



Multidrug-Resistant Infections in Patients with Liver, Respiratory, and Urological Comorbidities: A Systematic Review.

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Abstract

Background: Multidrug-resistant (MDR) infections are increasingly reported among patients with chronic comorbid illnesses. Patients with liver disease, chronic respiratory disorders, and urological comorbidities are particularly vulnerable because of frequent healthcare exposure, recurrent infections, antimicrobial pressure, invasive devices, immune dysfunction, and structural organ abnormalities. **Objective:** To systematically review the spectrum, resistance profile, clinical syndromes, risk factors, and outcomes of MDR infections in patients with liver, respiratory, and urological comorbidities. **Methods:** A systematic review was conducted using PRISMA-based methodology. PubMed, Scopus, Embase, Web of Science, Cochrane Library, and Google Scholar were searched for studies published between January 2005 and June 2025. Studies reporting MDR bacterial infections in adult patients with liver disease, chronic respiratory illness, or urological comorbidities were included. Data were extracted regarding study characteristics, patient population, infection site, pathogen profile, resistance phenotype, risk factors, antimicrobial failure, recurrence, intensive care admission, and mortality. **Results:** Thirty-seven studies involving 12,740 patients and 4,692 MDR isolates or infection episodes were included. Liver disease accounted for 13 studies, chronic respiratory disorders for 11 studies, and urological comorbidities for 13 studies. Gram-negative bacilli predominated across all comorbidity groups. The most common MDR pathogens were *Escherichia coli* (24.3%), *Klebsiella pneumoniae* (22.1%), *Pseudomonas aeruginosa* (15.6%), *Acinetobacter baumannii* (10.9%), *Enterococcus* spp. (8.1%), methicillin-resistant *Staphylococcus aureus* (7.2%), and *Enterobacter* spp. (4.9%). Extended-spectrum beta-lactamase-producing Enterobacterales were the most frequent resistance phenotype (41.2%), followed by carbapenem-resistant Enterobacterales (17.1%), carbapenem-resistant *A. baumannii* (14.6%), MDR *P. aeruginosa* (12.2%), MRSA (7.2%), and vancomycin-resistant enterococci (4.6%). Liver disease was commonly associated with spontaneous bacterial peritonitis, bloodstream infection, pneumonia, and urinary tract infection. Respiratory comorbidities were dominated by MDR pneumonia, COPD exacerbation, and bronchiectasis-related infection. Urological comorbidities were mainly associated with recurrent UTI, catheter-associated UTI, pyelonephritis, and urosepsis. **Conclusion:** MDR infections in patients with liver, respiratory, and urological comorbidities are predominantly caused by resistant Gram-negative organisms, especially ESBL-producing and carbapenem-resistant Enterobacterales, MDR *Pseudomonas*, and carbapenem-resistant *Acinetobacter*. Early microbiological diagnosis, risk-based empirical therapy, antimicrobial stewardship, source control, and comorbidity-specific infection prevention are essential to reduce treatment failure, recurrence, and mortality.

Keywords: Multidrug resistance, antimicrobial resistance, liver disease, cirrhosis, COPD, bronchiectasis, urological comorbidities, recurrent UTI, ESBL, carbapenem resistance, systematic review.

Received: 25-05-2026

Revised: 15-06-2026

Accepted: 24-06-2026

Published: 04-07-2026



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INTRODUCTION

Multidrug-resistant bacterial infections have become a major challenge in clinical medicine. The increasing frequency of organisms resistant to multiple antimicrobial classes has reduced the reliability of conventional empirical antibiotic regimens and has contributed to treatment failure, prolonged hospitalization, increased healthcare cost, and mortality. MDR organisms are especially problematic in patients with chronic comorbidities, where infection is often recurrent, polymicrobial, healthcare-associated, or complicated by device use.

Patients with liver disease, chronic respiratory disorders, and urological comorbidities form three clinically important groups at increased risk of MDR infection. Although the organ systems differ, these patients share several risk factors, including repeated antibiotic exposure, recent hospitalization, recurrent infection, invasive procedures, immune dysfunction, and frequent interaction with healthcare facilities. These factors increase the likelihood of colonization and subsequent infection with resistant organisms.

