



## Occurrence of isolates resistant to quaternary ammonium obtained from a healthcare environment in the metropolitan region of Belém-PA

Ocorrência de isolados resistentes à amônia quaternária obtidos de um ambiente de assistência à saúde na região metropolitana de Belém-PA

Ocurrencia de aislamientos resistentes al amonio cuaternario obtenidos en un ambiente de salud en la región metropolitana de Belém-PA

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### ABSTRACT

**Objective:** To carry out the phenotypic characterization of bacterial isolates resistant to quaternary ammonium to evaluate the effectiveness of the biocide in microbiological control. **Methods:** This was an experimental research, conducted based on the isolation of microbial species from contact surfaces in a regional hospital to identify bacterial strains resistant to quaternary ammonia. **Results:** 54 isolates were obtained from different areas of the hospital, 11% confirmed as gram-negative species of the Enterobacteriaceae family and 14% as *Staphylococcus* spp. The average Minimum Inhibitory Ammonia Concentration between the strains was lower than 0.2%/L, but some species revealed greater resistance. From the antibiogram, one of the phenotypes was found to be resistant to all antimicrobials tested. According to Pearson's correlation test, there was no significance between antibiotic halos and MIC. **Conclusion:** It is evident that quaternary ammonium had an effect on the majority of isolates, however, others resisted high concentrations of the biocide, suggesting an alert to the importance of monitoring to prevent the spread of resistant bacteria.

**Keywords:** Drug resistance bacterial, Disinfectants, Hospital.

### RESUMO

**Objetivo:** Realizar a caracterização fenotípica de isolados bacterianos resistentes à amônia quaternária para avaliar a eficácia do biocida no controle microbiológico. **Métodos:** Trata-se de uma pesquisa experimental, conduzida a partir do isolamento de espécies microbianas de superfícies de contato em um hospital Regional para a identificação de cepas bacterianas resistentes à amônia quaternária. **Resultados:** Foram obtidos 54 isolados em diferentes áreas do hospital, 11% confirmados como espécies gram negativas da família Enterobacteriaceae e 14% como *Staphylococcus* spp. A média da Concentração Inibitória Mínima de Amônia entre as cepas demonstrou-se menor que 0,2%/L, mas algumas espécies revelaram ter resistência maior. A partir do antibiograma, encontrou-se um dos fenótipos com resistência a todos os antimicrobianos testados. De acordo com o teste de correlação de Pearson, não houve significância entre os halos dos antibióticos e a CIM. **Conclusão:** É evidente que a amônia quaternária surtiu efeito sobre a maioria dos isolados, no entanto, outras resistiram em altas concentrações do biocida, sugerindo um alerta para a importância do monitoramento para evitar a disseminação de bactérias resistentes.

**Palavras-chave:** Farmacorresistência bacteriana, Desinfetantes, Hospital.

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## RESUMEN

**Objetivo:** Realizar la caracterización fenotípica de aislados bacterianos resistentes al amonio cuaternario para evaluar la efectividad del biocida en el control microbiológico. **Métodos:** Se trata de una investigación experimental, realizada a partir del aislamiento de especies microbianas de superficies de contacto en un hospital regional para identificar cepas de bacterias resistentes al amoníaco cuaternario. **Resultados:** Se obtuvieron 54 aislamientos de diferentes áreas del hospital, 11% confirmados como especies gramnegativas de la familia Enterobacteriaceae y 14% como *Staphylococcus* spp. La Concentración Mínima Inhibitoria de Amoníaco promedio entre las cepas fue inferior a 0,2%/L, pero algunas especies revelaron mayor resistencia. A partir del antibiograma, se encontró que uno de los fenotipos era resistente a todos los antimicrobianos probados. Según la prueba de correlación de Pearson no hubo significación entre los halos de antibióticos y la CIM. **Conclusión:** Es evidente que el amonio cuaternario tuvo efecto en la mayoría de los aislamientos, sin embargo, otros resistieron altas concentraciones del biocida, lo que sugiere una alerta sobre la importancia del monitoreo para prevenir la propagación de bacterias resistentes.

