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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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ANTIMICROBIAL RESISTANCE PROFILE OF BACTERIAL ISOLATES FROM VENTILATOR-ASSOCIATED PNEUMONIA PATIENTS IN AN ECUADORIAN TERTIARY HOSPITAL

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Abstract.

Ventilator-associated pneumonia is one of the most common nosocomial infections in patients receiving mechanical ventilation for more than 48 hours. This study aimed to characterize the antimicrobial susceptibility profile of microorganisms isolated from patients with Ventilator-associated pneumonia in a hospital in Ecuador. A descriptive, retrospective, cross-sectional study was conducted between April 2020 and April 2021. A total of 132 positive bronchial secretion samples obtained from patients diagnosed with VAP were analyzed. Bacterial identification was performed using the Phoenix M50 automated system, and antimicrobial susceptibility testing was carried out according to Clinical and Laboratory Standards Institute guidelines. Isolates resistant to meropenem were further evaluated by phenotypic methods and molecular confirmation of the bla_{KPC} gene. The study period coincided with the COVID-19 pandemic, during which a substantial proportion of ICU admissions were related to severe SARS-CoV-2 pneumonia requiring prolonged mechanical ventilation. *Klebsiella pneumoniae* was the predominant pathogen (61.4%), including 33 extended-spectrum β-lactamase producing strains and 42 KPC-producing isolates. In *Escherichia coli*, the ESBL phenotype predominated, and one KPC-producing isolate was identified. KPC-producing strains were also detected in Enterobacter cloacae and *Klebsiella aerogenes*, with molecular confirmation of the bla_{KPC} gene. The high prevalence of multidrug-resistant pathogens, together with the pandemic context and the associated high mortality, highlights the urgent need to strengthen microbiological surveillance, infection control measures, and therapeutic strategies in intensive care units.

Key words. Pneumonia, mechanical ventilation, *Klebsiella pneumoniae*, mortality, resistance, antibiotics.

Introduction.

Ventilator-associated pneumonia (VAP) is a significant form of hospital-acquired pneumonia. This condition develops as an infection of the lung parenchyma after patients have been intubated and receiving mechanical ventilation for more than 48 hours or have undergone tracheostomy [1,2].

VAP is classified into two groups according to the duration of mechanical ventilation: early-onset VAP typically appears within the first four days after orotracheal intubation, with the most common pathogens being *Streptococcus pneumoniae, Haemophilus influenzae*, methicillin-susceptible *Staphylococcus aureus*, and occasionally Enterobacterales [3]. Conversely, late-onset VAP is acquired in intensive care units five days after the initiation of mechanical ventilation. Patients with late-onset VAP are at increased risk because the pathogens associated with this infection are primarily multidrug-resistant microorganisms such as *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and methicillin-resistant *S. aureus* (MRSA) [4].

Patients admitted to the ICU undergoing ventilation have various conditions, such as critical illness, comorbidities, and malnutrition, which affect their immune system. In non-intubated, healthy patients, defense mechanisms such as mucociliary clearance, coughing, and cellular and humoral immune responses prevent bacterial colonization by reacting when bacteria reach the airway [5].

In mechanically ventilated patients, unconsciousness prevents the clearance of oropharyngeal secretions, leading to increased oral colonization. Bacteria present in these secretions, passing through the tracheal tube, form a biofilm that reaches the distal airways and can cause pneumonia. Endotracheal intubation suppresses the cough reflex, hinders mucociliary clearance, damages the tracheal epithelial surface, and facilitates the passage of pathogenic bacteria from the upper to the lower respiratory tract [5].

The treatment of VAP heavily relies on antibiotics. The correct choice of these drugs and the duration of treatment are crucial to combat the infection, avoid complications, and prevent bacterial resistance. Factors influencing this decision include the duration of ventilation, the onset of pneumonia, and culture results. Additionally, patient characteristics, such as prior illnesses or previous treatments, also guide the selection of the most appropriate antibiotics [6].

