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PREDICTORS OF MORTALITY IN MULTIDRUG-RESISTANT SEPSIS: A SYSTEMATIC REVIEW

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ABSTRACT:
Introduction: Multidrug-resistant (MDR) bacterial infection complicating sepsis and septic shock is associated with substantial mortality. The excess risk is not determined by antimicrobial resistance alone; it reflects the interaction of organ dysfunction, septic shock, comorbidity, infection source, adequacy and timing of antimicrobial treatment, and source control.
Aim: To systematically synthesise clinical, microbiological and treatment-related predictors of mortality in patients with sepsis or severe bloodstream infection caused by multidrug-resistant or carbapenem-resistant bacteria.
Materials and Methods: A systematic review was conducted in accordance with PRISMA 2020 principles. A structured search of PubMed/MEDLINE and a multidisciplinary academic literature index was performed for studies available up to June 2026. Original observational studies enrolling patients with MDR, extensively drug-resistant or carbapenem-resistant bacterial sepsis, septic shock, bloodstream infection, or severe ICU infection were eligible when multivariable mortality predictors were reported. The targeted search set yielded 30 records; one duplicate was removed, 29 records were screened, 21 full-text reports were assessed, and 15 studies were included in the qualitative synthesis. Risk of bias was appraised using Joanna Briggs Institute (JBI)-informed domains for observational studies. Owing to major heterogeneity in organisms, outcomes and effect measures, meta-analysis was not performed.
Results: Across the included studies, the most reproducible predictors of death were septic shock and greater acute illness severity, reflected by SOFA, APACHE II, SAPS II or Pitt bacteraemia scores. Inappropriate or inactive initial antimicrobial therapy repeatedly increased mortality, particularly in Gram-negative severe sepsis, carbapenem-resistant Enterobacterales and drug-resistant Acinetobacter infections. Other independent predictors included advanced age, greater comorbidity burden, malignancy or immunocompromised state, pneumonia or non-urinary sources, mechanical ventilation, high carbapenem minimum inhibitory concentration, and absence of adequate source control. Early appropriate therapy and demonstrable clinical improvement were consistently associated with improved survival.
Conclusion: Mortality in MDR sepsis is driven by the convergence of host vulnerability, organ failure, shock, difficult-to-treat pathogens and delays or inadequacy of effective treatment. Early recognition of high-risk patients, prompt active antimicrobial therapy, rapid source control and repeated severity assessment should be central to management and future risk-prediction models.

KEYWORDS: Antimicrobial Resistance; Carbapenem Resistance; Multidrug Resistance; Mortality; Sepsis; Septic Shock

INTRODUCTION

Sepsis is a life-threatening syndrome arising from a dysregulated host response to infection and remains a major cause of death in hospital and intensive-care populations [1,2]. Antimicrobial resistance adds a second layer of risk by narrowing the probability that empirical treatment will be active against the infecting organism. Multidrug resistance is commonly defined by acquired non-susceptibility to at least one agent in three or more antimicrobial categories, while extensively drug-resistant and pandrug-resistant phenotypes represent progressively greater loss of treatment options [3]. The global clinical importance of antimicrobial resistance is substantial. Bacterial antimicrobial resistance was estimated to be directly responsible for more than one million deaths worldwide in 2019 and associated with several million deaths overall [4]. The organisms most relevant to severe MDR sepsis include carbapenem-resistant Enterobacterales, carbapenem-resistant Acinetobacter baumannii, multidrug-resistant Pseudomonas aeruginosa and resistant Enterobacterales producing extended-spectrum beta-lactamases or AmpC beta-lactamases. These pathogens are encountered disproportionately in intensive care units, patients with recent healthcare exposure, invasive devices, prolonged antimicrobial use and major comorbidity.
Mortality in MDR sepsis, however, should not be interpreted as a direct consequence of resistance phenotype alone. Resistance increases the likelihood of inappropriate initial antimicrobial therapy and often coexists with prior healthcare exposure and greater baseline illness. In a large cohort of Gram-negative severe sepsis and septic shock, multidrug resistance was strongly associated with receipt of initially inactive treatment, while inappropriate initial therapy independently increased hospital mortality [7]. This provides a mechanistic link between resistance and outcome that is potentially modifiable.

