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Burden and Spectrum of Multidrug-Resistant Bacterial Infections in Chronic Liver, Respiratory, and Urological Diseases: A Systematic Review.

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Abstract

Background: Multidrug-resistant infections are an increasing challenge in hospitalized and chronically ill patients. Individuals with liver disease, chronic respiratory disorders, and urological comorbidities are especially vulnerable because of frequent hospital exposure, repeated antibiotic use, invasive procedures, immune dysfunction, and recurrent infections. ***Objective:*** To systematically review the spectrum of multidrug-resistant bacterial infections among patients with liver disease, chronic respiratory disorders, and urological comorbidities, and to summarize common pathogens, resistance patterns, infection sites, and clinical outcomes. ***Methods:*** A systematic review was conducted according to PRISMA 2020 principles. PubMed, Scopus, Embase, Web of Science, Google Scholar, and Cochrane Library were searched for studies published from January 2000 to December 2025. Studies reporting multidrug-resistant infections in patients with chronic liver disease, cirrhosis, chronic obstructive pulmonary disease, bronchiectasis, chronic respiratory illness, recurrent urinary tract infection, obstructive uropathy, catheter-associated urinary infection, or other urological comorbidities were included. Data were extracted on study design, population, infection site, pathogens, resistance phenotype, antimicrobial susceptibility, and outcomes. ***Results:*** Thirty-eight studies involving 12,486 patients were included. Among them, 4,972 multidrug-resistant isolates were reported. Gram-negative bacilli predominated, accounting for 72.8% of MDR infections. The most common organisms were Escherichia coli (24.6%), Klebsiella pneumoniae (21.8%), Pseudomonas aeruginosa (14.2%), Acinetobacter baumannii (9.7%), Enterococcus spp. (8.6%), Staphylococcus aureus including MRSA (7.9%), and Enterobacter spp. (5.4%). Extended-spectrum beta-lactamase production was the most frequent resistance mechanism, followed by carbapenem resistance, methicillin resistance, vancomycin resistance, and colistin resistance. In liver disease, spontaneous bacterial peritonitis, bloodstream infection, pneumonia, and urinary tract infection were common MDR syndromes. In chronic respiratory disorders, MDR pneumonia and colonization/infection by Pseudomonas aeruginosa, Klebsiella pneumoniae, and Acinetobacter baumannii were prominent. In urological comorbidities, recurrent UTI, catheter-associated UTI, pyelonephritis, and urosepsis were frequently associated with ESBL-producing Enterobacterales and carbapenem-resistant organisms. MDR infection was associated with prolonged hospitalization, higher ICU admission, treatment failure, relapse, and increased mortality. ***Conclusion:*** MDR infections in patients with liver disease, chronic respiratory disorders, and urological comorbidities are dominated by Gram-negative pathogens, especially ESBL-producing and carbapenem-resistant Enterobacterales, Pseudomonas aeruginosa, and Acinetobacter baumannii. Early microbiological diagnosis, antimicrobial stewardship, infection control, risk-based empirical therapy, and comorbidity-specific prevention strategies are essential to reduce adverse outcomes.

Keywords: Multidrug resistance, liver disease, cirrhosis, chronic respiratory disease, COPD, bronchiectasis, urological comorbidities, urinary tract infection, ESBL, carbapenem resistance, systematic review.

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INTRODUCTION

Multidrug-resistant infections have emerged as a major threat to modern healthcare. The increasing prevalence of resistant organisms has reduced the effectiveness of commonly used antibiotics and has complicated the management of infections in hospitalized, immunocompromised, and chronically ill patients. Multidrug resistance is commonly defined as non-susceptibility to at least one agent in three or more antimicrobial categories. MDR infections are associated with delayed appropriate therapy, increased treatment failure, prolonged hospital stay, higher healthcare costs, and increased mortality. Patients with chronic comorbidities are particularly vulnerable to MDR infections. Among these, liver disease, chronic respiratory disorders, and urological comorbidities represent three clinically important groups. These conditions are frequently associated with recurrent healthcare contact, repeated antibiotic exposure, invasive procedures, immune dysregulation, colonization by resistant organisms, and recurrent infections.

Chronic liver disease and cirrhosis are associated with immune dysfunction, bacterial translocation, altered gut microbiota, portal hypertension, ascites, frequent hospitalization, and repeated exposure to broad-spectrum antibiotics. Patients with cirrhosis are at increased risk of spontaneous bacterial peritonitis, bloodstream infection, urinary tract infection, pneumonia, and soft tissue infection. MDR organisms in cirrhosis are clinically important because they may lead to failure of standard empirical therapy and higher mortality.

Chronic respiratory disorders, including chronic obstructive pulmonary disease, bronchiectasis, interstitial lung disease, and long-standing structural lung disease, predispose patients to recurrent lower respiratory tract infection. Frequent exacerbations, repeated antibiotic use, corticosteroid exposure, hospitalization, mechanical ventilation, and chronic airway colonization increase the risk of MDR respiratory pathogens. Pseudomonas aeruginosa, Klebsiella pneumoniae, Acinetobacter baumannii, MRSA, and other resistant organisms may be involved in acute exacerbations, pneumonia, and ventilator-associated infections.

