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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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Содержание:

COMPARATIVE SUSCEPTIBILITY PROFILES OF CLINICAL AND REFERENCE BACTERIAL STRAINS ACROSS MULTIPLE ANTIBIOTIC CLASSES

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Abstract.

Antimicrobial resistance (AMR) is a major global public health threat, undermining the efficacy of commonly used antibiotics. Resistance patterns differ across bacterial taxa, including Enterobacteriaceae, non-fermenting Gram-negative bacilli, and Gram-positive cocci. This study aimed to provide a comparative analysis of antimicrobial susceptibility among **reference strains with defined susceptible and resistant phenotypes, alongside selected clinical isolates,** to evaluate the preservation of phenotypic traits and the impact of antibiotic use. Reference susceptibility strains exhibited high susceptibility across most antibiotics, whereas resistant reference strains demonstrated multidrug resistance. Among Enterobacteriaceae, **reference strains harboring ESBL and AmpC mechanisms** displayed resistance to penicillins, cephalosporins, and carbapenems. Non-fermenters, including *Pseudomonas aeruginosa* and *Acinetobacter baumannii,* showed both intrinsic and acquired resistance to multiple classes, particularly carbapenems and fluoroquinolones. Gram-positive cocci largely retained susceptibility to glycopeptides and linezolid, while MRSA, high-level aminoglycoside-resistant enterococci, and penicillin-resistant *Streptococcus pneumoniae* posed significant therapeutic challenges. Comparative analysis revealed that antimicrobial susceptibility is influenced not only by bacterial taxonomy but also by patterns of uncontrolled or inappropriate antibiotic use. Clinical strains of *Klebsiella pneumoniae* and *Streptococcus pneumoniae* displayed reduced and more variable susceptibility compared to the predictable profiles of reference strains.

These findings highlight the importance of continuous surveillance, strict adherence to antimicrobial stewardship, and the use of standardized reference strains to ensure reliable susceptibility testing. Early detection of emerging resistance patterns is essential to guide effective therapy and mitigate the public health impact of multidrug-resistant pathogens.

Key words. Antimicrobial resistance, reference strains, clinical isolates, Enterobacteriaceae, Gram-negative bacilli, Gram-positive cocci.

Introduction.

Antimicrobial resistance (AMR) has become one of the gravest public health threats of our time, undermining decades of progress in infectious disease control. According to a 2025 report by World Health Organization (WHO), one in six laboratory confirmed bacterial infections globally in 2023 was resistant to at least one of the commonly used antibiotics; between 2018 and 2023, over 40% of monitored pathogen–antibiotic combinations showed increasing resistance trends [1]. The problem is especially pronounced among Gram negative bacteria, which the report identifies as posing "the greatest threat," particularly in resource-limited settings where surveillance and treatment options are constrained [2,3].

These worrying global patterns underscore the need for comprehensive surveillance and analysis across diverse bacterial taxa. In clinical practice, the main culprits responsible for serious infections — urinary, bloodstream, respiratory, and nosocomial — frequently belong to three broad groups: Gram-negative Enterobacteriaceae, Gram-negative non-fermenters, and Gram-positive cocci. Each group has unique biology, ecology, and mechanisms of resistance, which influence how susceptibility evolves over time and across regions [4,5].

Gram-negative Enterobacteriaceae and the erosion of β-lactam efficacy: Historically, many Enterobacteriaceae — such as *Escherichia coli, Klebsiella pneumoniae*, and Proteus species — were reliably treated with penicillins and cephalosporins. However, over the past two decades, the global dissemination of extended-spectrum β-lactamases (ESBLs), AmpC β-lactamases, and carbapenemases has dramatically eroded that reliability. Recently, newer β lactam/β lactamase inhibitor combinations were developed to restore activity against ESBL- and carbapenemase-producing strains. Nevertheless, a 2025 systematic review and meta-analysis found that resistance to one such combination — Ceftazidime–avibactam — is rising globally among Gram-negative bacteria, both in Enterobacterales and non-fermenting species. This reflects the alarming reality that even latest-generation antibiotics are encountering resistance, underscoring the dynamic adaptability of bacterial pathogens [6-10].

Non fermenters: Intrinsic and Acquired Defences Amplify the Threat: Beyond Enterobacteriaceae, non fermenting Gram-negative bacilli — notably Pseudomonas aeruginosa and Acinetobacter baumannii — pose an even greater therapeutic challenge, due to both intrinsic and acquired resistance mechanisms. These organisms often resist multiple drug classes simultaneously because of impermeable outer membranes, efflux pumps, and ability to acquire carbapenemases or other β lactamases. A recent ICU based surveillance study (2022–2024) reported that resistance among *Pseudomonas* isolates to key antibiotics — including ceftazidime, ciprofloxacin, meropenem, and gentamicin — remains substantial, although some decline was observed in 2024 compared to 2022. MDPI Similarly, recent clinical data show that A. baumannii remains among the most resistant nosocomial pathogens, often requiring last-line agents for treatment [11-13].

