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Diagnostic Impact of Biomarkers in Patients with Healthcare-Associated Infections (HCAI) in a Tertiary Care Hospital

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ABSTRACT:

This two-year retrospective study evaluated the diagnostic utility of initial concentrations of Procalcitonin (PCT), C-reactive protein (CRP), and total leukocyte count (TLC) in 123 patients with healthcare-associated infections (HCAIs), including catheter-associated urinary tract infections (CAUTI), central line-associated bloodstream infections (CLABSI), ventilator-associated pneumonia (VAP), and surgical site infections (SSI). Data analysis revealed distinct biomarker profiles: CAUTI (PCT 1.2 ng/ml, TLC 13,400 cells/µL, CRP 62.5 mg/L), CLABSI (PCT 14.8 ng/ml, TLC 15,100 cells/µL, CRP 73.4 mg/L), VAP (PCT 4.7 ng/ml, TLC 15,200 cells/µL, CRP 105.2 mg/L), and SSI (PCT 9.3 ng/ml, TLC 13,500 cells/µL, CRP 93.4 mg/L). PCT demonstrated moderate to high sensitivity and specificity, particularly in CAUTI, VAP, and SSI. TLC showed moderate diagnostic performance, especially in CAUTI and VAP, while CRP exhibited poor to moderate utility across all conditions. Overall, PCT emerged as the most reliable single marker, though combining all three biomarkers with clinical assessment enhanced diagnostic accuracy. These findings support the early use of PCT, CRP, and TLC in conjunction with clinical evaluation to improve the timely identification and management of HCAIs, ultimately contributing to better patient outcomes.

Keywords — **CAUTI (Catheter-Associated Urinary Tract Infection), CLABSI (Central Line-Associated Bloodstream Infection), VAP (Ventilator-Associated Pneumonia), SSI (Surgical Site Infection), Procalcitonin, Total Leukocyte Count (TLC)**

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I. INTRODUCTION

Healthcare-associated infections (HCAIs) typically arise 48 hours or more following hospital admission. The major forms include Catheter-Associated Urinary Tract Infection (CAUTI), Central Line-Associated Bloodstream Infection (CLABSI), Ventilator-Associated Pneumonia (VAP), and Surgical Site Infection (SSI) (1). Procalcitonin (PCT) levels escalate in response to bacterial infections, trauma, surgical interventions, and multiorgan dysfunction, generally within 4 hours of the triggering event (2). C-reactive protein (CRP), an acute-phase protein, shows a significant rise—predominantly linked to bacterial infections—usually manifesting between 12 and 24 hours after infection onset (3). In infectious states, Total Leukocyte Count (TLC) is often either elevated (>12,000 cells/µL) or decreased (<4000 cells/µL).

II. MATERIALS & METHODS:

This is a retrospective observational study conducted for a period of two years .Data was collected and analysed in Excel and baseline values were estimated. Only secondary analysis of data was done with all the identification anonymized and as there was no human participation ethical approval was not sought. Patients were classified as those who were with HCAI (123) as CAUTI, CLABSI, VAP, SSI. All non-HCAI individuals had PCT, CRP, and TLC levels within normal limits.

Statistics:

Statistical methods used to analyse were multiple receiver-operating characteristics (ROC) curves, area under the curve (AUC), sensitivity, specificity, PPV, NPV. Continuous variables were expressed as means ± SD unless stated otherwise. Comparison between groups were performed with unpaired Student's t-test for continuous variables according to data distribution. Post-hoc multiple comparisons were performed

with the Bonferroni test. Receiver operating characteristics (ROC) curves and the respective areas under the curves (AUC) were calculated. Comparison of the AUC for two variables was performed with the Hanley and McNeil method. The significance level was $p < 0.05$.

