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Impact of COVID-19 on the prevalence of multidrug-resistant bacteria associated with nosocomial infections in the state of Puebla, Mexico

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Abstract

Antimicrobial resistance (AMR) is one of the leading threats to public health worldwide. This phenomenon, accelerated by the irrational use of antibiotics, has been exacerbated by the COVID-19 pandemic. In the city of Puebla, Mexico, the lack of a comprehensive analysis of the impact of SARS-CoV-2 on AMR in public hospitals justifies this study. The objective was to analyze this impact by comparing the pre-pandemic situation (2015-2020) with the post-pandemic situation (2022-2025). A comprehensive literature review was conducted using databases such as PubMed and Google Scholar, as well as reports from official organizations such as the RHOVE and PRUCA. Studies that reported data on multidrug-resistant bacteria and nosocomial infections in public hospitals in the region were selected. The findings revealed that pathogenic bacteria such as Escherichia coli, Pseudomonas aeruginosa, and Klebsiella pneumoniae were already prevalent before the pandemic. However, during the pandemic, the indiscriminate use of antibiotics in COVID-19 patients accelerated the presence of multidrug-resistant strains in hospitals in the region. Post-pandemic data show that these pathogens have established themselves as a persistent threat. The COVID-19 pandemic exacerbated AMR in Puebla, highlighting the urgent need to implement surveillance and antimicrobial stewardship programs to provide more appropriate treatments and reduce associated morbidity and mortality.

Keywords: Multidrug-resistant bacteria; Healthcare-associated infections; prevalence; COVID-19; Puebla; hospital.

1. Introduction

Today, bacterial resistance to antimicrobials constitutes one of the main challenges to public health and has been classified by the World Health Organization (WHO) as one of the ten most serious problems threatening humanity [1]. According to estimates by the WHO and the Centers for Disease Control and Prevention (CDC) of the United States, this phenomenon affects approximately two million people each year and causes approximately 29,000 deaths in that country [2]. Bacterial resistance is understood as the ability of bacteria to survive and proliferate when exposed to antimicrobial agents [3]. Those that show resistance to three or more classes of antibiotics are considered multi-resistant [2]. This phenomenon is part of a natural process of evolutionary adaptation that allows the survival of species, although it usually develops slowly and steadily over time [4]. Bacterial adaptation is manifested through various resistance mechanisms: intrinsic resistance, which corresponds to the natural and unique capacity of certain bacteria due to the presence of inherited genes that confer protection against antimicrobials; circumstantial resistance, associated with physiological or environmental conditions that limit the action of the antibiotic; and acquired resistance, which is the most clinically relevant. This resistance occurs when microorganisms modify, adapt and transmit resistance genes as a result of selective pressure derived from the use of antimicrobials [5, 6].

This latter type of resistance is favored by practices such as the irrational use of antibiotics, self-medication, and the administration of treatments without prior identification of the causative agent. As a result, an increase in healthcare-

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associated infections (HAIs) has been reported as one of the most frequent complications in the hospital setting. In order to establish a diagnostic framework, NOM-045-SSA2-2005 indicates that, in cases of bacterial infections, the incubation period between 48 and 72 hours after the patient's admission should be considered to classify them as nosocomial or extra-hospital infections [7, 8].

In Mexico, an alarming panorama has been documented, since the WHO has reported that the frequency of HAIs ranges between 2.1% and 15.8% in the hospital units, while in intensive care units (ICUs) the prevalence rises to 23.2% [9, 10]. Likewise, the Hospital Epidemiological Surveillance Network (RHOVE) has identified Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Klebsiella pneumoniae, Staphylococcus epidermidis, and Acinetobacter baumannii as the most frequent multidrug-resistant bacteria from January to May 2025. [11].

In this context, the SARS-CoV-2 pandemic aggravated the situation by generating a high hospital demand that resulted in widespread use of antibiotics due to the absence of a specific antiviral treatment and with the purpose of treating respiratory infections. However, in many cases this practice lacked diagnostic criteria for the causative pathogen, which contributed to the intensification of the bacterial resistance phenomenon [12-13]. In response to this, the WHO, through its Clinical Management Guide for COVID-19 published on January 25, 2021, advised against the indiscriminate use of antibiotics and recommended performing cultures prior to starting therapy, restricting its administration only to patients with confirmed nosocomial infection [12].