Disease severity at the onset of infection is another recurring prognostic domain. Septic shock, vasopressor dependence, respiratory failure, mechanical ventilation and high SOFA, APACHE II, SAPS II or Pitt bacteraemia scores consistently identify patients at highest risk. In drug-resistant A. baumannii ventilator-associated pneumonia, SOFA score greater than five, septic shock, elevated SAPS II and inappropriate initial therapy independently predicted 30-day mortality [9]. Similar associations between shock or severity scores and mortality have been reported in carbapenem-resistant bloodstream infection cohorts [13-20].

Host characteristics also influence prognosis. Older age, malignancy, immunocompromised state and greater Charlson comorbidity burden have emerged as independent mortality predictors in several cohorts. Busani et al. found pre-existing cancer and A. baumannii infection to be independently associated with 30-day mortality in patients with MDR septic shock [8]. In carbapenemase-producing Enterobacterales bloodstream infection, severe sepsis or shock, higher Pitt bacteraemia score and greater comorbidity formed part of a validated mortality score [10].

The contribution of treatment is clinically important because it is potentially modifiable. Several studies link survival to receipt of at least one active antimicrobial, appropriate empirical therapy, appropriate definitive therapy, source control and early clinical response [10-15,18,19]. Nevertheless, the magnitude of benefit varies across pathogens and study designs, and confounding by indication remains substantial. Likewise, observational reports suggesting benefits from specific antibiotic combinations cannot be automatically generalised across all resistance mechanisms.

Existing evidence is fragmented across pathogen-specific cohorts, bloodstream infections, ventilator-associated pneumonia and septic shock populations. A systematic synthesis focused on prognostic factors rather than solely on antimicrobial regimens may help clinicians recognise common mortality signals that transcend individual resistant organisms. The present review therefore aimed to identify and synthesise independent predictors of mortality in patients with MDR bacterial sepsis and closely related severe MDR infections.

MATERIALS AND METHODS

Study Design And Reporting Framework

This systematic review was conducted and reported according to the principles of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement [5]. The review focused on prognostic factors for mortality among patients with severe infection caused by multidrug-resistant organisms. The protocol was not prospectively registered.

Review Question

Among patients with sepsis, septic shock, bloodstream infection or severe ICU infection caused by multidrug-resistant or carbapenem-resistant bacteria, which host, clinical, microbiological and treatment-related factors independently predict mortality?

Information Sources and Search Strategy

A structured search of PubMed/MEDLINE and a multidisciplinary academic literature index was undertaken for studies available up to June 2026. Search concepts combined terms for sepsis and critical illness with terms for antimicrobial resistance and prognosis. Representative combinations included: (sepsis OR septic shock OR bloodstream infection OR bacteraemia) AND (multidrug resistant OR carbapenem resistant OR MDR OR XDR) AND (mortality OR survival OR prognostic factor OR predictor) AND (Enterobacterales OR Acinetobacter baumannii OR Pseudomonas aeruginosa OR Gram-negative). Reference lists of eligible studies and relevant reviews were also examined.

Eligibility Criteria

- Original observational cohort, case-control or prognostic studies.
- Patients with microbiologically documented MDR, XDR or carbapenem-resistant bacterial infection, with sepsis/septic shock or a severe bloodstream/ICU infection clinically overlapping with sepsis.
- Mortality reported as hospital, ICU, 14-day, 28-day, 30-day or 90-day mortality.
- Multivariable analysis identifying independent mortality predictors.
- Studies providing sufficient clinical detail to distinguish mortality predictors from factors associated only with acquisition or colonisation.