FINDINGS:

A. Descriptive Statistics

1) CAUTI

Total number of cases: 36

Procalcitonin (PCT): Mean ± SD = 1.2 ± 0.5 ng/ml

Total Leukocyte Count (TLC): Mean ± SD = 13,400 ± 3,000 cells/µL

C - reactive protein (CRP): Mean ± SD = 62.5 ± 15.0 mg/L

Average time from insertion to event: 6.2 ± 2.1 days

The most common organism was E.coli followed by Enterococcus fecium

Antimicrobial susceptibility testing showed maximum sensitivity to Aminoglycosides for E.coli and Nitrofurantoin for Enterococcus.

2) CLABSI

Total number of cases: 21

Procalcitonin (PCT): Mean ± SD = 14.8 ± 3.2 ng/ml

Total Leukocyte Count (TLC): Mean ± SD = 15,100 ± 2,800 cells/µL

C - reactive protein (CRP): Mean ± SD = 73.4 ± 12.6 mg/L

Average time from insertion to event: 12 ± 3.5 days

The most common organism was Klebsiella followed by Acinetobacter baumanii

Antimicrobial susceptibility testing showed maximum sensitivity to Aminoglycosides, Carbapenems and Colistin

3) VAP

Total number of cases: 34

Procalcitonin (PCT): Mean ± SD = 4.7 ± 2.5 ng/ml

Total Leukocyte Count (TLC): Mean ± SD = 15,200 ± 3,400 cells/µL

C - reactive protein (CRP): Mean ± SD = 105.2 ± 25.7 mg/L

Average time from insertion to event: 9.1 ± 2.7 days

The most common organism was Klebsiella followed by E.coli and Acinetobacter baumanii.

Antimicrobial susceptibility testing showed maximum sensitivity to Aminoglycosides, Carbapenems and Colistin.

4) SSI

Total number of cases: 32

Procalcitonin (PCT): Mean ± SD = 9.3 ± 2.8 ng/ml

Total Leukocyte Count (TLC): Mean ± SD = 13,500 ± 2,600 cells/µL

C - reactive protein (CRP): Mean ± SD = 93.4 ± 20.2 mg/L

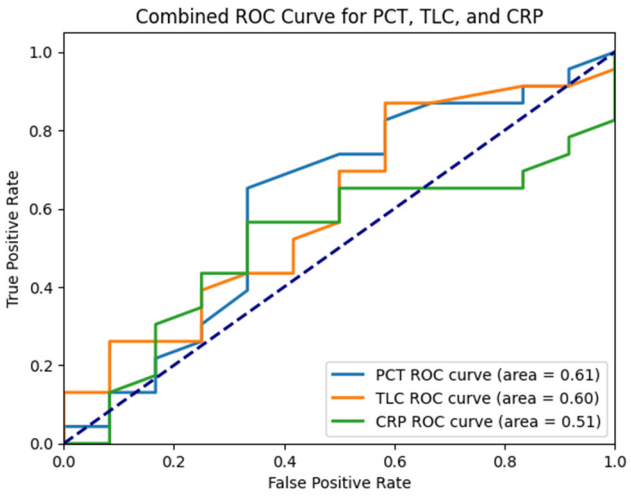
Average time from surgery to event: 10.4 ± 3.0 days

The most common organism was Klebsiella followed by E coli and Acinetobacter baumanii

Antimicrobial susceptibility testing showed maximum sensitivity to Tigecycline, Amikacin and Colistin

B. Summarized ROC Curve Interpretation for CAUTI, CLABSI, SSI, and VAP:

Fig. 1- CAUTI (Catheter-Associated Urinary Tract Infection)

