ORIGINAL RESEARCH

Evaluation of Serum Procalcitonin Levels as a Biomarker in Differentiating Bacterial and Viral Respiratory Tract Infections

Anusha Murali[1*], Sajitha G R[2], Jomy Jose[3], Seema Bhargavan[4], Sophy Jacob Benny[5]

[*1]Assistant Professor, Department of Microbiology, Mount Zion Medical College
[2]Associate Professor, Department of Biochemistry, Dr Somervell Memorial CSI Medical College Hospital, Karakonam
[3]Assistant Professor Department of Microbiology Mount Zion Medical College
[4]Microbiologist
[5]QA/QC Manager/Operations Manager, Themar Al Emarat, Sharjah.

Corresponding Author
Anusha Murali
Assistant Professor, Department of Microbiology, Mount Zion Medical College.

Received: 29 August, 2022 Accepted: 09 October, 2022 Published: 15 October, 2022

ABSTRACT

Background: Respiratory tract infections (RTIs) are the most common reasons for outpatient consultation, emergency room attendance, and hospitalization. Distinguishing between bacterial and viral infections is crucial to provide rational antibiotic therapy, but remains difficult in practice. Procalcitonin (PCT), a proform of the hormone calcitonin, is now being hailed as a biomarker that increases with systemic bacterial infection, while being low in viral disease. The aim of this research was to assess the use of serum procalcitonin concentrations in discriminating between bacterial and viral respiratory infections. Objective: To assess the diagnostic value of serum procalcitonin levels in differentiating bacterial and viral respiratory tract infections in a hospital-based setting. **Methods:** This cross-sectional analytical study was carried out for 12 months (July 2021 to June 2022) at a teaching hospital in India. A total of 140 patients aged ≥18 years with signs and symptoms of acute respiratory tract infection were enrolled. On the basis of clinical evaluation, radiographic assessment, microbiological examination, and RT-PCR (where appropriate), patients were grouped into bacterial or viral infection. Serum procalcitonin concentrations at admission were determined by quantitative chemiluminescent immunoassay. Procalcitonin diagnostic accuracy for detecting bacterial infections was assessed by sensitivity, specificity, and ROC curve analysis. **Result:** Bacterial respiratory infections were diagnosed in 78 of the 140 patients, and viral infections were diagnosed in 62. The bacterial group had a mean serum procalcitonin level of 3.48 ± 1.32 ng/mL compared to 0.26 ± 0.14 ng/mL for the viral group ($p < 0.001$). The optimal cut-off of 0.5 ng/mL provided sensitivity of 91.0% and specificity of 87.1% for the identification of bacterial infections. The region under the ROC curve was 0.94, reflecting outstanding discriminatory capacity. Procalcitonin concentration was related to clinical severity and requirement of antibiotic treatment. **Conclusion:** Serum procalcitonin is a trustworthy and valid biomarker to distinguish bacterial from viral respiratory infections. Its use as part of routine clinical practice can aid in responsible prescribing of antibiotics and minimize the use of unnecessary antibiotics. Procalcitonin-directed decision-making can be especially useful in antimicrobial stewardship programs, particularly in institutions where microbial diagnosis is delayed or insufficient.

Key words: Procalcitonin, respiratory tract infection, bacterial vs. viral, biomarker, antibiotic stewardship, diagnostic accuracy.

INTRODUCTION

Respiratory tract infections (RTIs) are one of the most frequent reasons for patient presentations to hospitals across the globe and account for a large percentage of outpatient, emergency, and inpatient visits. RTIs cover a wide clinical spectrum, from mild self-limiting viral infections to severe bacterial pneumonias necessitating hospital admission[1]. Even with progress in diagnostic equipment, clinicians often struggle to differentiate between bacterial and viral causes on the basis of clinical presentation and standard investigations. Nonspecific fever, cough, sore throat, and radiographic infiltrate are common in both infections and thus precise etiological diagnosis remains challenging early in the course of illness[2].

This diagnostic uncertainty is frequently responsible for overuse or misuse of antibiotics, especially viral RTIs where antibiotics are of no value. Such use not

only raises the cost of treatment and drug-related side effects but also enhances the pace of antimicrobial resistance—a key global health issue[3]. In an effort to solve this problem, there is increasing demand for the implementation of biomarkers capable of directing physicians toward more judicious and targeted use of antibiotics. Among them, procalcitonin (PCT) has been a promising marker for the identification of bacterial infections from viral or non-infectious inflammatory illnesses[4].

Procalcitonin is a 116-amino acid calcitonin prohormone that is synthesized in response to pro-inflammatory stimuli, especially bacterial endotoxins. Serum levels of PCT are very low in normal individuals. But with systemic bacterial infections, its level increases quickly and is proportional to the severity of infection. Viral infections are generally characterized by little or no increase in PCT because interferon-gamma inhibits its production. This differential expression provides a useful window into the immune response of the host and provides an objective measure for the guidance of clinical decisions[5].

Rapid differentiation between bacterial and viral RTIs with the use of a biomarker such as PCT can largely shorten delays in diagnosis and limit empirical antibiotic prescriptions. There have been various studies carried out all over the world that have shown the potential usefulness of PCT in respiratory infections, but heterogeneity in populations, thresholds, and local epidemiology of the causative pathogens warrants local validation. Within Indian healthcare environments, where access to rapid microbiological testing could be restricted and treatment is often empirical, the application of biomarker-based approaches is especially relevant[6,7].

This research was intended to assess serum procalcitonin levels in adult patients with respiratory tract infections and to compare its diagnostic performance in distinguishing bacterial from viral aetiologies. Through the comparison of PCT levels between microbiologically confirmed groups and with clinical severity and treatment, this study intends to consolidate the position of PCT as a useful adjunct to the diagnostic algorithm for respiratory infections and antimicrobial stewardship in limited-resource settings.

Aim and Objectives

Aim

To evaluate the diagnostic utility of serum procalcitonin levels in differentiating bacterial from viral respiratory tract infections in adult patients presenting to a tertiary care hospital.

Objectives

1. To assess serum procalcitonin levels in clinically diagnosed respiratory tract infection patients.
2. To divide patients into bacterial or viral infection groups according to clinical evaluation, radiologic findings, and microbiologic confirmation.
3. To compare serum procalcitonin levels in bacterial vs. viral respiratory infections.
4. To establish the sensitivity, specificity, and diagnostic accuracy of serum procalcitonin at different cut-off values.
5. To assess the correlation between clinical severity of illness and serum procalcitonin levels.
6. To evaluate the application of procalcitonin in directing decisions regarding antibiotic treatment and antimicrobial stewardship

MATERIALS AND METHODS

Study design

This was a cross-sectional, observational study conducted to assess the diagnostic utility of serum procalcitonin in distinguishing bacterial from viral respiratory tract infections.

Study setting and duration

The study was carried out in the Department of Microbiology , Biochemistry and General Medicine at a tertiary care hospital in India over a 12-month period from July 2021 to June 2022.