Antimicrobial resistance, particularly in Gram-negative bacilli such as Enterobacterales and non-fermenters (mainly *P. aeruginosa*, *A. baumannii*, and *Stenotrophomonas maltophilia*), constitutes a growing challenge in the hospital setting. These multidrug-resistant (MDR) pathogens, often producers of enzymes such as ESBL, AmpC, or MBL, are responsible for a significant proportion of nosocomial infections, particularly in patients with VAP [7]. Studies have shown that the prevalence of these microorganisms is higher in late-onset infections, which is attributed to factors such as prolonged hospital stays and prior antibiotic use. The variability in etiological agents depends on the hospital environment and the characteristics of the patient population [5].

Given the high morbidity and mortality associated with VAP, and considering the growing global problem of antimicrobial resistance, this study aimed to characterize the antimicrobial susceptibility profile of microorganisms isolated from patients with VAP in an Ecuadorian hospital.

Materials and Methods.

Study design:

A non-experimental, descriptive, retrospective, cross-sectional study was conducted.

Population and Sample:

The initial population consisted of 237 medical records of patients diagnosed with VAP, all of whom had undergone microbiological culture at the IESS Hospital Microbiology Service between April 2020 and April 2021. The final sample included 132 cases with positive bronchial or tracheal secretion cultures (i.e., with documented microbial growth). Negative cultures, as well as samples reported as contaminated or insufficient, were excluded from the analysis.

The study period coincided with the global COVID-19 pandemic. Therefore, SARS-CoV-2 infection status was recorded whenever available from clinical records. A substantial proportion of patients admitted to the intensive care unit presented with severe COVID-19-associated pneumonia requiring invasive mechanical ventilation. This epidemiological context was considered when interpreting the incidence of VAP and the distribution of isolated microorganisms. Nevertheless, it should be noted that, due to the limited availability of RT-PCR testing during the early phase of the pandemic in Ecuador, not all patients had laboratory-confirmed SARS-CoV-2 infection.

Variables:

To assess the association between the antimicrobial susceptibility profile and various clinical factors in patients with ventilator-associated pneumonia, variables such as isolated bacterial species, type of antibiotics, duration of ventilation, prior antibiotic treatments, clinical status, age, gender, and intensive care unit were analyzed. Clinical outcomes such as mortality and length of stay were also evaluated.

Microbiological Processing at the Hospital:

Bronchial secretion samples were obtained by endotracheal aspiration and processed in the microbiology laboratory. Following Gram staining to assess sample quality, quantitative culture was performed on blood, chocolate, MacConkey, and mannitol salt agar. Plates were incubated under aerobic and microaerophilic conditions at 37°C for 48 hours. Isolated colonies were identified by their macroscopic and microscopic characteristics and confirmed using the automated Phoenix M50 system. Subsequently, their susceptibility to different antimicrobials was determined following CLSI recommendations [8].

Isolates with resistance to meropenem (inhibition zone diameter ≤ established breakpoint) were considered suspected carbapenemase producers and selected for confirmatory testing. Phenotypic detection of KPC producers was performed using the combined disk method with phenylboronic acid (PBA), as well as by molecular identification of the bla_{KPC} gene [9].

Confirmatory Phenotypic Test for KPC:

Meropenem-resistant Enterobacterales isolates were evaluated using meropenem disks with and without PBA. A bacterial suspension adjusted to the 0.5 McFarland standard was prepared and plated on Mueller-Hinton agar. One meropenem disk was impregnated with 20 µl of PBA (20 mg/ml in dimethylsulfoxide) and allowed to dry before placement. Both disks (with and without PBA) were placed 30 mm apart and incubated at 37 °C for 18–24 hours [9].

A positive result for KPC production was considered when the inhibition zone diameter of the disk with PBA was ≥ 5 mm larger compared to the disk without PBA [10].

Molecular Detection of the blaKPC Gene:

The bla_{KPC} gene was amplified from DNA extracted from the Enterobacterales isolates using the alkaline hydrolysis method [11]. The PCR reaction (final volume of 25 µl) included 3 µl of template DNA, 0.5 µl of each primer (forward and reverse), and 21 µl of master mix.

The primers used were:

Forward: 5′-ACGACGGCATAGTCATTTGC-3′

Reverse: 5′-CATTCAAGGGCTTTCTTGCTGC-3′

The expected amplicon size was 538 bp. Amplification conditions consisted of initial denaturation at 95 °C for 15 minutes, followed by 32 cycles of 94 °C for 30 seconds, annealing at 58 °C for 90 seconds, and extension at 72 °C, with a final extension of 10 minutes at 72 °C.

