## MEDICAL MICROBIOLOGY

# A Comparison of the Antimicrobial Resistance Patterns of Gram-Positive Cocci Isolated from Community-Private and University-Affiliated Hospitals from Puerto Rico

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**The antimicrobial resistance patterns of 2,462 selected Gram-positive cocci obtained from three Community-Private Hospitals (CPH) and three University-Affiliated Hospitals (UAH) were evaluated utilizing the institutions' antimicrobial susceptibility reports for the year 2000. The objectives of this study were: 1) to evaluate the *in vitro* resistance to selected standard antibiotics of *Staphylococcus aureus*, *Enterococcus faecalis*, *Enterococcus faecium and Streptococcus pneumoniae* clinical isolates, and 2) to compare the antimicrobial resistance patterns between community-private (CPH) and university-affiliated hospitals (UAH). *Staphylococcus aureus* was the most common Gram-positive isolated organism in CPH (63.3%) followed by *E. faecalis* (31.0%). In UAH, the most prevalent cocci were *E. faecalis* (51.7%) followed by *S. aureus* (43.9%). *Enterococcus faecium* represented 2.3% and 4.4% of CPH and UAH isolates, respectively. *Streptococcus pneumoniae* represented 3.4% of the total Gram-positive isolates from CPH, no *S. pneumoniae* was reported in UAH. The antimicrobial susceptibility results showed that for *Staphylococcus aureus* there was a statistically significant higher resistance to methicillin and thrimethoprim sulfamethoxazole in UAH, while resistance to erythromycin was significantly higher in CPH. There was no difference in the resistance of *S. aureus* to other antimicrobial agents between hospitals groups. A statistically significant resistant to vancomycin was found between enterococcal isolates from UAH (43%) and CPH (12.7%). High-level aminoglycoside resistance (HLAR) was observed among UAH enterococcal isolates with *E. faecium* showing a higher resistance than *E. faecalis*, no data for HLAR in CPH could be obtained. For pneumococci 46% of CPH isolates were resistant to penicillin. In summary, there are important differences in the prevalence and antimicrobial resistance between the Gram-positive bacteria isolated from community and teaching hospitals.**

*Key words: Gram-positive cocci, Antibiotic resistance, Antimicrobial agents, Antimicrobial surveillance*

During the past decades, antimicrobial resistant bacteria have become an important health issue. Infections with these pathogens have been associated with significant increases in health care costs and patient's morbidity and mortality. Gram-positive organisms such as *S. aureus*, *S. pneumoniae*, and the enterococcal species, have been associated with resistance to multiple antibiotics. These bacteria, initially isolated from surgical and medical intensive care units and from large university affiliated hospitals, are now also being identified from community-acquired infections (18). In some institutions, over 40% of *S. aureus* isolates have shown resistance to methicillin-oxacillin (MRSA) (3,7,8,11). Enterococcal isolates resistant to penicillins, aminoglycosides (high-level aminoglycoside resistance, HLAR) and vancomycin (VRE) have been responsible for serious infections (11,14). A worldwide significant increase in penicillin resistant strains of *S. pneumoniae* (PRP) has been reported during the last two decades (1,2,3,20).

Since few studies have been performed in Puerto Rico on the antimicrobial resistance pattern of these Gram-positive cocci, this study was conducted to: 1) evaluate the *in vitro* antimicrobial resistance of *Staphylococcus aureus*, *Enterococcus faecalis*, *Enterococcus faecium and Streptococcus pneumoniae* clinical isolates, and 2) to

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compare the antimicrobial resistance patterns between community-private (CPH) and university-affiliated hospitals (UAH).

## Materials and Methods

The antimicrobial susceptibility reports for the year 2000 were obtained from 6 Metropolitan San Juan area hospitals. The hospitals were divided in two groups: Community-Private Hospitals (CPH), which included 3 institutions (A, B and C) with a total bed capacity of 772 and 3 (D, E and F) University-Affiliated Hospitals (UAH) with a total capacity of 701 beds. The following Gram-positive bacteria were selected for further analyses: *Staphylococcus aureus*, *Enterococcus faecalis, Enterococcus faecium*, and *Streptococcus pneumoniae*. The following data was evaluated and subjected to statistical analyses from each hospitals antimicrobial susceptibility reports: 1) the total number of each Gram-positive bacteria studied and 2) the antimicrobial susceptibility patterns of these organisms.