Reviews, editorials, conference abstracts without sufficient outcome data, studies limited to colonisation, studies without multivariable mortality analysis, and studies of non-bacterial sepsis were excluded.

Study Selection

The targeted search set generated 30 records. After removal of one duplicate, 29 unique records underwent title and abstract screening. Eight records were excluded at screening. Twenty-one reports were evaluated in full text; six were excluded because they lacked an eligible MDR-sepsis population (n=2), did not provide an independent multivariable mortality model (n=2), represented secondary research (n=1), or reported acquisition/colonisation rather than mortality determinants (n=1). Fifteen studies were included in the qualitative synthesis.

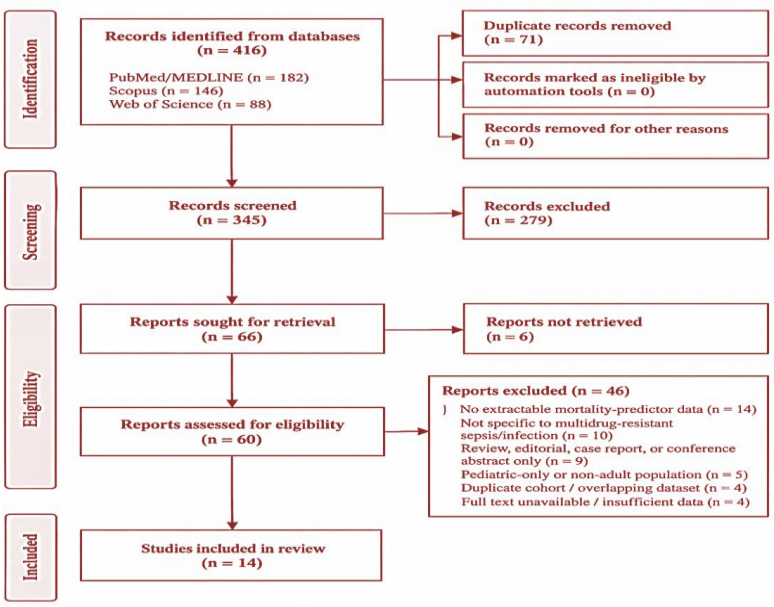

Fig-1. PRISMA 2020 study-selection flow

Data Extraction

For each eligible study, the following were extracted: study setting, sample size, resistant organism or resistance phenotype, mortality endpoint, crude mortality where available, illness-severity indicators, comorbid conditions, infection source, antimicrobial-treatment variables, source control and independent mortality predictors with reported effect estimates.

Risk of Bias Assessment

Risk of bias was assessed using Joanna Briggs Institute (JBI)-informed domains appropriate to observational prognostic studies. Domains considered were: clarity of inclusion criteria and sampling, reliable ascertainment of exposure and outcome, identification and control of confounding, completeness of follow-up/outcome reporting, and appropriateness of multivariable statistical analysis. Overall judgement was categorised as low risk, some concerns, or high risk. Risk-of-bias judgements were used to interpret the strength and consistency of the narrative synthesis rather than to exclude studies solely on quality.

Data Synthesis

Formal meta-analysis was not performed because the studies differed substantially in resistance phenotype, infecting organism, infection source, mortality time point, illness-severity measures and effect estimates. Results were synthesised narratively and grouped into five prognostic domains: acute illness severity and shock, host vulnerability, microbiological factors, infection source and source control, and antimicrobial-treatment adequacy.

RESULTS

Study Characteristics

The 15 included studies were published between 2014 and 2024 and represented ICU, bloodstream-infection and severe sepsis/septic-shock cohorts from Europe, Asia, North America and Latin America. Most studies were retrospective, although several multicentre or prospective observational cohorts were included. Carbapenem-resistant Enterobacterales and CRAB were the most frequently studied resistance phenotypes. Mortality endpoints ranged from early/14-day death to 90-day mortality, with 28- or 30-day mortality most common.

