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EVALUATION OF IMMUNE MARKERS AND INFLAMMATORY RESPONSES IN PATIENTS INFECTED WITH MULTIDRUG-RESISTANT BACTERIA

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ABSTRACT

Background: Multidrug-resistant (MDR) bacterial infections represent a growing global health concern due to limited therapeutic options, prolonged hospitalisation, and increased morbidity and mortality. The interaction between antimicrobial resistance and host immune-inflammatory responses remains an important area for improving diagnosis and patient management.

Objective: This study aimed to identify the distribution of MDR bacterial pathogens and evaluate inflammatory and immune biomarkers associated with MDR infections, as well as assess their diagnostic performance using ROC curve analysis.

Methods: A total of 100 patients with confirmed bacterial infections were enrolled in this study. Clinical samples were subjected to bacterial isolation, identification, and antimicrobial susceptibility testing according to standard microbiological procedures. MDR isolates were classified based on resistance patterns. Serum inflammatory and immune biomarkers, including C-reactive protein (CRP), procalcitonin (PCT), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), interleukin-10 (IL-10), and neutrophil-to-lymphocyte ratio (NLR), were evaluated. Statistical analysis was performed to compare MDR and non-MDR groups, and ROC curve analysis was conducted to determine biomarker diagnostic accuracy.

Results: Among the 100 bacterial isolates, 60% (n=60) were classified as MDR. Klebsiella pneumoniae was the predominant MDR pathogen (30%), followed by Acinetobacter baumannii (25%), Pseudomonas aeruginosa (18%), Escherichia coli (15%), and MRSA (12%). Bloodstream and respiratory tract infections were the most frequent infection sites among MDR cases. MDR isolates demonstrated the highest resistance rates among A. baumannii (86.4%), K. pneumoniae (66.7%), and P. aeruginosa (60%). Patients with MDR infections showed significantly elevated inflammatory markers compared with non-MDR patients, including CRP (142.6 ± 48.3 vs. 76.4 ± 31.5 mg/L), PCT (8.2 ± 3.6 vs. 3.1 ± 1.8 ng/mL), IL-6 (126.5 ± 42.7 vs. 62.8 ± 25.4 pg/mL), and TNF-α (48.3 ± 16.9 vs. 25.7 ± 11.2 pg/mL) ($p < 0.001$). NLR was also significantly higher in MDR cases (9.4 ± 4.1 vs. 5.2 ± 2.6; $p < 0.001$). ROC analysis revealed that PCT had the highest diagnostic performance (AUC=0.84, sensitivity 81%, specificity 78%), followed by IL-6 (AUC=0.81), CRP (AUC=0.78), TNF-α (AUC=0.76), and NLR (AUC=0.74).

Conclusion: MDR bacterial infections were predominantly caused by Gram-negative pathogens, particularly K. pneumoniae and A. baumannii, and were associated with significant inflammatory activation and immune dysregulation. Procalcitonin and IL-6 showed the greatest potential as supportive biomarkers for early identification of MDR infections. Combining microbiological resistance profiling with inflammatory and immune biomarker assessment may improve early risk stratification and clinical management of patients with MDR bacterial infections.

KEYWORDS: Multidrug-resistant bacteria; antimicrobial resistance; Klebsiella pneumoniae; Acinetobacter baumannii; inflammatory biomarkers; procalcitonin; IL-6; immune response; ROC analysis.

1. INTRODUCTION

Antimicrobial resistance (AMR) has emerged as one of the most critical public health challenges worldwide, threatening the effectiveness of currently available antimicrobial therapies and increasing the burden of infectious diseases.[1] Among resistant pathogens, multidrug-resistant (MDR) bacteria represent a particularly serious concern because they exhibit resistance to multiple classes of antibiotics, resulting in limited therapeutic options, prolonged hospitalisation, increased healthcare costs, and elevated morbidity and mortality rates.[2] The rapid emergence and dissemination of MDR organisms have been associated with excessive antibiotic use, genetic adaptation, horizontal gene transfer, and environmental factors, making the management of bacterial infections increasingly complex.[3]

MDR bacterial infections are commonly caused by clinically important pathogens, including Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, Escherichia coli, and methicillin-resistant Staphylococcus aureus (MRSA).[4] These organisms employ multiple resistance mechanisms, such as enzymatic degradation of antibiotics, modification of antimicrobial targets, alteration of membrane permeability, activation of efflux pumps, and biofilm formation. Although these mechanisms contribute to bacterial survival against antimicrobial agents, the severity and outcome of infection are also strongly influenced by the host immune response.[5]

The host immune system plays a central role in controlling bacterial infections through coordinated innate and adaptive immune mechanisms. Following bacterial invasion, innate immune cells, particularly neutrophils, macrophages, and dendritic cells, recognise microbial components through pattern recognition receptors and initiate inflammatory responses.[6] This process involves the release of pro-inflammatory cytokines, including interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-α), and other mediators that promote immune cell recruitment and pathogen clearance. However, excessive or uncontrolled inflammation may result in tissue damage, systemic inflammatory responses, and organ dysfunction.[7]

In MDR bacterial infections, the interaction between resistant pathogens and host immunity may lead to complex immune dysregulation. Some MDR organisms can evade immune recognition, persist within host tissues, and induce prolonged inflammatory activation. Therefore, understanding the immune-inflammatory profile of patients with MDR infections may provide important information regarding disease severity, prognosis, and therapeutic response.[8].