These findings highlight that non-fermenters are not merely "difficult to treat" but are continuously evolving, sometimes outpacing the development and deployment of new antibiotics.

Gram-Positive Cocci: Persistent Resistance Despite Long-Term Use of Targeted Therapies: Resistance is not confined to Gram-negatives. Among Gram-positive cocci — including *Staphylococcus aureus, Streptococcus pneumoniae*, and *Enterococcus faecalis* — the longstanding challenges of methicillin-resistance (MRSA), macrolide-resistance in pneumococci, and high-level aminoglycoside resistance in enterococci persist worldwide. A 2024 meta-analysis focusing on a Middle East region showed that ESBL-producing Enterobacteriaceae, carbapenem resistant non-fermenters, MRSA, and other resistant Gram positives are all prevalent and contribute significantly to clinical burden .Meanwhile, local and hospital-based studies continue to report high rates of multidrug resistance among Gram-positives: for instance, a 2023–2024 surveillance at a reference hospital in Romania identified 59% of Staphylococcaceae strains as multidrug-resistant (MDR), with a substantial proportion being MRSA or showing macrolide-lincosamide-streptogramin B (MLSB) resistance. MDPI These developments underscore that resistance among Gram-positive cocci remains dynamic, not static — driven by ongoing antibiotic pressure,

horizontal gene transfer, and selection in both community and hospital [14,15].

Given the divergent biology and resistance mechanisms across Enterobacteriaceae, non fermenters, and Gram-positive cocci, a comparative approach is essential. A narrow focus on one group or antibiotic class can overlook broader shifts in bacterial ecology and treatment efficacy. For example, reliance on new β lactam/β lactamase inhibitor agents may provide a temporary reprieve for Enterobacteriaceae, but non fermenters might still harbor high resistance. Similarly, while glycopeptides or linezolid remain effective against many Gram-positive cocci, emerging resistance patterns in other drug classes may compromise empirical therapy, especially in mixed or unknown pathogen infections. Global analyses corroborate this need: a broad meta-analysis spanning dozens of countries found a continuous upward trend in multidrug-resistant (MDR) infections, especially in low- and middle-income countries, where antibiotic misuse is more common and surveillance systems are weaker. A regional meta-analysis from 2024 demonstrated high incidences of resistant Gram-negatives and Gram-positives in a Middle-Eastern country, reflecting how global trends manifest locally [16-19]. Previously have been shown the influence of antibiotics on different pathogens strains isolated from sick patients [20].

The present study aims to perform a comparative analysis of antimicrobial susceptibility across three major bacterial groups — Enterobacteriaceae, non fermenting Gram-negative bacilli, and Gram-positive cocci — using reference both susceptible and resistant strains. This approach allows:

Ø A baseline comparison of "susceptible" profiles vs. resistant phenotypes.

Ø Cross-group evaluation to identify which antibiotic classes remain broadly effective and which have lost reliability.

Ø Insight into how resistance mechanisms (ESBLs, carbapenemases, efflux, altered PBPs, HLAR, etc.) influence overall susceptibility.

Ø Data to inform empirical therapy, antibiotic stewardship policies, and infection control strategies in light of evolving resistance.

By integrating these data, we aim to provide a current, evidence-based of the evolving landscape of antibiotic susceptibility — bridging local findings with global trends.

Aim: The aim of this research to support the development of effective therapeutic strategies and alternative approaches to conventional antibiotics against multidrug-resistant pathogens.

Materials and Methods.

Bacterial Strains and Sample Collection:

All strains were sourced from reference culture collections of the American Type Culture Collection (ATCC) (https://www.atcc.org/), the National Collection of Type Cultures of the United Kingdom (NCTC) (https://www.culturecollections.org.uk/collections/nctc), the Microbiological Quality Control Laboratory in Darmstadt, Germany (MQCL), and the type cultures provided by the United Kingdom National External Quality Assessment Service (UK NEQAS) (https://www.ukneqas.org.uk/).

Enterobacteriaceae: *Escherichia coli* (ATCC 25922, MQCL 6578), *Proteus mirabilis* (UKNEQAS 4571/5275, 5243/7400), *Klebsiella pneumoniae* (ATCC 13883, 700603).

Non-fermenters: *Pseudomonas aeruginosa* (ATCC 27853, UKNEQAS 5290/4576), *Acinetobacter baumannii* (UKNEQAS 7601/5307, ATCC 13301, OXA-48 positive).