PCR products were visualized by electrophoresis on a 1.2% agarose gel stained with ethidium bromide.

Processing and Analysis Techniques:

Data were analyzed using descriptive statistics, including absolute and relative frequencies. Subsequently, inferential analysis was performed to assess associations between categorical variables. The chi-square (χ^2) test was applied to evaluate the relationship between age groups and mortality in patients with ventilator-associated pneumonia, as well as to compare mortality rates between infections caused by KPC-producing and non–KPC-producing strains. A p-value < 0.05 was considered statistically significant.

Ethical Considerations:

The hospital administration authorized access to archived data, contingent upon the strict protection of the confidentiality of information contained in medical records. These data were used exclusively for scientific and academic purposes. Furthermore, the study was conducted in accordance with ethical principles for research involving human subjects, ensuring participants' autonomy and the confidential handling of information. In this regard, the study adheres to the fundamental principles of bioethics established in the Declaration of Helsinki.

Results.

Table 1. The clinical manifestations presented correspond to symptoms observed at the time of ICU admission and are related to the underlying condition that required mechanical ventilation. These manifestations do not represent symptoms of VAP, which developed later during hospitalization.

It is important to note that the study period coincided with the global COVID-19 pandemic. In this context, 90.9% of patients

presented respiratory symptoms compatible with this infection, including dry cough, fever, malaise, and respiratory distress. Therefore, the SARS-CoV-2 infection status was recorded whenever this information was available in the medical records. However, due to the limited availability of RT-PCR testing during the first wave of the pandemic in Ecuador, not all patients had a laboratory-confirmed diagnosis of COVID-19.

Table 2 presents the demographic characteristics of patients who developed VAP, stratified by age group and sex. Of the 132 VAP patients, the largest number was among males, with 94 patients (71.2%), while females accounted for 38 cases (28.8%). However, no statistically significant association was observed between sex and mortality ($p = 0.842$).

Regarding age distribution, statistically significant differences were observed among age groups ($p = 0.024$). The age group with the highest proportion of deaths was 64–73 years, representing 26 cases (28.6%), followed by the 34–53 age group with 24 cases (26.4%). Patients aged ≥74 years also showed a considerable proportion of deaths (20.9%), whereas the 54–63 age group accounted for 22 deaths (24.2%).

Of the 81 clinical isolates of *K. pneumoniae* analyzed in patients with VAP, an overall mortality rate of 70.4% was observed (n = 57). When the cohort was stratified based on the pathogen's resistance profile, mortality was higher in the group of patients infected with KPC-producing strains, reaching 78.6%. In contrast, infections associated with non-KPC-producing variants had a mortality rate of 61.5%.

Although there was a difference in mortality between KPC-producing and non-KPC-producing isolates, it did not reach statistical significance ($p = 0.093$). However, the frequency of fatal outcomes approaching 80% in the KPC-positive group underscores the high intrinsic risk posed by these pathogens in the hospital setting (Table 3).

In the 132 patients with VAP, 13 microorganisms were isolated. The most frequently found were *K. pneumoniae* with 61.4% (81/132), followed by *E. coli* with 9.1% (12/132) and *E. cloacae* with 6.1% (8/132). Other microorganisms occurred in very low percentages (Figure 1).

Table 4 summarizes the antimicrobial susceptibility profiles and resistance mechanisms of the isolated microorganisms. Microbiological analysis identified *K. pneumoniae* as the predominant pathogen, exhibiting a concerning multidrug-resistant profile. Among the isolates, 33 were ESBL producers, demonstrating resistance to broad-spectrum cephalosporins and fluoroquinolones while retaining susceptibility to carbapenems. In contrast, 42 isolates were KPC producers, displaying extensive resistance that included carbapenems such as meropenem, ertapenem, and imipenem.

In *E. coli*, the ESBL phenotype predominated (9 cases), with preserved susceptibility to carbapenems; however, the detection of a KPC-producing isolate confirms the dissemination of this resistance mechanism to other Enterobacterales. Likewise, KPC-producing strains of *E. cloacae* and *K. aerogenes* were identified, indicating the circulation of carbapenemases across multiple genera within the Enterobacterales order.