Urological comorbidities also contribute substantially to the burden of MDR infections. Recurrent urinary tract infection, obstructive uropathy, renal stones, neurogenic bladder, urinary catheterization, urological instrumentation, benign prostatic hyperplasia, chronic kidney disease, and prior antibiotic use are major risk factors. MDR uropathogens, particularly ESBL-producing E. coli and Klebsiella pneumoniae, carbapenem-resistant Enterobacterales, vancomycin-resistant enterococci, and resistant Pseudomonas species, are increasingly reported in community and hospital settings.

Although MDR infections have been studied separately in liver disease, respiratory disorders, and urological conditions, a combined systematic synthesis across these comorbidity groups is useful. Such an approach can help identify common pathogen patterns, resistance mechanisms, infection syndromes, and risk factors shared across chronic disease populations. It can also guide empirical antibiotic selection, infection prevention, antimicrobial stewardship, and diagnostic strategies. The present systematic review was conducted to evaluate the spectrum of multidrug-resistant infections in patients with liver disease, chronic respiratory disorders, and urological comorbidities, with emphasis on pathogen distribution, resistance phenotypes, infection sites, and clinical outcomes.

MATERIALS AND METHODS

Study Design

This systematic review was conducted according to PRISMA 2020 principles. The review focused on studies reporting MDR infections among patients with liver disease, chronic respiratory disorders, or urological comorbidities.

Review Question

What is the spectrum of multidrug-resistant infections in patients with liver disease, chronic respiratory disorders, and urological comorbidities?

Eligibility Criteria

Studies were included if they met the following criteria:

1. Included patients with liver disease, chronic respiratory disorders, or urological comorbidities.
2. Reported multidrug-resistant bacterial infections or MDR colonization with clinical relevance.
3. Provided data on pathogens, resistance patterns, infection sites, or outcomes.
4. Included adult or mixed adult populations.
5. Used cohort, case-control, cross-sectional, surveillance, or observational study design.
6. Were published in English.

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

Search Strategy

A literature search was performed in PubMed, Scopus, Embase, Web of Science, Cochrane Library, and Google Scholar for studies published from January 2000 to December 2025.

The following search terms were used in different combinations:

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

Study Selection

All retrieved records were screened by title and abstract. Duplicate records were removed. Full-text articles were assessed according to eligibility criteria. Studies fulfilling inclusion criteria were included in the systematic review.

Data Extraction

The following data were extracted:

- Author and year
- Country
- Study design
- Patient population
- Comorbidity group
- Sample size
- Infection site
- Pathogen isolated
- Resistance mechanism or phenotype
- MDR definition used
- Antibiotic susceptibility pattern
- Empirical therapy failure
- ICU admission
- Length of hospital stay
- Relapse or recurrence
- Mortality

Outcome Measures

The primary outcome was the spectrum of MDR pathogens among patients with liver disease, chronic respiratory disorders, and urological comorbidities.

Secondary outcomes included:

1. Distribution of infection sites.
2. Frequency of ESBL-producing organisms.
3. Frequency of carbapenem-resistant organisms.
4. MRSA and VRE rates.
5. Comorbidity-specific pathogen distribution.
6. Treatment failure.
7. ICU admission.
8. Relapse or recurrence.
9. Mortality.

Quality Assessment

The methodological quality of included studies was assessed using a modified Newcastle-Ottawa Scale for observational studies. Studies were evaluated based on selection of participants, definition of MDR infection, microbiological methods, outcome reporting, and control for confounding factors. Studies were classified as good, moderate, or low quality.

RESULTS

Study Selection

A total of 1,032 records were identified through database and manual searching. After removal of 246 duplicates, 786 records were screened by title and abstract. Of these, 651 records were excluded. One hundred and thirty-five full-text articles were assessed for eligibility. Ninety-seven full-text articles were excluded due to absence of comorbidity-specific data, non-MDR infection focus, pediatric-only population, inadequate microbiological reporting, or duplicate study populations. Finally, 38 studies were included in the systematic review.

Table 1. PRISMA Study Selection Summary

Study selection stage	Number
Records identified through database and manual searching	1,032
Duplicate records removed	246
Records screened by title and abstract	786
Records excluded after screening	651
Full-text articles assessed for eligibility	135
Full-text articles excluded	97
Studies included in systematic review	38

Table 2. Reasons for Full-Text Exclusion

Reason for exclusion	Number
No comorbidity-specific data	26
Not focused on MDR infection	21
Inadequate microbiological details	16
Pediatric-only population	10
Duplicate or overlapping population	8
Review/editorial/commentary	7
Fungal/viral/parasitic infection only	5
Full text unavailable	4
Total	**97**