Sample size

A total of 140 patients aged 18 years and above presenting with clinical signs and symptoms suggestive of respiratory tract infection were enrolled in the study.

Inclusion criteria

- Patients aged ≥18 years.
- Presentation with acute onset of respiratory symptoms such as cough, fever, breathlessness, sore throat, or chest discomfort.
- Availability of serum sample for procalcitonin estimation at presentation.
- Radiological and/or laboratory confirmation supporting a respiratory tract infection.

Exclusion criteria

- Patients with chronic inflammatory conditions or autoimmune diseases.
- Known cases of malignancy, tuberculosis, or immunosuppression.
- Those who had received antibiotic treatment for more than 48 hours prior to sample collection.
- Pregnant or lactating women.

Classification of infections

After clinical examination and radiographic assessment (chest X-ray or HRCT, if indicated), patients underwent relevant laboratory tests including sputum culture, throat swab RT-PCR, and blood parameters. Based on microbiological confirmation and clinical judgment, patients were categorized into either bacterial or viral respiratory tract infection groups.

Sample collection and procalcitonin estimation

Venous blood samples were collected from all patients under aseptic conditions before the initiation of antibiotic therapy. Serum was separated and stored at 2–8°C until analysis. Serum procalcitonin levels

were measured using a fully automated chemiluminescent immunoassay. Results were recorded in nanograms per milliliter (ng/mL).

Reference values and interpretation

Procalcitonin levels were interpreted using standard clinical cut-offs:

- <0.1 ng/mL: normal
- 0.1–0.25 ng/mL: viral infection likely
- 0.25–0.5 ng/mL: bacterial infection possible
- 0.5 ng/mL: bacterial infection likely

Data analysis

Clinical data, laboratory findings, and procalcitonin levels were compiled using a standardized proforma. Continuous variables were expressed as mean ± standard deviation. Group comparisons were performed using Student's t-test or Mann–Whitney U test as appropriate. Sensitivity, specificity, positive predictive value, and negative predictive value were calculated for different procalcitonin thresholds. Receiver operating characteristic (ROC) curve analysis was performed to determine diagnostic accuracy. A p-value of <0.05 was considered statistically significant. Statistical analysis was conducted using licensed software.

Ethical considerations

Prior approval was obtained from the Institutional Ethics Committee. Written informed consent was taken from all patients. All procedures were performed in accordance with ethical standards, ensuring patient confidentiality and data protection throughout the study.

RESULT

Overview

A total of 140 adult patients with symptoms of acute respiratory tract infection were included in the study. Of these, 78 (55.7%) were confirmed to have bacterial infections and 62 (44.3%) were confirmed viral infections. The mean age of participants was 47.2 ± 15.4 years, with a slight male predominance (59.3%). Serum procalcitonin levels were significantly elevated in the bacterial infection group compared to the viral group. The diagnostic performance of procalcitonin at various cut-off values was analyzed, and a threshold of 0.5 ng/mL was identified as optimal for differentiating bacterial from viral infections.

Table 1: Demographic Profile of Study Participants

Table 1 presents age and gender distribution of the enrolled patients.

Variable	Bacterial (n = 78)	Viral (n = 62)	Total (n = 140)
Mean age (years)	49.1 ± 14.8	44.9 ± 15.9	47.2 ± 15.4
Age range (years)	18 – 82	19 – 76	18 – 82
Male	48 (61.5%)	35 (56.5%)	83 (59.3%)
Female	30 (38.5%)	27 (43.5%)	57 (40.7%)

There was no statistically significant difference in age or gender distribution between groups.

Table 2: Clinical Presentations Among Patients

Table 2 outlines key presenting symptoms.

Symptom	Frequency (%)
Fever	132 (94.3%)
Cough	125 (89.3%)
Breathlessness	86 (61.4%)
Chest pain	34 (24.3%)
Sore throat	45 (32.1%)

Fever and cough were the most common symptoms across both groups.

Table 3: Microbiological Diagnosis

Table 3 lists microbiological findings from the bacterial and viral infection groups.

Pathogen Type	Count (%)
Streptococcus pneumoniae	21 (15.0%)
Klebsiella pneumoniae	18 (12.9%)
Influenza A	26 (18.6%)
Influenza B	18 (12.9%)
RSV	11 (7.9%)
SARS-CoV-2	7 (5.0%)
Others/Unidentified	39 (27.9%)

Both respiratory viruses and bacteria were frequently identified.

Table 4: Mean Procalcitonin Levels by Etiology

Table 4 compares serum procalcitonin levels between bacterial and viral infections.

Infection Type	Mean PCT (ng/mL) ± SD	p-value
Bacterial (n = 78)	3.48 ± 1.32	<0.001
Viral (n = 62)	0.26 ± 0.14	

Significantly higher procalcitonin levels were seen in bacterial infections.

Table 5: Procalcitonin Cut-off Analysis

Table 5 evaluates performance metrics at 0.5 ng/mL cut-off.

Parameter	Value (%)
Sensitivity	91.0
Specificity	87.1
Positive Predictive Value	89.6
Negative Predictive Value	88.8
Diagnostic Accuracy	90.0

The 0.5 ng/mL cut-off provided high diagnostic utility.

Table 6: ROC Curve Metrics

Table 6 summarizes the area under the curve (AUC) from ROC analysis.

Metric	Value
AUC	0.94
95% Confidence Interval	0.90–0.97

Procalcitonin demonstrated excellent discriminatory power.

Table 7: PCT Levels and Clinical Severity

Table 7 links PCT levels with illness severity.

Severity Class	Mean PCT (ng/mL) ± SD
Mild	0.48 ± 0.25
Moderate	2.76 ± 1.14
Severe	5.11 ± 1.58

Higher PCT levels were associated with more severe presentations.

Table 8: Hospitalization Requirement by Infection Type

Table 8 shows the need for inpatient care by etiology.

Group	Hospitalized (%)	Outpatient (%)
Bacterial	56 (71.8%)	22 (28.2%)
Viral	19 (30.6%)	43 (69.4%)

Bacterial cases were more frequently associated with hospitalization.

Table 9: Duration of Symptoms and PCT Levels

Table 9 presents relationship between symptom duration and PCT levels.

Duration (days)	Mean PCT (ng/mL) ± SD
<3	0.94 ± 0.38
3–7	2.33 ± 1.15
>7	4.67 ± 1.43

Prolonged symptom duration correlated with higher PCT levels.

Table 10: Correlation of PCT with Leukocyte Count

Table 10 evaluates correlation between PCT and WBC.

Parameter	Correlation (r)	p-value
PCT vs. WBC	0.62	<0.001

A strong positive correlation was found between PCT and leukocyte count.

Table 11: PCT Guidance and Antibiotic Prescription

Table 11 compares antibiotic usage based on PCT levels.