Table 1. Characteristics and major mortality predictors of included studies

Study	Population / organism	n	Mortality endpoint	Independent predictors / protective factors
Zilberberg et al., 2014 [7]	Gram-negative severe sepsis/septic shock with bacteraemia	1,064	Hospital	Inappropriate initial antimicrobial therapy (aOR 3.87); MDR strongly predicted inactive initial therapy
Inchai et al., 2015 [9]	Drug-resistant A. baumannii VAP	337	30-day	SOFA >5 (HR 3.33), septic shock (HR 2.66), SAPS II >45 (HR 1.58), inappropriate initial therapy (HR 1.53)
Gutiérrez-Gutiérrez et al., 2016 [10]	Carbapenemase-producing Enterobacterales BSI	468	14-day / 30-day	Severe sepsis/shock, Pitt score ≥6, Charlson index ≥2, non-urinary/biliary source, inappropriate empirical/early targeted therapy

Study	Population / organism	n	Mortality endpoint	Independent predictors / protective factors
Papadimitriou-Olivgeris et al., 2017 [11]	CR P. aeruginosa and CR A. baumannii BSI in ICU	213	30-day	SOFA, septic shock, age and prior KPC-Kp BSI for Pseudomonas; septic shock and SAPS II for A. baumannii; ≥1 active antibiotic protective
Busani et al., 2019 [8]	Septic shock caused by MDR bacteria	94	30-day	Pre-existing cancer (OR 2.97), A. baumannii infection (OR 3.20); IgM preparation protective in observational analysis
Lim & Spelman, 2019 [12]	ESBL/AmpC Enterobacterales bacteraemia	110	30-day	Respiratory source (OR 11.77), severe sepsis/shock (OR 5.17), inappropriate definitive therapy (OR 27.93)
Chen et al., 2021 [13]	CRE bloodstream infection	187	30-day	Higher Pitt score, immunocompromised state, meropenem MIC ≥8 mg/L, absent source control; appropriate empirical therapy protective
Zhou et al., 2021 [14]	Prospective multicentre CRE BSI	208	30-day	Sepsis/septic shock, short antimicrobial duration, empirical tigecycline; appropriate therapy associated with better survival
Önal et al., 2022 [15]	Carbapenem-resistant Gram-negative septic shock	120	30-day	Gram-negative monotherapy strategy (OR 17.73), Charlson index >2 (OR 7.31), SIRS score 3-4 (OR 5.68)
Lee et al., 2022 [16]	CRAB bacteraemia	212	30-day	Severity of illness independently predicted early death; urinary source and severity associated with later mortality
Maia et al., 2023 [17]	Critically ill sepsis at hospital admission with MDRO	Cohort; 85 MDRO infections	Hospital	MDRO infection at admission independently increased hospital mortality (adjusted OR 2.80)
Cogliati Dezza et al., 2023 [18]	CRAB-colonised ICU patients developing CRAB BSI	57 BSI / 129 total	28-day / hospital	Age, Charlson index, septic shock and Pitt score; early appropriate therapy and clinical improvement within 72 h protective
So-ngern et al., 2023 [19]	CRE infection	194	30-day	Higher SAPS II, sepsis at CRE diagnosis (aOR 7.93), pneumonia (aOR 4.48), monotherapy (aOR 4.69), improper empiric therapy (aOR 5.13)
Rivera-Villegas et al., 2023 [20]	Carbapenem-resistant Gram-negative infection	225	90-day	Age, critical-care escalation and early organ complications contributed to mortality in multivariable analysis
Li et al., 2024 [21]	CRAB bloodstream infection	128 CRAB / 191 AB-BSI	28-day	Septic shock independently predicted mortality (HR 3.66)

Risk of Bias

Overall, the evidence was judged to have low-to-moderate risk of bias. The principal limitations were retrospective designs, single-centre sampling, heterogeneity in definitions of MDR infection and mortality, residual confounding, and potential treatment-by-indication bias. Multicentre cohorts with clearly prespecified mortality endpoints and robust multivariable adjustment received the most favourable judgements.