**Palabras clave:** Farmacorresistencia bacteriana, Desinfectantes, Hospital.

## INTRODUCTION

Healthcare-associated infections affect patients in hospitals and other healthcare settings and are linked to the assistance provided in these locations. This issue is highly relevant to public health due to its contribution to hospital mortality, especially among immunocompromised patients, and is exacerbated by antimicrobial resistance (VICARI NG, et al., 2021). In this context, biocides are antimicrobial agents primarily used for microbiological control in healthcare environments (BARALDI M, 2022). However, their application has been debated, as improper use and incorrect concentrations can promote the selection of resistant strains in the environment (MAILLARD JY, 2018).

Exposing microorganisms to sub-inhibitory concentrations of biocides is not recommended as it may contribute to strain selection and cross-resistance. Cross-resistance occurs when microorganisms exposed to sub-inhibitory doses of a biocide become resistant to other unrelated antimicrobials, reducing the effectiveness of both biocides and antibiotics (PEREIRA BMP, et al., 2021). Negligence in hospital care—stemming from infrastructure deficiencies, poor infection control, and inadequate staffing—has been linked to the development of antimicrobial resistance to biocides in hospitals (DE MELO RC, et al., 2020). According to the World Health Organization (WHO), resistance among bacteria associated with sepsis in hospitals increased by 50% in 2022.

Few studies in Brazil have investigated or identified biocide-resistant strains. A study conducted by the Federal University of Espírito Santo (2022) analyzed the susceptibility of Gram-negative *Escherichia coli* strains to biocides, finding reduced susceptibility to 2% chlorhexidine digluconate (ABRANTES JM e NOGUEIRA JMR, 2021). In Natal, Rio Grande do Norte (2019), researchers found low susceptibility to biocides among most *Acinetobacter baumannii* isolates, with resistance often associated with chlorhexidine and the presence of the *qacE* gene. These resistant strains were more prevalent in public hospitals, suggesting microbiological control failures (ÉVORA BHSR, 2019).

Although antimicrobial resistance is a global concern, it remains underreported in low-income countries despite high mortality rates. Self-medication, improper drug use (often due to lack of accurate diagnosis), poor hygiene and sanitation, and the absence of regulation and control are factors that exacerbate cases of antimicrobial resistance and healthcare-associated infections (DADGOSTAR P, 2019). Thus, the objective of this study was to phenotypically characterize bacterial isolates resistant to quaternary ammonium compounds obtained from a hospital in the metropolitan region of Belém, PA.

## METHODS

### Sampling

The hospital, located in the metropolitan region of Belém, has been operational for 24 years and has the capacity for up to 500 monthly admissions across various specialties, in addition to outpatient care. Sampling involved collecting surface swabs from contact points (chairs, stretchers, doors, windows, and gurneys) in

different hospital wards between June and August 2024. A total of 20 samples were collected using sterile swabs, which were stored in tubes containing 12 mL of peptone water. The samples were transported in pre-disinfected isothermal containers.

### Pre-enrichment, Isolation, and Biochemical Identification

Resistant strain selection involved pre-enriching the samples in 20 tubes containing 45 mL of tryptic soy broth (TSB), followed by incubation at 36°C for 48 hours. Subsequently, 10 µL of culture were streaked onto tryptic soy agar (TSA) plates supplemented with ammonium and MacConkey agar and incubated again. The resulting colonies were transferred to inclined TSA tubes and incubated for 24 hours. According to the National Health Surveillance Agency (ANVISA) guidelines, isolates underwent Gram staining for morphological evaluation. Gram-negative bacteria were subjected to biochemical tests such as TSI, citrate, and motility assays to identify Enterobacteriaceae strains.

### MIC Determination and Antibiotic Sensitivity Profile

The MIC of quaternary ammonium compounds was determined using the microdilution method following ANVISA protocols (2008). Dilutions were prepared in Mueller-Hinton broth, ranging from 0.025% to 0.2%. Each isolate was adjusted to a turbidity equivalent to 0.5 McFarland standards and inoculated into the dilutions. After incubation at 36°C for 24 hours, the lowest concentration with no turbidity was recorded as the MIC. Antibiotic susceptibility testing by disk diffusion followed the Brazilian Committee on Antimicrobial Susceptibility Testing (BRCAST) guidelines, recommended by ANVISA (2021). Antibiotics tested included ciprofloxacin, amoxicillin, tetracycline, and azithromycin. Plates were incubated at 37°C for 24 hours.