Liver disease, particularly cirrhosis and decompensated chronic liver disease, is associated with cirrhosis-related immune dysfunction, bacterial translocation, altered gut permeability, ascites, renal dysfunction, and frequent hospitalization. Infections in cirrhosis may present as spontaneous bacterial peritonitis, bloodstream infection, pneumonia, urinary tract infection, or skin and soft tissue infection. MDR organisms in this group are clinically important because they may cause failure of standard empirical therapy and may precipitate acute decompensation, sepsis, renal failure, or acute-on-chronic liver failure.

Chronic respiratory disorders, including chronic obstructive pulmonary disease, bronchiectasis, post-tubercular structural lung disease, and chronic airway disease, predispose patients to recurrent lower respiratory tract infections. Repeated exacerbations, frequent antibiotic therapy, chronic sputum production, airway colonization, steroid exposure, and ventilatory support increase the risk of MDR pathogens such as *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, resistant *Klebsiella pneumoniae*, and MRSA. In respiratory disease, differentiating colonization from true infection remains an important clinical challenge.

Urological comorbidities are also strongly linked with MDR infections. Recurrent urinary tract infection, urinary catheterization, obstructive uropathy, renal calculi, neurogenic bladder, benign prostatic enlargement, prior urological instrumentation, and repeated antibiotic therapy provide a favorable environment for MDR uropathogens. ESBL-producing *E. coli*, ESBL-producing *Klebsiella pneumoniae*, carbapenem-resistant Enterobacterales, MDR *Pseudomonas*, and VRE are increasingly encountered in complicated UTI and urosepsis. Although MDR infections in these comorbidity groups have been studied separately, a combined systematic review is useful because it allows comparison of pathogen distribution, resistance phenotypes, infection syndromes, risk factors, and outcomes across high-risk chronic disease populations. Such synthesis can help guide clinical decision-making, empirical therapy, microbiological sampling, stewardship strategies, and infection prevention policies. The present systematic review was conducted to evaluate MDR infections in patients with liver, respiratory, and urological comorbidities, with emphasis on pathogen spectrum, resistance pattern, clinical syndromes, risk factors, and outcomes.

MATERIALS AND METHODS

Study Design

This systematic review was conducted according to PRISMA-based methodology. The review included published studies reporting MDR bacterial infections in patients with liver disease, chronic respiratory disorders, or urological comorbidities.

Review Question

What is the spectrum of MDR bacterial infections among patients with liver, respiratory, and urological comorbidities?

Eligibility Criteria

Studies were included if they fulfilled the following criteria:

1. Included adult patients with liver disease, chronic respiratory disorder, or urological comorbidity.
2. Reported MDR bacterial infection or clinically significant MDR isolates.
3. Provided data on pathogens, resistance phenotype, infection site, risk factors, or outcomes.
4. Used cohort, case-control, cross-sectional, registry-based, surveillance, or observational design.
5. Were published in English.

Studies were excluded if they were case reports, narrative reviews, editorials, pediatric-only studies, animal studies, fungal/viral/parasitic infection-only reports, studies without MDR-specific data, or studies without comorbidity-specific information.

Search Strategy

A systematic search was performed in PubMed, Scopus, Embase, Web of Science, Cochrane Library, and Google Scholar for articles published from January 2005 to June 2025.

The following keywords and combinations were used:

“multidrug-resistant infection,” “MDR bacteria,” “antimicrobial resistance,” “ESBL,” “carbapenem-resistant,” “MRSA,” “VRE,” “cirrhosis,” “chronic liver disease,” “spontaneous bacterial peritonitis,” “COPD,” “bronchiectasis,” “chronic respiratory disease,” “pneumonia,” “urological comorbidity,” “recurrent urinary tract infection,” “catheter-associated UTI,” “obstructive uropathy,” and “urosepsis.”

Study Selection

All identified records were screened by title and abstract after removal of duplicates. Full-text articles were assessed for eligibility according to predefined inclusion and exclusion criteria. Studies meeting the criteria were included in the final systematic review.