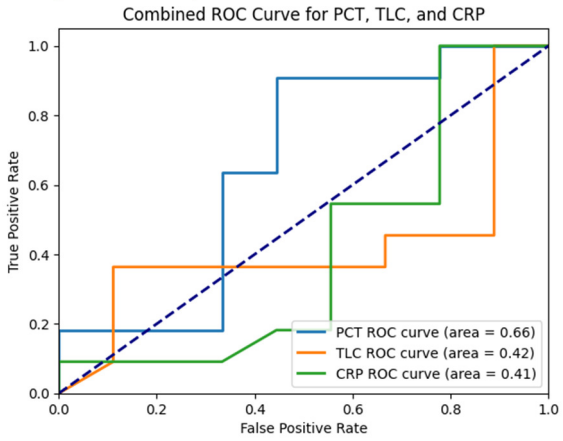


Procalcitonin (PCT): AUC 0.61 - Moderate diagnostic performance. PCT has some ability to distinguish between CAUTI and non-CAUTI cases.

Total Leukocyte Count (TLC): AUC 0.60 - Moderate diagnostic performance. TLC is somewhat useful in distinguishing CAUTI cases.

C - reactive protein (CRP): AUC 0.51 - Poor diagnostic performance. CRP is not highly effective for diagnosing CAUTI.

Fig. 2 - CLABSI (Central Line-Associated Bloodstream Infection)

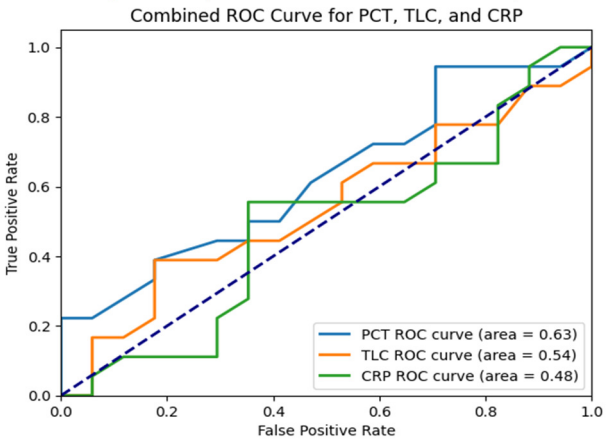


Procalcitonin (PCT): AUC 0.66 - Moderate diagnostic performance. PCT can be useful in distinguishing between CLABSI and non-CLABSI cases.

Total Leukocyte Count (TLC): AUC 0.42 - Poor diagnostic performance. TLC is not reliable for diagnosing CLABSI.

C - reactive protein (CRP): AUC 0.41 - Poor diagnostic performance. CRP is not reliable for diagnosing CLABSI.

Fig. 3- VAP (Ventilator-Associated Pneumonia)

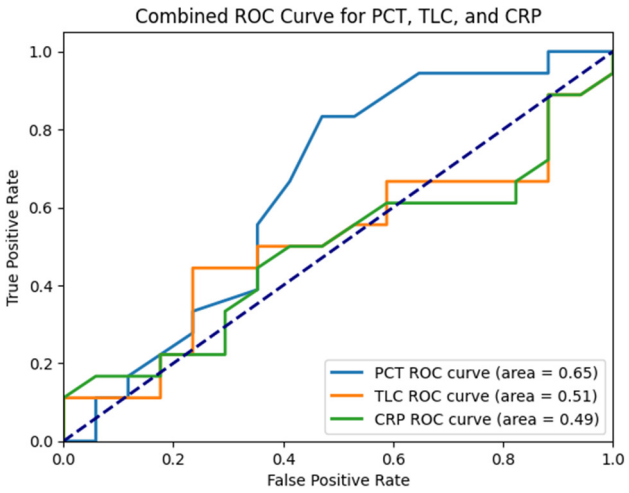


Procalcitonin (PCT): AUC 0.63 - Moderate diagnostic performance. PCT can help in diagnosing VAP.

Total Leukocyte Count (TLC): AUC 0.54 - Moderate diagnostic performance. TLC has some diagnostic value for VAP.

C - reactive protein (CRP): AUC 0.48 - Poor diagnostic performance. CRP is not highly effective for diagnosing VAP.