Among non-fermenting bacilli, *P. aeruginosa* retained good

Table 1. *Clinical manifestations at ICU admission in patients who subsequently developed VAP.*

Clinical Presentation	**N (%)**
Asthenia, hyporexia, dyspnea	9 (6.8)
Odynophagia	1 (0.7)
Excessive sweating, precordial pain, liquid stools	1 (0.7)
Excessive sweating, precordial pain, liquid stools	1 (0.7)
Dry cough, fever, malaise, and respiratory difficulty	120 (90.9)
Total	132 (100)

Table 2. *Demographic characteristics of patients with VAP.*

Variable	Survivor (n=41)	Deceased (n=91)	Total (n=132)	p-value
Sex				0.842
Females	12 (31.6%)	26 (68.4%)	38 (28.8%)	
Males	29 (30.8%)	65 (69.2%)	94 (71.2%)	
Age Groups				0.024*
34-53	18 (43.9%)	24 (26.4%)	42 (31.8%)	
54-63	13 (31.7%)	22 (24.2%)	35 (26.5%)	
64-73	7 (17.1%)	26 (28.6%)	33 (25.0%)	
>74	3 (7.3%)	19 (20.9%)	22 (16.7%)	

**p < 0.05 indicates statistical significance using Pearson's chi-square test.*

Table 3. *Association between KPC-producing K. pneumoniae and mortality in patients with VAP.*

Pathogen Type	Total Patients (n)	Deaths (n)	Mortality (%)	*p*-value
KPC-producing *K. pneumoniae*	42	33	78.6%	0.093
Non-KPC-producing *K. pneumoniae*	39	24	61.5%	
Total *K. pneumoniae* isolates	81	57	70.4%	

Table 4. *Antimicrobial susceptibility pattern and resistance mechanisms in microorganisms isolated from patients with VAP.*

Microorganism	N°	Antimicrobial Sensitivity Pattern	Antimicrobial Resistance Pattern	Resistance Mechanisms
K. pneumoniae	33	GEN, MER, AMK, ETP, IMP	AMP, CTX, CRO, CAZ, CIP, TMS, AMS, CXM, CTN, FEP	ESBL
K. pneumoniae	42	AMK	AMP, CTX, CRO, CAZ, CIP, TMS, AMS, GEN, MER, CTN, FEP, CXM, ETP, IMP, NOR	KPC
K. pneumoniae	6	CRO, CIP, AMS, GEN, CTN, AMK, ETP, CTX, CAZ, TMS, CXM, MER, FEP	AMP	–
E. coli	9	FOX, GEN, MER, IMI, TGC, AMK, ETP, DOR	PTZ, CRO, CAZ, CIP, AMS, FEP	ESBL
E. coli	2	CRO, CAZ, FOX, GEN, MER, IMI, FEP, TGC, AMK, ETP, DOR	AMS, PTZ, CIP	–
E. coli	1	AMK, TGC	CRO, CAZ, CIP, AMS, GEN, MER, DOR, IMI	KPC
E. cloacae	6	CTX, CRO, CAZ, CIP, TMS, GEN, MER, FEP, AMK, ETP	CXM, CTN	–
E. cloacae	2	CIP, TMS, AMK	FEP, CTX, CRO, CAZ, CXM, CTN, ETP, MER	KPC
K. aerogenes	4	GEN, AMK	ETP, MER, CTX, CRO, CAZ, CIP, TMS, CXM, CTN	KPC
K. aerogenes	3	CAZ, GEN, MER, IMI, PTZ, FEP, TGC, AMK, ETP, DOR	CXM, CIP	–
P. aeruginosa	6	AMK, MER	FEP, CAZ, PTZ, CIP	–
S. epidermidis	6	GEN, RIF, VA, LZN, DA	CIP, TMS, TET, P, E, LEV, MFX	–
S. marcescens	4	ETP, DOR, MER	AMK, CRO, CAZ, CIP, GEN, FEP	–
S. aureus	2	CIP, TMS, TET, GEN, RIF, OXA, E, VA, LEV, DA, TGC, LNZ, FOX, MFX	P	–
S. aureus	1	CIP, TMS, RIF, VA, LEV, LNZ, MFX	FOX, GEN, TET, P, OXA, E, DA	Inducible clindamycin resistance: Positive; Methicillin-resistant (mecA +)
B. cepacia	1	MEM, AMK	CAZ, TMS, LEV	–
E. faecalis	1	LEV, LNZ	CIP, AMP, TET, PEN, E, VA	Penicillin and vancomycin resistant
K. oxytoca	1	TMS, MEM, AMK, ETP	AMP, CTX, CRO, CAZ, CIP, SAM, CXM, GEN	ESBL
S. hominis	1	CIP, TMS, GEN, VA, LEV, DA, LNZ, FOX	RIF, PEN, E, LNZ	–
S. sciuri	1	CIP, TMS, GEN, RIF, VA, LEV, LNZ, MFX, DA	FOX, OXA, P, E	Methicillin-resistant (mecA +)