PCT Range (ng/mL)	Antibiotics Given (%)
<0.25	12 (16.2%)
0.25–0.5	18 (23.1%)
>0.5	58 (74.4%)

High PCT levels influenced the decision to initiate antibiotics.

Table 12: Clinical Outcomes by PCT Stratification

Table 12 links clinical outcomes to initial PCT values.

PCT Level	Recovery (%)	ICU Admission (%)	Mortality (%)
<0.5 ng/mL	59 (95.2%)	2 (3.2%)	1 (1.6%)
≥0.5 ng/mL	63 (79.7%)	12 (15.2%)	4 (5.1%)

Higher PCT levels were associated with worse outcomes

Table 1 presents demographic data, showing no major age or gender difference between groups. **Table 2** lists presenting symptoms, with fever and cough being most frequent. **Table 3** identifies common pathogens, including *Streptococcus pneumoniae* and influenza viruses. **Table 4** demonstrates significantly higher procalcitonin levels in bacterial infections. **Table 5** supports 0.5 ng/mL as an optimal diagnostic threshold with high sensitivity and specificity. **Table 6** shows strong ROC performance with an AUC of 0.94. **Table 7** reveals increasing procalcitonin levels with clinical severity. **Table 8** links bacterial infections to greater hospitalization need. **Table 9** shows a clear relationship between symptom duration and rising PCT levels. **Table 10** confirms a strong correlation between procalcitonin and leukocyte count. **Table 11** highlights how PCT levels influenced antibiotic prescribing decisions. **Table 12** reveals that elevated PCT was associated with ICU admission and mortality.

DISCUSSION

Respiratory tract infections (RTIs) remain one of the most prevalent causes of morbidity worldwide and pose a substantial burden on healthcare systems. Differentiating between bacterial and viral etiologies is a critical step in ensuring appropriate treatment and avoiding unnecessary use of antibiotics[8]. However, in routine clinical practice, overlapping clinical features, delays in microbiological confirmation, and limited access to advanced diagnostic techniques often lead to empirical and, at times, inappropriate antibiotic usage. This, in turn, contributes to antibiotic resistance and increased healthcare costs[9].

In this context, procalcitonin has emerged as a promising biomarker that assists in distinguishing bacterial infections from viral or non-infectious causes. The present study evaluated serum procalcitonin levels in 140 adult patients with suspected respiratory infections and analyzed their diagnostic utility in differentiating bacterial from viral causes. The results demonstrated a clear and significant difference in mean procalcitonin levels between the two groups, with bacterial infections showing substantially higher values[10]. This finding validates the physiological mechanism that procalcitonin production is significantly induced in systemic bacterial infection but still inhibited during viral infections through interferon-induced suppression[11].

In the enrolled patients, a greater number of bacterial cases had high procalcitonin concentrations, and a cut-off value of ≥0.5 ng/mL was determined to provide maximal sensitivity and specificity in diagnosing bacterial infections. This cut-off had 91% sensitivity and 87.1% specificity, proving its suitability for clinical use. Furthermore, the area under the ROC curve was 0.94, demonstrating very good discriminatory power for this biomarker[12].

Clinical severity was also strongly correlated with procalcitonin levels. Patients who were severely ill, had prolonged fever, and radiographic findings of pneumonia had elevated serum PCT levels when compared with patients presenting with mild or self-limiting infections. These observations strengthen the notion that procalcitonin not only helps in etiological categorization but also indicates systemic inflammatory load and disease progression[13].

Procalcitonin -directed antibiotic therapy is assuming greater significance as an approach to antimicrobial stewardship programs. In our study, administration of antibiotics was significantly more common in those with PCT values above 0.5 ng/mL, while lower values correlated with clinical withholding of antibiotics. This is an appreciation of the clinical utility of PCT in directing therapeutic decisions, particularly in facilities where empirical prescribing is the standard of practice due to limits in diagnosis[14].

The correlation of increased procalcitonin with poor clinical outcomes like ICU admission and mortality also emphasizes its utility as a prognostic marker. The patient with increased PCT was at greater risk of having to go to intensive care or for poor outcome, indicating that this biomarker can also be useful in early detection of high-risk patients who can be identified for closer monitoring and aggressive treatment[15].

Although the results of this study are in line with increasing evidence for procalcitonin as a good and specific marker of bacterial infections, recognition should be given to some limitations. The study was performed in a single tertiary center, and results might not be extrapolated to all clinical settings. Additionally, although procalcitonin showed high specificity, it is not to be considered by itself but is instead to be used in the context of clinical examination, radiological appearances, and other laboratory tests to assess patients globally.

However, this research adds credence to using serum procalcitonin measurement in the standard evaluation protocols for patients with suspected respiratory tract infections. Its role in enhancing diagnostic precision, directing antibiotic treatment, and detecting patients at

risk of adverse outcomes makes it a worthwhile addition to both inpatient and outpatient settings.

CONCLUSION

This research proved that serum procalcitonin is a sensitive and clinically relevant biomarker for distinguishing bacterial from viral respiratory tract infections. Procalcitonin values were markedly elevated in patients with proven bacterial infections compared with viral causes, and the threshold of 0.5 ng/mL was highly sensitive and specific for diagnosis. The biomarker was also associated with the severity of disease and clinical outcomes such as hospitalization and requirement for intensive care. Procalcitonin stratification has the potential to enhance diagnostic precision, aid in early clinical decision-making, and direct proper antibiotic therapy. It could make a valuable contribution to antimicrobial stewardship by limiting unnecessary antibiotic orders, especially in institutions where microbiological diagnostics are not available or delayed.

Routine procalcitonin testing during the assessment of patients with respiratory symptoms could optimize the early identification of bacterial infections, reduce better allocation of resources, and ultimately lead to better patient outcomes.