Most studies on drug-resistant bacteria in Mexican hospitals have been based on reports of patients with nosocomial infections in public institutions. However, in the city of Puebla, the available evidence is limited and primarily refers to studies conducted in higher education institutions. To date, there is no comprehensive analysis evaluating the impact of the SARS-CoV-2 pandemic on the prevalence of multidrug-resistant microorganisms associated with nosocomial infections. Therefore, this review aims to analyze this impact, comparing the epidemiological situation before and after the pandemic, in order to provide evidence that contributes to the understanding and control of bacterial resistance.

2. Methodology

2.1. Research Design

A longitudinal, comparative, and bibliographic study was conducted to analyze the prevalence of multidrug-resistant bacteria associated with nosocomial infections in secondary and tertiary public hospitals in the city of Puebla, Mexico. The analysis was structured into two periods: pre-pandemic (2015–2020) and post-pandemic (2022 and 2025), considering the impact of SARS-CoV-2 on antimicrobial resistance patterns.

Information was collected through an exhaustive search of scientific databases such as PubMed, ClinicalKey, ScienceDirect, Google Scholar, and Mendeley. Official national and international sources were also consulted, including the World Health Organization (WHO), the National Institute of Public Health, the Hospital Epidemiological Surveillance Network (RHOVE), the University Program for Antimicrobial Resistance Control (PUCRA), and the National Institute of Geography and Statistics (INEGI).

2.2. Data Sources

2.2.1. Inclusion Criteria

- Publications published between 2015 and 2025.
- Documents reporting data on multidrug-resistant bacteria and nosocomial infections in secondary and tertiary care hospitals in the city of Puebla, Mexico.
- Complete reports from official databases, both in the state of Puebla and nationally in Mexico.

2.2.2. Exclusion Criteria

- Reports without full text access.
- Studies presenting data from private hospitals in the city of Puebla.

2.3. Search Strategies

The search used combinations of keywords joined by Boolean operators (AND, OR), such as: "multidrug-resistant bacteria" AND "COVID-19" AND "hospitals" AND "Puebla", "nosocomial infections" OR "healthcare-associated infections". Filters were applied by year of publication, type of study, and full-text availability.

2.4. Study Area

The geographic scope of the study focused on the city of Puebla, with an emphasis on secondary and tertiary public hospitals. National data from Mexico were also incorporated.

3. Results and Discussion

3.1. Epidemiology of Nosocomial Pathogens in the Pre-Pandemic Period (2015-2020)

During the pre-pandemic period, the epidemiology of healthcare-associated infections (HAIs) in hospitals in the city of Puebla showed notable variability. A 2015 study at the Mexican Social Security Institute (IMSS) [14] documented that, of 844 samples, *E. coli* (23%) and *S. aureus* (17%) were the most frequent pathogens. In contrast, at the Puebla Women's Hospital (2015-2017), *P. aeruginosa* (49.5%) was the predominant microorganism, followed by *K. pneumoniae* (17.8%) [15]. These differences can be attributed to the specialties and patient profiles of each center. Furthermore, both reports agree on a high prevalence of clinically relevant pathogens, which also include S. epidermidis (12%) and A. baumannii (12%).

National trends were consistent with local findings. The 2015 Hospital Epidemiological Surveillance Network (RHOVE) [16] recorded that, of 34,884 isolates, *E. coli* was the most frequent (18.8%), followed by *P. aeruginosa* (12.4%) and *K. pneumoniae* (9.5%). Similarly, the University Antimicrobial Resistance Surveillance Program (PRUCA) (2017-2020) [17] confirmed that *E. coli* (29%), *S. aureus* (22%), and *K. pneumoniae* (17%) were the most prevalent pathogens in blood culture studies. These findings, supported by morbidity reports from the Puebla Ministry of Health (2018-2020) [18], underline that pathogens such as *E. coli*, *K. pneumoniae*, *P. aeruginosa*, and *S. aureus* already constituted a threat to public health before the pandemic.