Gram-positive cocci: *Staphylococcus aureus* (ATCC 29213, NCTC 12493, MRSA), *Streptococcus pneumoniae* (ATCC 49619, UK NEQAS 4907), *Enterococcus faecalis* (ATCC 29212, NCTC 13379, HLAR).

Clinical isolates: *Klebsiella pneumoniae* (n=13) and *Streptococcus pneumoniae* (n=33) isolated from hospitalized patients (throat, sputum, blood) in multiple medical centers in Armenia during the COVID-19 epidemic period. These isolates were included for comparative purposes only.

For the purposes of this study, individual microbial cultures with distinct tinctorial characteristics ("Gram-positive" and "Gram-negative"), belonging to different genera and classified as either "susceptible" or "resistant" to antimicrobial agents, were selected.

Bacterial Identification:

Enterobacteriaceae and non-fermenters: In order to study the preservation of the biochemical properties of the reference strains, identification was carried out using API systems and the VITEK 2 automated analyzer. The study of susceptibility/resistant to antibacterial drugs was carried out in accordance with the requirements of the European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines.

Gram-positive cocci: Identified via morphology, catalase/coagulase tests, optochin sensitivity, bile solubility, standard biochemical tests (API Staph/ Strep) https://www.biomerieux.com/products/api®, VITEK 2 as appropriate (https://www.biomerieux.com/products/vitek-2).

Antimicrobial Susceptibility Testing:

Studies on susceptibility to antimicrobial agents and the interpretation of the results were conducted in accordance with the guidelines of the European Committee on Antimicrobial Susceptibility Testing (EUCAST, https://www.eucast.org).

Antibiotic panels included: **Enterobacteriaceae:** β-lactams, cephalosporins (I–IV generation), monobactams, fluoroquinolones, aminoglycosides, carbapenems, sulfonamides, chloramphenicol, fosfomycin, nitrofurans, nitroxoline. **Non-fermenters:** Piperacillin-tazobactam, ceftazidime, ceftazidime-avibactam, cefepime, aztreonam, fluoroquinolones, aminoglycosides, carbapenems, trimethoprim-sulfamethoxazole. **Gram-positive cocci:** Penicillins, cephalosporins, fluoroquinolones, aminoglycosides, carbapenems, glycopeptides, oxazolidinones, tetracyclines, sulfonamides, macrolides, nitrofurans, fusidic acid.

Results were interpreted as susceptible (S), intermediate (I), or resistant (R) according to EUCASTbreakpoints.

Detection of Resistance Mechanisms.

Extended-spectrum β-lactamases (ESBLs) and AmpC β-lactamases: Detected using double-disk synergy tests and AmpC disk tests (https://www.cdc.gov/hai/settings/lab/ampc.html). **Carbapenemases:** The mechanisms were identified by a phenotypic method using a 10 μg meropenem disk and confirmed by combined disks, evaluated using modified Hodge test (https://www.cdc.gov/hai/organisms/cre/cre-toolkit/hodge-test.html), Carba NP test, and PCR assays targeting KPC, NDM (https://www.cdc.gov/hai/organisms/cre/technical-info.html), OXA-type genes (https://apps.who.int/iris/handle/10665/275454). **Methicillin resistance (MRSA):** The mechanism of MRSA resistance was determined using a 30 μg cefoxitin disk and PCR assay. **High-level aminoglycoside resistance (HLAR):** The mechanism of HLAR stability was revealed with a 30 μg gentamicin disk. For detected using cefoxitin disk screening, MIC determination, or molecular assays as appropriate.

Data Analysis.

Comparative analysis between reference strains was performed to evaluate erosion of susceptibility over time. Statistical analysis was conducted using SPSS v28 or R software, applying chi-square with $p<0.05$ considered significant.

Results.

Our findings from the antimicrobial susceptibility testing of reference Enterobacteriaceae strains including *E. coli, P. mirabilis*, and *K. pneumoniae*, against conventional antibiotics is summarized in Table 1.

Definition antimicrobial susceptibility testing of susceptible (S) and resistant (R) Enterobacteriaceae strains revealed the following trends: **β-lactams and penicillins:** S-strains (*E. coli* ATCC 25922, *K. pneumoniae* ATCC 13883) were mostly susceptible to amoxicillin-clavulanic acid, piperacillin-tazobactam, and cefotaxime. R -strains (*E. coli* MQCL 6578, *K. pneumoniae* ATCC 700603, P. mirabilis UKNEQAS 5243/7400) showed high resistance to older β-lactams and cephalosporins. **Carbapenems:** Most S-strains were fully susceptible, while R-strains showed variable susceptibility, with some *K. pneumoniae* isolates resistant to meropenem and ertapenem. **Fluoroquinolones and aminoglycosides:** S-strains were largely susceptible, while R-strains exhibited reduced susceptibility, particularly to ciprofloxacin and gentamicin. **Other antibiotics:** Fosfomycin and nitrofurans retained activity against some resistant isolates, whereas trimethoprim-sulfamethoxazole showed inconsistent efficacy.