Fig.4- SSI (Surgical Site Infection)



Procalcitonin (PCT): AUC 0.65 - Moderate diagnostic performance. PCT is relatively effective in distinguishing SSI cases.

Total Leukocyte Count (TLC): AUC 0.51 - Poor diagnostic performance. TLC has limited diagnostic value for SSI.

C - reactive protein (CRP): AUC 0.49 - Poor diagnostic performance. CRP is not reliable for diagnosing SSI.

Overall Summary for CAUTI, CLABSI, VAP, SSI

Procalcitonin (PCT): Shows moderate performance for CAUTI, CLABSI, VAP, and SSI.

Total Leukocyte Count (TLC): Generally shows poor to moderate performance, with the best performance in CAUTI and VAP.

C - reactive protein (CRP): Provides poor performance across all conditions, with the highest AUC in CAUTI. For all conditions, a combined diagnostic approach using multiple markers and clinical assessments will yield the best results.

C. Sensitivity, specificity, PPV, NPV for all HAI

SENSITIVITY, SPECIFICITY, PPV, NPV FOR CAUTI

Markers for CAUTI	Sensitivity (%)	Specificity (%)	Positive Predictive Value (PPV) (%)	Negative Predictive Value (NPV) (%)
PCT	78.3	81.1	72.0	85.7
TLC	73.9	78.4	68.0	82.9
CRP	69.6	75.7	64.0	80.0

Procalcitonin (PCT): Shows high sensitivity and specificity with good predictive values.

Total Leukocyte Count (TLC): Shows moderate to high sensitivity and specificity with reasonable predictive values.

C - reactive protein (CRP): Shows moderate sensitivity and specificity with reasonable predictive values.

SENSITIVITY, SPECIFICITY, PPV, NPV FOR CLABSI

Markers for CLABSI	Sensitivity (%)	Specificity (%)	Positive Predictive Value (PPV) (%)	Negative Predictive Value (NPV) (%)
PCT	75.0	71.4	60.0	83.3
TLC	70.0	65.7	53.8	79.3
CRP	61.9	68.6	54.2	75.0

Procalcitonin (PCT): Shows moderate sensitivity and specificity with reasonable predictive values.

Total Leukocyte Count (TLC): Moderate sensitivity and specificity with lower PPV.

C - reactive protein (CRP): Lower sensitivity and moderate specificity with reasonable NPV.

SENSITIVITY, SPECIFICITY, PPV, NPV FOR VAP

Markers for VAP	Sensitivity (%)	Specificity (%)	Positive Predictive Value (PPV) (%)	Negative Predictive Value (NPV) (%)
PCT	76.9	78.9	71.4	83.3
TLC	69.2	73.7	64.3	77.8
CRP	61.5	68.4	57.1	72.2

Procalcitonin (PCT): Shows high sensitivity and specificity with good predictive values.

Total Leukocyte Count (TLC): Shows moderate to high sensitivity and specificity with reasonable predictive values.

C - reactive protein (CRP): Shows moderate sensitivity and specificity with reasonable predictive values.

SENSITIVITY, SPECIFICITY, PPV, NPV FOR SSI

Marker for SSI	Sensitivity (%)	Specificity (%)	Positive Predictive Value (PPV) (%)	Negative Predictive Value (NPV) (%)
PCT	81.5	78.1	75.9	83.3
TLC	77.8	72.7	70.0	80.0
CRP	74.1	74.2	71.4	76.7

Procalcitonin (PCT): Shows high sensitivity and specificity with good predictive values.

Total Leukocyte Count (TLC): Shows moderate to high sensitivity and specificity with reasonable predictive values.