The following frequently used antibiotics were selected to evaluate the resistance patterns of the studied Gram-positive cocci:

***Staphylococcus aureus:*** methicillin/oxacillin (Met/Oxa); vancomycin (Vanco); ciprofloxacin (Cipro); erythromycin (Erythro); cefazolin (Cefa); and thrimethoprim sulfamethoxazole (TMP/SXT).

***Enterococcus* species:** ampicillin/penicillin (Amp/Pen); vancomycin (Vanco); gentamicin (Genta) and streptomycin (Strepto).

***Streptococcus pneumoniae:*** oxacillin/penicillin G (Oxa/PenG); levofloxacin (Levo); ceftriaxone (Ceftri); vancomycin (Vanco); erythromycin (Erythro) and thrimethoprim sulfamethoxazole (TMP/SXT).

Statistical analysis, utilizing Chi Square test, was performed to determine any significant differences between total number of isolates and their susceptibility patterns obtained from CPH and UAH. A P value $\leq 0.05$ was considered as being statistically significant.

## Results

A total of 11,574 unselected Gram-positive and Gram-negative bacteria isolates were collected during the year 2000 from the 6 hospitals (3 CPH and 3 UAH). Of these isolates, 8,052 were selected for further analysis and included 2,462 Gram-positive cocci and 5,590 Gram-negative bacilli. All isolated organisms identified as *Staphylococcus aureus, Enterococcus faecalis, Enterococcus faecium,* and *Streptococcus pneumoniae* were selected for further analysis (Figures 1 and 2). Table 1 shows the total number of unselected and selected Gram-positive bacteria from each participating hospital. Gram-positive bacteria were significantly more common in CPH than in UAH (39.1% vs. 22.6%; $P \leq 0.05$) where as Gram-negative bacteria were significantly more common (77.4% vs 60.9%) in UAH as shown in Figure 1. The susceptibility of the Gram-negative bacteria was not considered for this report. The distribution of selected 1,546 Gram-positive cocci from CPH and 916 from UAH is shown in Figure 2.

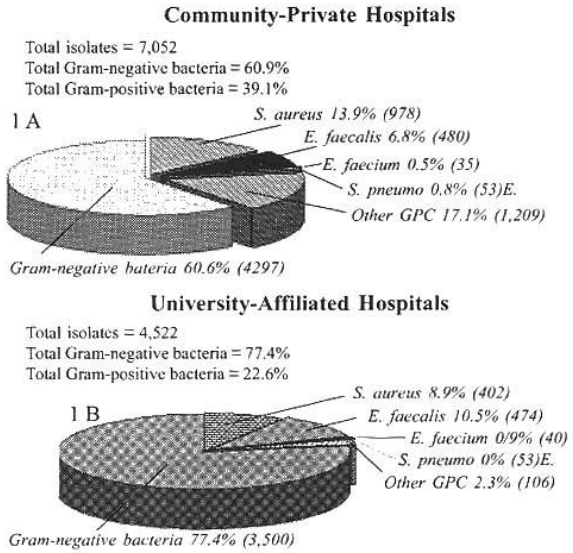



**Figure 1.** Total and percent of Gram-positive and negative bacteria insolated from Community-private and University-affiliated hospital