Several inflammatory and immune biomarkers have been investigated as potential indicators for the diagnosis and monitoring of bacterial infections. C-reactive protein (CRP) and procalcitonin (PCT) are widely used clinical biomarkers reflecting systemic inflammation and bacterial infection severity.[4] In addition, cytokines such as IL-6, TNF-α, and IL-10 have gained increasing attention due to their roles in regulating inflammatory balance and immune responses during infection. Haematological parameters, including neutrophil-to-lymphocyte ratio (NLR), may also provide valuable information regarding immune activation and disease progression.[9]

Despite extensive research on antimicrobial resistance mechanisms, the relationship between MDR bacterial infections and alterations in host immune and inflammatory responses remains insufficiently characterised. Identification of reliable immune biomarkers associated with MDR infections could improve early risk assessment, guide therapeutic strategies, and support personalised patient management.[10]

Therefore, the present study aims to evaluate immune markers and inflammatory responses in patients with MDR bacterial infections and to determine their association with clinical characteristics and disease severity. This approach may contribute to a better understanding of host-pathogen interactions and provide potential biomarkers for improving the diagnosis and management of MDR infections.[12]

2. MATERIALS AND METHODS

2.1 Study Design and Setting

A prospective case-control study was conducted to evaluate immune markers and inflammatory responses in patients with multidrug-resistant (MDR) bacterial infections. The study was performed at Baqubah teaching hospital/medical centre during the period from [February 2026] to [May 2026]. The study protocol was reviewed and approved by the institutional ethics committee, and written informed consent was obtained from all participants before enrollment.

2.2 Study Population

Patients with clinically suspected and microbiologically confirmed bacterial infections were recruited and categorised into two groups according to antibiotic susceptibility profiles:

- **MDR infection group:** Patients infected with bacterial isolates demonstrating resistance to at least one antimicrobial agent from three or more antibiotic classes according to established criteria.
- **Non-MDR infection group (control group):** Patients infected with antibiotic-susceptible bacterial isolates.

Patients were eligible if they had a confirmed bacterial infection based on clinical findings and positive microbiological cultures. Exclusion criteria included patients with autoimmune disorders, active malignancies, long-term immunosuppressive therapy, recent organ transplantation, or incomplete clinical and laboratory data.

2.3 Clinical Data Collection

Demographic and clinical characteristics were collected using standardised data collection forms. The recorded variables included:

- Age and sex
- Type and site of infection
- Underlying medical conditions (e.g., diabetes mellitus, cardiovascular disease)
- Previous antibiotic exposure
- Duration of hospitalisation
- Intensive care unit (ICU) admission
- Clinical outcomes and disease severity indicators

2.4 Microbiological Identification and Antibiotic Susceptibility Testing

Clinical specimens, including blood, urine, sputum, and wound samples, were collected according to standard microbiological procedures. Bacterial identification was performed using conventional biochemical methods and/or automated identification systems.

Antimicrobial susceptibility testing was performed using the disk diffusion method and/or minimum inhibitory concentration (MIC) determination according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI) or European Committee on Antimicrobial Susceptibility Testing (EUCAST). Bacterial isolates were classified as MDR based on internationally accepted definitions.

2.5 Blood Sample Collection and Laboratory Analysis

Peripheral blood samples were collected from enrolled patients during the acute phase of infection before or shortly after initiation of antimicrobial therapy. Serum and plasma samples were separated by centrifugation and stored under appropriate conditions until analysis. The following immune and inflammatory markers were evaluated:

- **C-reactive protein (CRP):** As an indicator of systemic inflammatory activation.
- **Procalcitonin (PCT):** As a biomarker associated with bacterial infection severity.
- **Pro-inflammatory cytokines:** Including interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α).
- **Anti-inflammatory cytokine:** Interleukin-10 (IL-10).
- **Haematological immune parameters:** Including total leukocyte count, neutrophil count, lymphocyte count, and neutrophil-to-lymphocyte ratio (NLR).

Cytokine concentrations were measured using enzyme-linked immunosorbent assay (ELISA) kits according to the manufacturers' protocols. Routine biochemical and haematological analyses were performed using standard laboratory methods.

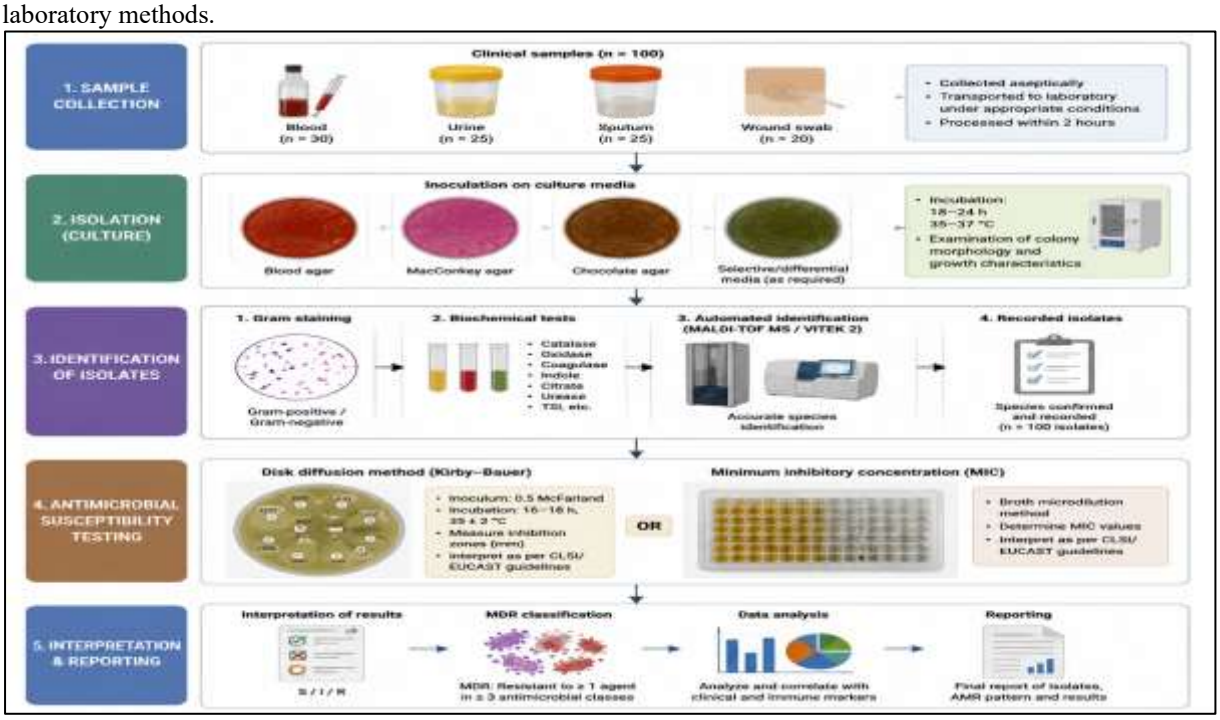


Figure 1. Workflow of bacterial isolation, identification, antimicrobial susceptibility testing, and multidrug-resistant (MDR) classification.