As shown in Table 1, susceptibility outcomes across a panel of 27 antibiotics differed markedly between susceptible reference strains and resistant phenotypes, confirming expected EUCAST-defined resistance profiles. As expected, the susceptible control strains (*E. coli* ATCC 25922, *P. mirabilis* UKNEQAS 4571/5275, and *K. pneumoniae* ATCC 13883) demonstrated consistent susceptibility to nearly all antibiotics tested, confirming the reliability and accuracy of the susceptibility testing procedures.

In contrast, the resistant strains—including ESBL-producing *E. coli* MQCL 6578, resistant *P. mirabilis* UKNEQAS 5243/7400, and *K. pneumoniae* ATCC 700603 (ESBL, AmpC)—exhibited widespread resistance across multiple antibiotic classes. The high number of resistant outcomes (9, 19 and 19 resistant readings respectively) reflects the significant impact of β-lactamase production on the effectiveness of commonly used antimicrobials. Only minimal intermediate responses were observed, indicating that most antibiotics were either clearly effective or clearly ineffective.

Overall, the results highlight extensive resistance patterns associated with ESBL and AmpC mechanisms when tested across a broad panel of 27 antibiotics. This emphasizes the need for continuous monitoring, careful antibiotic selection, and strengthened antimicrobial stewardship to manage and prevent the spread of these resistant Enterobacteriaceae strains.

Definition antimicrobial susceptibility testing of susceptible (S) and resistant (R) *Pseudomonas aeruginosa* and *Acinetobacter baumannii* showed: **β-lactams:** S-strains were partially susceptible to piperacillin-tazobactam, ceftazidime, and cefepime. R-strains were largely resistant to penicillins and cephalosporins, though ceftazidime-avibactam retained activity against some *P. aeruginosa* strains. **Fluoroquinolones:** S-strains showed intermediate susceptibility to ciprofloxacin and levofloxacin, whereas resistant isolates were mostly resistant. **Aminoglycosides:** Activity was preserved in S-strains but reduced in resistant isolates. **Carbapenems:** S-strains were generally susceptible; *R- A. baumannii* strains showed high resistance to imipenem, meropenem, and doripenem. **Sulfonamides:** Trimethoprim-sulfamethoxazole showed limited activity, with most resistant isolates classified as resistant. So non-fermenters demonstrated intrinsic and acquired resistance, particularly in ICU-associated isolates, emphasizing their therapeutic challenge.

The results obtained for the susceptibility of Gram-Negative Non-Fermenting Bacteria such as *Pseudomonas aeruginosa* and *Acinetobacter baumannii* strains to conventional antibiotics is summarized in Table 2.

As shown in Table 2, susceptibility outcomes across a panel of 14 antibiotics differed markedly between susceptible reference strains and resistant phenotypes, confirming expected EUCAST-defined resistance profiles. As expected, the quality-control strains *Pseudomonas aeruginosa* ATCC 27853 and *Acinetobacter baumannii* UKNEQAS 7601/5307 showed predominantly susceptible or intermediate responses, confirming appropriate test performance.

In contrast, the resistant reference strains—*P. aeruginosa* UKNEQAS 5290/4576 and *A. baumannii* ATCC 13301 (OXA-48)—exhibited extensive resistance across nearly all antibiotics tested. Notably, *P. aeruginosa* UKNEQAS showed complete resistance to all 14 antibiotics, while the OXA-48–producing *A. baumannii* displayed high resistance (10 resistant results) with limited susceptibility. These findings highlight the severe therapeutic challenge posed by resistant non-fermenters, especially those harboring carbapenemase enzymes such as OXA-48. Overall, the data reveal that although susceptible control strains behave predictably, resistant strains of *Pseudomonas* and *Acinetobacter* demonstrate broad and clinically significant antimicrobial resistance. This underscores the essential need for rigorous antimicrobial stewardship, rapid detection of carbapenemase-producing organisms, and continuous surveillance to mitigate the spread of highly resistant non-fermenting Gram-negative bacteria.