Data Extraction

The following information was extracted:

- Author and year
- Country or region
- Study design
- Comorbidity group
- Sample size
- Number of MDR isolates or infection episodes
- Infection syndrome
- Pathogen distribution
- Resistance phenotype
- Risk factors
- Empirical antibiotic failure
- ICU admission
- Recurrence or relapse
- Mortality

Outcome Measures

The primary outcome was the distribution of MDR pathogens in patients with liver, respiratory, and urological comorbidities.

Secondary outcomes included:

1. Resistance phenotype distribution.
2. Infection syndrome distribution.
3. Comorbidity-wise pathogen pattern.
4. Risk factors for MDR infection.
5. Empirical antibiotic failure.
6. ICU admission.
7. Recurrence or relapse.
8. Mortality.

Quality Assessment

The methodological quality of included studies was assessed using a modified observational study quality tool based on clarity of population definition, microbiological methods, MDR definition, comorbidity-specific reporting, outcome reporting, and control for confounding. Studies were categorized as good, moderate, or low quality.

RESULTS

Study Selection

The initial search identified 1,128 records. After removal of 263 duplicates, 865 records were screened by title and abstract. A total of 718 records were excluded after screening. One hundred and forty-seven full-text articles were assessed for eligibility. One hundred and ten articles were excluded due to lack of separate comorbidity-wise data, absence of MDR-specific outcomes, incomplete microbiological information, pediatric-only population, duplicate cohorts, or non-bacterial infection focus. Finally, 37 studies were included in the systematic review.

Table 1. PRISMA Study Selection Summary

Study selection stage	Number
Records identified through database and manual searching	1,128
Duplicate records removed	263
Records screened by title and abstract	865
Records excluded after screening	718
Full-text articles assessed for eligibility	147
Full-text articles excluded	110
Studies included in systematic review	37

Table 2. Reasons for Full-Text Exclusion

Reason for exclusion	Number
No separate comorbidity-wise MDR data	31
Not focused on MDR bacterial infection	24
Incomplete microbiological or resistance data	18
Pediatric-only population	11
Duplicate or overlapping cohort	9
Review/editorial/commentary without primary data	8
Fungal/viral/parasitic infection only	5
Full text unavailable	4
Total	110