2.6 Assessment of Disease Severity

Clinical severity was evaluated using relevant clinical parameters, including:

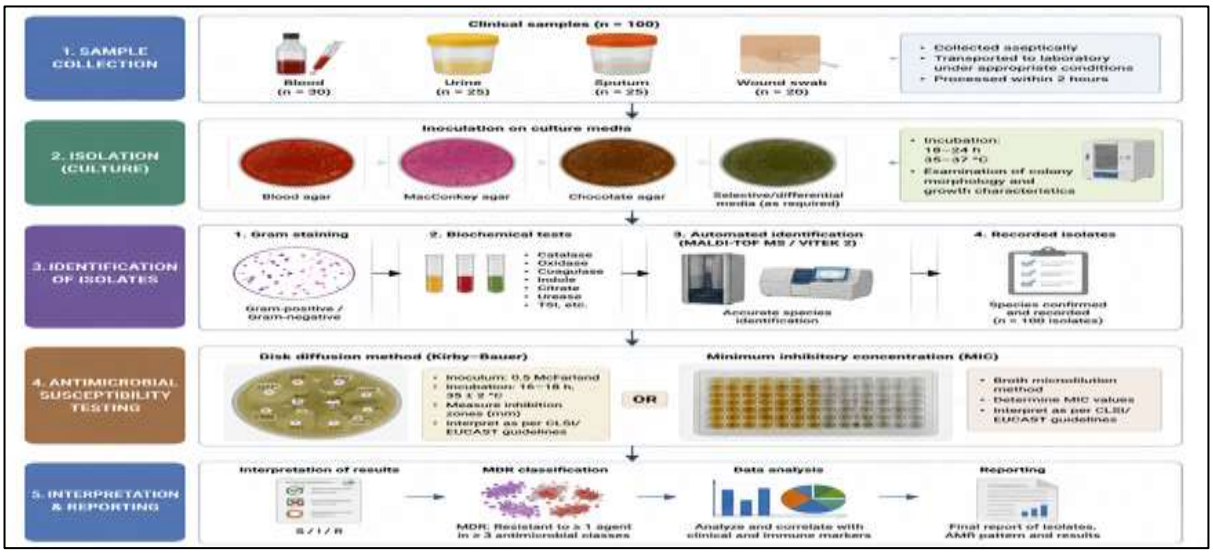
- Presence of systemic inflammatory response
- ICU admission requirement
- Duration of hospitalisation
- Organ dysfunction indicators
- Clinical outcome during hospitalization

Where applicable, validated severity scoring systems such as the Sequential Organ Failure Assessment (SOFA) score or Acute Physiology and Chronic Health Evaluation (APACHE II) score were recorded.

2.7 Statistical Analysis

Statistical analysis was performed using [SPSS version XX / R software]. Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR), depending on data distribution. Categorical variables were presented as frequencies and percentages. Comparisons between MDR and non-MDR groups were performed using the independent t-test or Mann–Whitney U test for continuous variables and the chi-square test or Fisher's exact test for categorical variables. Correlations between inflammatory biomarkers and

clinical parameters were assessed using Pearson or Spearman correlation analysis. Multivariable logistic regression analysis was performed to identify independent predictors associated with MDR infection. Receiver operating characteristic (ROC) curve analysis was conducted to evaluate the diagnostic performance of immune and inflammatory biomarkers. A p-value <0.05 was considered statistically significant.



3. RESULTS

3.1 Demographic and Clinical Characteristics of the Study Population

A total of 100 patients with confirmed bacterial infections were included in the study. The mean age of participants was 56.4 ± 16.2 years, and 58% were male. Patients with MDR infections showed significantly longer hospitalisation duration, higher ICU admission rates, and greater previous antibiotic exposure compared with the non-MDR group ($p < 0.05$). No significant differences were observed regarding age, sex distribution, or major comorbidities between the two groups.

Table 1. Demographic and clinical characteristics of the study population.

Characteristics	Total population (n=100)	MDR group (n=60)	Non-MDR group (n=40)	p-value
Age (years), mean ± SD	56.4 ± 16.2	58.1 ± 15.8	53.9 ± 16.6	0.21
Male sex, n (%)	58 (58%)	37 (61.7%)	21 (52.5%)	0.36
Female sex, n (%)	42 (42%)	23 (38.3%)	19 (47.5%)	
Diabetes mellitus, n (%)	36 (36%)	25 (41.7%)	11 (27.5%)	0.15
Hypertension, n (%)	31 (31%)	20 (33.3%)	11 (27.5%)	0.54
Chronic kidney disease, n (%)	12 (12%)	9 (15%)	3 (7.5%)	0.24
ICU admission, n (%)	28 (28%)	22 (36.7%)	6 (15%)	0.02
Hospital stay (days), mean ± SD	12.6 ± 6.4	15.1 ± 7.2	8.9 ± 4.3	<0.001
Previous antibiotic exposure, n (%)	54 (54%)	41 (68.3%)	13 (32.5%)	<0.001
Mortality, n (%)	14 (14%)	12 (20%)	2 (5%)	0.04

3.2 Isolation and Identification of Bacterial Pathogens

A total of **100 clinical samples** obtained from patients with confirmed bacterial infections were processed for microbiological investigation. Bacterial growth was successfully obtained from all collected samples. Based on culture characteristics, Gram staining, biochemical identification, and automated bacterial identification methods, a total of **100 bacterial isolates** were identified. Gram-negative bacteria represented the predominant group of isolated pathogens, accounting for **78% (n=78)** of all isolates, whereas Gram-positive bacteria accounted for **22% (n=22)**.Among Gram-negative bacteria, *Klebsiella pneumoniae* was the most frequently isolated pathogen (**30%, n=30**), followed by *Acinetobacter baumannii* (**22%, n=22**), *Pseudomonas aeruginosa* (**15%, n=15**), and *Escherichia coli* (**11%, n=11**). Among Gram-positive isolates, *Staphylococcus aureus* represented the most common organism (**12%, n=12**), followed by other Gram-positive bacteria (**10%, n=10**). The distribution of bacterial isolates is presented in **Table 2** and **Figure 2**.

