Chlorhexidine gluconate (CHG) susceptibility of *Klebsiella pneumoniae* carbapenemase (KPC)-producing *K. pneumoniae* isolates from skin cultures of patients in long-term acute care hospitals (LTACHs)

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Abstract

Background: Routine skin cleansing with CHG is an effective strategy to prevent infection and cross-transmission of bacterial pathogens in healthcare settings. Whether daily CHG bathing selects for CHG resistance is unresolved.

Methods: We collected swab samples of patients' skin to monitor minimal inhibitory concentrations (MICs) of CHG for KPC-producing *Enterobacteriaceae* during a bundled infection control intervention that was conducted in 4 Chicago LTACHs. During the intervention, all patients were bathed daily with CHG. From May 2012 - June 2013, patients who were rectal carriers of KPC and who had received at least three daily CHG baths were evaluated. Cultures were collected using dual Dacron swabs (BBL) from five skin sites: Antecubital fossa, axilla, back, neck, and inguinal area, and the rectum. Swabs were screened for KPC-producing organisms using an ertapenem disk method; bla_{KPC} was confirmed by PCR. Species were identified by MicroScan Walkaway 96 system (Siemens). *K. pneumoniae* isolates were identified presumptively as multilocus sequence type 258 (ST258) by PCR assay for the ST258-*tonB79* cluster. CHG MICs were tested by broth microdilution. For investigation of change in MIC over time, the study period was divided into 4 intervals that were each 3-4 months long and that included approximately equal numbers of observations.

Results: 217 KPC-positive isolates were cultured from 62 patients. 195 (90%) isolates were *K. pneumoniae*, 13 (6%) *Escherichia coli*, 4 (1.8%) *Enterobacter aerogenes,* 3 (1.4%) *Providencia stuartii,* and 2 (1%) *Citrobacter koseri*. 119 (61%) *K. pneumoniae* isolates were members of the ST258 lineage. For *K. pneumoniae,* the CHG MIC_{50}/MIC_{90} was 32 µg/mL in period 1; 64 µg/mL/128 µg/mL in period 2; and was 32 µg/mL/64 µg/mL in periods 3 and 4 (Figure 1). *K. pneumoniae* ST258 isolates had a significantly higher geometric mean CHG MIC compared to non-ST258 *K. pneumoniae* (32 µg/mL vs. 18 µg/mL, p=.002). In an analysis of variance that corrected for person and anatomic site, no increase in geometric mean MIC was observed over time among *K. pneumoniae*, p=.84.

Conclusion: Daily CHG bathing of LTACH patients over 14 months was not associated with development of reduced susceptibility to CHG in KPC-producing *K. pneumoniae* isolates.

Background

- CHG is used increasingly for routine bathing to decrease bloodstream infections and reduce cross-transmission of multidrug-resistant organisms.
- Whether exposure of bacteria to CHG over time leads to reduced CHG susceptibility remains a concern.

Methods

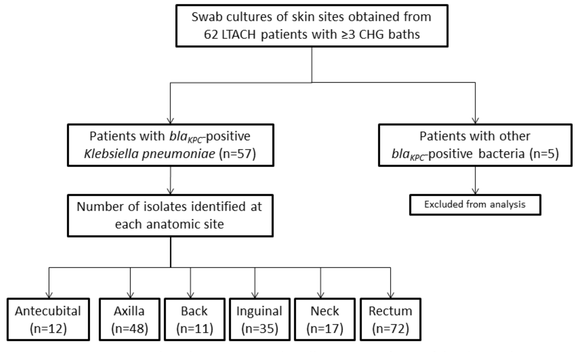

Figure 1. Patients and isolates studied. All patients (N=62) had ≥1 skin site that grew bla_{KPC}-positive Enterobacteriaceae and 13 patients had >1 bla_{KPC}-positive bacterial species identified. Other bla_{KPC}-positive organisms isolated include 13 *Escherichia coli*, 4 *Enterobacter aerogenes*, 3 *Providencia stuartii*, and 2 *Citrobacter koseri*. Further analysis was done only *on K. pneumoniae* because it is the dominant bla_{KPC}-positive organism in Chicago LTACH patients. (See reference no. 2 for additional analyses of these isolates.)

- Gram-negative bacilli were tested for bla_{KPC} by qPCR using a modified assay.[3,4]
- Bacterial isolates were identified to the species by MicroScan WalkAway 96 (Siemens, Tarrytown, NY).
- MICs were determined using broth microdilution with chlorhexidine digluconate (Sigma Aldrich, St. Louis, MO).
- bla_{KPC}-positive isolates were tested using a modified qPCR assay to identify two single nucleotide polymorphisms in the *tonB79* allele that correspond to multilocus sequence type (MLST) 258.[5]

Results

In an analysis of variance that included all 195 *K. pneumoniae* isolates and that was corrected for person and anatomic site of isolation, the geometric mean MIC of CHG for *K. pneumoniae* isolates did not increase over time. (Range of geometric mean MICs, 18 – 29 µg/mL, p=.84)

