

NOSOCOMIAL INFECTIONS CAUSED BY *ACINETOBACTER* IN THE REPUBLIC OF MOLDOVA

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Septic nosocomial infections continue to be one of the main causes of mortality in hospital settings. In this regard, nosocomial infections caused by new etiological agents from the genus *Acinetobacter* are an urgent issue. This chapter presents data on the distribution of nosocomial infections caused by *Acinetobacter baumannii* across the Republic of Moldova.

Keywords: nosocomial infections, *Acinetobacter baumannii*, distribution, etiological agents.

STUDY RELEVANCE

Nosocomial infections (NIs), also known as healthcare-associated infections (HAIs), currently represent a major and evolving issue, both in terms of medical and socio-economic aspects, due to the increasing incidence, development of severe clinical forms, high mortality rates, and significant medical, economic, and moral impact [1–5].

The studies conducted previously within the Scientific Laboratory “Nosocomial Infections” at the “Nicolae Testemițanu” State University of Medicine and Pharmacy [6–10] have highlighted both the existing problem and the epidemiological characteristics of nosocomial infections depending on the profile of inpatient treatment. The conducted studies have also demonstrated that the key elements involve the etiological peculiarities of these infections, notably the ever-growing multitude of microorganism species responsible for nosocomial infections. Moreover, these infections exhibit a high level of resistance to antibiotics, presenting additional burden in combating them effectively.

Lately, an increasing number of severe cases of nosocomial infections with high mortality caused by microorganisms from the *Acinetobacter* genus have been reported. In 2017, the World Health Organization (WHO) released a comprehensive list outlining the most pressing threats to public health. Within this critical compilation, *Acinetobacter baumannii*

microorganisms were identified as the most perilous agents responsible for nosocomial infections, presenting as highly resistant bacteria [11].

Acinetobacter microorganisms, initially discovered in 1911 by Martinus Beijerinck from soil samples, were long disregarded in terms of their clinical significance, since rare cases of patient illness and the strains' high antibiotic sensitivity contributed to this oversight. However, in the late 20th century (1970s–1990s), reports of nosocomial outbreaks caused by *Acinetobacter* started to surface. In certain regions, this microorganism was already among the first pathogens of nosocomial infections. Since the 21st century, there has been a rapid spread of *A. baumannii* strains, eventually reaching global priority status. By 2013, the European Centre for Disease Prevention and Control had already reported a significant occurrence of *Acinetobacter* strains, accounting for 3.6% of healthcare-associated infections, of which 81.2% were resistant to carbapenems [12–19].

STATUS OF NOSOCOMIAL INFECTIONS WITH *ACINETOBACTER* IN THE REPUBLIC OF MOLDOVA

According to the findings of epidemiological studies conducted at the Scientific Laboratory for “Nosocomial Infections” within the “Nicolae

Testemițanu” State University of Medicine and Pharmacy, as part of the State Program “Investigation of Nosocomial Infections with *Acinetobacter*, *Pseudomonas*, and Methicillin-Resistant *Staphylococcus*”, project number 00059.80.03A/MS, running from 2015 to 2019 [18–20], it has been established that the first cases of

nosocomial infections with *Acinetobacter* in the Republic of Moldova were reported in 1997. Over a span of 22 years, a total of 166 cases of nosocomial infections with *Acinetobacter* have been documented, displaying a noticeable upward trend in recent years (see Fig. 1), according to data from the Chișinău Public Health Center.