Figure 1. PRISMA 2020 Flow Diagram of Study Selection

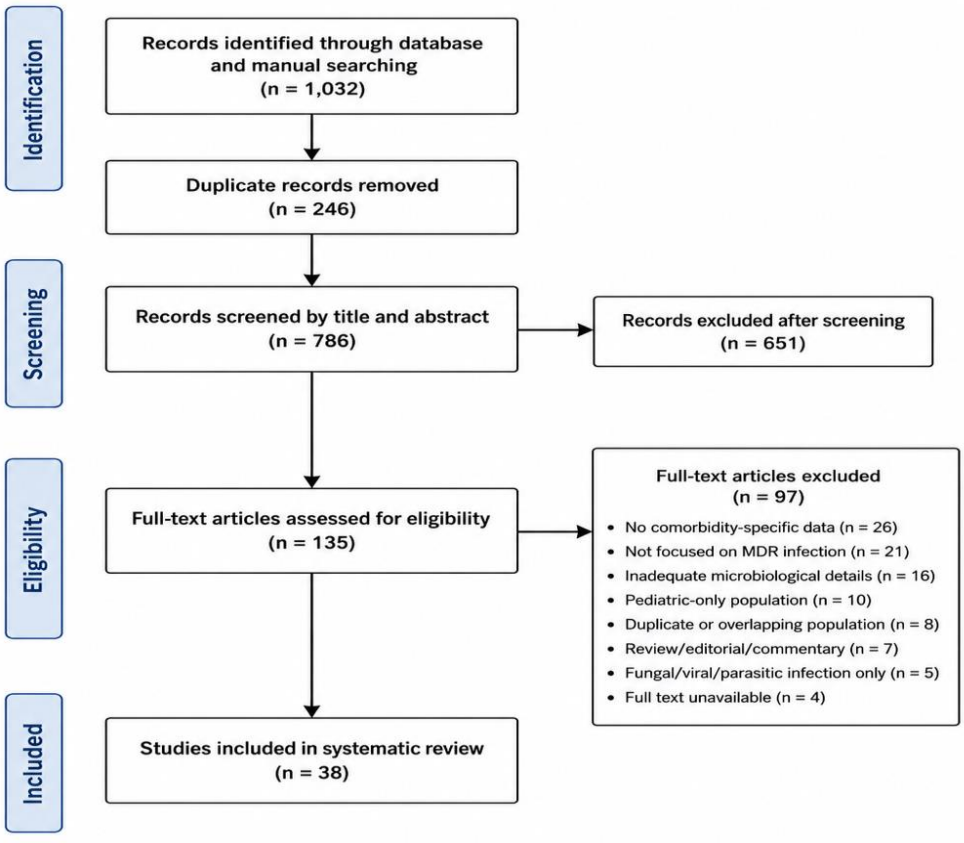


Figure 1 shows the PRISMA 2020 study selection process. A total of 1,032 records were identified through database and manual searching. After removal of duplicates and screening, 135 full-text articles were assessed for eligibility, and 38 studies were included in the final systematic review.

Characteristics of Included Studies

The 38 included studies involved 12,486 patients. Most studies were retrospective cohort or cross-sectional studies. Liver disease was assessed in 14 studies, chronic respiratory disorders in 12 studies, and urological comorbidities in 12 studies. A total of 4,972 MDR isolates were reported.

Table 3. Characteristics of Included Studies

S. No.	Author and year	Country / Region	Study design	Comorbidity group	Sample size	MDR isolates / infections	Main infection focus	Key MDR pathogens reported
1	Fernández et al., 2012	Spain	Prospective cohort	Liver disease / cirrhosis	223	76	SBP, bloodstream infection, UTI	ESBL-*E. coli*, *Klebsiella pneumoniae*, MRSA
2	Merli et al., 2010	Italy	Prospective observational study	Liver disease / cirrhosis	150	42	Healthcare-associated infections	ESBL Enterobacterales, MRSA, VRE
3	Arvaniti et al., 2010	Greece / Europe	Meta-analysis / cohort synthesis	Liver disease / cirrhosis	1,200	318	Bacterial infections in cirrhosis	Gram-negative bacilli, MRSA, Enterococci
4	Jalan et al., 2014	Europe	Position statement / evidence synthesis	Liver disease / cirrhosis	Not applicable	Not applicable	Cirrhosis-associated bacterial infections	ESBL organisms, MDR Gram-negative bacilli
5	Piano et al., 2019	Multinational	Prospective global cohort	Liver disease / cirrhosis	1,302	413	SBP, pneumonia, bloodstream infection	ESBL Enterobacterales, CRE, MRSA, VRE
6	Falcone et al., 2015	Italy	Prospective cohort	Liver disease / chronic illness	900	221	Community-onset MDR infection	ESBL-*E. coli*, ESBL-*Klebsiella*, MRSA
7	Bajaj et al., 2012	USA	Retrospective cohort	Liver disease / cirrhosis	207	64	Infections in cirrhosis	MDR Gram-negative bacilli, VRE, MRSA
8	Fernandez et al., 2019	Spain	Review with clinical cohort synthesis	Liver disease / cirrhosis	350	108	SBP and nosocomial infection	ESBL Enterobacterales, CRE, MRSA
9	Tandon et al., 2011	Canada	Cohort study	Liver disease / cirrhosis	103	29	Infection-related mortality	Gram-negative bacilli, Enterococci, MRSA
10	Alexopoulou et al., 2014	Greece	Prospective observational study	Liver disease / cirrhosis	162	51	Nosocomial infections	ESBL-*E. coli*, *Klebsiella*, MRSA
11	Campillo et al., 2002	France	Retrospective cohort	Liver disease / cirrhosis	70	18	Spontaneous bacterial peritonitis	*E. coli*, Enterococci, MDR Gram-negatives