### Data Analysis

Data were organized in Microsoft Excel (2019) spreadsheets for descriptive statistical analysis, including box plot graphs and tables. Pearson's correlation test was used to analyze the relationship between the MIC of quaternary ammonium compounds and inhibition zone diameters observed in the antibiotic disk diffusion test. The statistical analysis was performed using BioEstat software (Ayres M, et al., 2007), and p-values < 0.05 were considered significant.

## RESULTS

A total of 54 isolates were obtained from the collected samples (**Table 1**). Most strains were retrieved from surfaces frequently in contact with patients and staff.

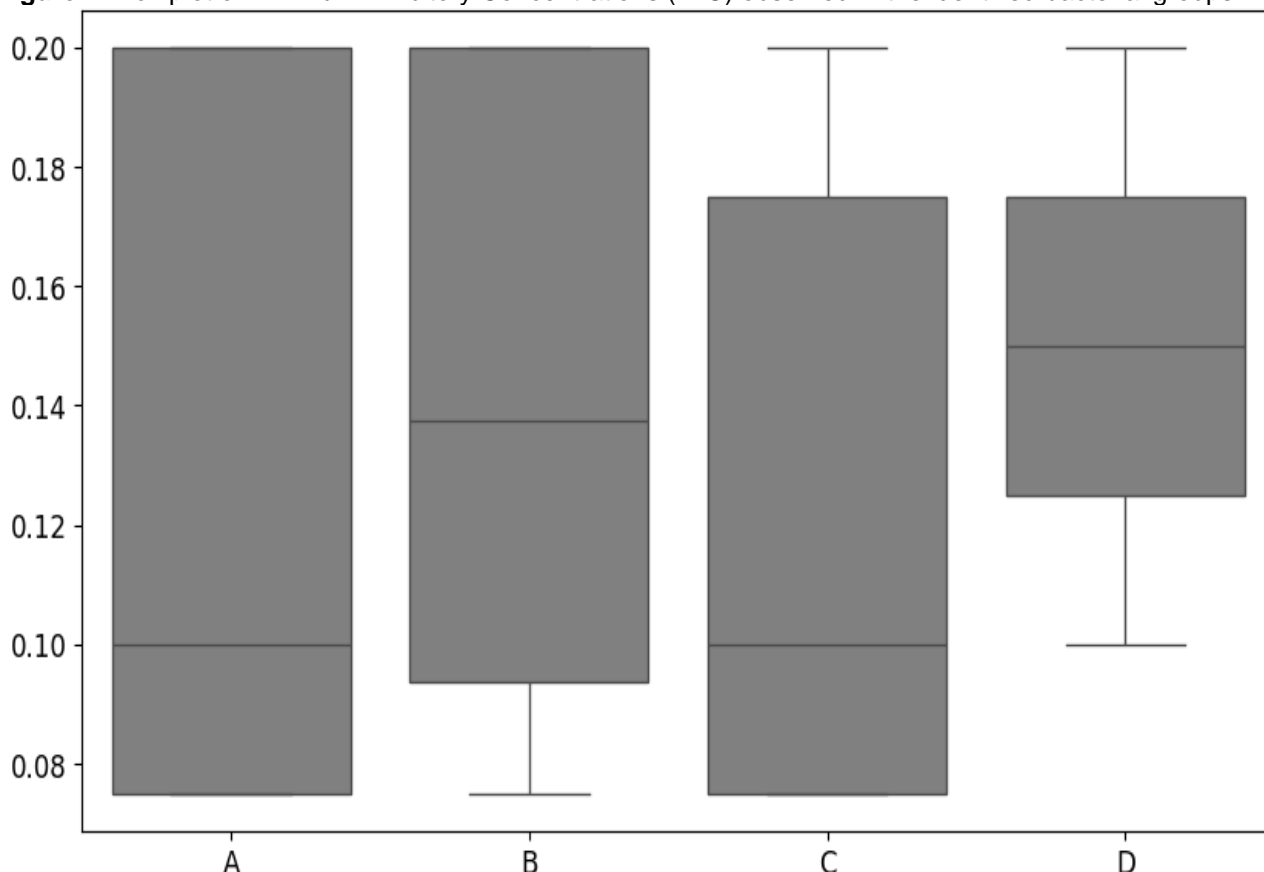
**Table 1-** Percentage of bacterial group isolated and identified by collection site at the Hospital in the Metropolitan Region of Belém.