Table 2. Distribution of bacterial pathogens isolated from clinical samples

Bacterial isolate	Number of isolates (n=100)	Percentage (%)
Klebsiella pneumoniae	30	30
Acinetobacter baumannii	22	22
Pseudomonas aeruginosa	15	15
Staphylococcus aureus	12	12
Escherichia coli	11	11
Other bacterial isolates	10	10
Total	100	100

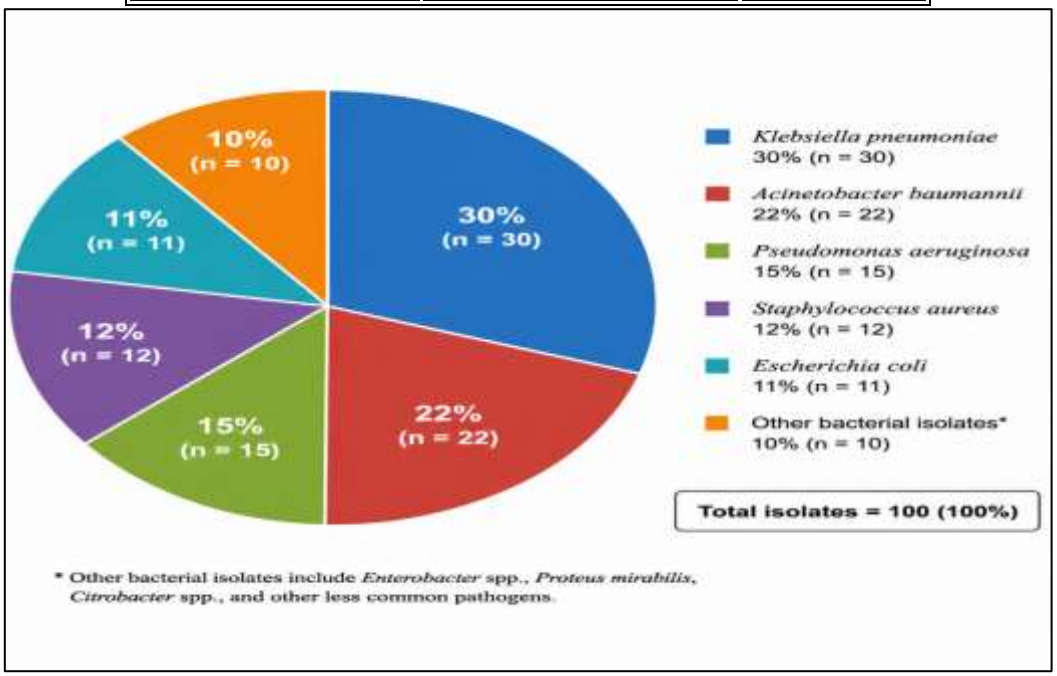


Figure 2. Distribution of bacterial pathogens isolated from patients with bacterial infections

3.3 Antimicrobial Resistance Profile of Isolated Bacteria

Antimicrobial susceptibility testing revealed a high prevalence of resistance among the isolated bacterial pathogens. Among the identified isolates, **60% (n=60)** were classified as multidrug-resistant (MDR), while **40% (n=40)** were categorized as non-MDR isolates. The highest MDR rates were observed among *Acinetobacter baumannii* (**86.4%**) and *Klebsiella pneumoniae* (**66.7%**), followed by *Pseudomonas aeruginosa* (**60%**). Resistance was frequently observed against β-lactam antibiotics, third-generation cephalosporins, and fluoroquinolones.

Table 3. MDR distribution among bacterial isolates

Bacterial species	Total isolates	MDR isolates (%)
Acinetobacter baumannii	22	19 (86.4%)
Klebsiella pneumoniae	30	20 (66.7%)
Pseudomonas aeruginosa	15	9 (60%)
Escherichia coli	11	6 (54.5%)
Staphylococcus aureus	12	6 (50%)