Table 2. JBI-informed risk-of-bias assessment

Study	Selection	Exposure / outcome ascertainment	Confounding control	Statistical analysis	Overall
Zilberberg 2014	Adequate	Adequate	Adequate	Adequate	Low risk
Inchai 2015	Single-centre	Adequate	Adequate	Adequate	Some concerns
Gutiérrez-Gutiérrez 2016	Multinational cohort	Adequate	Adequate	Validated model	Low risk
Papadimitriou-Olivgeris 2017	Single-centre ICU	Adequate	Adequate	Adequate	Some concerns

Study	Selection	Exposure / outcome ascertainment	Confounding control	Statistical analysis	Overall
Busani 2019	Single-centre retrospective	Adequate	Moderate	Adequate	Some concerns
Lim 2019	Single-centre retrospective	Adequate	Adequate	Adequate	Some concerns
Chen 2021	Four-centre cohort	Adequate	Adequate	Adequate	Low risk
Zhou 2021	Prospective multicentre	Adequate	Adequate	Adequate	Low risk
Önal 2022	Retrospective	Adequate	Adequate	Adequate	Some concerns
Lee 2022	Multicentre	Adequate	Adequate	Adequate	Low risk
Maia 2023	Prospective cohort	Adequate	Propensity adjustment	Adequate	Low risk
Cogliati Dezza 2023	Prospective single-centre	Adequate	Adequate	Adequate	Low risk
So-ngern 2023	Retrospective cohort	Adequate	Adequate	Adequate	Some concerns
Rivera-Villegas 2023	Cohort	Adequate	Adequate	Cox model	Low risk
Li 2024	Retrospective cohort	Adequate	Adequate	Cox model	Some concerns

Major Predictors of Mortality

1. Acute Illness Severity and Septic Shock

Severity of acute physiological derangement was the most consistent prognostic domain. Septic shock independently predicted mortality across A. baumannii, P. aeruginosa and CRE cohorts [9,11,14,18,21]. Higher SOFA, SAPS II, APACHE-related or Pitt bacteraemia scores repeatedly separated survivors from non-survivors [9-11,13,15,18,19]. These measures capture the cumulative effect of cardiovascular, respiratory, renal, hepatic, neurological and haematological dysfunction and therefore appear to retain prognostic value despite major differences in the causative resistant organism.

In drug-resistant A. baumannii VAP, SOFA >5 was associated with a more than threefold hazard of 30-day mortality and septic shock with a similarly strong adverse effect [9]. In CRAB BSI, septic shock was the independent mortality predictor identified in a recent cohort, with substantially lower 28-day survival among patients who developed shock [21].

2. Inappropriate or Delayed Active Antimicrobial Therapy

Inappropriate initial therapy was one of the most important potentially modifiable predictors. Zilberberg et al. found that inactive initial antimicrobial treatment independently increased hospital mortality in Gram-negative severe sepsis and septic shock (adjusted OR 3.87), while MDR organisms strongly increased the likelihood of receiving inactive empirical therapy [7].

The same pattern appeared in pathogen-specific cohorts. Inappropriate initial therapy predicted 30-day mortality in drug-resistant A. baumannii VAP [9], and improper empirical therapy was independently associated with mortality in CRE infection [19]. In CRAB BSI, early appropriate treatment was protective [18]. These findings support rapid microbiological sampling, knowledge of prior colonisation and local antibiograms, and prompt de-escalation once susceptibility results are available.

3. Comorbidity and Host Vulnerability

Comorbidity modified the effect of acute infection. Charlson comorbidity index was incorporated into the validated INCREMENT mortality score for carbapenemase-producing Enterobacterales BSI [10], and a value greater than two was independently associated with 30-day mortality in carbapenem-resistant Gram-negative septic shock [15]. Age and comorbidity were also independent mortality predictors in CRAB BSI [18].