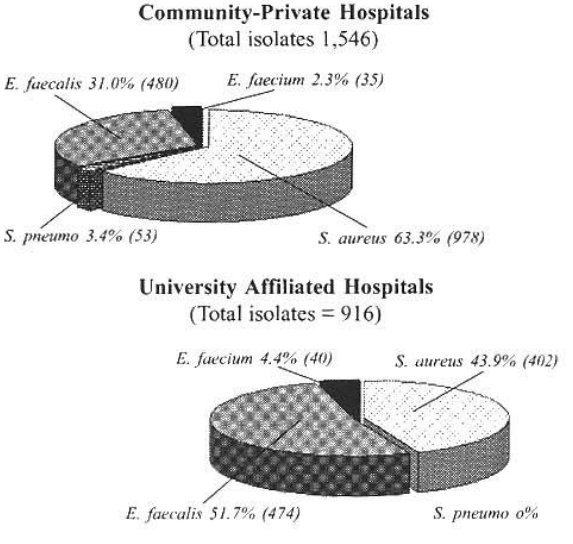



**Figure 2.** Distribution of Gram-positive cocci isolated from Community-private and University-affiliated hospitals

**Table 1.** Total Gram Positive Bacteria and Selected Gram-Positive Cocci per Hospital

| Hospital | Unselected | S. aureus | | E. faecalis | | E. faecium | | S. pneumo | | Total Selected |
|---|---|---|---|---|---|---|---|---|---|---|
| CPH | Gram + Bacteria | Total | % | Total | % | Total | % | Total | % | Gram + Cocci |
| A | 956 | 306 | 32.0 | 148 | 16 | 8 | 0.8 | 12 | 1.3 | 474 |
| B | 619 | 279 | 45 | 127 | 21 | 6 | 1.0 | 17 | 2.7 | 429 |
| C | 1180 | 393 | 33 | 205 | 17 | 21 | 1.8 | 24 | 2.0 | 643 |
| **Total CPH** | **2755** | **978** | **36** | **480** | **17.4** | **35** | **1.3** | **53** | **1.9** | **1546** |
| **UAH** | | | | | | | | | | |
| D | 418 | 167 | 40.0 | 214 | 51 | 24 | 5.7 | NR | NR | 405 |
| E | 242 | 80 | 33 | 107 | 44 | 4 | 1.7 | NR | NR | 191 |
| F | 362 | 155 | 43 | 153 | 42 | 12 | 3.3 | NR | NR | 320 |
| **Total UAH** | **1022** | **402** | **39.3** | **474** | **46.4** | **40** | **3.9** | **NR** | **NR** | **916** |

CPH = Community-Private Hospital, UAH = University-Affiliated Hospital, NR = Not Reported
Unselected = All isolated Gram-positive bacteria
Selected = S. aureus, E. faecalis, E. faecium and S. pneumoniae

The antimicrobial susceptibility pattern and the distribution of the studied Gram-positive cocci were as follows:

***Staphylococcus aureus.*** As shown in Figure 2, *S. aureus* was the most common Gram-positive bacterium isolated from CPH, representing 63.3% (978) of the Gram-positive isolates. In UAH, however, *E. faecalis* (51.7%) was the most common Gram-positive followed by *S. aureus* (43.9%), this difference was statistically significant to a $P \leq 0.05$. Figure 3 summarizes the antimicrobial resistance results of *S. aureus* against selected antibiotics according to the hospitals group (CPH vs. UAH). University-Affiliated

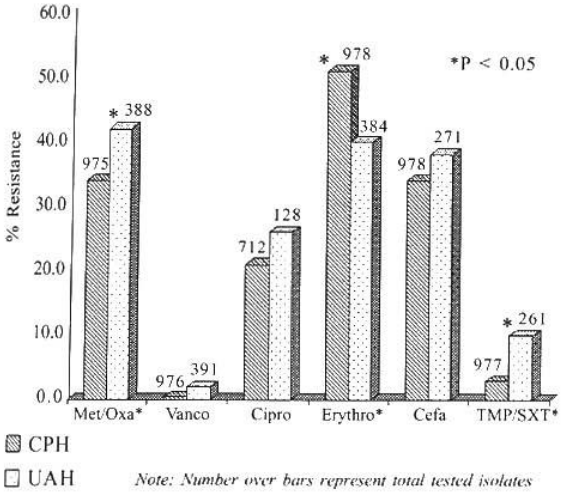



**Figure 3.** % Resistance of *S. aureus* to selected antibiotics according to hospitals group
(Total isolates: CPH = 978; UAH = 402)

Hospitals demonstrated a statistically significant higher resistance of *S. aureus* to oxacillin (42.8% vs. 35.2%; $P \leq 0.05$) and thrimethoprim-sulfamethoxazole (UAH 11.1% and CPH 2.4%; $P \leq 0.05$). There was a significantly higher resistance to erythromycin in CPH than in UAH (51.5% vs. 41.0%; $P \leq 0.05$). No significant differences in antimicrobial resistance between the two hospital groups were observed for the following antibiotics: vancomycin, cefazolin and ciproflaxocin.