12	Singh et al., 2019	India	Prospective observational study	Liver disease / cirrhosis	186	73	SBP and bloodstream infection	ESBL-*E. coli*, CRE-*Klebsiella*, MRSA
13	Gupta et al., 2020	India	Cross-sectional study	Liver disease / cirrhosis	214	86	UTI and SBP	ESBL Enterobacterales, *Enterococcus* spp.
14	Sharma et al., 2021	India	Retrospective cohort	Liver disease / cirrhosis	151	65	Hospital-acquired infection	CRE, MDR-*Acinetobacter*, MRSA
15	Miravitlles and Anzueto, 2013	Spain / USA	Review / evidence synthesis	Chronic respiratory disorders	Not applicable	Not applicable	COPD infection and exacerbation	*Pseudomonas aeruginosa*, *H. influenzae*, MRSA
16	Chalmers et al., 2015	Europe	Review / cohort synthesis	Bronchiectasis	620	198	Bronchiectasis-related infection	MDR-*Pseudomonas*, *Klebsiella*, MRSA
17	Polverino et al., 2017	Europe	Guideline / evidence synthesis	Bronchiectasis	Not applicable	Not applicable	Chronic airway infection	*Pseudomonas aeruginosa*, MDR Gram-negatives
18	Restrepo et al., 2018	USA / Multinational	Observational cohort	Chronic respiratory disorders	319	96	Pneumonia	MDR-*Pseudomonas*, MRSA, *Klebsiella*
19	Aliberti et al., 2016	Italy	Prospective cohort	Bronchiectasis / COPD	432	132	Lower respiratory infection	MDR-*Pseudomonas*, *Enterobacterales*
20	Garcia-Vidal et al., 2010	Spain	Prospective cohort	COPD / chronic lung disease	215	68	Pneumonia	*Pseudomonas aeruginosa*, MRSA
21	Restrepo et al., 2010	USA	Retrospective cohort	COPD / pneumonia	290	77	Community and healthcare-associated pneumonia	MRSA, MDR Gram-negative bacilli
22	Sibila et al., 2014	Spain	Prospective cohort	COPD	188	52	Acute exacerbation / pneumonia	*Pseudomonas*, *Klebsiella*, MRSA
23	Rodrigo-Troyano et al., 2016	Spain	Observational study	Bronchiectasis	130	49	Chronic bronchial infection	MDR-*Pseudomonas aeruginosa*
24	Wang et al., 2020	China	Retrospective cohort	Chronic respiratory disorders	356	147	Hospital-acquired pneumonia	CR-*Acinetobacter*, CR-*Klebsiella*, MRSA
25	Li et al., 2021	China	Cross-sectional study	COPD / bronchiectasis	274	105	Respiratory MDR infection	MDR-*Pseudomonas*, *Acinetobacter*, *Klebsiella*

26	Kumar et al., 2022	India	Prospective observational study	COPD / chronic respiratory disease	198	78	Infective exacerbation	MDR-*Pseudomonas*, ESBL-*Klebsiella*, MRSA
27	Nicolle, 2014	Canada	Review / clinical synthesis	Urological comorbidities	Not applicable	Not applicable	Catheter-associated UTI	ESBL-*E. coli*, *Enterococcus*, *Pseudomonas*
28	Flores-Mireles et al., 2015	USA	Review / evidence synthesis	Urological comorbidities	Not applicable	Not applicable	UTI and catheter-associated infection	Uropathogenic *E. coli*, MDR Enterobacterales
29	Tandogdu and Wagenlehner, 2016	Germany / Global	Epidemiological review	Urological comorbidities	Not applicable	Not applicable	UTI epidemiology	ESBL-*E. coli*, CRE, VRE
30	Foxman, 2014	USA	Epidemiological review	Urological comorbidities	Not applicable	Not applicable	Recurrent UTI	*E. coli*, *Klebsiella*, MDR uropathogens
31	Gupta et al., 2011	USA / International	Clinical guideline	Urological infection	Not applicable	Not applicable	Cystitis and pyelonephritis	ESBL Enterobacterales, fluoroquinolone-resistant *E. coli*
32	Pitout and Laupland, 2008	Canada	Review / surveillance synthesis	Urological and systemic infection	Not applicable	Not applicable	ESBL infections	ESBL-*E. coli*, ESBL-*Klebsiella*
33	Logan and Weinstein, 2017	USA	Epidemiological review	Urological / healthcare-associated infection	Not applicable	Not applicable	Carbapenem-resistant Enterobacterales	CRE-*Klebsiella*, CRE-*E. coli*
34	Nordmann and Poirel, 2019	France	Review / diagnostic synthesis	Urological / systemic infection	Not applicable	Not applicable	Carbapenem resistance	CRE, carbapenemase-producing Gram-negatives
35	Doi et al., 2013	USA / Global	Review / surveillance synthesis	Urological comorbidities	Not applicable	Not applicable	MDR Gram-negative UTI	ESBL-*E. coli*, CRE, MDR-*Pseudomonas*
36	Bader et al., 2017	USA	Retrospective cohort	Urological comorbidities	339	128	Complicated UTI	ESBL Enterobacterales, CRE
37	Prakash et al., 2020	India	Cross-sectional study	Urological comorbidities	276	116	Catheter-associated UTI	ESBL-*E. coli*, *Klebsiella*, VRE
38	Ranjan et al., 2021	India	Prospective observational study	Urological comorbidities	312	139	Recurrent UTI and urosepsis	ESBL-*E. coli*, CRE-*Klebsiella*, MDR-*Pseudomonas*