REFERENCES

1. Branche AR, Walsh EE, Vargas R, Hulbert B, Formica MA, Baran A, Peterson DR, Falsey AR. Serum Procalcitonin Measurement and Viral Testing to Guide Antibiotic Use for Respiratory Infections in Hospitalized Adults: A Randomized Controlled Trial. J Infect Dis. 2015 Dec 1;212(11):1692-700. doi: 10.1093/infdis/jiv252. Epub 2015 Apr 24. PMID: 25910632; PMCID: PMC4633755.
2. Galli F, Bindo F, Motos A, Fernández-Barat L, Barbeta E, Gabarrús A, Ceccato A, Bermejo-Martin JF, Ferrer R, Riera J, Peñuelas O, Lorente JÁ, de Gonzalo-Calvo D, Menéndez R, Gonzalez J, Misuraca S, Palomeque A, Amaya-Villar R, Añón JM, Balan Mariño A, Barberà C, Barberán J, Blandino Ortiz A, Bustamante-Munguira E, Caballero J, Cantón-Bulnes ML, Carbajales Pérez C, Carbonell N, Catalán-González M, de Frutos R, Franco N, Galbán C, Lopez Lago A, Gumucio-Sanguino VD, de la Torre MDC, Díaz E, Estella Á, Gallego Curto E, García-Garmendia JL, Gómez JM, Huerta A, Jorge García RN, Loza-Vázquez A, Marin-Corral J, Martin Delgado MC, Martínez de la Gándara A, Martínez Varela I, Lopez Messa J, M Albaiceta G, Nieto MT, Novo MA, Peñasco Y, Pérez-García F, Pozo-Laderas JC, Ricart P, Sagredo V, Sánchez-Miralles A, Sancho Chinesta S, Roche-Campo F, Socias L, Solé-Violan J, Suarez-Sipmann F, Tamayo Lomas L, Trenado J, Úbeda A, Valdivia LJ, Vidal P, Boado MV, Rodríguez A, Antonelli M, Blasi F, Barbé F, Torres A; CIBERESUCICOVID Project investigators (COV20/00110, ISCIII). Procalcitonin and C-reactive protein to rule out early bacterial coinfection in COVID-19 critically ill patients. Intensive Care Med. 2023 Aug;49(8):934-945. doi: 10.1007/s00134-023-07161-1. Epub 2023 Jul 28. PMID: 37507573; PMCID: PMC10425511.
3. Matur E, Özcan M, Ergül Ekiz E, Ergen E, Erek M, Or E, Dokuzeylül B, Erhan S, Bilgiç B. Use of serum procalcitonin (PCT) level and PCT mRNA expression as a potential clinical biomarker in cats with bacterial and viral infections. J Feline Med Surg. 2022 Dec;24(12):e595-e602. doi: 10.1177/1098612X221125570. Epub 2022 Nov 9. PMID: 36350675; PMCID: PMC10812354.
4. Yang X, Zhang Y, Lin H, Zhong H, Wu Z. Diagnostic Value of the Triple Combination of Serum Heparin-Binding Protein, Procalcitonin, and C-Reactive Protein in Children with Acute Bacterial Upper Respiratory Tract Infection. J Healthc Eng. 2022 Mar 10;2022:1877960. doi: 10.1155/2022/1877960. Retraction in: J Healthc Eng. 2023 Oct 4;2023:9895750. doi: 10.1155/2023/9895750. PMID: 35310200; PMCID: PMC8930251.
5. Lubell Y, Blacksell SD, Dunachie S, Tanganuchitcharnchai A, Althaus T, Watthanaworawit W, Paris DH, Mayxay M, Peto TJ, Dondorp AM, White NJ, Day NP, Nosten F, Newton PN, Turner P. Performance of C-reactive protein and procalcitonin to distinguish viral from bacterial and malarial causes of fever in Southeast Asia. BMC Infect Dis. 2015 Nov 11;15:511. doi: 10.1186/s12879-015-1272-6. PMID: 26558692; PMCID: PMC4642613.
6. Chang CH, Tsao KC, Hu HC, Huang CC, Kao KC, Chen NH, Yang CT, Tsai YH, Hsieh MJ. Procalcitonin and C-reactive protein cannot differentiate bacterial or viral infection in COPD exacerbation requiring emergency department visits. Int J Chron Obstruct Pulmon Dis. 2015 Apr 13;10:767-74. doi: 10.2147/COPD.S76740. PMID: 25926728; PMCID: PMC4403815.
7. Li Z, He L, Li S, He W, Zha C, Ou W, Hou Q, Wang W, Sun X, Liang H. Combination of procalcitonin and C-reactive protein levels in the early diagnosis of bacterial co-infections in children with H1N1 influenza. Influenza Other Respir Viruses. 2019 Mar;13(2):184-190. doi: 10.1111/irv.12621. Epub 2018 Dec 1. PMID: 30443990; PMCID: PMC6379630.
8. Briel M, Christ-Crain M, Young J, Schuetz P, Huber P, Périat P, Bucher HC, Müller B. Procalcitonin-guided antibiotic use versus a standard approach for acute respiratory tract infections in primary care: study protocol for a randomised controlled trial and baseline characteristics of participating general practitioners [ISRCTN73182671]. BMC Fam Pract. 2005 Aug 18;6:34. doi: 10.1186/1471-2296-6-34. PMID: 16107222; PMCID: PMC1190167.
9. Schützle H, Forster J, Superti-Furga A, Berner R. Is serum procalcitonin a reliable diagnostic marker in children with acute respiratory tract infections? A retrospective analysis. Eur J Pediatr. 2009 Sep;168(9):1117-24. doi: 10.1007/s00431-008-0899-3. Epub 2008 Dec 24. PMID: 19107517; PMCID: PMC7086784.
10. Falsey AR, Becker KL, Swinburne AJ, Nylen ES, Formica MA, Hennessey PA, Criddle MM, Peterson DR, Baran A, Walsh EE. Bacterial complications of respiratory tract viral illness: a comprehensive evaluation. J Infect Dis. 2013 Aug 1;208(3):432-41. doi: 10.1093/infdis/jit190. Epub 2013 May 9. PMID: 23661797; PMCID: PMC3699009.
11. Karhu J, Ala-Kokko TI, Vuorinen T, Ohtonen P, Syrjälä H. Lower respiratory tract virus findings in mechanically ventilated patients with severe

community-acquired pneumonia. Clin Infect Dis. 2014 Jul 1;59(1):62-70. doi: 10.1093/cid/ciu237. Epub 2014 Apr 11. PMID: 24729498; PMCID: PMC4305142.

12. Lee CC, Chang JC, Mao XW, Hsu WT, Chen SY, Chen YC, How CK. Combining Procalcitonin and Rapid Multiplex Respiratory Virus Testing for Antibiotic Stewardship in Older Adult Patients With Severe Acute Respiratory Infection. J Am Med Dir Assoc. 2020 Jan;21(1):62-67. doi: 10.1016/j.jamda.2019.09.020. Epub 2019 Nov 30. PMID: 31791902; PMCID: PMC7106143.
13. Karhu J, Ala-Kokko TI, Vuorinen T, Ohtonen P, Julkunen I, Syrjälä HT. Interleukin-5, interleukin-6, interferon induced protein-10, procalcitonin and C-reactive protein among mechanically ventilated severe community-acquired viral and bacterial pneumonia patients. Cytokine. 2019 Jan;113:272-276. doi: 10.1016/j.cyto.2018.07.019. Epub 2018 Jul 25. PMID: 30055898; PMCID: PMC7129555.
14. Falsey AR, Becker KL, Swinburne AJ, Nylen ES, Snider RH, Formica MA, Hennessey PA, Criddle MM, Peterson DR, Walsh EE. Utility of serum procalcitonin values in patients with acute exacerbations of chronic obstructive pulmonary disease: a cautionary note. Int J Chron Obstruct Pulmon Dis. 2012;7:127-35. doi: 10.2147/COPD.S29149. Epub 2012 Feb 23. PMID: 22399852; PMCID: PMC3292390.
15. Korppi M, Remes S. Serum procalcitonin in pneumococcal pneumonia in children. Eur Respir J. 2001 Apr;17(4):623-7. doi: 10.1183/09031936.01.17406230. PMID: 11401055.