***Enterococcus faecalis.*** As shown in Figure 2, *E. faecalis* represented 31.0% (480) of the total Gram-positive bacterial isolates in CPH and 51.7% (474) of the UAH isolates; this difference was statistically significant ($P \leq 0.05$). Figure 4 shows the resistance of *E. faecalis* to selected antibiotics according to the hospital groups. In UAH there was a significantly higher resistance to vancomycin (21.1% vs 9.6%; $P \leq 0.05$) and to ampicillin/penicillin (3.7% vs 0%, $P \leq 0.05$). *E. faecalis* aminoglycoside resistance in UAH was 86.0% to streptomycin and 22.2% to gentamicin. No data from CPH institutions was available for statistical comparison.

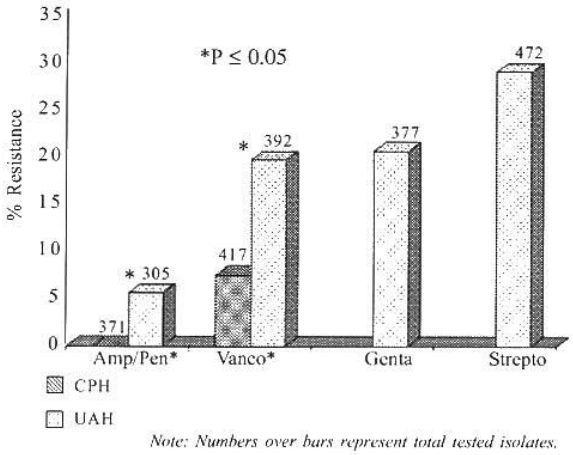
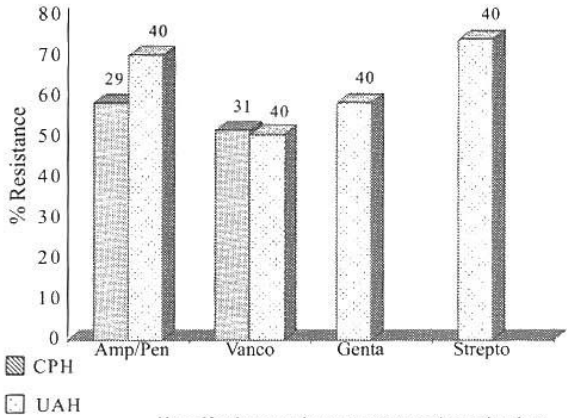



**Figure 4.** % Resistance of E. faecalis to selected antibiotics according to hospitals group
(Total isolates: CPH = 480; UAH = 474)

***Enterococcus faecium.*** As shown in Figure 2, a total of 35 (2.3%) and 40 (4.4%) *E. faecium* isolates were identified in CPH and UAH, respectively. Figure 5 shows the resistance of *E. faecium* to selected antibiotics according to hospital groups. There was no significant difference in

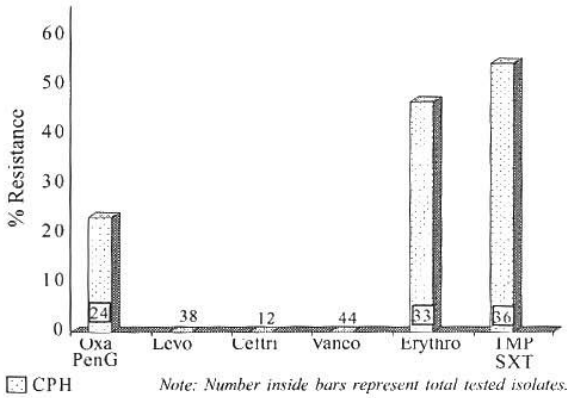



*Note: Number over bars represent total tested isolates.*

**Figure 5.** % Resistance of *E. faecium* to selected antibiotics according to hospitals group.
(Total isolates: CPH = 35; UAH = 40)

the number of *E. faecium* isolates resistant to vancomycin (CPH 55.9%, UAH 54.9%) or to ampicillin/penicillin (CPH 62.1%, UAH 74.8%) between the hospitals groups. In UAH, 62.3% of *E. faecium* isolates were resistant to gentamicin and 77.4% to streptomycin. No data for aminoglycosides resistance from CPH institutions was available for statistical comparison.

***Streptococcus pneumoniae.*** *S. pneumoniae* represented 3.4% (53 isolates) of the CPH selected Gram-positive bacteria (Figure 2); no *S. pneumoniae* isolates were reported from UAH. Figure 6 shows the antimicrobial




*Note: Number inside bars represent total tested isolates.*

**Figure 6.** % Resistance of *S. pneumoniae* isolated from community-private hospitals to selected antibiotics.
(Total isolates: CPH = 53; UAH = 0)

resistance patterns to selected antibiotics. Fifty-five percent of *S. pneumoniae* isolates were resistant to oxacillin/penicillin, 48.5% were resistance to erythromycin and 58.3% to trimethoprim-sulfamethoxazole. No resistance to levofloxacin, ceftriaxone and vancomycin was observed.