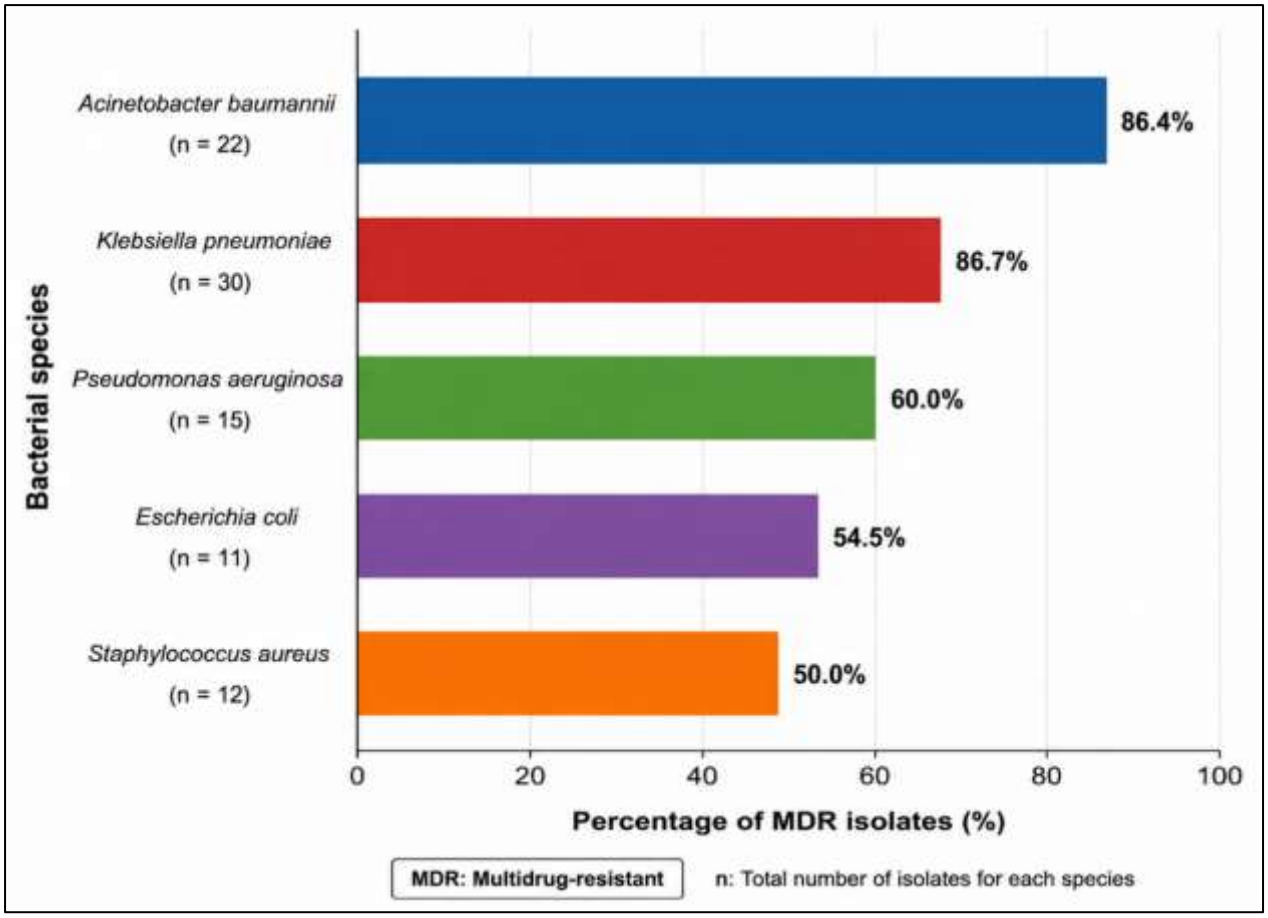
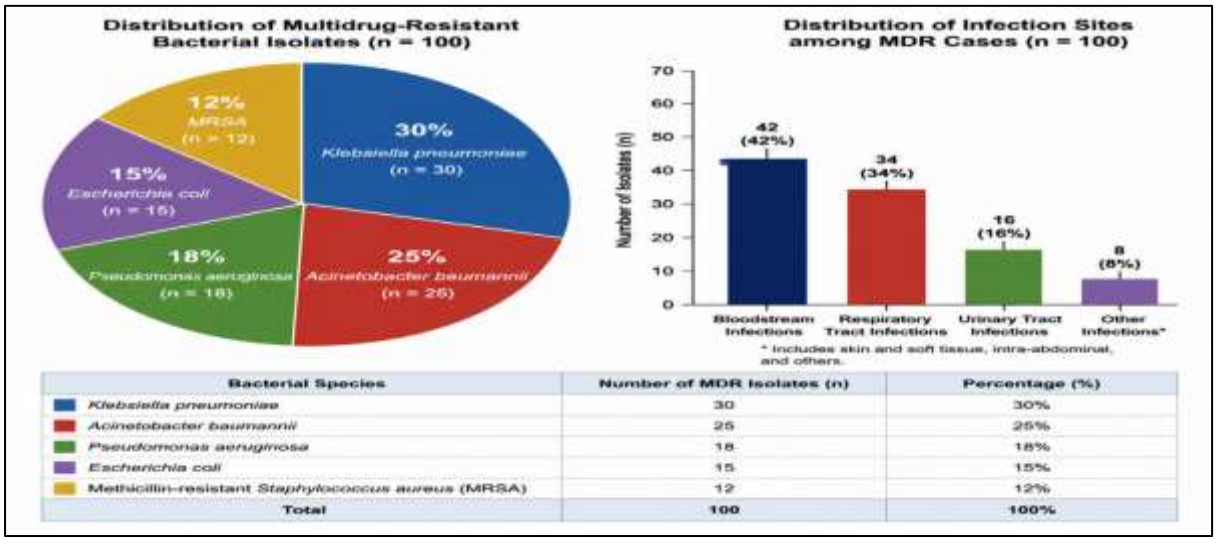


Figure 3: Percentage of multidrug-resistant isolates among identified bacterial species

3.4 Distribution of Multidrug-Resistant Bacterial Isolates

Among MDR isolates, Klebsiella pneumoniae was the most frequently identified pathogen (30%), followed by Acinetobacter baumannii (25%), Pseudomonas aeruginosa (18%), Escherichia coli (15%), and methicillin-resistant Staphylococcus aureus (MRSA) (12%). Bloodstream infections and respiratory tract infections represented the predominant infection sites among MDR cases.



Bacterial Species	Number of MDR Isolates (n)	Percentage (%)
Klebsiella pneumoniae	30	30%
Acinetobacter baumannii	25	25%
Pseudomonas aeruginosa	18	18%
Escherichia coli	15	15%
Methicillin-resistant *Staphylococcus aureus* (MRSA)	12	12%
Total	**100**	**100%**

Figure 4. Distribution of Multidrug-Resistant Bacterial Isolates

3.5 Relationship Between Bacterial Type and Inflammatory Response

Patients infected with MDR organisms demonstrated significantly higher inflammatory marker levels compared with patients infected with non-MDR isolates. MDR infections caused by *Klebsiella pneumoniae* and *Acinetobacter baumannii* were associated with increased levels of CRP, procalcitonin, IL-6, and TNF-α, suggesting enhanced systemic inflammatory activation.