Bacterial Group Isolated	N (%)	Sampling locations
Not identified	24 (44%)	Main Door; Nursing Door; Office Door 2; Emergency Room Chair; ICU Door
Gram-positive Cocci	13 (24%)	Main Door; Emergency Room Door; Stretcher and Chair; ICU Door; Reception Chair
<i>Staphylococcus</i> spp.	8 (14%)	Reception Chair; Emergency Room Door and Stretcher; ICU Door; Operating Room Door; Central Door
<i>Escherichia coli</i>	6 (11%)	Emergency Room Chair and Stretcher; ICU Door; Operating Room Door; Nursing Door
Gram-positive bacilli	2 (3%)	Emergency Stretcher
Gram-negative cocci	1 (1%)	Emergency Chair

**Source:** Costa ES, et al., 2025.

Among the identified isolates, Gram-positive cocci were the most frequent group (24.1%), followed by *Staphylococcus* spp. (14.8%). After biochemical identification, MIC evaluations of the identified bacteria were conducted (**Figure 1**).

**Figure 1-** Box plot of Minimum Inhibitory Concentrations (MIC) observed in the identified bacterial groups.



**Legend:** A – *Escherichia coli*; B – *Staphylococcus* spp.; C – Cocos Gram positivos; D – Bacilos Gram positivos. **Source:** Costa ES, et al., 2025.

The average MIC across all strains was approximately below 0.2%/L. *Escherichia coli* displayed a wide range of MIC values (0.08 to 0.20), with a median of 0.10. In contrast, *Staphylococcus* spp. (Group B) exhibited a more asymmetric distribution, with most data concentrated at lower values. Some Gram-positive isolates were inhibited only at a concentration of 0.175% quaternary ammonium. Due to their small representation, Gram-negative cocci were excluded from the box plot analysis.

Subsequent antibiotic susceptibility tests revealed distinct phenotypic profiles. For *Escherichia coli*, four phenotypes (A, B, C, and D) were identified, all classified as multidrug-resistant. For *Staphylococcus* spp., three phenotypes (E, F, and G) were identified (**Table 2**). The most frequent phenotype, A, exhibited resistance to all tested antibiotics (amoxicillin, azithromycin, tetracycline and ciprofloxacin).

It is important to note that resistance to Azithromycin was the most observed, with the exception of phenotype F, which was sensitive not only to this, but to the other two antimicrobials tested. In some phenotypes, it was not possible to identify the halos formed in the face of all antibiotics due to their absence.

This phenotypic profile of antibiotic-resistant strains was drawn using only the isolates identified as *Escherichia coli* of the Enterobacteriaceae family, and *Staphylococcus* spp., since the BRCast (2021) and ANVISA (2021) manuals establish the cutoff points for defining the sensitivity profile according to the species/family taxonomic level, making it impossible to define the profile of the other groups.

**Table 2-** Phenotypic profiles of *Escherichia coli* and *Staphylococcus* spp. resistant to quaternary ammonium, determined through antibiotic sensitivity tests (disk diffusion).

Antimicrobial					
Phenotypes	Nº Strains	Amoxicillin (20 µg)	Azithromycin (15 µg)	Tetracycline (30 µg)	Ciprofloxacin (5 µg)
A	3	Resistant	Resistant	Resistant	Resistant
B	1	Resistant	Resistant	Resistant	Unidentified
C	2	Unidentified	Resistant	Resistant	Resistant
D	1	Unidentified	Resistant	Resistant	Unidentified
E	1	Resistant	Resistant	Unidentified	Resistant
F	2	Unidentified	Susceptible	Susceptible	Susceptible
G	1	Unidentified	Resistant	Susceptible	Resistant

**Legend:** A, B, C e D represent *Escherichia coli*; E, F e G represent *Staphylococcus* spp. **Source:** Costa ES, et al., 2025.