Definition antimicrobial susceptibility testing of susceptible (S) and resistant (R) of Gram-Positive Cocci revealed the following trends: ***Staphylococcus aureus:*** S-strains were susceptible to most β-lactams, fluoroquinolones, glycopeptides, linezolid, and tetracycline. MRSA isolates (NCTC 12493) were resistant to oxacillin, cefoxitin, and multiple other β-lactams. ***Streptococcus pneumoniae:*** S-strains remained susceptible to penicillin and levofloxacin, while resistant isolates showed resistance to benzylpenicillin and ceftriaxone. ***Enterococcus faecalis:*** S-strains were susceptible to ampicillin, vancomycin, linezolid, and teicoplanin. HLAR strains exhibited high-level resistance to aminoglycosides and partial resistance to β-lactams. Those resistance among Gram-positive cocci persists, with MRSA, HLAR enterococci, and penicillin-resistant pneumococci representing a continuing clinical challenge. The suspectibility of Gram-positive cocci, including *Staphylococcus aureus, Streptococcus pneumoniae*, and *Enterococcus faecalis*, to conventional antibiotics is summarized in Table 3.

As shown in Table 3, susceptibility outcomes across a panel of 26 antibiotics differed markedly between susceptible reference strains and resistant phenotypes, confirming expected EUCAST-defined resistance profiles. The susceptible control strains—*Staphylococcus aureus* ATCC 29213, *Streptococcus pneumoniae* ATCC 49619, and *Enterococcus faecalis* ATCC 29212—demonstrated high levels of susceptibility, confirming valid test performance and appropriate antibiotic activity against non-resistant strains.

In contrast, the resistant strains exhibited substantial resistance across multiple antibiotic classes. The MRSA strain (*S. aureus* NCTC 12493) showed increased resistance (4 resistant readings), consistent with its methicillin-resistant phenotype. The resistant *S. pneumoniae* UK NEQAS 4907 strain showed a pronounced shift toward resistance (10 resistant results), reflecting reduced susceptibility particularly to β-lactams and related agents. The high-level aminoglycoside-resistant (HLAR) *Enterococcus faecalis* NCTC 13379 also displayed reduced susceptibility, with 3 resistant outcomes and no intermediate responses, consistent with the HLAR phenotype that compromises synergistic therapy options.

Overall, the results illustrate distinct differences between susceptible and resistant Gram-positive cocci, with resistant strains demonstrating notable multidrug resistance across the 26 antibiotics tested. These findings emphasize the ongoing clinical challenge posed by MRSA, drug-resistant *S. pneumoniae*, and HLAR enterococci, underscoring the importance of antimicrobial stewardship, careful antibiotic selection, and continuous resistance surveillance.

Table 1. *Antimicrobial susceptibility summary of reference Enterobacteriaceae strains (27 antibiotics tested).*

Strain (reference)	Resistance phenotype	Susceptible (S)	Intermediate (I)	Resistant (R)
E. coli ATCC 25922	Susceptible control	27	0	0
E. coli MQCL 6578	ESBL producer	18	0	9
P. mirabilis UKNEQAS 4571/5275	Susceptible control	25	0	2
P. mirabilis UKNEQAS 5243/7400	Resistant	7	1	19
K. pneumoniae ATCC 13883	Susceptible control	26	0	1
K. pneumoniae ATCC 700603	ESBL, AmpC	8	0	19

Footnote: *Values represent the number of antibiotics classified as susceptible (S), intermediate (I), or resistant (R) according to EUCAST breakpoints. Reference strains were used for comparative and quality-control purposes.*

Table 2. *Antimicrobial susceptibility summary of reference Gram-negative non-fermenting bacteria based on EUCAST interpretation (14 antibiotics tested).*

Strain (reference)	Resistance phenotype of reference strains	Susceptible (S)	Intermediate (I)	Resistant (R)
P. aeruginosa ATCC 27853	Susceptible control	4	8	2
P. aeruginosa UKNEQAS 5290/4576	Multidrug-resistant	0	0	14
A. baumannii UKNEQAS 7601/5307	Susceptible control	8	2	4
A. baumannii ATCC 13301	OXA-48 producer	3	1	10

Footnote*: Susceptibility categories were assigned according to EUCAST guidelines. Values indicate the number of antibiotics within the tested panel.*

Table 3. *Antimicrobial susceptibility summary of reference Gram-positive cocci based on EUCAST interpretation (26 antibiotics tested).*

Strain (reference)	Resistance phenotype of reference strains	Susceptible (S)	Intermediate (I)	Resistant (R)
S. aureus ATCC 29213	Susceptible control	15	3	2
S. aureus NCTC 12493	MRSA	13	3	4
S. pneumoniae ATCC 49619	Susceptible control	13	0	1
S. pneumoniae UK NEQAS 4907	Resistant control	3	1	10
E. faecalis ATCC 29212	Susceptible control	11	1	0
E. faecalis NCTC 13379	HLAR	8	0	3