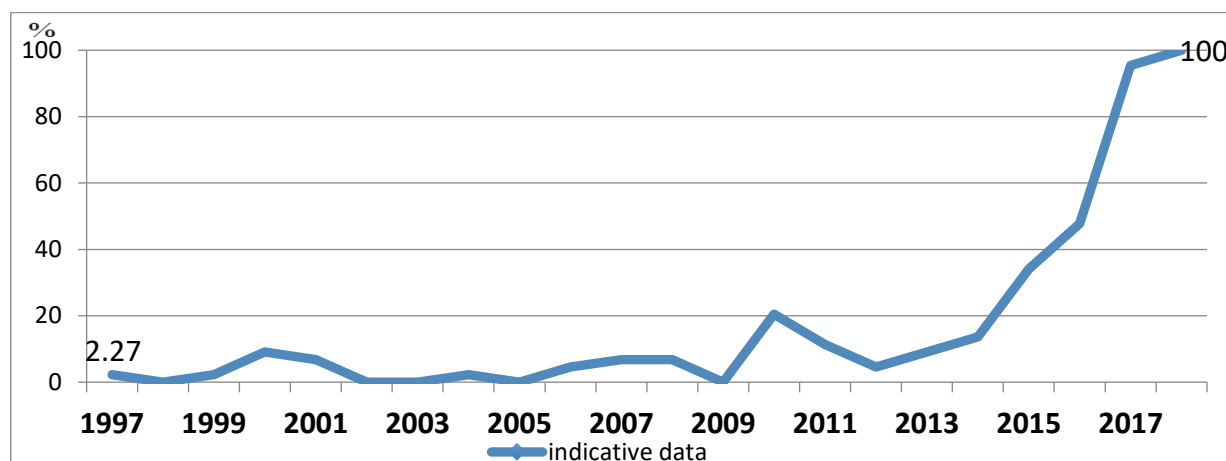


Fig. 1 – Long-term dynamics of nosocomial *Acinetobacter* infections officially registered in the Republic of Moldova (indicative data).

However, the officially recorded data do not reflect the real situation regarding *Acinetobacter* infections. A comprehensive retrospective epidemiological study was conducted to actively diagnose patients with *Acinetobacter*, based on the laboratory investigations of patients with nosocomial septic infections. The primary objective was to ascertain the actual epidemiological situation regarding *Acinetobacter* infections in the Republic of Moldova. The findings revealed a staggering incidence rate, approximately 14 times higher than reported.

Further evidence of the increasing spread of *Acinetobacter* strains can also be provided by the results of the study regarding the proportion of

these microorganisms in the overall structure of causative agents in nosocomial infections, as well as their proportion in the overall structure of Gram-negative microorganisms isolated from patients with nosocomial septic infections over multiple years. In 2010, the proportion of *Acinetobacter* microorganisms, out of the total number of strains isolated from patients with septic infections, was 3.07%. However, by 2018, this proportion had surged to 9.01%, and in 2022, it reached an alarming 12.89% (Fig. 2). Concurrently, the proportion of *Acinetobacter* strains within the broader spectrum of Gram-negative microorganisms increased from 7.45% in 2010 to a significant 21.80% in 2022 (Fig. 3).

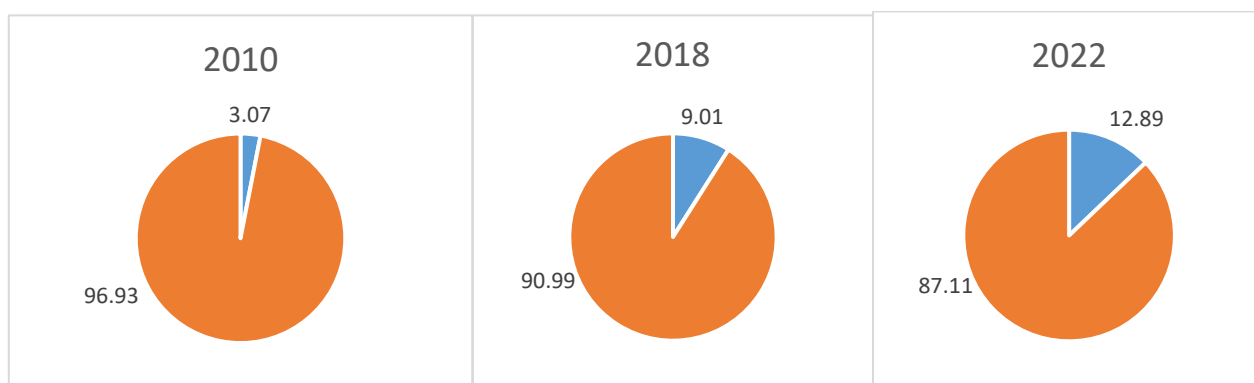


Fig. 2 – Distribution of *Acinetobacter* spp. strains among the total number of microorganism strains identified in patients with nosocomial septic infections.