3.2. The Impact of the Pandemic (2020-2021)

The arrival of the COVID-19 pandemic in 2020 represented a turning point in healthcare systems worldwide, and Mexico was no exception. According to data from INEGI (National Institute of Statistics and Geography), 747,784 deaths were recorded in the country in 2019, rising to 1,122,249 cases in 2021, of which 92.5% were linked to health-related causes. This increase in mortality is primarily attributed to the impact of SARS-CoV-2, especially in older adults [19].

In the hospital setting, given the high demand for patients with SARS-CoV-2 and the lack of curative treatment, medical staff opted for early empirical antibiotic therapy [20]. This strategy, justified by bacterial coinfections, was later questioned because studies showed that, in most cases, microbiological isolations were not performed, therefore, they did not document improvements in the patient's health [21].

Data reported from the Puebla region reflect these global trends. International studies in Spain, France, and China [22, 23, 24] documented coinfections with resistant pathogens such as S. pneumoniae, *S. aureus*, *P. aeruginosa*, *K. pneumoniae*, Enterococcus faecium, and A. baumannii; an analysis at the Regional Hospital of the Institute of Security and Social Services for State Workers (ISSSTE) in Puebla (2020–2021) [25] identified that these pathogens, including *E. coli*, were responsible for 36% of coinfections in 103 patients with pneumonia. The identified pathogens are consistent with international reports and, crucially, are known for their resistance to first-line antibiotics.

The massive and indiscriminate use of broad-spectrum antibiotics such as carbapenems during this period accelerated the detection of multi-resistant strains. Furthermore, a study by the Mexican Social Security Institute (IMSS) in Puebla (2020-2023) [26] showed that, of 704 blood cultures, the most isolated pathogens were *E. coli* (27%), S. epidermidis (26%), and S. hominis (14%).

3.3. Post-Pandemic Patterns

During 2023, 799,869 deaths were recorded in Mexico, with a crude death rate of 619 deaths per-100,000 inhabitants. Of the total deaths, 89.5% were related to medical causes. In this case, adults aged 65 years and older constituted the most vulnerable group, representing 63% of all deaths, with respiratory system diseases being the main cause. This demonstrates the susceptibility of this population to acute and chronic respiratory infections. In contrast, among children under five years of age, the most frequent causes of death were diarrheal diseases and gastroenteritis of presumed infectious origin, followed by respiratory infections such as pneumonia and bronchitis, according to data from INEGI [27].

In this context, the persistence of respiratory and infectious diseases in the Mexican population allows them to be associated with the bacterial resistance that has remained or increased in the years following the pandemic. National surveillance by the RHOVE (2022-2025) [11, 28, 29, 30] has reported *E. coli, P. aeruginosa, and K. pneumoniae* as the main etiological agents of HAIs. This phenomenon is clearly visible when comparing the data from 2015 with those from the post-pandemic period (Figure 1) [11, 26, 28, 30], which demonstrates the persistence of these microorganisms as a threat.