Footnote: *S = susceptible; I = intermediate; R = resistant. Values indicate the number of antibiotics meeting EUCAST criteria within the tested panel.*

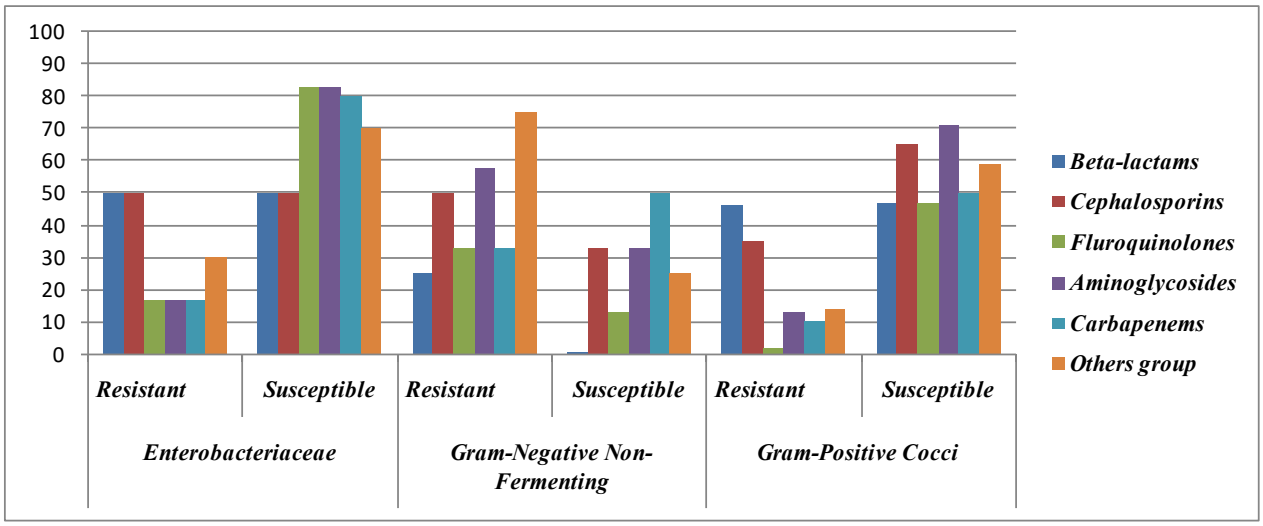
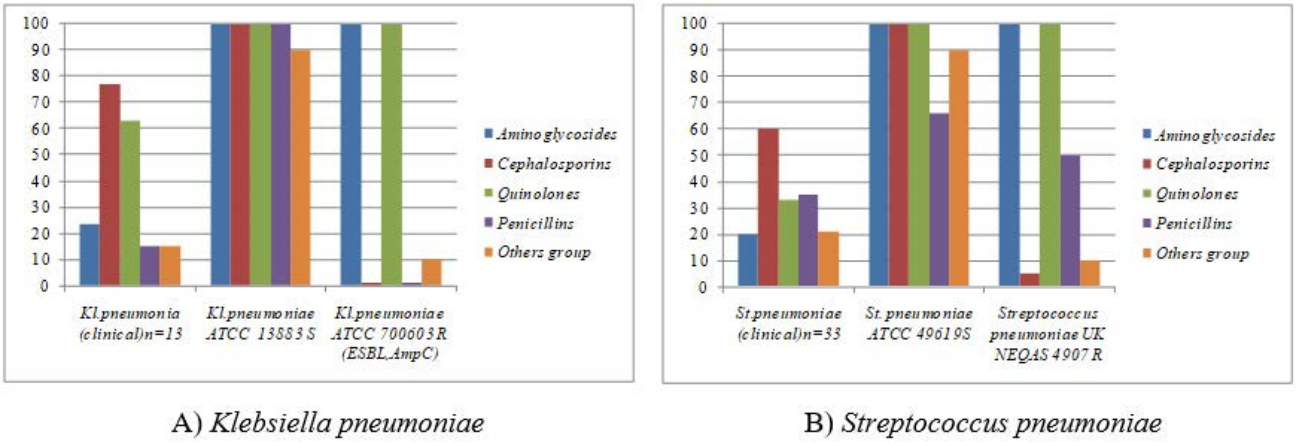


Figure 1. *The comparative analysis of antimicrobial classes across Enterobacteriaceae, Gram-negative non-fermenters, and Gram-positive cocci (%).*



A) *Klebsiella pneumoniae* B) *Streptococcus pneumoniae*

Figure 2. *Comparative analysis of antimicrobial susceptibility patterns among selected clinical isolates and corresponding reference strains.*

The comparative analysis of antimicrobial classes across Enterobacteriaceae, Gram-negative non-fermenters, and Gram-positive cocci reveals distinct susceptibility and resistance trends that align with the intrinsic and acquired resistance mechanisms of each group are shown in Figure 1.