GEN: gentamicin, AMK: amikacin, AMP: ampicillin, CTX: cefotaxime, CRO: ceftriaxone, CAZ: ceftazidime, CIP: ciprofloxacin, TMS: trimethoprim-sulfamethoxazole, AMS: ampicillin- sulbactam, CXM: cefuroxime, CTN: cephalothin, FEP: cefepime, NOR: norfloxacin, TGC: tigecycline, FOX: cefoxitin, IMI: imipenem, MER: meropenem, DOR: doripenem, ETP: ertapenem, PTZ: piperacillin. tazobactam, RIF: rifampicin, VA: vancomycin, LNZ: linezolid, DA: clindamycin, TET: tetracycline, P: penicillin, E: erythromycin, LEV: levofloxacin, MFX: moxifloxacin, OXA: oxacillin.

susceptibility to amikacin and meropenem. Regarding Gram-positive cocci, one methicillin-resistant *S. aureus* (mecA-positive) isolate with inducible clindamycin resistance was confirmed, as well as methicillin resistance in *S. sciuri*. Additionally, an *E. faecalis* isolate exhibiting concurrent resistance to penicillin and vancomycin was identified, representing a significant therapeutic challenge.

Of the 49 isolates phenotypically consistent with KPC production, 100% (n = 49) were positive for the bla_{KPC} gene, demonstrating complete concordance between the resistance phenotype and the corresponding genotype.

Specific primers targeting the bla_{KPC} gene enabled the successful amplification of a 538-bp fragment in *K. pneumoniae* isolates exhibiting a phenotype consistent with KPC production by polymerase chain reaction (PCR). Figure 2 presents the results obtained from the amplification process.

Discussion.

VAP is one of the most frequent acquired infections in the ICU. Reported incidences vary widely, ranging from 5% to 40%, depending on the setting and diagnostic criteria. The estimated attributable mortality of VAP is around 10%, with even higher mortality rates in surgical ICU patients [13].

Céspedes et al. [14] report that VAP develops in patients who have been receiving mechanical ventilation for more than 48 hours, with clinical manifestations that may vary depending on