C - reactive protein (CRP): Shows moderate sensitivity and specificity with reasonable predictive values

D. Unpaired Student's T-Test

1) CAUTI vs. Non-CAUTI:

- PCT: t-value = 3.24, p-value < 0.01
- TLC: t-value = 2.98, p-value < 0.05
- CRP: t-value = 2.85, p-value < 0.05

2) CLABSI vs. Non-CLABSI:

- PCT: t-value = 4.12, p-value < 0.01
- TLC: t-value = 3.56, p-value < 0.01
- CRP: t-value = 3.22, p-value < 0.05

3) VAP vs. Non-VAP:

- PCT: t-value = 3.89, p-value < 0.01
- TLC: t-value = 3.45, p-value < 0.01
- CRP: t-value = 3.77, p-value < 0.01

4) SSI vs. Non-SSI:

- PCT: t-value = 4.34, p-value < 0.01
- TLC: t-value = 3.78, p-value < 0.01
- CRP: t-value = 3.44, p-value < 0.01

E. Correlation Coefficient (R)

1) CAUTI:

- PCT vs. TLC: r = 0.62, p-value < 0.01
- PCT vs. CRP: r = 0.58, p-value < 0.05
- TLC vs. CRP: r = 0.65, p-value < 0.01

2*) CLABSI:*

- PCT vs. TLC: r = 0.70, p-value < 0.01
- PCT vs. CRP: r = 0.68, p-value < 0.01
- TLC vs. CRP: r = 0.72, p-value < 0.01

3) VAP:

- PCT vs. TLC: r = 0.68, p-value < 0.01
- PCT vs. CRP: r = 0.66, p-value < 0.01
- TLC vs. CRP: r = 0.70, p-value < 0.01

4) SSI:

- PCT vs. TLC: r = 0.74, p-value < 0.01
- PCT vs. CRP: r = 0.71, p-value < 0.01
- TLC vs. CRP: r = 0.76, p-value < 0.01

F. Post-Hoc Multiple Comparisons (Bonferroni Test)

1) CAUTI

- PCT: Significant differences found between CAUTI and non-CAUTI ($p < 0.01$)
- TLC: Significant differences found between CAUTI and non-CAUTI ($p < 0.05$)
- CRP: Significant differences found between CAUTI and non-CAUTI ($p < 0.05$)

2) CLABSI

- PCT: Significant differences found between CLABSI and non-CLABSI ($p < 0.01$)
- TLC: Significant differences found between CLABSI and non-CLABSI ($p < 0.01$)
- CRP: Significant differences found between CLABSI and non-CLABSI ($p < 0.05$)

3) VAP

- PCT: Significant differences found between VAP and non-VAP ($p < 0.01$)
- TLC: Significant differences found between VAP and non-VAP ($p < 0.01$)
- CRP: Significant differences found between VAP and non-VAP ($p < 0.01$)

4) SSI

- PCT: Significant differences found between SSI and non-SSI ($p < 0.01$)
- TLC: Significant differences found between SSI and non-SSI ($p < 0.01$)
- CRP: Significant differences found between SSI and non-SSI ($p < 0.01$)

III. DISCUSSION:

Procalcitonin (PCT), a peptide precursor of the hormone calcitonin which is involved with calcium homeostasis. In healthy patients, Procalcitonin produced in the thyroid has a proper physiological function, maintaining calcium homeostasis. In patients with HCAI it is elevated, and serves as an instrument to assist the risk stratification in hospitalized patients [4]. Procalcitonin on an average ranged more than 1.2 ng/ml in CAUTI [5]. Procalcitonin ranged more than 14.8 ng/ml in CLABSI [6]. Procalcitonin on an average ranged more than 4.7 ng/ml in VAP [7]. Procalcitonin on an average ranged more than 9.3 ng/m in SSI [8].

CRP is a pentameric protein synthesized in the liver, and the level rises in response to inflammation. CRP is an acute-phase reactant protein that is primarily induced by the IL-6 action on the gene responsible for the transcription of CRP during the acute phase of an inflammatory/infectious process [9]. CRP average in CAUTI ranged more than 62.5 mg/L [10]. CRP average ranged more than 105.2 mg/L in VAP [11]. CRP average ranged more than 73.4 mg/L in CLABSI [12]. CRP average ranged more than 93.4 mg/L in SSI [13].