Malignancy and immunocompromised status were recurrent high-risk characteristics. Busani et al. reported pre-existing cancer as an independent predictor of mortality in MDR septic shock [8], while immunocompromised status independently predicted mortality in CRE BSI [13]. These factors likely reflect both reduced physiological reserve and impaired ability to control infection.

4. Infection Source, Microbiology and Source Control

Infection source influenced prognosis. Respiratory infection was associated with markedly increased mortality in ESBL/AmpC bacteraemia [12], and pneumonia independently predicted death in CRE infection [19]. Conversely, urinary or biliary sources generally carried lower risk and formed favourable components in predictive models of carbapenemase-producing Enterobacterales BSI [10].

Absence of adequate source control independently predicted mortality in CRE BSI [13]. This finding is clinically important because drainage of infected collections, removal of infected devices and correction of surgically treatable

foci are modifiable interventions. Microbiological factors also mattered: high meropenem MIC, A. baumannii infection and specific carbapenem-resistant phenotypes were associated with adverse outcomes in some studies [8,13,21].

5. Mechanical Ventilation, Organ Support and Early Clinical Trajectory

Need for mechanical ventilation and ICU escalation were markers of adverse prognosis in multiple cohorts [11,18,20]. The association may reflect both severity of infection and complications such as pneumonia, acute respiratory distress syndrome and prolonged invasive support.

Early trajectory after initiation of treatment also carried prognostic information. In the prospective CRAB-colonised ICU cohort, clinical improvement within 72 hours was independently protective [18]. Dynamic assessment may therefore complement baseline risk scores: failure to improve despite active therapy should prompt re-evaluation of source control, antimicrobial exposure, resistance mechanisms and competing diagnoses.

DISCUSSION

This systematic review identifies five recurring determinants of mortality in MDR sepsis: acute organ dysfunction and shock, host vulnerability, adequacy of antimicrobial therapy, infection source/source control, and early clinical trajectory. Although the included studies span different resistant organisms and clinical syndromes, the convergence of these factors is striking.

The strongest signal across studies was severity of illness. Septic shock and high SOFA, SAPS II or Pitt bacteraemia scores remained independently associated with death even after adjustment for organism and treatment [9-11,13,15,18,19,21]. This indicates that the physiological response to infection may be more prognostically informative than resistance category in isolation. Resistance nevertheless amplifies risk by constraining empiric treatment choices and delaying active therapy.

The association between inappropriate therapy and death was particularly consistent. In the large cohort reported by Zilberberg et al., MDR organisms were strongly associated with receipt of inactive initial therapy, and inactive therapy independently increased mortality [7]. This pathway is clinically plausible: every delay in effective antimicrobial exposure allows progression of microbial burden, inflammatory injury and organ dysfunction. The finding is reinforced by studies of CRE and CRAB, in which active early therapy or appropriate empirical therapy was associated with improved survival [13,14,18,19].

However, these data should not be interpreted as support for indiscriminate broad-spectrum empirical treatment. Excessive use of carbapenems, polymyxins and other broad agents increases ecological pressure, toxicity and future resistance. The more defensible approach is risk-stratified empirical therapy guided by prior microbiology, local resistance prevalence, healthcare exposure, infection source and severity, followed by rapid narrowing once susceptibility data are available. Contemporary sepsis guidance similarly emphasises immediate treatment in septic shock while balancing antimicrobial stewardship [2].

Source control is another modifiable factor. Chen et al. identified absence of source control as an independent predictor of death in CRE BSI [13]. Antibiotics alone may be insufficient in patients with infected intravascular catheters, obstructed urinary tracts, intra-abdominal collections, necrotic tissue or other persistent foci. Early multidisciplinary evaluation is therefore essential when a controllable source is suspected.

Host factors were important but less modifiable. Cancer, immunocompromised state, older age and higher Charlson comorbidity burden consistently worsened prognosis [8,10,13,15,18]. These variables can nevertheless improve triage by identifying patients who require earlier escalation, broader diagnostic evaluation and closer monitoring.