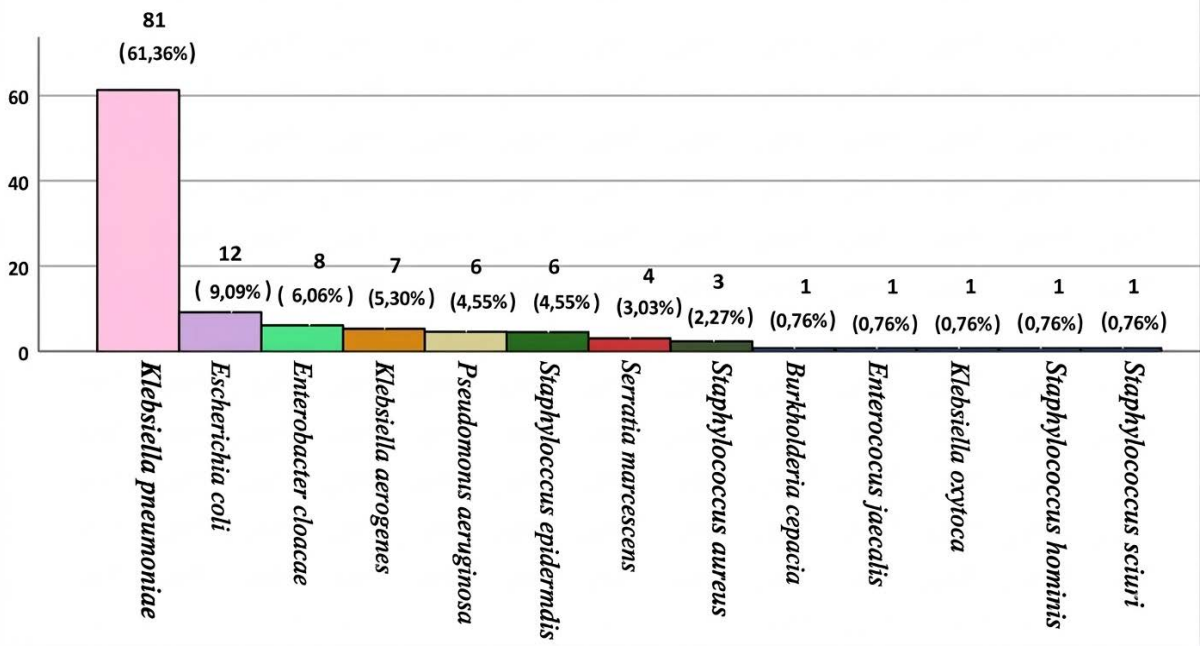

Figure 1. *Microorganisms isolated in VAP in hospitalized patients.*

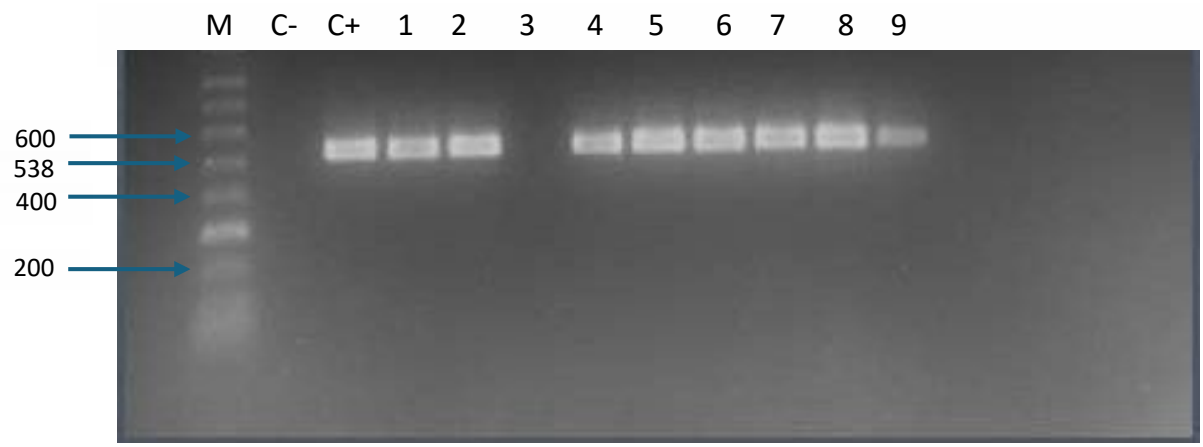

Figure 2. *Agarose gel electrophoresis analysis of PCR products amplified using primers specific for the bla_{KPC} gene from the isolated samples. Lane M: 1 kb DNA size marker (100–1000 bp); Lane C−: negative control; Lane C+: positive control; Lanes 1, 2, 4, 5, 6, 7, 8, and 9: K. pneumoniae isolates positive for the bla_{KPC} gene; Lane 3: empty well (no sample loaded).*

the underlying etiology and severity of the infection. Similarly, Karunarathna et al. [15] describe that symptoms such as cough, sputum production, fever, and chest pain are commonly associated with pneumonia. In the specific context of VAP, additional clinical findings—including leukocytosis, purulent respiratory secretions, abnormalities in blood gas parameters, and persistent fever—are considered key indicators supporting the diagnosis of nosocomial pneumonia.

In our study, 90.9% of patients were admitted to the ICU presenting respiratory symptoms such as dry cough, fever, malaise, and respiratory distress. However, these manifestations correspond to the clinical condition present at the time of ICU admission and are related to the underlying disease that required mechanical ventilation. Therefore, they should not be interpreted as symptoms of VAP, which was diagnosed subsequently during the course of hospitalization.