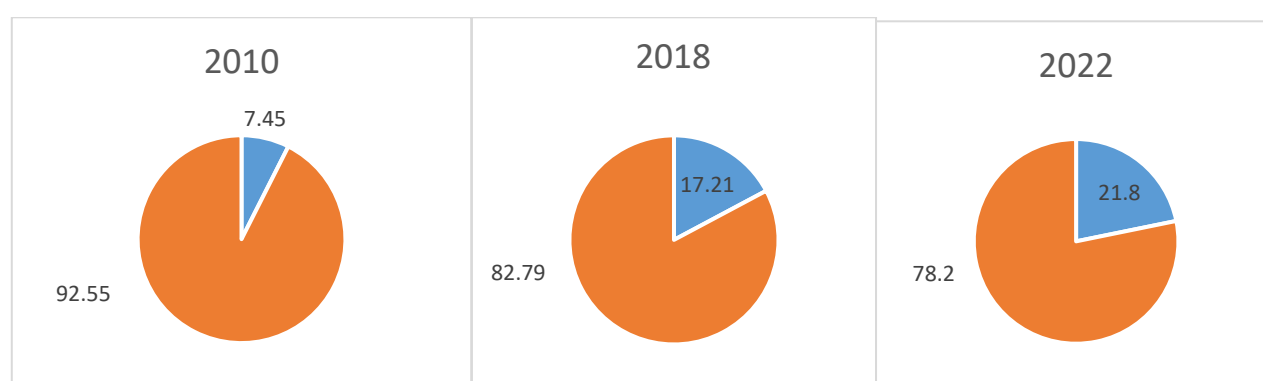


Fig. 3 – Proportion of *Acinetobacter* spp. strains within the total number of Gram-negative microorganism strains isolated from patients with nosocomial septic infections.

Among the group of *Acinetobacter* microorganisms, which serve as causative agents in nosocomial septic infections, *A. baumannii* is referred as the predominant species, accounting for 98.18% of the cases. The remaining species within the *Acinetobacter* genus were isolated as follows: *A. lwoffii* – 1.11%, *A. haemolyticus* – 0.61%, and *A. junii* – 0.10%.

Strains of *Acinetobacter baumannii* were primarily isolated in monocultures (68.60%) from the septic foci, while in 31.40% of cases they were found in association with other species of microorganisms. *Acinetobacter baumannii* strains were associated with gram-

negative microorganisms in 71.21% of cases, 15.37% of cases with gram-positive microorganisms, and 6.42% with various species of fungi.

Severe and generalized clinical forms predominantly characterize the structure of nosocomial infections caused by *Acinetobacter baumannii*, accounting for 56.30% of cases. These include pulmonary sepsis (25.59%), abdominal sepsis (11.81%), septicemia (9.45%), cutaneous sepsis (6.30%), cholangiogenic sepsis (1.97%), and uronephrogenic sepsis (1.18%). Among the local infections caused by *Acinetobacter baumannii*, wound infection predominates – 16.93% and pneumonia – 14.57% (Fig. 4).

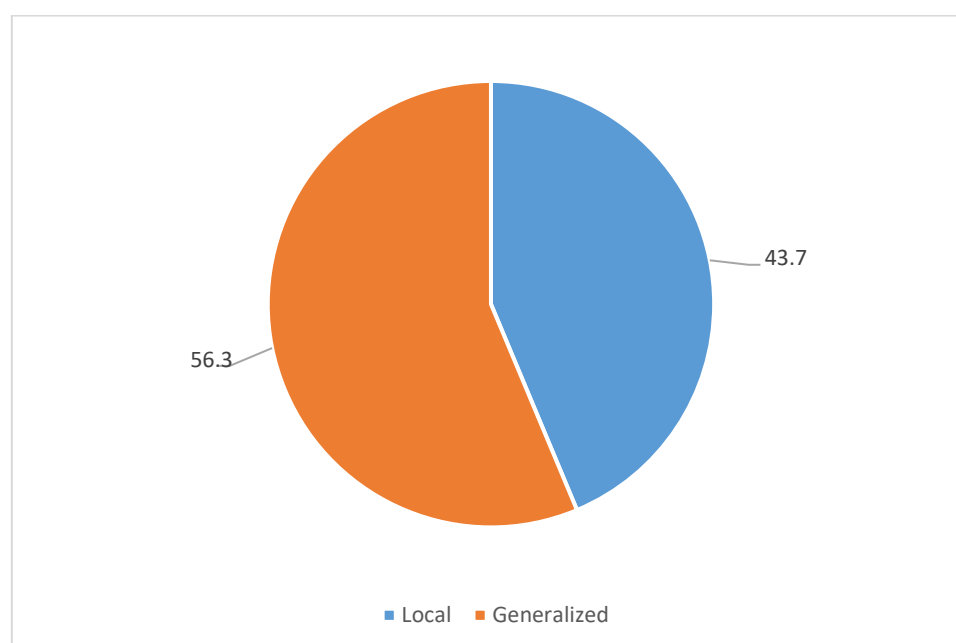


Fig. 4 – Structure of clinical forms in nosocomial septic infections caused by *Acinetobacter baumannii*.