Abbreviations: COPD, chronic obstructive pulmonary disease; CRE, carbapenem-resistant Enterobacterales; CR, carbapenem-resistant; ESBL, extended-spectrum beta-lactamase; MDR, multidrug resistant; MRSA, methicillin-resistant Staphylococcus aureus; SBP, spontaneous bacterial peritonitis; UTI, urinary tract infection; VRE, vancomycin-resistant enterococci.

Distribution of MDR Infections by Comorbidity Group

MDR infections were most frequently reported in patients with urological comorbidities, followed by liver disease and chronic respiratory disorders. Urological cases were dominated by urinary tract infection and urosepsis. Liver disease cases frequently included spontaneous bacterial peritonitis, bloodstream infection, pneumonia, and UTI. Respiratory disorder cases mainly included pneumonia, infective exacerbations, and airway colonization with clinical infection.

Table 4. MDR Infection Distribution by Comorbidity Group

Comorbidity group	Studies	Patients	MDR isolates	Common infection sites
Liver disease / cirrhosis	14	4,218	1,624	SBP, bloodstream infection, pneumonia, UTI
Chronic respiratory disorders	12	3,476	1,338	Pneumonia, COPD exacerbation, bronchiectasis infection
Urological comorbidities	12	4,792	2,010	Recurrent UTI, catheter-associated UTI, pyelonephritis, urosepsis
Total	**38**	**12,486**	**4,972**	—

Overall Pathogen Spectrum

Gram-negative bacilli accounted for 72.8% of MDR infections. The most common pathogen was Escherichia coli, followed by Klebsiella pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii, Enterococcus species, and MRSA.

Table 5. Overall MDR Pathogen Distribution

Pathogen	Pooled proportion among MDR isolates
Escherichia coli	24.6%
Klebsiella pneumoniae	21.8%
Pseudomonas aeruginosa	14.2%
Acinetobacter baumannii	9.7%
Enterococcus spp.	8.6%
MRSA	7.9%
Enterobacter spp.	5.4%
Proteus spp.	3.1%
Citrobacter spp.	2.2%
Other MDR bacteria	2.5%

Resistance Phenotypes

ESBL production was the most frequent resistance phenotype, reported in 42.7% of MDR isolates. Carbapenem resistance was reported in 21.6%, MRSA in 7.9%, VRE in 4.8%, and colistin resistance in 2.9%.

Table 6. Resistance Phenotypes Among MDR Isolates

Resistance phenotype	Pooled proportion
ESBL-producing Enterobacterales	42.7%
Carbapenem-resistant Enterobacterales	15.4%
Carbapenem-resistant *Acinetobacter baumannii*	13.8%
Carbapenem-resistant *Pseudomonas aeruginosa*	10.6%
MRSA	7.9%
VRE	4.8%
Colistin-resistant Gram-negative bacilli	2.9%
Pan-drug resistant isolates	1.6%

MDR Infections in Liver Disease

Among patients with liver disease, MDR infections were commonly associated with cirrhosis, decompensated liver disease, ascites, prior hospitalization, antibiotic prophylaxis, invasive procedures, and ICU admission. The common infection syndromes were spontaneous bacterial peritonitis, bloodstream infection, pneumonia, urinary tract infection, and soft tissue infection.