Pearson's correlation test evaluated potential relationships between MIC values for quaternary ammonium and inhibition zones observed in the disk diffusion tests for each antibiotic (**Table 3**). No significant correlation was identified between these variables.

**Table 3-** Pearson Correlation Coefficients (r) between Minimum Inhibitory Concentrations (MIC) of Quaternary Ammonium and Antibiotic Inhibition Zones.

Variable Comparison	r Value	p Value
MIC and Amoxicillin Halos	-0.119	0.588
MIC and Azithromycin Halos	-0.078	0.633
MIC and Ciprofloxacin Halos	-0.243	0.147
MIC and Tetracycline Halos	0.036	0.825

**Source:** Costa ES, et al., 2025.

## DISCUSSION

In hospitals and healthcare environments, there is a constant flow of individuals, including patients and professionals, which increases the risk of infectious agent transmission (**Table 1**). This highlights the importance of ensuring proper sanitation in critical areas, particularly those involving the handling of equipment and the circulation of people. The presence of certain bacterial groups may indicate a risk within the context of nosocomial infections (FERREIRA MA, et al., 2023).

Some bacterial groups identified in the sampling sites (**Table 1**) suggest the occurrence of cross-contamination. This is likely due to the inadequate sanitization of contact surfaces, leading to the accumulation of microorganisms originating from the skin microbiota (CORREIA ER, et al., 2021). In this context, it was observed that 24% of the isolates belonged to the group of Gram-positive cocci. This may be related to their ability to persist on surfaces for extended periods, attributed to their morphology. This group constitutes part of the normal microbiota and features a cell wall composed of a thick peptidoglycan layer, which aids in resistance to diverse environmental conditions (ERKMANN VF, et al., 2023).

Additionally, the presence of isolates from the genus *Staphylococcus* spp. (14%) (**Table 1**) was noted. This is a common group found on the skin, capable of causing diseases ranging from minor infections, such as boils, to more severe conditions, such as meningitis and pneumonia (NORBERG AN, et al., 2022).

Furthermore, the occurrence of *Escherichia coli* (11%) (**Table 1**) is noteworthy. This species is typically found in the gastrointestinal tract, and its presence on contact surfaces may indicate fecal contamination. This raises concerns about the effectiveness of hand hygiene practices among both healthcare professionals and patients in these environments (SIMPLÍCIO IOB, et al., 2021).

The efficiency of cleaning and disinfection of hospital surfaces can be directly related to the training of the team involved and the correct choice and application of the products used, when these practices are neglected, the risk of failures in infection control increases significantly, compromising the safety of the hospital



environment, so the training of cleaning professionals is essential, however, the lack of adequate training is a reality in many health services (CORREA JS, et al., 2022).

It was also noted that 44% of the isolates could not be identified (**Table 1**), even after cultivation on growth media. This may be related to the environmental conditions from which the samples were collected, as contact surfaces influence bacterial physiology and, consequently, nutrient absorption necessary for their development. Nutrient scarcity, biofilm formation and environmental stressors are factors that highlight atypical bacterial growth patterns under varying environmental pressures (MADIGAN MT, et al., 2018).

Contact surfaces such as door handles, stretchers, doors, and chairs, which were the sites of sample collection, provide limited nutrients for bacteria. Consequently, bacterial metabolism is reduced, altering the physiology of their cell walls—structures that determine morphology and Gram staining identification. Additionally, external factors such as dehydration and high temperatures act as stressors, directly affecting cellular growth (MADIGAN MT, et al., 2018).

In this study, a potential explanation for the observed hygiene protocol failures is the resistance of all isolates to quaternary ammonium compounds. In this context, variability in the minimum inhibitory concentration (MIC) was observed among the different bacterial groups. The average MICs for the strains were below 0.2% w/v, indicating that most isolates were susceptible to this biocide according to the standards recommended by ANVISA.