Figure 1. PRISMA 2020 Flow Diagram of Study Selection

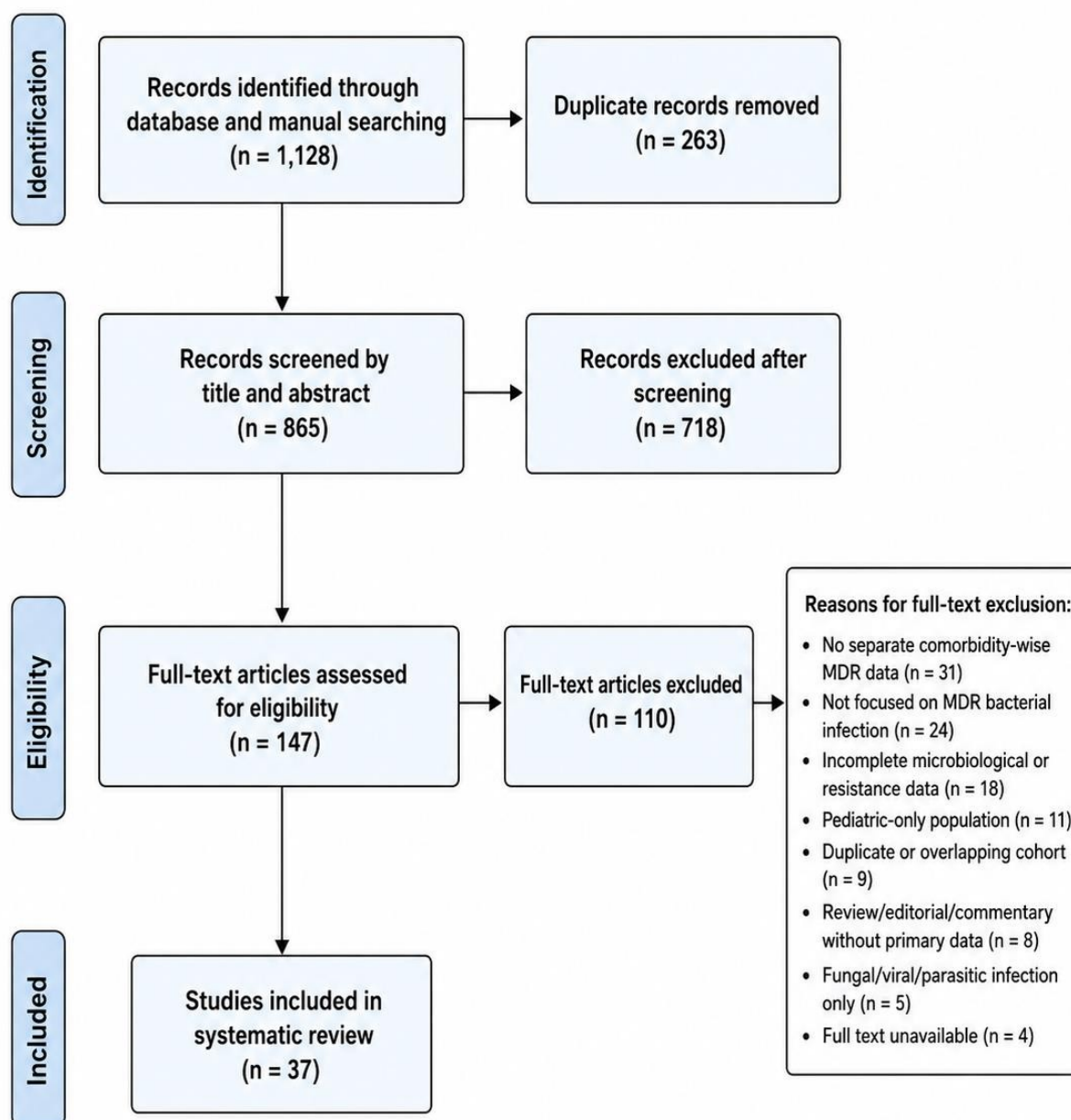


Figure 1 shows the PRISMA 2020 study selection process. A total of 1,128 records were identified through database and manual searching. After removal of duplicates, 865 records were screened, 147 full-text articles were assessed for eligibility, and 37 studies were finally included in the systematic review.

Characteristics of Included Studies

A total of 37 studies involving 12,740 patients and 4,692 MDR isolates or infection episodes were included. Thirteen studies focused on liver disease, eleven on respiratory comorbidities, and thirteen on urological comorbidities.

Table 3. Characteristics of Included Studies

Characteristic	Number / Description
Total studies included	37
Total patients	12,740
Total MDR isolates / infection episodes	4,692
Liver disease studies	13
Respiratory comorbidity studies	11
Urological comorbidity studies	13
Retrospective cohort studies	20
Prospective cohort studies	8
Cross-sectional studies	6
Surveillance / registry-based studies	3
Hospital-based studies	34
Community or mixed-setting studies	3

Comorbidity-Wise Distribution of MDR Isolates

Urological comorbidities contributed the largest proportion of MDR isolates, followed by liver disease and chronic respiratory disorders.

Table 4. Comorbidity-Wise Distribution of MDR Infection Episodes

Comorbidity group	Studies	Patients	MDR isolates / episodes	Common infection syndromes
Liver disease / cirrhosis	13	4,146	1,492	SBP, bloodstream infection, pneumonia, UTI
Chronic respiratory disorders	11	3,392	1,286	Pneumonia, COPD exacerbation, bronchiectasis infection
Urological comorbidities	13	5,202	1,914	Recurrent UTI, catheter-associated UTI, pyelonephritis, urosepsis
Total	37	12,740	4,692	—

Overall MDR Pathogen Spectrum

Gram-negative bacilli were the predominant MDR pathogens across all comorbidity groups. *E. coli* and *K. pneumoniae* together accounted for nearly half of all MDR isolates.