An important feature of the currently prevalent strains of *Acinetobacter baumannii* in healthcare

settings is their high resistance to antibiotics commonly employed in medical practice (Fig. 5).

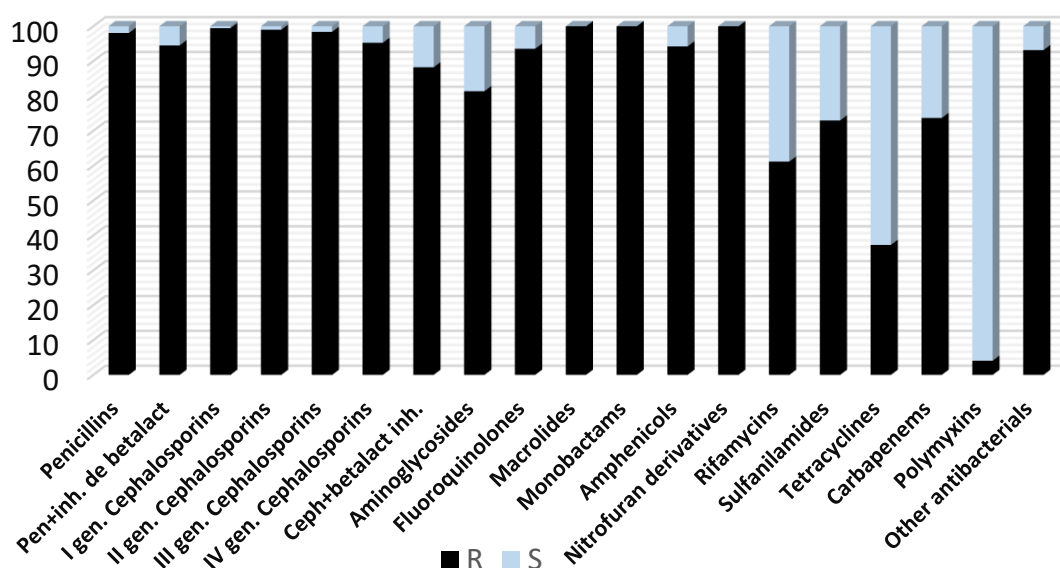


Fig. 5 – Antibiotic resistance/susceptibility of *Acinetobacter baumannii* strains according to the antibiotic group.

Of the total strains of *Acinetobacter baumannii* isolated from patients with nosocomial septic infections, 98.82% showed resistance to penicillins, including penicillins with beta-lactamase inhibitors – 93.20%. *Acinetobacter baumannii* strains showed very high resistance to macrolides – 98.82%,

cephalosporins – 97.65%, fluoroquinolones – 87.16%, nitrofur derivatives – 99.03%, carbapenems – 65.2%, and to monobactams in 100% of the samples.

Additionally, there is a constant increase in the overall resistance of *Acinetobacter baumannii* strains to antibiotics (Fig. 6).