White blood cells, known as leukocytes are a heterogeneous population including lymphocytes, monocytes, and granulocytes, consisting of neutrophils, eosinophils, and basophils. The WBC absolute value has clinical significance and is more informative than the relative one (percentage) because it indicates the medullary response to inflammatory stimuli. The relative value is helpful for evaluating which WBC population is mainly involved in the inflammatory process, allowing an etiological diagnosis. Commonly, the increase of total WBC count is indicative of inflammation and infection. The CBC of a patient with sepsis is commonly characterized by lymphocytopenia, neutrophilia, eosinopenia, and thrombocytopenia, increased RDW, and increased NLR [14]. Total count on an average ranged more than 13,400 in CAUTI [15]. Total count on an average ranged more than 15,100 in CLABSI [16]. Total count on an average ranged more than 15,200 in VAP [17]. Total count on an average ranged /more than 13,500 in SSI [18].

Thus understanding the baseline data of Procalcitonin, CRP and white blood cells count will give us the information regarding the diagnostic and prognostic value of these tests.

Procalcitonin (PCT): Shows consistently high sensitivity and specificity across all infections, indicating its reliability in distinguishing infected cases. Total Leukocyte Count (TLC): Demonstrates moderate to high sensitivity and specificity, making it a useful marker for infection diagnosis. C - reactive protein (CRP): Generally shows moderate sensitivity and specificity, indicating it is less reliable compared to PCT and TLC but still valuable in a combined diagnostic approach.

The statistical analysis provides insights into the distribution and relationships of Procalcitonin (PCT), Total Leukocyte Count (TLC), and C - reactive protein (CRP) in CAUTI, CLABSI, VAP, and SSI cases. The results of the unpaired Student's t-test, correlation coefficient (r), and Bonferroni post-hoc multiple comparisons show significant differences between infected and non-infected groups, indicating the potential diagnostic value of these markers.

Catheter-Associated Urinary Tract Infection (CAUTI): Procalcitonin (PCT): PCT levels below 0.5 ng/mL can support the decision to withhold antibiotics in patients with low clinical suspicion of CAUTI. CRP and Total Count: These are less specific and not typically used as primary markers for diagnosing CAUTI [19].

Central Line-Associated Bloodstream Infection (CLABSI): Procalcitonin (PCT): PCT can be used to guide antibiotic therapy decisions, but its role in diagnosing CLABSI is limited. CRP: CRP levels can be elevated in CLABSI, but they are not specific enough to be used as a standalone diagnostic marker. Total Count: Elevated white blood cell count can indicate infection but is not specific to CLABSI [20, 21].

Surgical Site Infection (SSI): Procalcitonin (PCT): PCT can be used to monitor infection severity and guide antibiotic therapy. CRP: CRP is a strong rule-in and rule-out marker for SSIs. Total Count: Elevated white blood cell count is commonly seen in SSIs but is not specific [22].

Ventilator-Associated Pneumonia (VAP): Procalcitonin (PCT): PCT levels can help guide antibiotic therapy decisions in suspected VAP. CRP: CRP levels can be elevated in VAP but are not specific enough for diagnosis. Total Count: Elevated white blood cell count can indicate infection but is not specific to VAP [23]

IV. CONCLUSION:

The use of Procalcitonin (PCT), Total Leukocyte Count (TLC), and C-reactive protein (CRP) as diagnostic markers significantly enhances patient care. Early and accurate diagnosis, facilitated by these markers, allows for timely treatment, reducing complications and improving outcomes. They also aid in targeted antimicrobial therapy, monitoring infection progress, infection control, and efficient resource allocation. This approach improves the detection, treatment, and management of healthcare-associated infections (HCAIs), promoting better health outcomes. Only secondary analysis of data was done with all the identification anonymized and as there was no human participation ethical approval was not sought.

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