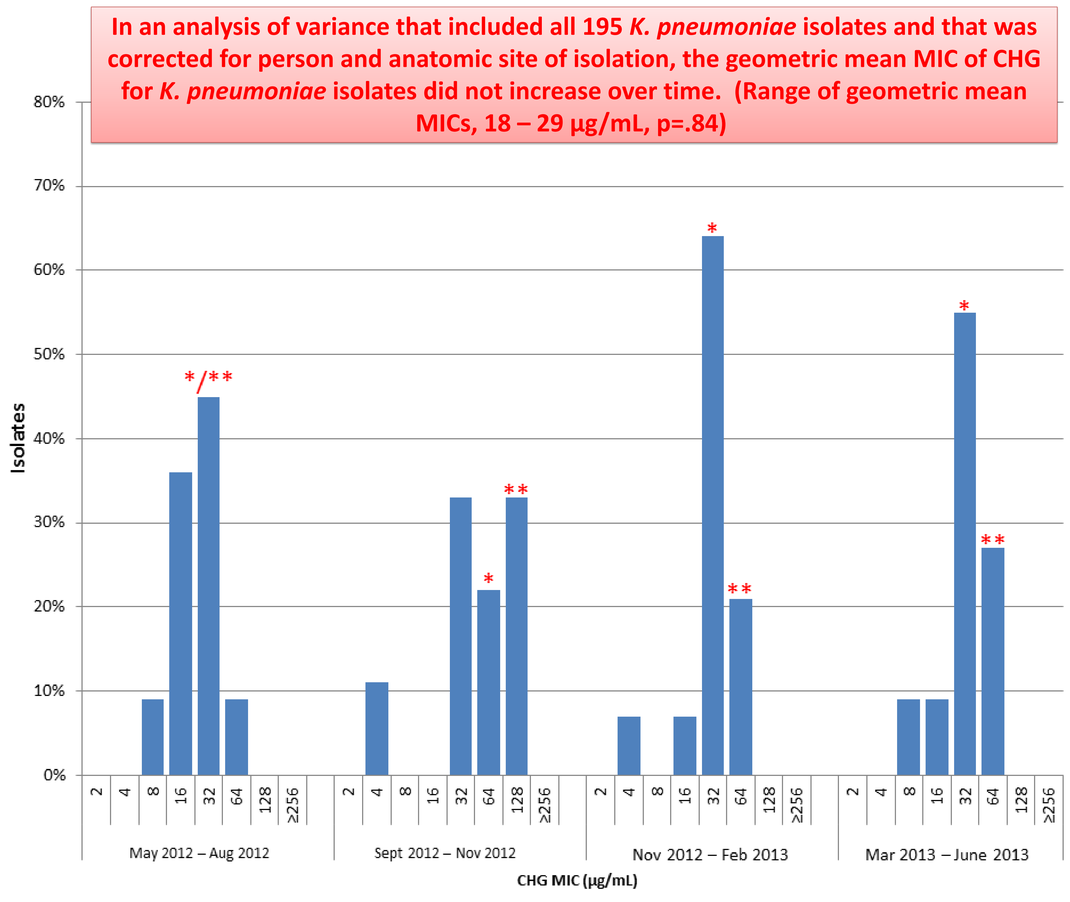

Figure 2. Distribution of CHG MICs among bla_{KPC}-positive *K. pneumoniae* skin isolates. Only one isolate per patient is presented, which represents the isolate with the highest CHG MIC. Period 1, 11 isolates; period 2, 12 isolates; period 3, 20 isolates; period 4, 14 isolates.*MIC_{50}; **MIC_{90}.

Range of CHG MICs differed between ST258 and non-ST258 *K. pneumoniae,* but the MIC_{50}/MIC_{90} were the same

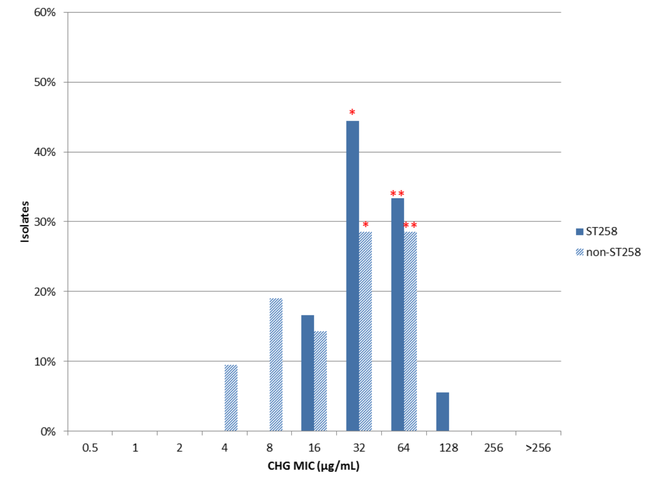

Figure 3. Comparison of CHG MICs between ST258 and non-ST258 *K. pneumoniae* skin isolates. *MIC50; **MIC90.

	ST258	
Period	**Negative**	**Positive**
May 2012 – August 2012	6 (54.5%)	5 (45.5%)
September 2012 – November 2012	4 (33.3%)	8 (66.7%)
November 2012 – February 2013	8 (40.0%)	12 (60.0%)
March 2013 – June 2013	3 (21.4%)	11 (78.6%)
Total	**21 (36.8%)**	**36 (63.2%)**

Table 1. Distribution of *bla*KPC-positive *K. pneumoniae* ST258 isolates.

Conclusions

- Despite daily bathing of LTACH patients for 14 months with 2% CHG wipes, the mean and range of CHG MICs did not increase over time.
- The range of CHG MICs was higher for ST258 than for non-ST258 strains of bla_{KPC}-positive *K. pneumoniae*, but the MIC_{50}/MIC_{90} were the same for both groups.

References

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