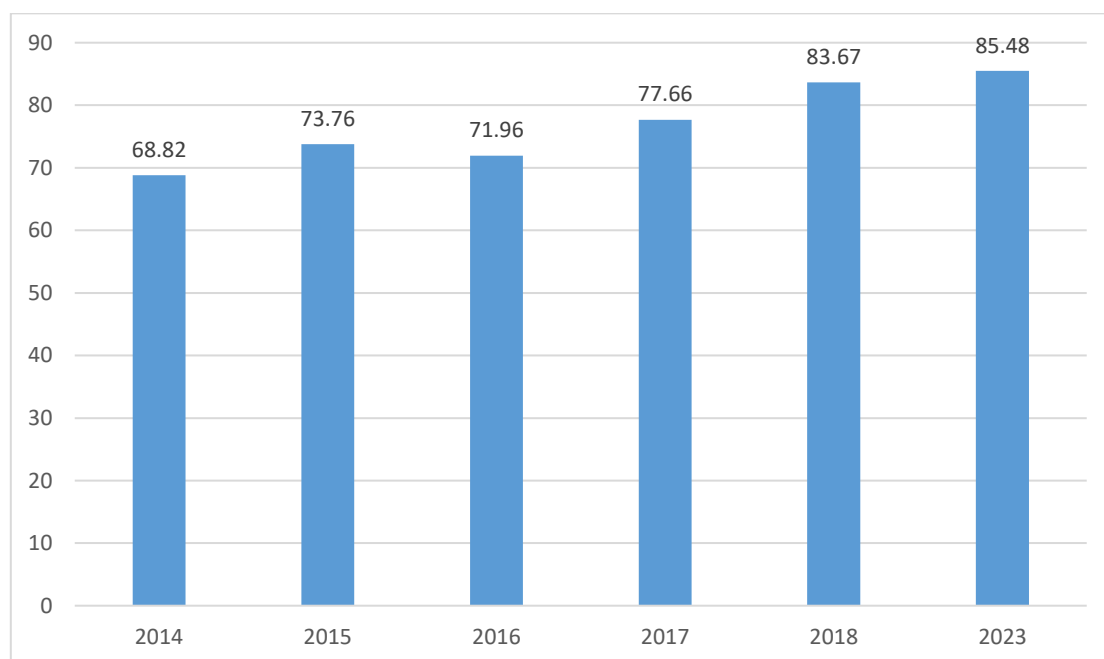


Fig. 6 – Evolution of overall antibiotic resistance in *Acinetobacter baumannii* strains over multiple years.

Acinetobacter baumannii strains have exhibited a greater sensitivity towards polymyxins, though their resistance has already increased to an alarming 5.6%. This significant increase poses a grave concern

in terms of therapeutic interventions for these patients.

Moreover, a staggering 93.08% of *Acinetobacter baumannii* strains isolated from patients with nosocomial septic infections display a multidrug-resistant phenotype (Fig. 7).

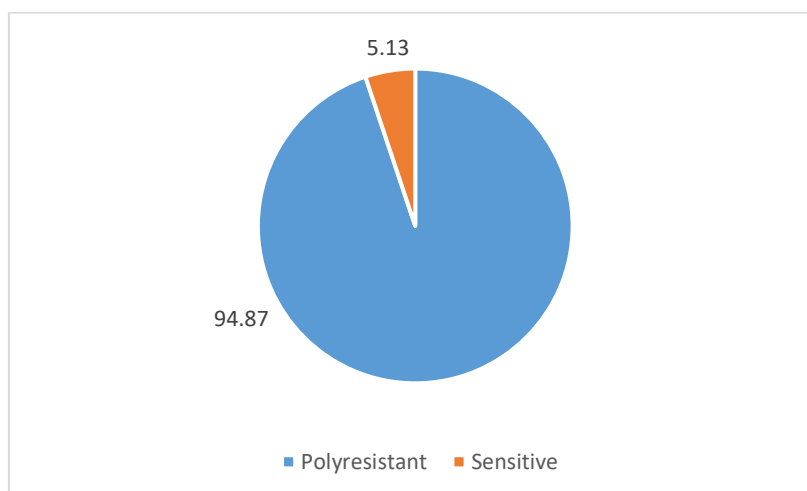


Fig. 7 – Antibiotic multi-resistance of *Acinetobacter baumannii* strains isolated from patients with nosocomial septic infections.

Acinetobacter microorganisms have become more widespread in resuscitation and intensive care units. Out of all the *Acinetobacter baumannii*

strains, 68.28% were isolated from patients with septic infections in these units, with surgical profile wards ranking second (Fig. 8).