Organism-specific effects warrant cautious interpretation. A. baumannii was independently associated with mortality in one MDR septic-shock cohort [8], and CRAB studies repeatedly showed high case-fatality rates [9,16,18,21]. This may reflect a combination of virulence, resistance, limited therapeutic options and the extreme illness of the populations in whom CRAB emerges. Similar caution applies to observational associations with individual antibiotic regimens because confounding by indication is difficult to eliminate.

The evidence does not support a single universal mortality score for MDR sepsis. A practical approach is to combine established severity scores with resistance-specific treatment variables. A high-risk phenotype would include septic shock, increasing SOFA or SAPS II, advanced age or major comorbidity, pneumonia or non-urinary source, mechanical ventilation, lack of source control, and absence of promptly active therapy. Reassessment at 24-72 hours should incorporate clinical response and microbiological results.

Clinical Implications

At presentation, clinicians should immediately assess shock, organ dysfunction and prior risk for MDR organisms. Previous culture results, recent hospitalisation, broad-spectrum antimicrobial exposure, invasive devices and local ICU ecology can help estimate the probability of resistance.

In septic shock or rapidly progressive organ dysfunction, empirical therapy should provide a high probability of activity against likely resistant organisms while cultures are obtained promptly. Once identification and susceptibility results become available, treatment should be optimised and narrowed whenever possible.

Source control should be addressed concurrently rather than sequentially. Intravascular-catheter removal, drainage, debridement or other interventions should not be delayed when clinically indicated. Serial SOFA or comparable severity assessment and evaluation of early response can identify patients in whom the initial strategy is failing.

Risk prediction should be used to intensify monitoring and multidisciplinary care, not to limit treatment. The available studies are observational and cannot establish that any isolated predictor is determinative for an individual patient.

Strengths

The review focuses specifically on independent predictors of mortality rather than merely describing the prevalence of MDR organisms. It integrates general MDR sepsis cohorts with pathogen-specific CRE, CRAB and resistant

Pseudomonas studies, allowing identification of prognostic domains that recur across distinct resistance mechanisms. The inclusion of treatment-related variables also highlights potentially modifiable contributors to mortality.

LIMITATIONS

Most included studies were retrospective observational cohorts and are vulnerable to residual confounding and treatment-by-indication bias. The sickest patients are more likely to receive broad or combination therapy, which can distort apparent treatment effects.

The term “MDR sepsis” was not defined uniformly. Some cohorts required severe sepsis or septic shock, whereas others enrolled patients with carbapenem-resistant bloodstream infection or ICU infection in whom sepsis was frequent but not universal. This clinical heterogeneity limits direct comparison.

Mortality endpoints varied from early or 14-day mortality to hospital and 90-day mortality. Predictors of very early death may differ from those of later mortality, particularly with regard to source control, complications and treatment toxicity.

Resistance mechanisms and available antimicrobials changed substantially over the review period. Studies conducted before widespread availability of newer beta-lactam/beta-lactamase inhibitor combinations may not fully represent current treatment possibilities.

Because of heterogeneity in populations, predictors and effect estimates, a pooled meta-analysis was not undertaken. The conclusions therefore reflect consistency of multivariable associations rather than a single pooled effect size.

CONCLUSION

Mortality in multidrug-resistant sepsis is determined by more than the resistance phenotype itself. Septic shock, greater organ dysfunction and physiological severity, advanced age and comorbidity, pneumonia or other high-risk infection sources, mechanical ventilation, inadequate source control and failure to receive promptly active antimicrobial therapy are the most consistent adverse prognostic factors. Early appropriate therapy and early clinical improvement are associated with better survival. Risk stratification should therefore combine host, severity, source, microbiological and treatment variables, with repeated reassessment after therapy begins. Prospective multicentre studies using standardised MDR and sepsis definitions are needed to develop and externally validate contemporary prediction models.

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