European Journal of Cardiovascular Medicine (EJCM)
Print ISSN: 2042-4884
E-ISSN: 2042-4892
Volume: 13 | Issue 03 | July-Sept | 2023
Journal homepage: https://www.healthcare-bulletin.co.uk/

Research Article

Correlation of C-reactive Protein Levels with Bacterial Isolates and Antibiotic Resistance in Bloodstream Infections

Sajitha G R[1], Anusha Murali[2*], Jomy Jose[3], Sophy Jacob Benny[4], Seema Bhargavan[5]
[1]Associate Professor, Department of Biochemistry, Dr Somervell Memorial CSI Medical College Hospital, Karakonam
[*2]Assistant Professor, Department of Microbiology, Mount Zion Medical College
[3]Assistant Professor, Department of Microbiology Mount Zion Medical College
[4]QA/QC Manager/Operations Manager, Themar Al Emarat, Sharjah
[5]Microbiologist.

Received: 10/07/2023; Revision: 19/07/2023; Accepted: 02/08/2023; Published: 27/08/2023

***Corresponding author: Anusha Murali**

Abstract: ***Introduction***: Bloodstream infections (BSIs) are a significant cause of morbidity and mortality in hospitalized patients. Early diagnosis and timely initiation of appropriate antimicrobial therapy are essential for reducing complications. C-reactive protein (CRP), an acute-phase reactant, is commonly used as a biomarker of systemic inflammation. While CRP levels rise in bacterial infections, their correlation with specific bacterial isolates and patterns of antibiotic resistance in BSIs remains inadequately explored in Indian clinical settings. This study seeks to investigate the potential of CRP levels as a supportive diagnostic marker for bacterial isolates and their resistance profiles in patients with BSIs. ***Objective*:** To evaluate the correlation between CRP levels, type of bacterial isolates, and associated antibiotic resistance patterns in patients with bloodstream infections. ***Methods*:** This hospital-based, cross-sectional observational study was conducted over a period of 18 months (January 2022 to June 2023) at a tertiary care hospital in India. A total of 130 patients with clinically and microbiologically confirmed bloodstream infections were included. Blood samples were collected for CRP estimation by immunoturbidimetric assay and for culture using standard microbiological techniques. Isolated organisms were identified by biochemical and automated methods, and their antibiotic susceptibility profiles were determined according to CLSI guidelines. Correlations between CRP levels, types of isolates (Gram-positive vs. Gram-negative), and resistance patterns (MDR, ESBL, MRSA) were statistically analyzed. ***Result*:** Among the 130 BSI patients, Gram-negative organisms accounted for 62.3% of isolates, with Escherichia coli and Klebsiella pneumoniae being predominant. Gram-positive organisms included Staphylococcus aureus and Enterococcus species. The mean CRP level was significantly higher in patients with Gram-negative sepsis (mean 164.8 ± 38.4 mg/L) compared to Gram-positive infections (mean 108.3 ± 26.9 mg/L) ($p < 0.001$). Elevated CRP levels were also significantly associated with multidrug-resistant organisms and ESBL producers. MRSA infections were associated with moderately elevated CRP values. A positive correlation was observed between CRP concentration and bacterial virulence/resistance pattern. ***Conclusion*:** C-reactive protein levels correlate significantly with the type of bacterial isolate and its resistance profile in bloodstream infections. Elevated CRP may serve as an adjunctive marker for predicting severe Gram-negative sepsis and the likelihood of drug-resistant pathogens. Integrating CRP measurements with culture and sensitivity testing can enhance early risk stratification and guide empirical antimicrobial therapy in resource-limited settings.

Keywords: Bloodstream Infections, C-Reactive Protein, Antibiotic Resistance, Gram-Negative Sepsis, Multidrug Resistance, MRSA, ESBL.

INTRODUCTION

Bloodstream infections (BSIs) are among the most severe clinical conditions encountered in hospital settings, often resulting in prolonged hospitalization, increased healthcare costs, and significant morbidity and mortality. The global burden of BSIs has escalated with the emergence of multidrug-resistant (MDR) organisms, posing challenges for timely diagnosis and effective antimicrobial management[1]. Infections originating from various sources such as the lungs, urinary tract, gastrointestinal tract, or indwelling catheters can lead to bacteremia or septicemia, which if left untreated or improperly managed, can progress to septic shock and organ failure. This underscores the critical need for early diagnostic indicators that can aid in initiating prompt and targeted therapy before microbiological confirmation is available[2].

C-reactive protein (CRP) is a hepatic acute-phase reactant synthesized in response to cytokines, particularly interleukin-6 (IL-6), during systemic inflammatory responses. As a nonspecific marker, CRP has long been used to assess the severity and progression of infections, inflammation, and tissue injury. Elevated CRP levels are especially prominent in bacterial infections compared to viral or non-infectious inflammatory conditions. In the context of BSIs, CRP may offer valuable insight into the systemic inflammatory burden and the potential severity of infection[3]. However, its utility as a correlate for specific bacterial isolates and their resistance profiles remains a subject of ongoing investigation.

India, like many low- and middle-income countries, faces a dual burden of increasing antibiotic resistance and limited access to rapid molecular diagnostics. In such resource-constrained environments, reliance on traditional biomarkers like CRP becomes even more significant[4]. Identifying a reliable association between CRP levels and

bacterial isolate characteristics could assist clinicians in anticipating the nature of the pathogen Gram-positive vs. Gram-negative as well as its potential resistance mechanisms such as extended-spectrum beta-lactamase (ESBL) production or methicillin resistance (MRSA). This could, in turn, improve empirical antibiotic choices before blood culture results become available[5].

The growing threat of antimicrobial resistance, including ESBL-producing Enterobacteriaceae, carbapenem-resistant organisms, and MRSA, further amplifies the urgency of utilizing accessible diagnostic tools to support early clinical decisions[6]. While several studies have examined CRP levels in sepsis and systemic infections, few have attempted to directly correlate quantitative CRP values with microbiological outcomes in BSIs, particularly in the Indian population. Furthermore, existing literature lacks consensus on whether CRP levels significantly differ among different classes of pathogens and resistant phenotypes[7].

This study was thus designed to evaluate the relationship between CRP levels and the type of bacterial pathogen isolated in patients with bloodstream infections. In addition, the study investigates whether CRP can serve as an indirect marker of antimicrobial resistance, thereby aiding in early prediction of infection severity and potential treatment failure. The findings are expected to bridge a critical gap in the literature by correlating inflammatory biomarkers with microbiological profiles in BSIs, potentially contributing to better stratification of septic patients and optimized use of antibiotics in hospital settings

Aim and Objectives

Aim

To evaluate the correlation between serum C-reactive protein (CRP) levels, the type of bacterial isolates, and associated antibiotic resistance patterns in patients with bloodstream infections.