However, the *Escherichia coli* strains (Group A - **Figure 1**) exhibited a wide range of MIC values, fluctuating between 0.08 and 0.20, with a median of 0.10. This suggests that certain strains are more resistant to 0.2% quaternary ammonium, requiring a higher concentration of the biocide to inhibit growth. The observed variability may indicate that *E. coli* possesses different resistance profiles, consistent with studies that identify this bacterium as one of the most prone to developing antimicrobial resistance (AGOSTINHO JMA, et al., 2020).

Conversely, the *Staphylococcus* spp. group (Group B - **Figure 1**) displayed a more concentrated distribution of MIC values at lower levels, with a median of 0.12. This lower variability and MIC concentration suggest greater sensitivity of these strains to the tested antimicrobial, indicating that these bacteria may be more susceptible to microbial control (BIER D, et al., 2022).

Other groups also presented values within the acceptable range, with specific variations, such as the group of Gram-positive cocci, as some isolates were only inhibited at a concentration of 0.175%. This may be attributed to the morphology of the isolates, which renders them more resistant to certain concentrations of quaternary ammonium and highlights a concern for potentially resistant strains circulating in the region (ERKMANN VF, et al., 2023). Therefore, the obtained data suggest the presence of distinct phenotypic profiles within a single bacterial group (**Figure 1**).

According to Furtado et al. (2019), one of the primary concerns regarding the rational application of antimicrobials is directly associated with their inappropriate use. A considerable variation in antimicrobial usage is observed across hospitals. Hence, broader and more rigorous monitoring of excessive antimicrobial use and the circulating strains in hospital environments is required. Regarding the antibiotic susceptibility profile (**Table 2**), it is evident that among the *Escherichia coli* isolates, from the Enterobacteriaceae family, phenotype A exhibits resistance to all tested antibiotics, classifying it as multidrug-resistant. Multidrug resistance poses a significant clinical concern due to the increase in hospitalization rates, resulting in higher morbidity and mortality rates.

The mechanisms of bacterial resistance are directly linked to this multidrug resistance, as they can inhibit the desired effects of the drugs (ROZWADOWSKI M and GAWEL D, 2022). *Escherichia coli* can cause infections in various parts of the body. Its antibiotic treatment depends on the type of infection and the strain involved. For instance, in urinary tract infections, common antibiotics include ciprofloxacin and amoxicillin. However, these bacteria can develop resistance mechanisms to antimicrobials, and the spread of these resistant strains may be linked to the excessive prescription of such antibiotics, complicating the treatment of these infections (LEITE MS, et al., 2019).

The *Staphylococcus* spp. isolates (F and G) were susceptible to tetracycline, whereas phenotype E demonstrated resistance to amoxicillin, azithromycin, and ciprofloxacin. A higher prevalence of resistance to azithromycin was notable, explained by Gessner MF (2022), who highlighted that the improper use of this antibiotic significantly increases bacterial resistance rates. During the COVID-19 pandemic, numerous attempts to combat the SARS-CoV-2 virus were observed, with azithromycin being widely prescribed during this period. This antibiotic was intended to inhibit viral replication and act as an immunomodulator. However, azithromycin's efficacy against COVID-19 remains unproven, and its indiscriminate use during the pandemic led to a significant number of adverse drug reactions, including gastrointestinal disturbances and elevated liver transaminase levels.

The improper treatment of COVID-19 with various medications and the use of antibiotics as preventive measures may have contributed to antimicrobial resistance (TANWIR S, et al., 2024). Among all tested antibiotics, tetracycline demonstrated the highest efficacy against the strains due to its use in treating a wide range of bacterial infections. According to Kounatidis D, et al. (2024), tetracycline's efficacy may be linked to its broad spectrum; however, a significant number of resistant bacteria has been observed.

The identification of resistance to commonly used antibiotics, such as amoxicillin and ciprofloxacin, challenges the limits of conventional antimicrobial treatments, necessitating the search for compounds with mechanisms of action less susceptible to resistance development (OSHIRO BK and MARTINS DM, 2024). Thus, the resistance to each tested antibiotic was evaluated, and no relationship with resistance to quaternary ammonium was observed.