For Enterobacteriaceae, the highest susceptibility was observed with cephalosporins, fluoroquinolones, and carbapenems, indicating these classes remain largely effective against many isolates. However, notable resistance was seen in beta-lactams and aminoglycosides, reflecting the influence of ESBL and AmpC producers in this group and highlighting ongoing pressure on commonly used antibiotics. Among Gram-negative non-fermenters, particularly *Pseudomonas* and *Acinetobacter*, resistance was markedly higher across almost all antimicrobial classes. Beta-lactams, carbapenems, and aminoglycosides showed substantial resistance levels, consistent with multidrug-resistant phenotypes and carbapenemase production. Susceptibility was most preserved in fluoroquinolones and some agents in the "other" category, though overall effectiveness remains limited. For *Gram-positive cocci*, susceptibility rates were considerably higher than in the Gram-negative groups. Beta-lactams and cephalosporins showed strong activity against susceptible strains, whereas resistance was expectedly higher in MRSA and HLAR enterococci. Carbapenems—though not routinely used for many Gram-positive infections—also showed high susceptibility values in the dataset.

Overall, the chart demonstrates that Gram-negative non-fermenters exhibit the highest levels of multidrug resistance, followed by Enterobacteriaceae, whereas Gram-positive cocci remain comparatively more susceptible across most antimicrobial classes. These patterns reinforce the need for targeted antibiotic stewardship, routine susceptibility testing, and continuous surveillance to manage evolving resistance profiles across bacterial groups.

Were investigation the antimicrobial comparison among *K. pneumoniae* and *S. pneumoniae* clinical isolates, the susceptible *K. pneumoniae* ATCC 13883 and *S. pneomaniae* ATCC 49619 strains, and the resistant ESBL/AmpC-producing *K. pneumoniae* ATCC 700603 and *S. pneumoniae* UK NEQAS 4907 strains, reveals substantial differences in susceptibility patterns across antibiotic classes (Figure 2).

In Figure 2A the clinical isolates showed moderate to high resistance across most antibiotic groups, with particularly elevated resistance to cephalosporins and quinolones, reflecting the growing prevalence of extended-spectrum β-lactamase (ESBL) production and other resistance mechanisms in clinical *K. pneumoniae*. Penicillins and agents in the "others" category showed the lowest activity, indicating limited treatment options when resistance is present. The susceptible ATCC 13883 strain demonstrated uniform susceptibility (100%) to all antibiotic classes tested, functioning effectively as a control and validating the accuracy of the susceptibility testing conditions. In contrast, the ESBL/AmpC-producing ATCC 700603 strain displayed extensive resistance across nearly all antibiotic classes. Resistance was particularly pronounced for cephalosporins, penicillins, and "other" group antibiotics, consistent with the enzymatic inactivation caused by ESBL and AmpC β-lactamases. Only quinolones retained notable activity, though even these showed reduced susceptibility compared to the fully sensitive strain.

Overall, the data illustrate the marked therapeutic challenge posed by resistant *K. pneumoniae* strains. While the susceptible control confirms reliable antibiotic performance, the sharp decline in susceptibility in clinical and ESBL/AmpC isolates underscores the urgent necessity for antimicrobial stewardship, early detection of β-lactamase-producing strains, and the strategic use of last-line agents to preserve their efficacy.

In Figure 2B the susceptibility profiles demonstrate clear differences between clinical *S. pneumoniae* isolates and reference strains. The ATCC 49619 strain exhibited uniformly high susceptibility to all major antimicrobial classes, confirming its reliability as a quality-control strain. In contrast, clinical isolates showed notably lower susceptibility, particularly to aminoglycosides, quinolones, and penicillins, reflecting the expected variability and reduced sensitivity typically seen in circulating clinical strains. The UK NEQAS 4907 strain displayed a mixed profile: while it maintained high susceptibility to aminoglycosides, cephalosporins, quinolones, and penicillins, it showed markedly reduced susceptibility within the "other" antibiotic group, consistent with its role as a resistant control strain.

Overall, the comparison highlights the preserved susceptibility of reference control strains versus the diminished and more heterogeneous susceptibility observed in clinical isolates. These findings underline the importance of using both susceptible and resistant controls for validating antimicrobial susceptibility testing and for monitoring potential erosion of antimicrobial effectiveness in clinical populations.