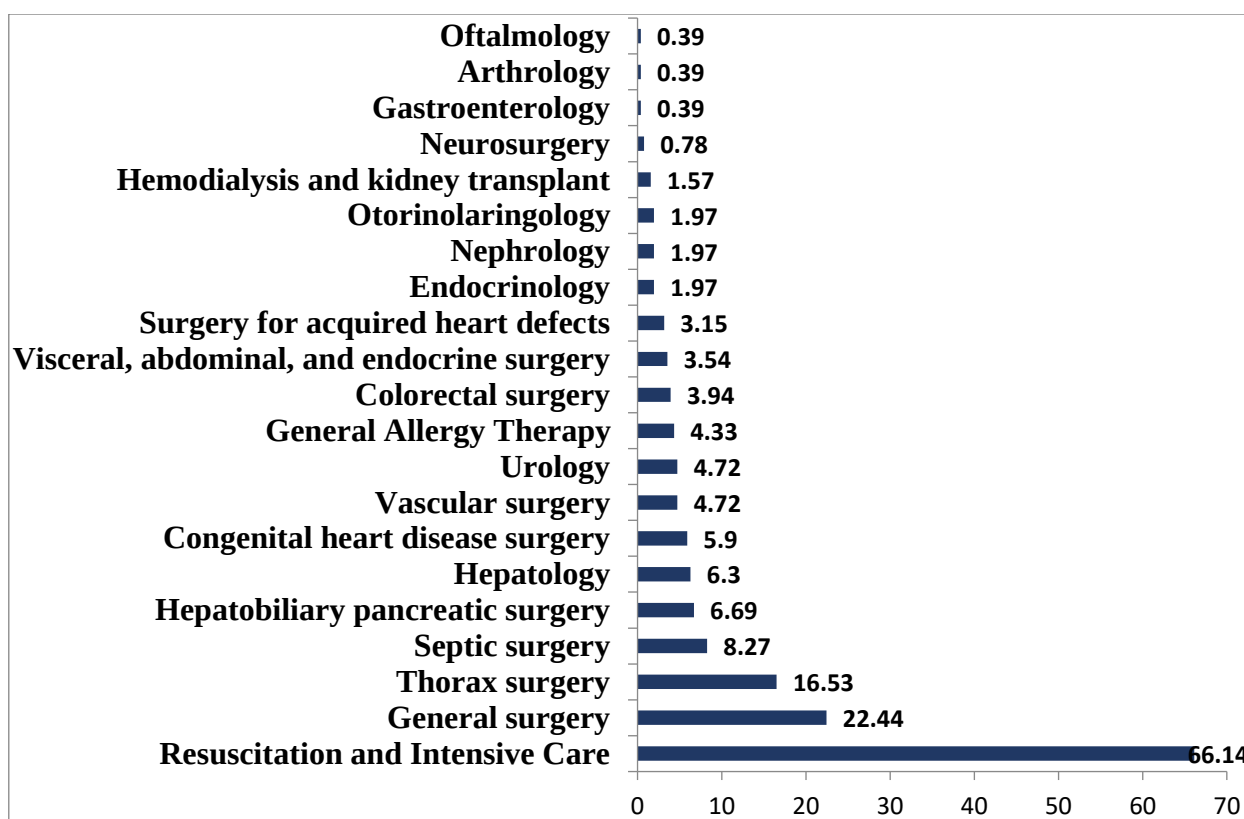


Fig. 8 – Rate of *Acinetobacter baumannii* strains isolated from patients with septic infections, according to the hospital unit profile.

The clinical and economic impact of infections caused by *Acinetobacter baumannii* is significant. It includes a lengthy inpatient treatment, averaging 20.42 days, considerable expenses for hospitalization and treatment (4119 US dollars per patient), and a high mortality rate of 25.98% in *Acinetobacter baumannii* infections.

CONCLUSIONS

Nosocomial infections with *Acinetobacter baumannii* currently represent a pressing issue for healthcare institutions. These infections are

increasingly occurring in severe and widespread forms, resulting in a significant clinical and socio-economic impact. It is crucial to raise awareness about the rapid rise in the incidence of nosocomial infections caused by *Acinetobacter* microorganisms, particularly the antibiotic-resistant *Acinetobacter baumannii*. Further irrational use of antibiotics, without considering antimicrobial susceptibility testing, will contribute to the widespread dissemination of antibiotic-resistant strains of *Acinetobacter baumannii* in medical practice, which could soon become the “plague of the 21st century”.

Given the situation, it is imperative for all medical institutions to prioritize the monitoring of *Acinetobacter spp* strains, including assessing their circulation and antibiotic resistance levels. Microbiological diagnosis, along with antibiotic susceptibility testing, plays a crucial role in the personalized therapy of patients with septic infections, especially those acquired in healthcare settings.

Furthermore, there is a growing need to address the challenge of enhancing therapeutic effectiveness by developing new antibacterial agents that can effectively target multidrug-resistant *Acinetobacter* strains.

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