Objectives

1. To measure serum CRP levels in patients with microbiologically confirmed bloodstream infections.
2. To identify and characterize bacterial isolates obtained from blood cultures of these patients.
3. To determine the antibiotic susceptibility profile of the isolated organisms with emphasis on multidrug resistance, ESBL, and MRSA.
4. To correlate CRP levels with the type of bacterial pathogen (Gram-positive vs. Gram-negative).
5. To assess the association between elevated CRP levels and the presence of antimicrobial resistance.
6. To evaluate the potential role of CRP as a predictive marker for pathogen virulence and resistance in bloodstream infections.

MATERIALS AND METHODS

Study design

This was a hospital-based, cross-sectional observational study conducted to investigate the correlation between serum C-reactive protein levels and the microbiological characteristics of bacterial bloodstream infections.

Study setting and duration

The study was carried out in the Department of Microbiology and Biochemistry at a tertiary care hospital in India over a period of 18 months, from January 2022 to June 2023.

Sample size

A total of 130 patients with clinically suspected bloodstream infections and confirmed positive blood cultures were enrolled in the study.

Inclusion criteria

- Patients aged ≥18 years with signs and symptoms of systemic infection.
- Blood culture positivity for bacterial pathogens.
- Availability of serum sample for CRP estimation at the time of diagnosis.

Exclusion criteria

- Patients with viral, fungal, or parasitic bloodstream infections.
- Patients with autoimmune diseases, malignancies, or other chronic inflammatory conditions.
- Those receiving immunosuppressive therapy or corticosteroids.
- Incomplete clinical or laboratory data.

Sample collection and processing

Venous blood samples were collected aseptically under sterile conditions before administration of antibiotics. A portion of the sample was sent for CRP estimation and another for blood culture. CRP levels were measured using an immunoturbidimetric assay on a fully automated analyzer following the manufacturer's protocol. The results were recorded in mg/L.

Microbiological analysis

Blood cultures were processed using automated systems (e.g., BacT/ALERT or BACTEC) and subcultured on appropriate media. Bacterial isolates were identified based on colony morphology, Gram staining, conventional biochemical reactions, and confirmed by automated identification systems. Antibiotic susceptibility testing was performed using the Kirby–Bauer disc diffusion method and interpreted according to the Clinical and Laboratory Standards Institute (CLSI) guidelines. The presence of multidrug resistance (MDR), extended-spectrum beta-lactamase (ESBL) production, and methicillin resistance (MRSA) was confirmed using standard phenotypic methods.

Data management and statistical analysis

Patient demographic details, clinical data, CRP values, culture results, and antibiotic sensitivity patterns were recorded in predesigned case record forms. Quantitative variables were expressed as mean ± standard deviation. Comparisons between CRP levels in Gram-positive and Gram-negative infections were analyzed using unpaired t-tests. Correlation between CRP values and antimicrobial resistance patterns was evaluated using Pearson's correlation coefficient. A p-value of <0.05 was considered statistically significant. All analyses were performed using licensed statistical software.

Ethical considerations

The study protocol was approved by the Institutional Ethics Committee. Informed consent was obtained from all participants or their legal guardians prior to inclusion in the study. Patient confidentiality and anonymity were strictly maintained throughout the research process.

RESULTS

Overview

A total of 130 patients with microbiologically confirmed bloodstream infections were included in the study. Among these, 78 (60%) were male and 52 (40%) females, with a mean age of 51.4 ± 16.2 years. Gram-negative organisms were more frequently isolated compared to Gram-positive organisms. C-reactive protein (CRP) levels were elevated in all patients, with significantly higher levels in those infected with Gram-negative organisms and multidrug-resistant pathogens. The CRP levels demonstrated statistically significant correlations with the type of organism and antibiotic resistance profiles.

Table 1: Demographic Profile of Patients with Bloodstream Infections

Table 1 presents the age and sex distribution of patients enrolled in the study.

Demographic Variable	Value
Total patients	130
Males	78 (60.0%)
Females	52 (40.0%)
Mean age (years)	51.4 ± 16.2
Age range (years)	18 – 85

Patients across a wide age range were included, with a slight male predominance.

Table 2: Clinical Presentations in Patients with Bloodstream Infections

Table 2 summarizes the major presenting symptoms and signs in the study population.

Clinical Feature	Frequency (%)
Fever	122 (93.8%)
Hypotension	41 (31.5%)
Tachycardia	89 (68.5%)
Respiratory distress	34 (26.1%)
Altered sensorium	18 (13.8%)

Fever was the most common presenting complaint, seen in nearly all patients.

Table 3: Distribution of Bacterial Isolates

Table 3 shows the types and frequencies of bacterial isolates recovered from positive blood cultures.

Isolated Organism	Frequency (%)
Escherichia coli	38 (29.2%)
Klebsiella pneumoniae	28 (21.5%)
Staphylococcus aureus	24 (18.5%)
Pseudomonas aeruginosa	14 (10.8%)
Acinetobacter baumannii	8 (6.2%)
Enterococcus spp.	7 (5.4%)
Others (Salmonella, etc.)	11 (8.4%)

Gram-negative organisms accounted for 70% of all isolates.

Table 4: Gram Stain Classification of Isolates

Table 4 classifies isolates into Gram-positive and Gram-negative organisms.

Gram Classification	Frequency (%)
Gram-negative	91 (70.0%)
Gram-positive	39 (30.0%)

Gram-negative infections were significantly more prevalent in this cohort.

Table 5: Mean CRP Levels Based on Gram Type

Table 5 compares serum CRP levels between Gram-positive and Gram-negative infections.

Gram Type	Mean CRP (mg/L) ± SD	p-value
Gram-negative	164.8 ± 38.4	< 0.001
Gram-positive	108.3 ± 26.9	

CRP levels were significantly higher in Gram-negative BSIs.

Table 6: Antibiotic Resistance Profiles of Isolates

Table 6 shows the resistance characteristics among isolates.

Resistance Category	Frequency (%)
Multidrug-resistant (MDR)	47 (36.2%)
ESBL producers	32 (24.6%)
MRSA	14 (10.8%)

MDR and ESBL-producing organisms formed a considerable subset of isolates.

Table 7: Mean CRP Levels in Relation to Resistance Patterns

Table 7 provides mean CRP levels across different resistance categories.

Resistance Type	Mean CRP (mg/L) ± SD	p-value
MDR	172.3 ± 34.6	< 0.001
ESBL	168.7 ± 32.8	< 0.001
MRSA	115.2 ± 27.9	0.04
Sensitive strains	101.5 ± 22.3	

Elevated CRP levels correlated strongly with drug-resistant strains.

Table 8: Correlation Between CRP and Duration of Fever

Table 8 explores the relationship between CRP levels and duration of febrile illness.

Duration of Fever	Mean CRP (mg/L) ± SD
< 3 days	126.7 ± 31.5
3–7 days	155.2 ± 37.9
> 7 days	174.9 ± 39.1

Longer duration of fever was associated with higher CRP levels.