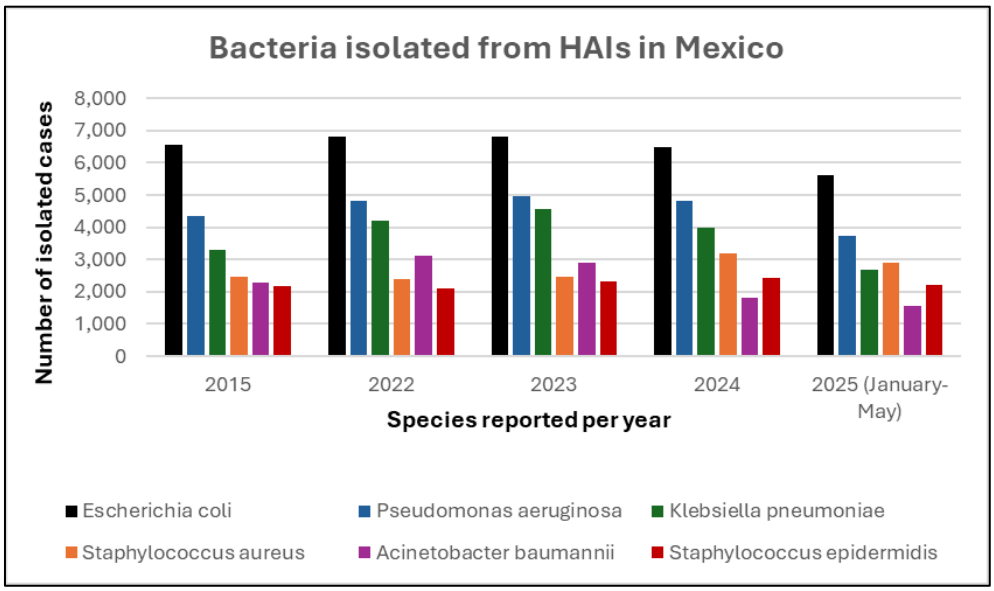

Figure 1 Comparison of the main isolated microorganisms responsible for healthcare-associated infections (HAIs) in Mexico during the years 2015, 2022, 2023, 2024 and the period from January to May 2025. No official reports are available between the years 2016 and 2021

This increase in the prevalence of multi-resistant pathogens coincides with the total number of reported cases of the main HAIs at the national level (Figure 2) [11, 16, 28, 30].

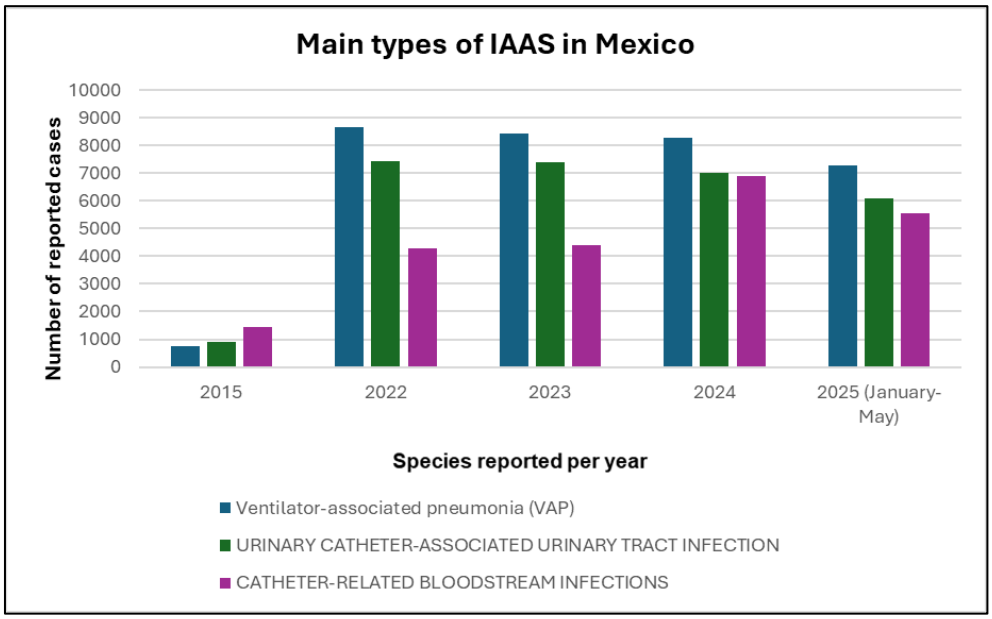

Figure 2 Reported cases of the main healthcare-associated infections (HAIs) in Mexico during the years 2015, 2022, 2023, 2024 and the period from January to May 2025. No official records are available between 2016 and 2021 according to reports from the Hospital Epidemiological Surveillance Network

The reviewed data show a direct correlation between *E. coli* as the most prevalent multidrug-resistant microorganism and urinary tract infections (UTIs), which are consistently among the top cases reported in public hospitals in Puebla. This association is clinically relevant, since *E. coli* is the main producer of extended-spectrum beta-lactamases (ESBLs), these enzymes confer resistance to commonly used antibiotics such as cephalosporins, ampicillin, and penicillin. At the hospital level, UTIs are frequently treated empirically without prior urine cultures, which favors the selection of resistant strains and hinders therapeutic management [31, 32].