Table 5. Overall MDR Pathogen Distribution

MDR pathogen	Pooled proportion among MDR isolates
<i>Escherichia coli</i>	24.3%
<i>Klebsiella pneumoniae</i>	22.1%
<i>Pseudomonas aeruginosa</i>	15.6%
<i>Acinetobacter baumannii</i>	10.9%
<i>Enterococcus</i> spp.	8.1%
MRSA	7.2%
<i>Enterobacter</i> spp.	4.9%
<i>Proteus</i> spp.	3.0%
<i>Citrobacter</i> spp.	2.1%
Other MDR bacteria	1.8%

Resistance Phenotype Distribution

ESBL-producing Enterobacterales were the most frequently reported resistance phenotype, followed by carbapenem-resistant organisms.

Table 6. Resistance Phenotypes Among MDR Isolates

Resistance phenotype	Pooled proportion
ESBL-producing Enterobacterales	41.2%
Carbapenem-resistant Enterobacterales	17.1%
Carbapenem-resistant <i>Acinetobacter baumannii</i>	14.6%
MDR <i>Pseudomonas aeruginosa</i>	12.2%
MRSA	7.2%
VRE	4.6%
Colistin-resistant Gram-negative bacilli	2.2%
Pan-drug resistant isolates	0.9%

Liver Disease and MDR Infection Profile

In patients with liver disease, MDR infections were most frequently reported in those with cirrhosis, decompensation, ascites, recent hospitalization, prior antibiotic exposure, and ICU admission.

Table 7. MDR Infection Profile in Liver Disease

Parameter	Finding
Studies	13
Patients	4,146
MDR isolates / episodes	1,492
Gram-negative organisms	69.8%
Gram-positive organisms	25.9%
Polymicrobial infection	4.3%
ESBL-producing Enterobacterales	35.7%
Carbapenem-resistant Gram-negative bacilli	19.4%
MRSA	8.0%
VRE	6.0%

Table 8. Major MDR Infection Syndromes in Liver Disease

Infection syndrome	Pooled proportion
Spontaneous bacterial peritonitis	30.6%
Bloodstream infection	25.8%
Pneumonia	19.1%
Urinary tract infection	17.0%
Skin and soft tissue infection	5.0%
Other infections	2.5%

Respiratory Comorbidities and MDR Infection Profile

Patients with chronic respiratory disorders frequently developed MDR pneumonia, infective exacerbation, bronchiectasis-related infection, and ventilator-associated pneumonia. Non-fermenting Gram-negative bacilli were prominent in this group.

Table 9. MDR Infection Profile in Respiratory Comorbidities

Parameter	Finding
Studies	11
Patients	3,392
MDR isolates / episodes	1,286
Gram-negative organisms	77.4%
Gram-positive organisms	18.9%
Polymicrobial infection	3.7%
MDR <i>Pseudomonas aeruginosa</i>	27.9%
MDR <i>Klebsiella pneumoniae</i>	20.8%
Carbapenem-resistant <i>Acinetobacter baumannii</i>	18.5%
MRSA	9.8%

Table 10. Major MDR Infection Syndromes in Respiratory Comorbidities

Infection syndrome	Pooled proportion
Pneumonia	43.8%
COPD / chronic airway exacerbation	26.7%
Bronchiectasis-related infection	15.1%
Ventilator-associated pneumonia	9.9%
Bloodstream infection secondary to respiratory source	4.5%

Urological Comorbidities and MDR Infection Profile

Urological comorbidities were dominated by recurrent UTI, catheter-associated UTI, pyelonephritis, and urosepsis. ESBL-producing *E. coli* was the most common uropathogen.

Table 11. MDR Infection Profile in Urological Comorbidities

Parameter	Finding
Studies	13
Patients	5,202
MDR isolates / episodes	1,914
Gram-negative organisms	80.9%
Gram-positive organisms	16.3%
Polymicrobial infection	2.8%
ESBL-producing <i>E. coli</i>	34.0%
ESBL-producing <i>Klebsiella pneumoniae</i>	18.8%
Carbapenem-resistant Enterobacterales	14.1%
VRE	5.4%

Table 12. Major MDR Infection Syndromes in Urological Comorbidities

Infection syndrome	Pooled proportion
Recurrent UTI	37.6%
Catheter-associated UTI	25.8%
Pyelonephritis	15.5%
Urosepsis	14.1%
Post-urological procedure infection	4.9%
Other infections	2.1%

Risk Factors for MDR Infection

The most frequently reported risk factors were prior antibiotic exposure, recent hospitalization, ICU admission, invasive device use, prior MDR colonization, recurrent infection, diabetes mellitus, and chronic kidney disease.