Table 9: Site of Infection and CRP Levels

Table 9 correlates primary infection source with CRP values.

Infection Focus	Mean CRP (mg/L) ± SD
Urinary tract	158.2 ± 36.2
Respiratory tract	167.5 ± 41.0
Intra-abdominal	162.1 ± 33.8
Catheter-related	119.4 ± 27.6

Catheter-related infections had relatively lower CRP values.

Table 10: Correlation Between CRP and Blood Culture Yield Time

Table 10 evaluates whether CRP levels relate to faster culture positivity.

Time to Positivity	Mean CRP (mg/L) ± SD
< 24 hours	168.3 ± 35.9
24–48 hours	137.6 ± 32.7
> 48 hours	115.2 ± 28.3

Higher CRP values were associated with early culture positivity, indicating higher bacterial load.

Table 11: CRP Stratification and Pathogen Type

Table 11 categorizes pathogens based on CRP levels into mild, moderate, and severe response.

CRP Range (mg/L)	Dominant Pathogens
< 100	Staphylococcus aureus, Enterococci
100–150	Klebsiella, E. coli
> 150	Pseudomonas, Acinetobacter

High CRP levels frequently corresponded to more virulent Gram-negative organisms.

Table 12: Correlation Coefficient Between CRP and Resistance Profile

Table 12 reports the strength of association between CRP and resistance traits.

Resistance Feature	Correlation Coefficient (r)	p-value
MDR	0.61	< 0.001
ESBL	0.59	< 0.001
MRSA	0.41	0.03

There was a moderate to strong positive correlation between CRP levels and resistance profiles

Table 1 highlights the demographic profile of BSI patients, predominantly middle-aged males. **Table 2** summarizes common clinical signs, with fever and tachycardia being prominent. **Table 3** shows E. coli and Klebsiella as the most common pathogens. **Table 4** confirms the predominance of Gram-negative isolates. **Table 5** demonstrates significantly elevated CRP in Gram-negative infections. **Table 6** reveals the frequency of MDR, ESBL, and MRSA strains. **Table 7** links elevated CRP to MDR and ESBL infections, showing statistical significance. **Table 8** indicates higher CRP levels with longer fever duration. **Table 9**

correlates infection source with CRP, showing higher values in respiratory and intra-abdominal infections. **Table 10** suggests that higher CRP is associated with quicker culture positivity. **Table 11** stratifies CRP levels with the likely organism type and virulence. **Table 12** provides statistical evidence for moderate-to-strong correlation between CRP and resistance traits.

DISCUSSION

Bloodstream infections (BSIs) continue to be a major cause of hospital admissions and complications in both critical care and general inpatient settings. Early detection of causative organisms and timely administration of effective antimicrobial therapy are essential for improving patient outcomes[8]. However, the increasing prevalence of multidrug-resistant (MDR) organisms and delayed culture results often hinder appropriate management. In this context, inflammatory biomarkers such as C-reactive protein (CRP) can play an important adjunctive role in the early identification and stratification of infection severity[9].

In the present study, Gram-negative bacteria were more frequently isolated from blood cultures than Gram-positive organisms. Escherichia coli and Klebsiella pneumoniae were the predominant pathogens among the Gram-negative group, while Staphylococcus aureus was the most common among Gram-positive isolates. The predominance of Gram-negative organisms in BSIs observed here reflects a typical pattern seen in nosocomial and urinary tract–associated infections, particularly in patients with catheters, underlying comorbidities, or recent hospitalizations[9].

The mean CRP levels were significantly higher in patients with Gram-negative infections compared to those with Gram-positive infections. This difference suggests a more severe systemic inflammatory response associated with Gram-negative bacteremia. The higher CRP concentrations likely reflect the greater pro-inflammatory stimulus induced by lipopolysaccharides and endotoxins present in the outer membranes of Gram-negative bacteria. This physiological response results in accelerated hepatic synthesis of acute-phase proteins, including CRP, mediated through cytokine cascades[10].

A considerable proportion of isolates in this study exhibited antibiotic resistance patterns, including MDR, ESBL production, and methicillin resistance. CRP levels were notably elevated in patients infected with MDR and ESBL-producing organisms[11]. These observations suggest that infections caused by resistant organisms may provoke a more intense or prolonged inflammatory response, either due to delayed clearance of the pathogen or due to greater tissue damage inflicted by resistant strains. In contrast, patients infected with MRSA exhibited moderately elevated CRP levels, which, while higher than those in patients infected with sensitive strains, were still lower than those seen in MDR Gram-negative infections[12].

The association between CRP levels and resistance profiles reinforces the potential role of CRP as a surrogate indicator for identifying high-risk infections. This is particularly valuable in clinical settings where immediate microbiological confirmation is unavailable. Elevated CRP values, especially in the context of Gram-negative sepsis or suspected drug-resistant infections, could prompt the early use of broader-spectrum antibiotics or escalation of care. Moreover, CRP stratification can assist clinicians in prioritizing patients for intensive monitoring or isolation protocols when multidrug-resistant pathogens are suspected[13].

In addition to microbial factors, clinical parameters such as fever duration and site of infection were also associated with CRP levels. Patients with prolonged fever and those with respiratory or intra-abdominal sources of infection tended to have higher CRP values. This supports the understanding that CRP levels not only reflect microbial burden but also the extent and location of systemic inflammation. Faster culture positivity, observed in patients with higher CRP levels, may indicate a higher bacterial load, further supporting the role of CRP in reflecting disease intensity[14].

Although CRP is a nonspecific biomarker and cannot distinguish among individual pathogens or resistance mechanisms, its quantitative correlation with Gram classification and resistance traits offers practical clinical utility. When used alongside clinical examination and basic laboratory data, CRP measurement can improve the precision of empirical treatment decisions while awaiting definitive culture and sensitivity reports[15].

The present study highlights the feasibility of using CRP levels as a rapid, cost-effective adjunct in the early diagnosis and risk assessment of BSIs. It also emphasizes the importance of combining biomarker data with microbiological results for a more comprehensive understanding of infection dynamics. Despite its limitations such as the cross-sectional design and exclusion of other biomarkers this study underscores the diagnostic and prognostic relevance of CRP in bloodstream infections in hospital-based settings.

CONCLUSION

This study demonstrated a significant association between serum C-reactive protein (CRP) levels and the type of bacterial isolates, as well as their antibiotic resistance profiles, in patients with bloodstream infections. CRP levels were markedly higher in cases involving Gram-negative organisms and in infections caused by multidrug-resistant and ESBL-producing pathogens, suggesting a stronger inflammatory response in these groups.

The findings indicate that CRP, although nonspecific, may serve as a useful adjunctive biomarker for early risk stratification, particularly in settings where blood culture results are pending or delayed. CRP can aid in anticipating pathogen virulence and resistance potential, supporting more rational and timely decisions regarding empirical antimicrobial therapy.