On the other hand, the high incidence of COVID-19 [33], which ranked as the third leading cause of hospital admissions in Puebla, led to a significant increase in cases of respiratory failure and pneumonia, requiring widespread use of mechanical ventilation. This condition increased patients' exposure to nosocomial bacterial infections and the administration of broad-spectrum antibiotic therapies [34].

In this context, *P. aeruginosa* has been reported as the main etiological agent of ventilator-associated pneumonia (VAP), due to its ability to form biofilms on endotracheal tubes and its high prevalence in intensive care units (ICUs) [35]. Likewise, *K. pneumoniae* has also been identified as a cause of VAP, in addition to being one of the microorganisms most frequently implicated in catheter-associated bloodstream infections [36].

These trends align with the epidemiological situation in the state of Puebla, where acute respiratory, intestinal, and urinary tract infections were the leading causes of hospital morbidity in 2021 [32], despite clinical guidelines recommending that, antibiotic treatment be initiated only after microbiological confirmation of the pathogen and a reassessment after 72 hours [21, 37]. During the pandemic, irrational use of antimicrobials was observed due to the urgency of treatment, which favored the development of bacterial resistance and caused some adverse effects such as organ damage and allergic reactions [21, 38].

According to Figure 2, it was expected that, starting in 2022, during and after the COVID-19 pandemic, the prevalence of healthcare-associated infections (HAIs) would show a steady increase, especially due to the intensive use of invasive devices and the high demand on medical personnel. However, the data do not reflect significant increases in subsequent years. This situation could suggest that priority was given to the care of patients with SARS-CoV-2, neglecting the capacity of hospital systems to report and notify HAI cases, thus weakening epidemiological surveillance [39]. Furthermore, when antibiotic therapy was implemented in COVID-19 patients without isolation to confirm bacterial coinfections, many of these patients were treated on an outpatient basis without hospitalization, which limited the reporting of HAI cases. In addition, according to INEGI data, in 2021, 47.3% of deaths in Mexico were registered at home, most of them related to medical causes [19]. The high proportion of out-of-hospital deaths suggests that HAI cases were not followed up or considered for epidemiological recording.

3.4. Limitations of the study

A significant limitation of this study is the scarcity of consistent and centralized reports on the notification of pathogens and healthcare-associated infections (HAIs), in public hospitals in the state of Puebla between 2015 and 2025. The lack of systematic records hinders obtaining a comprehensive view of the dynamics and evolution of multidrug-resistant bacteria in the region. Therefore, the available data, while valuable, exhibit heterogeneity that highlights the need to promote the systematization and publication of research that more consistently documents the frequency and distribution of multidrug-resistant bacteria in the state.

4. Conclusion

The COVID-19 pandemic accelerated the emergence and spread of multidrug-resistant pathogens in the state of Puebla and nationwide. The high prevalence of microorganisms such as *E. coli*, *P. aeruginosa* and *K. pneumoniae*, which was already a problem before the pandemic, was exacerbated by the irrational use of broad-spectrum antibiotics in the treatment of patients with SARS-CoV-2 and for prevalent infections such as ventilator-associated pneumonia, urinary tract infections, and catheter-associated bloodstream infections. This practice generated massive selection pressure in the hospital setting, contributing to the consolidation of these microorganisms as a persistent threat.

This study demonstrates that, despite the limited number of studies specifically focused on the Puebla region, the local problem is clearly consistent with national and international trends. The lack of a unified surveillance system and consistent reporting hinders comprehensive monitoring of antimicrobial resistance and the implementation of effective public health policies.

To mitigate this problem, it is urgent to strengthen infection control measures and promote the rational use of antibiotics in Puebla hospitals. This includes implementing antimicrobial stewardship monitoring programs. Simultaneously, public awareness campaigns regarding bacterial resistance should be promoted, using language accessible to the general public, to foster social awareness of the impact of nosocomial infections on public health.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of ethical approval

The present research work does not contain any studies performed on animals/humans' subjects by any of the authors"

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