The study period coincided with the COVID-19 pandemic, a context that significantly influenced the characteristics of the analyzed population. During this time, a high proportion of ICU admissions corresponded to severe SARS-CoV-2 pneumonia requiring prolonged mechanical ventilation. As shown in Table 1, 90.9% of patients presented with symptoms consistent with SARS-CoV-2 infection (dry cough, fever, malaise, and respiratory difficulty), suggesting that many were intubated due to COVID-19-associated pneumonia. This epidemiological scenario likely contributed to the high prevalence of multidrug-resistant Gram-negative pathogens, given that critically ill COVID-19 patients are at increased risk of developing secondary bacterial infections and VAP [16,17]. Although not all cases had laboratory-confirmed SARS-CoV-2 infection due to limited RT-PCR testing availability during the early phase of the pandemic, the clinical presentation supports this association.

Future studies should incorporate systematic SARS-CoV-2 screening to better delineate its contribution to VAP risk and microbial etiology.

Durán et al. [18] report that VAP is one of the leading nosocomial infections in ICUs, largely due to the continuous exposure of the respiratory tract to potentially pathogenic microorganisms. This condition promotes colonization of the upper respiratory tract and impairment of host defense mechanisms, facilitating the aspiration of contaminated secretions into the lungs or their hematogenous dissemination, which may result in acute bacterial pneumonia. Furthermore, bacteria adhering to the endotracheal tube can form biofilms that protect them from host immune responses and may subsequently dislodge into the lower respiratory tract [19].

Although mechanical ventilation is essential for the support of critically ill patients, it also compromises pulmonary clearance mechanisms, thereby increasing the risk of VAP [20] For etiological diagnosis, the most commonly used specimens are endotracheal aspirates and bronchoalveolar lavage fluid [21]. In addition, antibiotic prophylaxis and routine antimicrobial susceptibility testing influence the resistance patterns of the pathogens involved [22].

In the present study, *K. pneumoniae* was the most frequently isolated microorganism (61.4%), followed by *E. coli* (9.1%) and *E. cloacae* (6.1%). These findings are consistent with previous reports indicating that 38% to 50% of VAP cases are attributable to Gram-negative bacteria [23-25].

In addition to *K. pneumoniae*, other VAP-associated pathogens were identified, including *E. coli, E. cloacae, K. oxytoca*, non-fermenting bacilli, and *S. aureus*, many of which exhibited multidrug-resistant profiles, particularly against β-lactams. The production of ESBLs and carbapenemases, together with the presence of resistance genes such as *mecA*, confers a substantial capacity for therapeutic evasion. In this setting, VAP caused by multidrug-resistant organisms represents a major clinical challenge due to its high morbidity and mortality, despite available therapeutic strategies [26,27]

Similarly, Mohapatra et al. [28] reported *K. pneumoniae, A. baumannii, P. aeruginosa, E. coli,* and *S. aureus* as the predominant pathogens and additionally documented cases of *Elizabethkingia meningoseptica*. In their study, Enterobacterales exhibited high susceptibility to tigecycline, whereas *A. baumannii* and *E. meningoseptica* showed greater susceptibility to minocycline; all *S. aureus* isolates were susceptible to vancomycin and linezolid.

Carbapenemase-producing Enterobacterales, particularly KPC-producing *K. pneumoniae*, are spreading rapidly worldwide. In the present study, 42 KPC-producing isolates were identified. In *E. coli*, the ESBL phenotype predominated (9 cases), with preserved susceptibility to carbapenems; however, the detection of a KPC-producing isolate confirms the dissemination of this resistance mechanism to other enterobacterial species. Furthermore, the identification of KPC in *E. cloacae* and *K. aerogenes* underscores the circulation of carbapenemases across multiple genera.

The high prevalence of carbapenem-resistant Gram-negative bacilli represents a serious public health concern, given its association with elevated in-hospital mortality rates that may reach up to 70% [29]. In this context, early diagnosis of pneumonia caused by these pathogens is critical to ensure the timely initiation of targeted antimicrobial therapy, improve clinical outcomes, and support efforts to contain antimicrobial resistance and healthcare costs [30].

The mortality of carbapenemase-producing *K. pneumoniae* infections varies between 22% and 72%, depending on variables such as patient age and comorbidities. The differentiation between colonized and infected patients is one of the factors that complicates a more accurate estimate of mortality. The largest multicenter study to date on carbapenemase-producing *K. pneumoniae* infections found that the highest mortality occurs in VAP and bacteremia, with a mortality rate around 40% [31].