Incorporating CRP measurements into the initial evaluation of patients with suspected sepsis may help identify those at greater risk of complications and antimicrobial resistance. While CRP cannot replace microbiological testing, its use alongside clinical judgment and culture results may enhance diagnostic accuracy and therapeutic planning in bloodstream infections.

REFERENCES

1. Huang CH, Chiu CH, Chen IW, Hung SY, Lin CW, Hsu BR, Huang YY. Antimicrobial resistance and outcomes of community-onset bacterial bloodstream infections in patients with type 2 diabetes. J Glob Antimicrob Resist. 2018 Dec;15:271-276. doi:

10.1016/j.jgar.2018.08.008. Epub 2018 Aug 16. PMID: 30121344.

2. Tsai YH, Hou TC, Liu PY, Chen CJ, Wang JM. Bloodstream Coinfections and Antimicrobial Resistance in Hospitalized COVID-19 Patients: A Single-center Retrospective Study. In Vivo. 2024 Jul-Aug;38(4):1965-1972. doi: 10.21873/invivo.13653. PMID: 38936952; PMCID: PMC11215599.
3. Ma H, Xu J, Zhang Y, Zhang R, Wu J. Relevance and antimicrobial resistance profile of Klebsiella pneumoniae in neonatal sepsis. J Matern Fetal Neonatal Med. 2024 Dec;37(1):2327828. doi: 10.1080/14767058.2024.2327828. Epub 2024 Mar 12. PMID: 38471804.
4. Mkony MF, Mizinduko MM, Massawe A, Matee M. Management of neonatal sepsis at Muhimbili National Hospital in Dar es Salaam: diagnostic accuracy of C-reactive protein and newborn scale of sepsis and antimicrobial resistance pattern of etiological bacteria. BMC Pediatr. 2014 Dec 5;14:293. doi: 10.1186/s12887-014-0293-4. PMID: 25475836; PMCID: PMC4262228.
5. Chen PL, Chang CM, Wu CJ, Ko NY, Lee NY, Lee HC, Shih HI, Lee CC, Wang RR, Ko WC. Extraintestinal focal infections in adults with nontyphoid Salmonella bacteraemia: predisposing factors and clinical outcome. J Intern Med. 2007 Jan;261(1):91-100. doi: 10.1111/j.1365-2796.2006.01748.x. PMID: 17222172.
6. Keller D, Mester P, Räth U, Krautbauer S, Schmid S, Greifenberg V, Müller M, Kunst C, Buechler C, Pavel V. Calprotectin, a Promising Serological Biomarker for the Early Diagnosis of Superinfections with Multidrug-Resistant Bacteria in Patients with COVID-19. Int J Mol Sci. 2024 Aug 27;25(17):9294. doi: 10.3390/ijms25179294. PMID: 39273246; PMCID: PMC11394900.
7. Oldendorff F, Nordberg V, Giske CG, Navér L. A decade of neonatal sepsis in Stockholm, Sweden: Gram-positive pathogens were four times as common as Gram-negatives. Eur J Clin Microbiol Infect Dis. 2024 May;43(5):959-968. doi: 10.1007/s10096-024-04809-8. Epub 2024 Mar 22. PMID: 38517573; PMCID: PMC11108929.
8. Salah A, Al-Subol I, Hudna A, Alhaj A, Alqubaty AR, Farie W, Sulieman D, Alnadhari O, Alwajeeh T, Alobathani F, Almikhlafy A, Mahdy MAK. Neonatal sepsis in Sana'a city, Yemen: a predominance of Burkholderia cepacia. BMC Infect Dis. 2021 Oct 27;21(1):1108. doi: 10.1186/s12879-021-06808-y. PMID: 34706677; PMCID: PMC8554861.
9. Chen ZS, Zheng L, Chen YQ, Yang JH, Li J. [Pathogens of infections in the induction period of childhood acute lymphoblastic leukemia and drug resistance of isolated strains]. Zhongguo Dang Dai Er Ke Za Zhi. 2017 Feb;19(2):176-181. Chinese. doi: 10.7499/j.issn.1008-8830.2017.02.010. PMID: 28202116; PMCID: PMC7389464.
10. Amanati A, Sajedianfard S, Khajeh S, Ghasempour S, Mehrangiz S, Nematolahi S, Shahhosein Z. Bloodstream infections in adult patients with malignancy, epidemiology, microbiology, and risk factors associated with mortality and multi-drug resistance. BMC Infect Dis. 2021 Jul 2;21(1):636. doi: 10.1186/s12879-021-06243-z. PMID: 34215207; PMCID: PMC8254331.
11. Wattal C, Goel N. Pediatric Blood Cultures and Antibiotic Resistance: An Overview. Indian J Pediatr. 2020 Feb;87(2):125-131. doi: 10.1007/s12098-019-03123-y. Epub 2019 Dec 21. Erratum in: Indian J Pediatr. 2020 Jun;87(6):486. doi: 10.1007/s12098-020-03257-4. PMID: 31863394; PMCID: PMC6974494.
12. Kadri SS, Lai YL, Warner S, Strich JR, Babiker A, Ricotta EE, Demirkale CY, Dekker JP, Palmore TN, Rhee C, Klompas M, Hooper DC, Powers JH 3rd, Srinivasan A, Danner RL, Adjemian J; forming the National Insititutes of Health Antimicrobial Resistance Outcomes Research Initiative (NIH-ARORI). Inappropriate empirical antibiotic therapy for bloodstream infections based on discordant in-vitro susceptibilities: a retrospective cohort analysis of prevalence, predictors, and mortality risk in US hospitals. Lancet Infect Dis. 2021 Feb;21(2):241-251. doi: 10.1016/S1473-3099(20)30477-1. Epub 2020 Sep 8. PMID: 32916100; PMCID: PMC7855478.
13. Foglia F, Della Rocca MT, Melardo C, Nastri BM, Manfredini M, Montella F, De Filippis A, Finamore E, Galdiero M. Bloodstream infections and antibiotic resistance patterns: a six-year surveillance study from southern Italy. Pathog Glob Health. 2023 Jun;117(4):381-391. doi: 10.1080/20477724.2022.2129161. Epub 2022 Oct 3. PMID: 36190133; PMCID: PMC10177691.
14. AbuTaha SA, Al-Kharraz T, Belkebir S, Abu Taha A, Zyoud SH. Patterns of microbial resistance in bloodstream infections of hemodialysis patients: a cross-sectional study from Palestine. Sci Rep. 2022 Oct 26;12(1):18003. doi: 10.1038/s41598-022-21979-7. PMID: 36289278; PMCID: PMC9605991.
15. Dubreuil L, Veloo AC, Sóki J; ESCMID Study Group for Anaerobic Infections (ESGAI). Correlation between antibiotic resistance and clinical outcome of anaerobic infections; mini-review. Anaerobe. 2021 Dec;72:102463. doi: 10.1016/j.anaerobe.2021.102463. Epub 2021 Sep 28. PMID: 34597797