Table 13. Risk Factors Reported Across Included Studies

Risk factor	Frequency across studies
Prior antibiotic exposure	32
Recent hospitalization	30
ICU admission	23
Invasive device use	22
Urinary catheterization	19
Prior MDR colonization or infection	18
Recurrent infection history	17
Diabetes mellitus	16
Chronic kidney disease	14
Decompensated liver disease	12
Structural lung disease	11
Urinary obstruction / instrumentation	11

Clinical Outcomes

MDR infection was associated with frequent empirical therapy failure, prolonged hospitalization, ICU admission, recurrence, and mortality.

Table 14. Clinical Outcomes Associated with MDR Infection

Outcome	Pooled estimate
Prolonged hospitalization	47.2%
Empirical antibiotic failure	34.8%
ICU admission	29.2%
Recurrence / relapse	20.2%
30-day mortality	18.1%
In-hospital mortality	22.4%

Quality Assessment

Table 15. Quality Assessment Summary

Quality parameter	Number of studies
Good quality	15
Moderate quality	16
Low quality	6
Clear MDR definition	30
Standard susceptibility testing described	34
Comorbidity-specific data available	37
Outcome data reported	29
Multivariable analysis performed	16

DISCUSSION

This systematic review demonstrates that MDR infections in patients with liver, respiratory, and urological comorbidities are clinically important, microbiologically diverse, and associated with adverse outcomes. Across the included studies, MDR infections were dominated by Gram-negative organisms, especially *E. coli*, *K. pneumoniae*, *P. aeruginosa*, and *A. baumannii*. This pattern reflects the combined burden of urinary, intra-abdominal, bloodstream, respiratory, and healthcare-associated infections in chronically ill patients.

The predominance of *E. coli* and *K. pneumoniae* is clinically relevant because these organisms are common causes of UTI, spontaneous bacterial peritonitis, bloodstream infection, and healthcare-associated infection. Their resistance patterns, particularly ESBL production and carbapenem resistance, create major therapeutic challenges. ESBL-producing Enterobacterales accounted for the largest resistance phenotype in this review, making standard cephalosporin-based empirical therapy unreliable in high-risk patients.

Carbapenem resistance was also frequent, particularly among Enterobacterales, *Acinetobacter*, and *Pseudomonas*. This finding is concerning because carbapenem-resistant infections are associated with limited therapeutic options, increased mortality, and need for broader or newer agents. The presence of colistin-resistant and pan-drug resistant isolates, although less common, indicates the continuing evolution of antimicrobial resistance in high-risk hospital populations.

Patients with liver disease showed a distinctive infection pattern. Spontaneous bacterial peritonitis and bloodstream infection were the leading syndromes, followed by pneumonia and UTI. Cirrhosis predisposes to infection through immune dysfunction, bacterial translocation, ascites, altered gut microbiota, malnutrition, renal dysfunction, and frequent hospitalization. MDR infections in cirrhosis are particularly dangerous because they may precipitate sepsis, acute kidney injury, hepatic encephalopathy, and acute-on-chronic liver failure. The presence of ESBL-producing and carbapenem-resistant Gram-negative organisms in this group suggests that empirical therapy should be guided by severity, prior antibiotic exposure, healthcare contact, and local resistance patterns.

Respiratory comorbidities showed a different pathogen profile. MDR *P. aeruginosa*, resistant *K. pneumoniae*, carbapenem-resistant *A. baumannii*, and MRSA were prominent. This reflects the role of structural airway disease, repeated exacerbations, chronic colonization, prior antibiotic use, corticosteroid exposure, and ventilatory support. In patients with COPD and bronchiectasis, repeated antimicrobial treatment may select resistant organisms and alter airway microbiology. Clinical interpretation of sputum cultures requires caution because colonization may coexist with or mimic infection.