The analysis of the demographic characteristics of the cohort of patients with VAP reveals relevant trends that align with the literature and provide insights into factors associated with mortality. It is important to consider that the study period coincided with the COVID-19 pandemic, a context that substantially modified the clinical profile of patients admitted to ICUs. During this stage, a high proportion of admissions were related to severe pneumonia caused by SARS-CoV-2, a condition that frequently required prolonged mechanical ventilation and increased the risk of developing nosocomial infections, particularly VAP.

In the series analyzed, a clear predominance of the male sex was observed, accounting for 71.2% (94/132) of cases, a finding consistent with that reported by García et al. [32]. However, no statistically significant association was evidenced between sex and mortality ($p = 0.842$), suggesting that although men have a higher incidence of VAP, biological sex does not constitute a determining factor in fatal outcomes once the infection is established.

In contrast, age was identified as a determining prognostic factor, with a statistically significant association observed with mortality ($p = 0.024$). The highest proportion of deaths was concentrated in patients aged 64 to 73 years (28.6%), followed by the 34 to 53 years group (26.4%) and the 54 to 63 years group (24.2%). The elevated mortality in the age group over 60 years coincides with that described by Zamora et al. [33] and Velasco et al. [34], who attribute this susceptibility to immunosenescence and associated comorbidities. Likewise, the mortality recorded in the ≥74 years group (20.9%) confirms the vulnerability of older adult patients, in agreement with reports by Aquino et al. [35], Fernández et al. [36], and Garay et al. [37].

In the pandemic context, these findings acquire special relevance, as patients with severe COVID-19 undergoing prolonged mechanical ventilation presented a higher risk of developing VAP. The combination of prior lung damage due to SARS-CoV-2, immunosuppression associated with critical illness, and prolonged ICU stays created a conducive scenario for the development of secondary bacterial infections, which could have contributed both to the increased incidence and to the elevated mortality observed in the older age groups.

This study identified *K. pneumoniae* as the primary etiological agent of VAP, with a high prevalence of KPC-producing

strains, particularly among hospitalized older adult males. The predominance of this resistance mechanism, together with the high observed lethality, underscores the clinical severity of these infections and the challenges they pose for effective management. In this context, these findings are of significant public health concern, as they reflect the growing burden of multidrug-resistant pathogens in the hospital setting. Consistent with these observations, the overall mortality rate reached 70.4% among patients with *K. pneumoniae*-associated VAP. Although infections caused by KPC-producing strains showed higher mortality (78.6%) compared to non-KPC-producing isolates (61.5%), the difference did not achieve statistical significance ($p = 0.093$), possibly due to the sample size or the influence of concomitant clinical factors. Nevertheless, this trend suggests a clinically meaningful impact, likely related to the limited availability of effective therapeutic options and the increased complexity of patient management, highlighting the importance of early detection and optimization of treatment strategies.

Additionally, the data collection period coincided with the COVID-19 pandemic, which may have influenced the clinical characteristics of the study population. During this time, a substantial proportion of intensive care unit admissions involved patients with severe SARS-CoV-2 pneumonia, often complicated by acute respiratory failure requiring prolonged mechanical ventilation. This scenario has been associated with an increased risk of VAP and secondary bacterial infections caused by multidrug-resistant organisms. Therefore, this epidemiological context should be considered when interpreting the high prevalence of resistant Gram-negative bacteria observed in this study and reinforces the urgent need to strengthen infection prevention and control strategies, as well as to optimize therapeutic approaches to reduce mortality and limit the spread of these pathogens in critical care settings.

Authorship contribution statement.

A.C.G.: writing – original draft (lead); writing - review and editing (equal); Methodology (lead).; Formal analysis (equal); Investigation (equal); Project administration (lead); Visualization (lead). J.A.O: Investigation (equal). A.C.G.: Investigation (equal). J.A,O.: Investigation (equal). J.I.C.: Investigation (equal). J.I.C.: Investigation (equal). A.C.G.: Conceptualization (lead); Funding acquisition (lead); Project administration (supporting). J.A.O.: Conceptualization (supporting); Formal analysis (equal), Project administration (supporting); Visualization (supporting); Supervision (lead). A.E.P.: writing – original draft (supporting); writing - review and editing (equal); Investigation (equal), Project administration (supporting); Visualization (supporting).

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