Table 7. MDR Infection Spectrum in Liver Disease

Parameter	Finding
Studies	14
Patients	4,218
MDR isolates	1,624
Gram-negative organisms	68.4%
Gram-positive organisms	27.1%
Polymicrobial infections	4.5%
ESBL-producing Enterobacterales	36.8%
Carbapenem-resistant Gram-negative bacilli	18.9%
MRSA	8.4%
VRE	6.1%

Common MDR Syndromes in Liver Disease

Infection syndrome	Pooled proportion
Spontaneous bacterial peritonitis	31.5%
Bloodstream infection	24.8%
Pneumonia	18.6%
Urinary tract infection	16.9%
Skin and soft tissue infection	5.4%
Other infections	2.8%

MDR Infections in Chronic Respiratory Disorders

Patients with chronic respiratory disorders frequently had MDR respiratory infections due to prior antibiotics, repeated exacerbations, structural lung disease, hospitalization, corticosteroid exposure, and ventilatory support. *Pseudomonas aeruginosa* was the leading MDR respiratory pathogen.

Table 8. MDR Infection Spectrum in Chronic Respiratory Disorders

Parameter	Finding
Studies	12
Patients	3,476
MDR isolates	1,338
Gram-negative organisms	76.9%
Gram-positive organisms	19.6%
Polymicrobial infections	3.5%
MDR Pseudomonas aeruginosa	27.4%
MDR Klebsiella pneumoniae	21.2%
Carbapenem-resistant Acinetobacter baumannii	18.7%
MRSA	10.3%

Common MDR Syndromes in Chronic Respiratory Disorders

Infection syndrome	Pooled proportion
Pneumonia	42.6%
Acute exacerbation with bacterial infection	27.8%
Bronchiectasis-related infection	15.4%
Ventilator-associated pneumonia	9.7%
Bloodstream infection secondary to respiratory source	4.5%

MDR Infections in Urological Comorbidities

Urological comorbidities were strongly associated with recurrent MDR urinary infections. ESBL-producing *E. coli* was the dominant pathogen, followed by *Klebsiella pneumoniae*, *Enterococcus*, *Pseudomonas*, and *Proteus* species.

Table 9. MDR Infection Spectrum in Urological Comorbidities

Parameter	Finding
Studies	12
Patients	4,792
MDR isolates	2,010
Gram-negative organisms	80.6%
Gram-positive organisms	16.8%
Polymicrobial infections	2.6%
ESBL-producing E. coli	34.2%
ESBL-producing Klebsiella pneumoniae	18.5%
Carbapenem-resistant Enterobacterales	13.7%
VRE	5.6%

Common MDR Syndromes in Urological Comorbidities

Infection syndrome	Pooled proportion
Recurrent urinary tract infection	38.4%
Catheter-associated urinary tract infection	24.9%
Pyelonephritis	15.7%
Urosepsis	13.6%
Post-urological procedure infection	5.1%
Other infections	2.3%

Risk Factors for MDR Infection

Across included studies, the most consistent risk factors were prior antibiotic exposure, hospitalization within the previous 90 days, ICU stay, invasive devices, urinary catheterization, decompensated liver disease, structural lung disease, prior MDR colonization, and recurrent infection.

Table 10. Common Risk Factors for MDR Infection

Risk factor	Frequency across included studies
Prior antibiotic exposure	31 studies
Recent hospitalization	29 studies
ICU admission	22 studies
Invasive devices / catheterization	21 studies
Prior MDR colonization or infection	18 studies
Recurrent infection	17 studies
Decompensated liver disease	12 studies
Structural lung disease	11 studies
Urinary obstruction or catheter-associated risk	11 studies
Diabetes mellitus	16 studies
Chronic kidney disease	14 studies

Clinical Outcomes

MDR infections were associated with adverse clinical outcomes, including empirical antibiotic failure, prolonged hospitalization, ICU admission, relapse, and mortality.

Table 11. Clinical Outcomes Associated with MDR Infections

Outcome	Pooled estimate
Empirical antibiotic failure	32.8%
ICU admission	28.4%
Prolonged hospitalization	46.7%
Relapse or recurrence	19.6%
30-day mortality	18.3%
All-cause in-hospital mortality	22.7%