## Discussion

Antimicrobial resistant bacteria have become a major health issue for the 21st century. The emergence of these bacteria has been associated with several risk factors such as: length of hospital stay, proximity to a hospital, severity of illness, recent surgery, immunosuppression, patterns of hospital and community antimicrobial utilization, large inner city or teaching hospital, and special areas within hospitals, among others (13).

The present study has an important caveat; there was no distinction between community and nosocomial isolates. This might have shifted our results towards an over representation of antibiotic susceptible organisms which are expected to be more frequent in community isolates. In spite of this limitation, our data showed a large number of resistant Gram-positive organisms in both hospital groups.

University-affiliated hospitals had a significantly higher number of MRSA than CPH. Since these isolates have been associated with serious sporadic and nosocomial infections, the surveillance of this pathogen's antimicrobial resistance pattern is of foremost importance (9,17). The prevalence of MRSA reported in the SENTRY Antimicrobial Surveillance Program (3) varies according to geographical regions from 1.8% in Switzerland to 73.8% in Hong Kong. Our resistant rates of 35.2% in CPH and 42.8% in UAH are slightly higher than the 34.2% MRSA reported from the USA in the previously mentioned study (3). The results for trimethoprim-sulfamethoxazole against *S. aureus* isolates in UAH and CPH demonstrated a significant difference in the former (11.1% UAH vs 2.4% CPH), which could suggest extensive usage of this antibiotic in UAH for the treatment of conditions such as *Pneumocystis carinii* pneumonia among others.

*Staphylococcus aureus* resistance to erythromycin was significantly higher in CPH than in UAH (51.5 % vs 41.0 %; $P \leq 0.05$). The reason for this difference is not clear, as higher resistance to erythromycin is usually observed in institutions with significant numbers of MRSA isolates. The reported resistance of methicillin-susceptible *S. aureus* to erythromycin is 35.6% in the United States and 30.2% in Canada, while for methicillin-resistant *S. aureus* the resistance to erythromycin is 94.3% and 82.7%, respectively (3). No other statistically significant (51.7%)

differences were observed in the resistance of *S. aureus* to other tested antibiotics in both hospitals groups.

Enterococcal species are an important cause of nosocomial bacteremia, urinary tract and surgical wound infections (19). *Enterococcus faecalis* was the most frequent Gram-positive bacteria isolated from UAH (51.7% vs 31.0% CPH) and the most prevalent enterococcal species in both hospital groups. In the USA, *E. faecalis* represents 60% of the enterococcal species isolated; in Latin America this number increases to 76.8% (12). Our results demonstrated that 92.3 % of all isolated enterococci were *E. faecalis*. *Enterococcus faecium* represented 4.4% and 2.3% of the enterococcal isolates in UAH and CPH, respectively. In the United States, *E. faecium* accounts for about 20% of the enterococcal species isolates (12). Similar to other large-scale studies, our findings showed a consistently higher resistance of *E. faecium* to antimicrobial agents when compared to *E. faecalis* (11,12).

The emergence of VRE isolates is a cause for major concern because of the limited therapeutic options for treating serious infections and because of their potential to transfer vancomycin-resistance genes to other organisms (12). ). In UAH, the enterococcal resistance to vancomycin (43.0%) was significantly higher than the observed resistance in CPH (12.7%). Combining both hospital groups, our data demonstrated that 18.6% of enterococci (*E. faecalis* and *faecium*) were resistant to vancomycin. This finding is similar to the 17.7% of VRE reported from the United States (12). Ampicillin/penicillin G resistance was higher in UAH (9.2%) than in CPH (4.5%). The reported resistance to ampicillin/penicillin G in the United States and Canada is 24.0% (12). High-level aminoglycoside resistance (HLAR) of 25.3% to gentamicin and 32.9% to streptomycin was observed in UAH isolates. In the United States a 36.0% resistance to gentamicin and 40.0% to streptomycin among the enterococcal species has been reported (12).