Certain microorganisms can develop resistance mechanisms to both biocides and antibiotics, known as cross-resistance. This occurs because the mechanisms used to resist antibiotics are often similar to those employed to withstand biocides, such as efflux pumps that expel both biocides and antibiotics from within the cell. As explained by Da Silva LOP et al. (2023), certain biocides, such as triclosan, chlorhexidine, quaternary ammonium, and alcohols (ethanol and isopropanol), demonstrate a relationship with antibiotic cross-resistance. This is of great interest in hospital environments, as intensive biocide use may contribute to increased bacterial resistance (ÉVORA BHSR, 2019).

Therefore, the Pearson Correlation Test was applied to analyze this cross-resistance among the isolates (**Table 3**). However, no significance was observed, indicating no statistically significant linear relationship between the MIC values and the inhibition zones in the antibiogram for quaternary ammonium. This could be attributed to the microorganism's ability to develop different resistance mechanisms to quaternary ammonium and the tested antibiotics or the asymmetry between the bacterial species found (BOYCE JM, 2023).

The resistance mechanisms developed against ammonium compounds differ from those commonly observed for antibiotics, which may also explain the lack of correlation in the results. For ammonium, membrane alterations may occur as a reaction to the biocide, such as changes in fatty acid composition that increase the cell's lipid content, rendering it more rigid. In contrast, antibiotic resistance arises from the production of enzymes, such as  $\beta$ -lactamases, efflux pumps, or modifications to the antibiotic binding site (KWASNIEWSKA D, et al., 2020).

According to Kwasniewska et al. (2020), efflux pumps operate differently for antibiotics and biocides. For antibiotics, they act specifically to prevent the accumulation of the drug within the cell, maintaining subinhibitory concentrations and allowing the microorganism to survive. For biocides, the action is non-specific. Since biocides generally target the membrane, efflux pumps function to remove the biocide before it can disrupt organelles, thereby limiting its action, as it directly affects the membrane.

Another potential mechanism involves reducing or modifying porin production. Porins are membrane proteins in bacteria that facilitate the entry of hydrophilic substances, such as antibiotics. With reduced outer permeability, the antibiotic cannot exert its function effectively. This reaction primarily occurs against tetracycline and fluoroquinolone. For quaternary ammonium compounds, this may occur; however, as these biocides do not rely solely on porins, their action is more indirect and involves, above all, changes in membrane composition (WANG S, et al., 2023).

This could also explain the resistance observed in phenotypes A, B, C, and D against tetracycline and **ciprofloxacin (Table 2)**, even though they were predominantly inhibited at concentrations near 0.2% in broth microdilution with quaternary ammonium. Resistance to quaternary ammonium compounds typically involves physical and structural modifications to microbial cells, whereas resistance to antibiotics involves molecular changes (KWASNIEWSKA D, et al., 2020).

## CONCLUSION

This study identified the occurrence of bacterial strains resistant to quaternary ammonium, particularly on surfaces frequently handled in hospital environments. The resistance observed in *Escherichia coli* and *Staphylococcus spp.* strains to quaternary ammonium concentrations, coupled with their multidrug resistance to antibiotics, raises concerns regarding potential failures in disinfection practices and biocide usage. The lack of a significant correlation between the minimum inhibitory concentration (MIC) of quaternary ammonium and antibiotic resistance suggests that resistance mechanisms differ substantially between these agents. Furthermore, the presence of multidrug-resistant strains to common antibiotics, such as amoxicillin and ciprofloxacin, underscores the challenges in treating healthcare-associated infections. The growing resistance to antimicrobials, combined with biocide resistance, demands immediate interventions in infection management and control, including the implementation of more robust public policies and the rational use of antimicrobials to prevent the worsening of this concerning scenario. Despite these findings, the use of quaternary ammonium remains essential for reducing the emergence of resistant microorganisms responsible for healthcare-associated infections (HAIs) in patients. Thus, this study highlights the main characteristics of quaternary ammonium-resistant strains, reinforcing the importance of continuously monitoring the efficacy of these antimicrobial agents, particularly in critical areas.

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