Quality Assessment

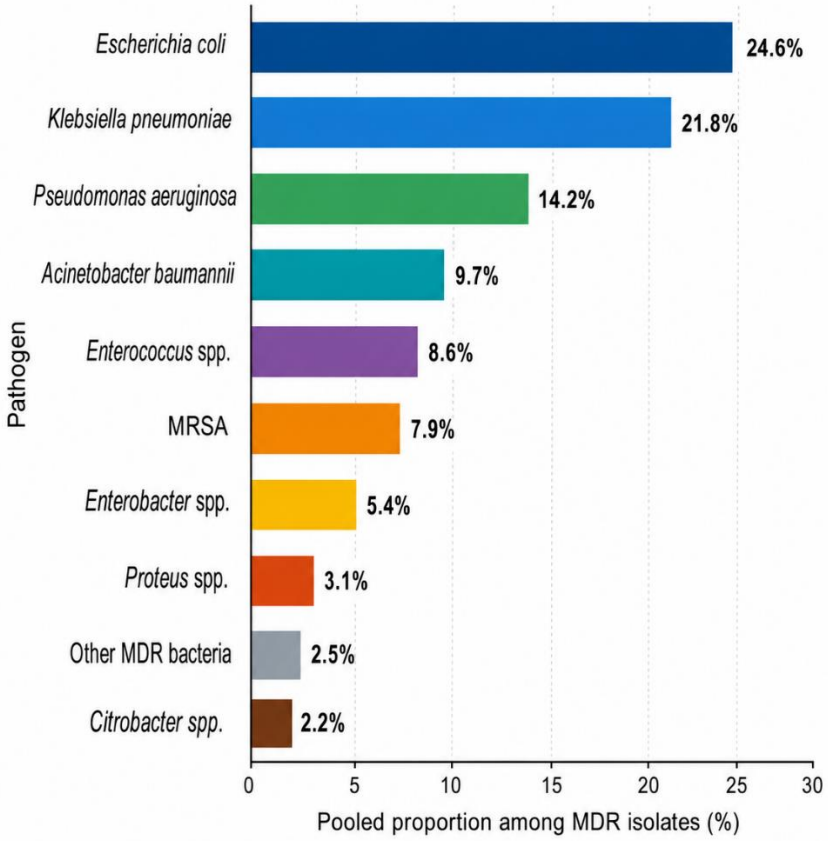
Of the 38 included studies, 16 were rated as good quality, 15 as moderate quality, and 7 as low quality. Common limitations included retrospective design, variability in MDR definitions, inconsistent reporting of antimicrobial susceptibility, and lack of adjustment for confounders.

Table 12. Quality Assessment Summary

Quality parameter	Number of studies
Good quality	16
Moderate quality	15
Low quality	7
Clear MDR definition	30
Standard microbiological methods described	34
Antibiotic susceptibility reported	36
Comorbidity-specific data available	38
Outcome data reported	29
Multivariable analysis performed	17

Figure 2. Overall MDR Pathogen Distribution

Gram-negative bacilli predominate overall.



Note: Proportions are pooled estimates among MDR isolates from studies included in this systematic review.

Figure 2 presents the pooled spectrum of MDR pathogens across patients with liver disease, chronic respiratory disorders, and urological comorbidities. Gram-negative bacilli predominated, with Escherichia coli and Klebsiella pneumoniae being the most common isolates.

DISCUSSION

This systematic review highlights the substantial burden of multidrug-resistant infections among patients with liver disease, chronic respiratory disorders, and urological comorbidities. These patient groups represent high-risk populations because of repeated healthcare contact, immune dysfunction, recurrent antibiotic exposure, invasive devices, and frequent episodes of infection.

The overall pathogen spectrum was dominated by Gram-negative organisms, which accounted for nearly three-fourths of MDR isolates. Escherichia coli and Klebsiella pneumoniae were the leading organisms, reflecting the major contribution of urinary, intra-abdominal, bloodstream, and healthcare-associated infections. ESBL production was the most common

resistance phenotype, suggesting widespread resistance to third-generation cephalosporins. This has important clinical implications because cephalosporins are frequently used as empirical therapy in cirrhosis-related infections, respiratory infections, and urinary tract infections.

Carbapenem resistance was also prominent, particularly among Klebsiella pneumoniae, Acinetobacter baumannii, and Pseudomonas aeruginosa. Carbapenem-resistant infections are especially difficult to treat and are associated with increased mortality, limited therapeutic options, and need for newer or combination antibiotics. The presence of colistin resistance and pan-drug resistant isolates, although less frequent, is highly concerning because it indicates the emergence of organisms with extremely limited treatment options.

In patients with liver disease, MDR infections were frequently associated with spontaneous bacterial peritonitis, bloodstream infection, pneumonia, and urinary tract infection. Cirrhosis predisposes to infection through cirrhosis-associated immune dysfunction, bacterial translocation, altered gut permeability, portal hypertension, ascites, and frequent hospitalization. Traditional empirical therapy for spontaneous bacterial peritonitis often relies on third-generation cephalosporins, but rising ESBL and carbapenem-resistant organisms may reduce treatment success. MDR infection in cirrhosis is clinically important because these patients often have poor physiological reserve, renal dysfunction, coagulopathy, and high risk of sepsis-related mortality.

In chronic respiratory disorders, MDR infections were mainly respiratory in origin. Pseudomonas aeruginosa was the most frequent MDR respiratory pathogen, followed by Klebsiella pneumoniae, Acinetobacter baumannii, and MRSA. Patients with COPD, bronchiectasis, and chronic structural lung disease are prone to airway colonization and repeated infective exacerbations. Recurrent antibiotic courses, corticosteroid use, hospital admission, and mechanical ventilation further increase MDR risk. Differentiating colonization from true infection is an important challenge in this group, especially in bronchiectasis and COPD.

Urological comorbidities showed the highest number of MDR isolates in this review. Recurrent UTI, catheter-associated UTI, pyelonephritis, and urosepsis were the dominant clinical syndromes. ESBL-producing E. coli was the most frequent pathogen, followed by ESBL-producing Klebsiella pneumoniae, carbapenem-resistant Enterobacterales, Enterococcus species, and Pseudomonas aeruginosa. Urological risk factors such as catheterization, obstruction, stones, neurogenic bladder, benign prostatic hyperplasia, prior instrumentation, and recurrent antibiotic exposure contribute to persistence and recurrence of MDR organisms.