A progressive and alarming increase in the number of highly penicillin resistant pneumococci (PRP) isolates has been found worldwide ranging from 4.0% in Canada to 22.0% in Europe (6,8). In a study involving 25 European university hospitals, 32.0% of the pneumococcal isolates demonstrated some degree of penicillin resistance (5). Our data demonstrated that 55.0% of CPH pneumococcal isolates were either intermediate or highly resistant to oxacillin/penicillin G. All pneumococcal isolates were 100% susceptible to vancomycin, levofloxacin, and ceftriaxione and about half of our isolates were resistant to erythromycin and TMP/SXT. These results were similar to those reported from the Unites States, Latin America, and Europe (5,6). It should be noted, however, that the number of pneumococcal isolates in our study was small and not amenable for statistical analysis. It is unclear why such a small number of pneumococci were identified in this study. Possible reasons to explain this finding are: 1) poorly taken samples, 2) inadequate handling of the specimen, 3) laboratory misidentification, among others.

## Conclusions

In both community-private and university-affiliated hospitals, a prominent number of antimicrobial resistant Gram-positive cocci were identified. The percent of antimicrobial resistance observed was similar to, or higher, than those reported from other geographic areas. University-affiliated hospitals had a significantly higher number of resistant organisms than community-private hospitals. *Staphylococcus aureus* resistant to methicillin and TMP/SXT, and vancomycin resistant *E. faecalis* were significantly more prevalent in UAH than CPH. High-level aminoglycoside resistance in the enterococcal species were identified in UAH isolates, while penicillin resistant pneumococci were observed in the community-private hospitals.

The differences in antimicrobial susceptibility between the two hospital groups could be partly explained by the type of patients served by the institutions, outpatient or inpatient antimicrobial prescription pattern, severity of illness, and number of medical personnel caring for the patient.

Ongoing antimicrobial resistance surveillance studies coupled with the judicious use of antimicrobial agents should be a priority in patient hospital care. It is imperative that an Island-wide antimicrobial susceptibility program be established to monitor the susceptibility trends of the most common bacterial pathogens.

## Resumen

El patrón de resistencia a antibióticos de 2,462 bacterias Gram-positivas obtenidas de 3 hospitales privados de la comunidad (CPH) y 3 hospitales afiliados a la universidad (UAH) fueron evaluados utilizando los reportes de susceptibilidad a antibióticos hechos por cada hospital para el año 2000. Los objetivos de este estudio son: 1) evaluar las resistencia a antibióticos *in vitro* de aislados clínicos de *Estafilococos aureus, Enterococos faecalis, Enterococos faecium y Estreptococos pneumoniae* a ciertos antibióticos, y 2) comparar los patrones de resistencia a antibióticos entre los hospitales privados de la comunidad (CPH) y los afiliados a la universidad (UAH). *Estafilococos aureus* fue la bacteria Gram-positiva que más se aisló en CPH (63%) seguida de *E. faecalis* (31%). En UAH, los cocos más prevalecientes fueron *E. faecalis*

seguido de *S. aureus* (43.9%). *Enterococcus faecium* representó el 2.3% y el 4.4% del total de aislados en CPH y UAH, respectivamente. *Estreptococos pneumoniae* representó el 3.4% del total de cocos Gram-positivos aislados en CPH. En UAH no se reportó ningún aislado de *S. pneumoniae*. Los resultados de susceptibilidad para *S. aureus* en UAH mostraron una alta resistencia a meticilina y trimetroprim-sulfamethoxazole, la cual fue estadísticamente significativa, mientras que la resistencia a eritromicina fue estadísticamente significativa más alta en CPH. No hubo diferencia entre los grupos de hospitales en la resistencia de *S. aureus* a los otros antibióticos estudiados. Los enterococos resistentes a vancomicina (VRE) se encontraron en un 12.7% y un 43% en los aislados de CPH y UAH, respectivamente. Esta resistencia fue estadísticamente significativa. La resistencia a aminoglicosidos de alto nivel (HLAR) se observó entre los enterococos aislados de UAH, mostrando *E. faecium* una mayor resistencia que *E. faecalis*. No se pudo obtener ningún dato de los enterococos HLAR en CPH. Para los neumococos, el 46% de los aislados en CPH fueron resistentes a penicilina. En resumen, hay diferencias importantes en la prevalencia y en la resistencia a antibiótico entre las bacterias Gram-positivas aisladas en hospitales de la comunidad y de enseñanza.

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