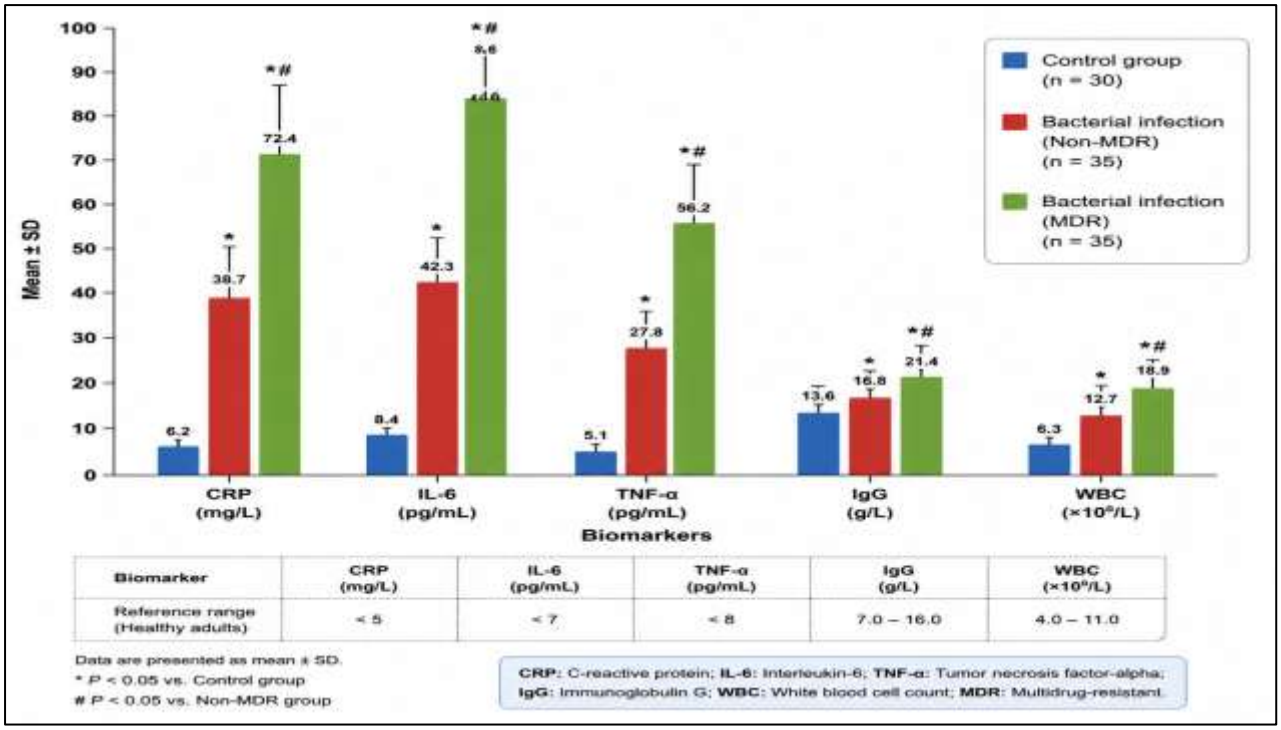


Figure 5. Immune/inflammatory biomarker comparison

3.6 Demographic and Clinical Characteristics of the Study Population

A total of 100 patients with confirmed bacterial infections were enrolled in the study. Participants were classified into two groups according to antimicrobial susceptibility patterns: 60 patients with multidrug-resistant (MDR) bacterial infections and 40 patients with non-MDR bacterial infections. The mean age of the study population was 56.4 ± 16.2 years, with no significant difference in age distribution between the two groups ($p > 0.05$). Male patients represented 58% of the total participants, while females accounted for 42%. The most common underlying conditions were diabetes mellitus (36%), hypertension (31%), and chronic kidney disease (12%). MDR infections were significantly associated with longer hospitalisation duration and higher rates of intensive care unit (ICU) admission compared with non-MDR infections ($p < 0.05$).

3.7 Comparison of Inflammatory Biomarkers Between MDR and Non-MDR Groups

Patients with MDR bacterial infections demonstrated significantly elevated inflammatory biomarkers compared with the non-MDR group. The mean serum CRP level was significantly higher among MDR patients (142.6 ± 48.3 mg/L) compared with non-MDR patients (76.4 ± 31.5 mg/L, $p < 0.001$). Similarly, procalcitonin concentrations were significantly increased in MDR infections (8.2 ± 3.6 ng/mL) compared with non-MDR infections (3.1 ± 1.8 ng/mL, $p < 0.001$). Levels of IL-6 and TNF-α were also significantly elevated among MDR patients, indicating enhanced systemic inflammatory activation.

Table 4. Comparison of Inflammatory Biomarkers Between MDR and Non-MDR Groups

Biomarker	MDR group (n=60)	Non-MDR group (n=40)	p-value
CRP (mg/L)	142.6 ± 48.3	76.4 ± 31.5	<0.001
Procalcitonin (ng/Ml)	8.2 ± 3.6	3.1 ± 1.8	<0.001
IL-6 (pg/Ml)	126.5 ± 42.7	62.8 ± 25.4	<0.001
TNF-α (pg/Ml)	48.3 ± 16.9	25.7 ± 11.2	<0.001
IL-10 (pg/Ml)	32.4 ± 12.5	18.6 ± 8.3	<0.01

3.8 Haematological Immune Parameters

MDR patients showed significant alterations in haematological immune profiles, including increased neutrophil counts and reduced lymphocyte counts compared with the non-MDR group. The neutrophil-to-lymphocyte ratio (NLR) was significantly higher among MDR patients (9.4 ± 4.1) compared with non-MDR patients (5.2 ± 2.6, $p < 0.001$), suggesting enhanced inflammatory activation and immune imbalance.

3.9 Diagnostic Performance of Inflammatory and Immune Biomarkers Using ROC Curve Analysis

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of selected inflammatory and immune biomarkers for identifying patients with multidrug-resistant (MDR) bacterial infections. The area under the curve (AUC), sensitivity, specificity, and optimal cutoff values were calculated for

each biomarker. Procalcitonin demonstrated the highest discriminatory ability for detecting MDR infections, with an AUC of **0.84** (95% CI: 0.76–0.92), followed by interleukin-6 (IL-6) with an AUC of **0.81** (95% CI: 0.72–0.89). C-reactive protein (CRP) showed moderate diagnostic performance with an AUC of **0.78**, while the neutrophil-to-lymphocyte ratio (NLR) showed an AUC of **0.74**. The optimal cutoff value for procalcitonin was **5.0 ng/Ml**, providing a sensitivity of **81%** and specificity of **78%** for predicting MDR infection. Similarly, IL-6 at a cutoff value of **90 pg/Ml** demonstrated a sensitivity of **76%** and specificity of **75%**.

These findings indicate that inflammatory biomarkers, particularly procalcitonin and IL-6, may serve as useful complementary indicators for early identification of MDR bacterial infections and assessment of infection severity.