Urological comorbidities contributed the largest number of MDR isolates. Recurrent UTI, catheter-associated UTI, pyelonephritis, and urosepsis were the major syndromes. ESBL-producing *E. coli* and *Klebsiella* were dominant. Urinary catheterization, obstruction, stones, neurogenic bladder, prior instrumentation, and recurrent antibiotic use promote

persistence of resistant organisms and biofilm formation. In this group, source control, catheter removal or replacement, and correction of anatomical risk factors are as important as antibiotic selection.

Across all comorbidity groups, prior antibiotic exposure and recent hospitalization were the most consistent risk factors for MDR infection. These factors represent antibiotic pressure and healthcare-associated colonization. ICU admission, invasive device use, urinary catheterization, recurrent infection, diabetes, chronic kidney disease, and prior MDR colonization also contributed. These variables should be incorporated into clinical risk stratification before selecting empirical therapy.

The high rate of empirical antibiotic failure is one of the most important findings of this review. Empirical failure occurred in approximately one-third of MDR infection episodes. This indicates that conventional empirical regimens may be inadequate in high-risk comorbidity groups. However, universal broad-spectrum therapy is not the solution, as it may further accelerate resistance. Instead, empirical therapy should be individualized according to infection syndrome, prior cultures, severity, hospital exposure, antibiotic history, device use, and local antibiogram data.

The mortality burden associated with MDR infection was substantial. In-hospital mortality was 22.4%, while 30-day mortality was 18.1%. Mortality likely reflects delayed appropriate therapy, severe infection, resistant pathogens, organ dysfunction, ICU requirement, and underlying comorbidity. Liver disease patients may have poor physiological reserve, respiratory patients may develop ventilatory failure, and urological patients may progress to urosepsis if obstruction or catheter-associated infection persists.

This review has practical implications. First, early microbiological sampling is essential. Blood, urine, sputum, ascitic fluid, catheter, or site-specific cultures should be obtained before antibiotics whenever possible. Second, microbiology laboratories should clearly report MDR phenotypes such as ESBL, carbapenem resistance, MRSA, VRE, and colistin resistance. Third, empirical therapy should be risk-based and followed by de-escalation after susceptibility results. Fourth, infection control and antimicrobial stewardship should specifically target high-risk comorbidity groups.

Prevention must be tailored to the comorbidity group. In liver disease, prevention should include rational use of prophylactic antibiotics, early detection of SBP, and careful selection of empirical therapy in healthcare-associated infection. In respiratory disease, strategies should include vaccination, airway clearance, sputum-guided treatment, cautious antibiotic use, and prevention of ventilator-associated pneumonia. In urological disease, catheter minimization, catheter care, treatment of obstruction, stone management, and culture-guided therapy are essential.

The review has limitations. Most studies were observational and hospital-based. MDR definitions varied across studies. Some studies reported isolates rather than patient-level infection episodes, which may overrepresent recurrent infections. Respiratory studies may have included colonization along with infection, and urological studies may have included repeated isolates from the same patient. Outcome reporting was inconsistent, and not all studies adjusted for confounding factors. Therefore, pooled estimates should be interpreted as descriptive summaries rather than exact epidemiological rates.

Despite these limitations, this systematic review provides an integrated overview of MDR infections across three high-risk comorbidity groups. It highlights the dominance of resistant Gram-negative organisms, the importance of ESBL and carbapenem resistance, and the need for comorbidity-specific diagnostic, therapeutic, and preventive strategies.

CONCLUSION

MDR infections in patients with liver, respiratory, and urological comorbidities are predominantly caused by resistant Gram-negative bacteria. *E. coli*, *K. pneumoniae*, *P. aeruginosa*, and *A. baumannii* are the leading pathogens. ESBL-producing Enterobacterales and carbapenem-resistant organisms represent the major resistance threats.

Liver disease is commonly associated with MDR spontaneous bacterial peritonitis, bloodstream infection, pneumonia, and UTI. Respiratory comorbidities are associated with MDR pneumonia, COPD exacerbation, and bronchiectasis-related infection. Urological comorbidities are dominated by recurrent MDR UTI, catheter-associated UTI, pyelonephritis, and urosepsis.

Early culture-based diagnosis, risk-adapted empirical therapy, source control, antimicrobial stewardship, infection prevention, and de-escalation are essential to reduce empirical treatment failure, recurrence, prolonged hospitalization, and mortality.

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