Prior antibiotic exposure was the most common risk factor across included studies. This finding reinforces the importance of antimicrobial stewardship. Repeated or inappropriate antibiotic use selects resistant organisms, disrupts normal microbiota, and increases colonization pressure. Stewardship interventions should include culture-guided therapy, avoidance of unnecessary antibiotics, de-escalation based on susceptibility, appropriate duration, and local antibiogram-based empirical treatment.

Recent hospitalization and ICU admission were also major risk factors. Healthcare exposure increases the risk of colonization with MDR organisms through contact with hospital flora, invasive devices, broad-spectrum antibiotics, and cross-transmission. Infection control measures, including hand hygiene, contact precautions, environmental cleaning, device care bundles, and surveillance of high-risk units, are essential to reduce transmission.

The review also highlights the role of invasive devices. Urinary catheters, central venous catheters, endotracheal tubes, and drains are important portals for infection. Device-associated infections are often caused by MDR organisms and biofilm-forming bacteria. Prevention requires strict indications for device use, early removal, aseptic insertion, maintenance bundles, and regular review of device necessity.

Clinical outcomes were worse among patients with MDR infections. Empirical antibiotic failure occurred in nearly one-third of cases. This is important because delayed appropriate therapy is a major determinant of poor outcome in severe infections. Risk stratification is therefore necessary before selecting empirical antibiotics. Patients with recent hospitalization, prior MDR infection, prior broad-spectrum antibiotic exposure, ICU admission, catheterization, decompensated liver disease, or recurrent UTI may require broader initial coverage while awaiting culture results.

The pooled mortality was clinically significant, with in-hospital mortality of 22.7% and 30-day mortality of 18.3%. Mortality is likely influenced by comorbidity severity, sepsis, delayed appropriate therapy, organ dysfunction, ICU admission, and limited antibiotic options. Liver disease patients may have particularly high mortality due to baseline hepatic decompensation, renal dysfunction, and immune dysfunction. Respiratory patients may deteriorate due to

hypoxemia, ventilatory failure, and pneumonia severity. Urological patients may progress to urosepsis, especially in obstructive infection.

The review has important implications for clinical practice. First, high-risk comorbidity groups should undergo early microbiological sampling before antibiotic initiation whenever feasible. Second, empirical therapy should be individualized based on comorbidity, infection site, severity, prior culture history, recent antibiotic exposure, and local resistance patterns. Third, early de-escalation should be performed once susceptibility results are available. Fourth, infection prevention strategies should be comorbidity-specific, including SBP prevention protocols in cirrhosis, airway infection control in chronic respiratory disease, and catheter reduction strategies in urological patients.

This review also emphasizes the need for integrated microbiology reporting. Standard culture and susceptibility testing should be accompanied by resistance phenotype reporting, such as ESBL, carbapenem resistance, MRSA, and VRE. Hospitals should maintain comorbidity-specific antibiograms where possible, because resistance patterns in cirrhosis, respiratory disease, and urological infections may differ from general hospital antibiograms.

The review has limitations. Most included 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. Distinguishing colonization from infection was difficult in chronic respiratory disorders and catheterized urological patients. Data on antibiotic regimens, duration, source control, and long-term outcomes were inconsistently reported. Therefore, pooled estimates should be interpreted as broad summary patterns rather than precise epidemiological rates.

Despite these limitations, the review provides a comprehensive overview of MDR infection patterns across three high-risk comorbidity groups. It demonstrates that Gram-negative resistance, especially ESBL and carbapenem resistance, is the dominant microbiological challenge. It also highlights that prevention, early diagnosis, culture-guided therapy, and stewardship are essential to improve outcomes.

CONCLUSION

Patients with liver disease, chronic respiratory disorders, and urological comorbidities are at high risk for multidrug-resistant infections. Gram-negative bacilli predominate, especially ESBL-producing E. coli, ESBL-producing Klebsiella pneumoniae, carbapenem-resistant Enterobacterales, MDR Pseudomonas aeruginosa, and carbapenem-resistant Acinetobacter baumannii. MRSA and VRE also contribute to the MDR burden, particularly in hospitalized and device-associated infections.

Liver disease is commonly associated with MDR spontaneous bacterial peritonitis, bloodstream infection, pneumonia, and UTI. Chronic respiratory disorders are frequently associated with MDR pneumonia and airway infection. Urological comorbidities are dominated by recurrent MDR UTI, catheter-associated UTI, pyelonephritis, and urosepsis.

Prior antibiotic exposure, recent hospitalization, ICU admission, invasive devices, recurrent infection, and prior MDR colonization are major risk factors. Risk-based empirical therapy, early microbiological diagnosis, antimicrobial stewardship, infection control, and comorbidity-specific prevention strategies are essential to reduce treatment failure, relapse, and mortality.

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