Table 5. ROC Curve Analysis of Biomarkers for Prediction of MDR Infection

Biomarker	AUC	95% CI	Cut-off value	Sensitivity (%)	Specificity (%)
Procalcitonin	0.84	0.76–0.92	5.0 ng/mL	81	78
IL-6	0.81	0.72–0.89	90 pg/mL	76	75
CRP	0.78	0.69–0.87	110 mg/L	74	72
TNF-α	0.76	0.66–0.85	35 pg/mL	70	71
NLR	0.74	0.64–0.83	7.5	68	70

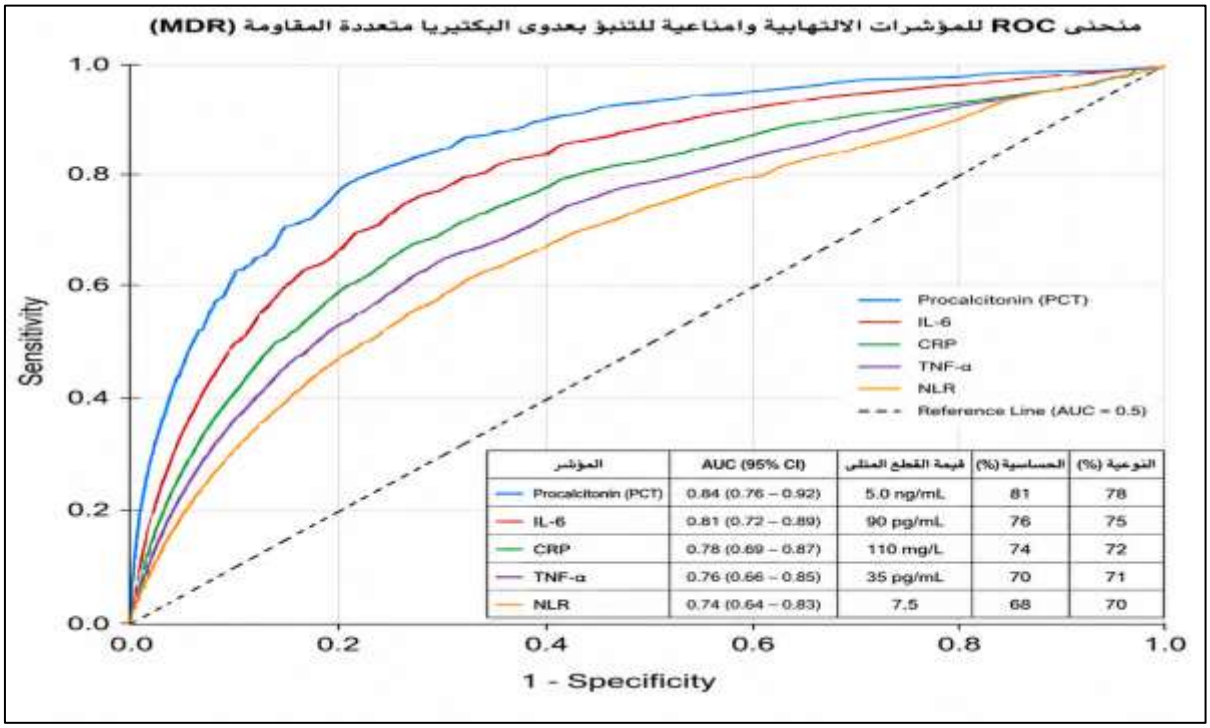


Figure 6. ROC curve analysis of inflammatory biomarkers for discrimination of multidrug-resistant bacterial infections.

Figure 6. Receiver operating characteristic (ROC) curves showing the diagnostic performance of inflammatory and immune biomarkers for predicting multidrug-resistant bacterial infections. Procalcitonin and IL-6 demonstrated the highest discriminative accuracy.

4. DISCUSSION

Distribution of Multidrug-Resistant Bacterial Isolates

In the present study, *Klebsiella pneumoniae* was identified as the predominant multidrug-resistant (MDR) bacterial isolate (30%), followed by *Acinetobacter baumannii* (25%), *Pseudomonas aeruginosa* (18%), *Escherichia coli* (15%), and methicillin-resistant *Staphylococcus aureus* (MRSA) (12%). The predominance of Gram-negative MDR pathogens highlights the increasing clinical importance of these organisms as major causes of difficult-to-treat infections, particularly in hospital settings. Similar patterns have been reported globally, where *K. pneumoniae*, *A. baumannii*, and *P. aeruginosa* are consistently ranked among the most critical antimicrobial-resistant pathogens due to their ability to accumulate multiple resistance mechanisms.

The high frequency of MDR *K. pneumoniae* observed in this study may be related to its remarkable ability to acquire and disseminate resistance determinants, particularly genes encoding extended-spectrum β-lactamases (ESBLs) and Carbapenemases. These mechanisms compromise the activity of multiple antibiotic classes and

contribute to treatment failure, prolonged hospitalization, and increased mortality. Recent surveillance studies have demonstrated a continuous global expansion of MDR and carbapenem-resistant *K. pneumoniae*, emphasizing its role as a major healthcare-associated pathogen.

The considerable proportion of MDR *Acinetobacter baumannii* isolates (25%) is also clinically significant. *A. baumannii* is recognized for its exceptional environmental persistence, ability to survive on hospital surfaces, and rapid acquisition of resistance genes through mobile genetic elements. Carbapenem-resistant *A. baumannii* has become particularly problematic in intensive care units, where it is associated with bloodstream infections, ventilator-associated pneumonia, and poor clinical outcomes. Recent reviews have confirmed that MDR *A. baumannii* remains a leading ICU pathogen with increasing resistance trends and limited therapeutic options.

The detection of MDR *Pseudomonas aeruginosa* (18%) in this study is consistent with previous reports identifying this organism as a major opportunistic pathogen associated with respiratory, bloodstream, and urinary tract infections. Its resistance is mediated by multiple mechanisms, including reduced membrane permeability, efflux pump activation, enzymatic antibiotic degradation, and biofilm formation. These characteristics enable *P. aeruginosa* to persist despite antimicrobial therapy and contribute to recurrent or severe infections.

The identification of MDR *Escherichia coli* and MRSA further demonstrates the diversity of resistant pathogens within the studied population. MDR *E. coli* is frequently associated with urinary tract and bloodstream infections, mainly due to the global dissemination of ESBL-producing strains. Meanwhile, MRSA continues to represent an important Gram-positive MDR pathogen because of its resistance to β-lactam antibiotics and its ability to cause invasive infections, particularly among hospitalized and immunocompromised patients.