The comparative analysis of antibiotic susceptibility among clinical and reference strains demonstrates that antimicrobial response is influenced by more than just bacterial taxonomy. While reference strains such as ATCC and UK NEQAS isolates maintained high and predictable susceptibility profiles, clinical strains of both *K. pneumoniae* and *S. pneumoniae* exhibited markedly reduced and more variable susceptibility across multiple antibiotic classes. This contrast highlights the impact of uncontrolled or inappropriate antibiotic use in clinical settings, which contributes to the emergence and persistence of resistant phenotypes. Overall, the findings reinforce the need for continuous surveillance, strict adherence to antimicrobial stewardship practices, and the use of standardized reference strains to ensure reliable susceptibility testing and early detection of resistance trends.

Discussion.

This study provides a comprehensive comparative assessment of antimicrobial susceptibility across three major bacterial groups—Enterobacteriaceae, non-fermenting Gram-negative bacilli, and Gram-positive cocci—using both susceptible reference strains and multidrug-resistant phenotypes, including ESBL-, AmpC-, MRSA-, HLAR-, and carbapenemase-producing isolates, as well as selected clinical isolates of *K. pneumoniae* and *S. pneumoniae* obtained from hospitals in Armenia. The observed inhibitory effects were associated with the intrinsic characteristics of the pathogen strains rather than the geographic origin of the isolates. Across all taxa, a consistent trend emerged: reference susceptible strains demonstrated predictable and broad susceptibility, whereas resistant strains exhibited extensive multidrug resistance affecting multiple antibiotic classes. Among Enterobacteriaceae, ESBL- and AmpC-producing isolates showed substantial resistance to penicillins, cephalosporins, and, in some cases, carbapenems, highlighting the continued erosion of β-lactam efficacy. Although carbapenems and fluoroquinolones retained activity against susceptible isolates, their reduced effectiveness against resistant strains reflects the growing prevalence of plasmid-mediated β-lactamases. Non-fermenting Gram-negative bacilli—particularly *Pseudomonas aeruginosa* and *Acinetobacter baumannii*—displayed the highest resistance levels across all groups, with some isolates resistant to nearly all conventional agents. Their pronounced resistance to β-lactams, carbapenems, and aminoglycosides underscores the combined influence of intrinsic defense mechanisms (e.g., efflux pumps and reduced permeability) and acquired carbapenemase genes. These findings are consistent with global reports identifying non-fermenters as leading drivers of persistent and hard-to-treat nosocomial infections. Gram-positive cocci generally retained susceptibility to glycopeptides and linezolid, though the presence of MRSA, penicillin-resistant pneumococci, and HLAR enterococci posed significant therapeutic challenges. These resistant phenotypes exhibited multidrug resistance patterns that compromise standard treatment options and necessitate careful regimen selection.

Comparison across bacterial groups revealed a clear gradient of antimicrobial resistance: non-fermenters demonstrated the greatest resistance burden, followed by Enterobacteriaceae, while Gram-positive cocci remained comparatively more susceptible, yet still affected by notable resistance mechanisms. The evaluation of *Kl. pneumonia* and *St. pneumoniae* subgroups reinforced these trends, demonstrating marked differences in susceptibility between clinical isolates, fully susceptible reference strains, and ESBL/AmpC producers.

Overall, these findings underscore the dynamic and evolving nature of antimicrobial resistance, driven by diverse mechanisms across bacterial taxa. The study highlights the critical importance of integrated surveillance, routine antimicrobial susceptibility testing, and robust stewardship programs to guide empirical therapy and contain the spread of resistance. Continuous monitoring, coupled with rational antibiotic use, remains essential for preserving the effectiveness of existing antimicrobials and mitigating the global AMR burden.

Conclusion.

In the last decade, the first comparative analysis of the susceptibility of AMR reference and clinical strains to commonly used antibiotics was conducted. This study contributes to the global understanding of different antimicrobial resistance (AMR) and provides a foundation for developing effective treatment and infection control strategies. Comparative analysis revealed notable differences in susceptibility patterns across bacterial taxa, highlighting antibiotics that remain broadly effective and those whose efficacy is declining. The findings emphasize the dynamic and evolving nature of AMR and underscore the need for integrated surveillance across multiple bacterial groups. Coordinated global and local efforts are essential to track resistance trends, guide empirical therapy, inform antimicrobial stewardship programs, and support evidence-based clinical decision-making. Continuous monitoring and prudent antibiotic use remain critical to mitigating the growing burden of AMR.

Author contributions.

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Availability of data and materials.

Raw data can be provided upon request to the corresponding author.

Declarations.

Competing interests.

The authors declare no competing interests.

Conflict of interest.

The authors declare no conflict of interest.

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