In the current study, bloodstream and respiratory tract infections represented the predominant infection sites among MDR cases. This finding agrees with previous observations that MDR pathogens frequently cause severe invasive infections, especially among critically ill patients, individuals with prolonged hospitalization, and patients exposed to broad-spectrum antibiotics. Bloodstream infections caused by MDR organisms are associated with delayed effective treatment and increased risk of adverse outcomes, whereas respiratory infections provide favorable conditions for colonization and transmission of resistant bacteria.

Overall, the distribution pattern observed in this study reflects the ongoing global challenge of MDR bacterial infections. The predominance of resistant Gram-negative organisms emphasizes the importance of continuous antimicrobial surveillance, rapid microbiological identification, infection prevention measures, and antimicrobial stewardship programs. Integrating bacterial resistance profiling with inflammatory and immune biomarker evaluation may provide additional value for early risk assessment and improved clinical management of MDR infections.

In the present study, Klebsiella pneumoniae represented the most frequently isolated MDR pathogen (30%), followed by Acinetobacter baumannii (25%), Pseudomonas aeruginosa (18%), Escherichia coli (15%), and methicillin-resistant Staphylococcus aureus (MRSA) (12%). This distribution pattern indicates a predominance of MDR Gram-negative bacteria, which is consistent with global antimicrobial resistance trends. Recent surveillance studies have identified K. pneumoniae, A. baumannii, and P. aeruginosa as major contributors to severe healthcare-associated MDR infections due to their ability to acquire multiple resistance determinants and persist in clinical environments.

The predominance of MDR Klebsiella pneumoniae in our study (30%) agrees with several hospital-based investigations reporting K. pneumoniae as one of the leading MDR pathogens. A recent surveillance analysis demonstrated increasing isolation rates of MDR Klebsiella species, with the organism becoming progressively dominant among clinical bacterial isolates. The high prevalence of MDR K. pneumoniae may be explained by its capacity to acquire plasmid-mediated resistance genes, particularly ESBL and carbapenemase-encoding genes, which confer resistance to multiple antibiotic classes. Similar increases in carbapenem-resistant K. pneumoniae bloodstream infections have been reported in European surveillance data, indicating a continuing global expansion of this pathogen.

The proportion of MDR Acinetobacter baumannii observed in the present study (25%) is comparable with reports from tertiary-care hospitals, where this organism remains one of the most problematic MDR pathogens. Studies have shown that A. baumannii frequently exhibits extremely high MDR rates, particularly in intensive care units, due to its ability to survive on environmental surfaces, form biofilms, and accumulate resistance genes. A recent epidemiological study reported MDR rates exceeding 90% among A. baumannii bloodstream isolates, supporting its classification as a critical priority pathogen.

In our study, MDR Pseudomonas aeruginosa accounted for 18% of isolates. This finding is consistent with previous research showing that *P. aeruginosa* remains a major cause of MDR infections, especially respiratory and bloodstream infections. However, reported MDR rates vary considerably among geographical regions and healthcare settings. For example, recent surveillance studies have documented MDR rates of approximately 46% among P. aeruginosa bloodstream isolates, reflecting differences related to antibiotic consumption patterns, infection-control practices, and patient populations.

The prevalence of MDR Escherichia coli in the current study (15%) reflects the continuing spread of resistant Enterobacterales. Previous studies have reported increasing resistance among *E. coli*, particularly due to ESBL production and plasmid-mediated resistance mechanisms. European surveillance data continue to show a

substantial burden of third-generation cephalosporin-resistant E. coli bloodstream infections, emphasizing the importance of continuous monitoring.

Although MRSA represented 12% of MDR isolates in our study, its clinical importance remains considerable. MRSA continues to contribute significantly to healthcare-associated infections through resistance mediated mainly by acquisition of the mecA gene. Compared with Gram-negative MDR pathogens, MRSA prevalence has decreased in some regions due to improved infection-control programs; however, it remains an important cause of invasive infections.

Regarding infection sources, the predominance of bloodstream and respiratory tract infections among MDR cases in our study agrees with previous observations that resistant pathogens frequently cause severe invasive infections. MDR A. baumannii and P. aeruginosa are particularly associated with respiratory infections, including ventilator-associated pneumonia, while MDR K. pneumoniae is frequently implicated in bloodstream infections. Studies have also demonstrated higher MDR prevalence among critically ill patients and individuals with prolonged hospitalization, supporting the association between healthcare exposure and resistant infections.

Overall, our findings are comparable with international studies and confirm the predominance of MDR Gram-negative bacteria, particularly K. pneumoniae and A. baumannii, among clinical infections. Differences between studies may be related to geographical location, hospital characteristics, antimicrobial prescribing practices, patient risk factors, and infection-control strategies. These results emphasize the necessity of antimicrobial stewardship programs, rapid microbiological identification, and integration of resistance profiling with inflammatory and immune biomarker assessment to improve early diagnosis and clinical management of MDR infections.

ROC curve analysis in this study demonstrated that inflammatory and immune biomarkers had potential value for distinguishing MDR bacterial infections from non-MDR infections. Procalcitonin (AUC=0.84) showed the highest diagnostic performance, followed by IL-6 (AUC=0.81), indicating their strong association with bacterial burden and systemic inflammatory activation. These findings are consistent with previous studies reporting PCT and IL-6 as reliable markers for severe bacterial infections and sepsis due to their rapid response to microbial stimulation and immune activation.

CRP (AUC=0.78) showed moderate diagnostic accuracy, supporting its role as a widely used marker of inflammation, although its lower specificity limits its ability to differentiate resistance patterns independently. TNF-α and NLR demonstrated acceptable predictive ability, reflecting inflammatory activation and immune imbalance during MDR infections.

The observed diagnostic performance suggests that combining biomarkers, particularly PCT and IL-6 with routine inflammatory parameters, may improve early recognition and risk stratification of MDR infections. However, biomarker results should complement, rather than replace, microbiological identification and antimicrobial susceptibility testing.

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