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Concise Communication

Socioeconomic disparities in the prevalence of multidrug resistance in Enterobacterales

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Abstract

We examined the association between multidrug resistance and socioeconomic status (SES), analyzing microbiological and ZIP-code–level socioeconomic data. Using generalized linear models, we determined that multidrug resistance is significantly and persistently more prevalent in samples taken from patients residing in low-income ZIP codes versus high-income ZIP codes in North Carolina.

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Antibacterial resistance represents a growing threat to public health[1]; multidrug-resistant Enterobacterales are increasingly isolated from clinical cultures in the United States.[2] Past data suggest that socioeconomic disparities may be linked to increased rates of infections caused by multidrug-resistant bacteria.[3,4] Understanding the socioeconomic factors that contribute to disparities in infectious disease burden is crucial in developing approaches to address the challenges of multidrug resistance. To that end, we explored the associations of population-level markers of socioeconomic status with multidrug resistance in Enterobacterales in North Carolina.

Methods

Multidrug resistance in Enterobacterales

We estimated the proportion of multidrug resistance in Enterobacterales isolates taken from patients treated in the UNC Health system in North Carolina (including UNC's main hospital, several regional hospitals and hundreds of local clinics across the state) from 2014 to 2021, using data from institutional electronic health records.[5] We included all patients having at least 1 Enterobacterales-positive clinical culture who were at least 18 years old when the culture was obtained. To avoid correlation between isolates, we included only the first instance of a given *Enterobacter* spp isolated per patient. In total, 90,129 isolates were included, taken from 76,118 unique patients.

Microbiological data were obtained from the UNC Hospitals Clinical Laboratory, including species and antibiotic susceptibility data, and standardized to current Clinical and Laboratory Standards Institute (CSLI) susceptibility breakpoints. Approximately 20% of results from susceptibility testing were MICs not reported as an exact dilution and therefore could not be reclassified; for these, the original interpretation was retained.

Species–antibiotic combinations that met current CLSI criteria for "intermediate" or "resistant" were classified as nonsusceptible. An isolate was classified as resistant to an antibiotic class if it was nonsusceptible to at least 1 member of that class, after removing results corresponding to intrinsically resistant species–antibiotic combinations. Multidrug-resistant isolates were classified as those that were nonsusceptible to at least 1 antibiotic from at least 3 separate antibiotic classes.[6] We removed susceptibility results for carbapenems due to low levels of nonsusceptibility throughout the study period and for first-generation cephalosporins due to separate cefazolin breakpoints depending on infection type (eg, for complicated vs uncomplicated urinary tract infections).

Socioeconomic variables

Using the methodology previously described by the Centers for Disease Control and Prevention (www.atsdr.cdc.gov/placeandhealth/svi/index.html), the SES subscore of the Social Vulnerability Index was calculated for each ZIP code in North Carolina. The score represents the summed percentile ranking of a given ZIP code in 5 areas: poverty rate, unemployment rate, cost-burdened housing rate, the percentage of residents that lack health insurance, and the percentage of adult residents that lack a high-school diploma. Data on these variables were obtained from the 2020 5-year American Community Survey (data.census.gov).

Statistical analyses

To allow readier interpretation of the association between multidrug resistance and SES, ZIP codes were organized into equal-sized SES quartiles: high, medium-high, medium-low, and low. Using the ZIP code of the patient from whom each culture was taken, we linked the microbiological data and SES scores.

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Table 1. Raw Multidrug Resistance (MDR) Percentage and Unadjusted Prevalence Ratios for Each Socioeconomic Status (SES) Quartile, 2014–2021

SES Quartile (Total Isolates)	MDR Isolates, No. (%; 95% CI)	Prevalence Ratio, (95% CI)
High (N=22,788)	3,602 (15.8; 15.3–16.3))	Referent
Medium-High (N=22,788)	3,776 (16.6; 16.1–17.1)	1.05 (1.00–1.10)
Medium-Low (N=22,787)	4,484 (19.7; 19.2–20.2)	1.24 (1.19–1.30)
Low (N=22,787)	4,528 (19.9;19.4–20.4)	1.26 (1.20–1.31)

Note. CI, confidence interval.

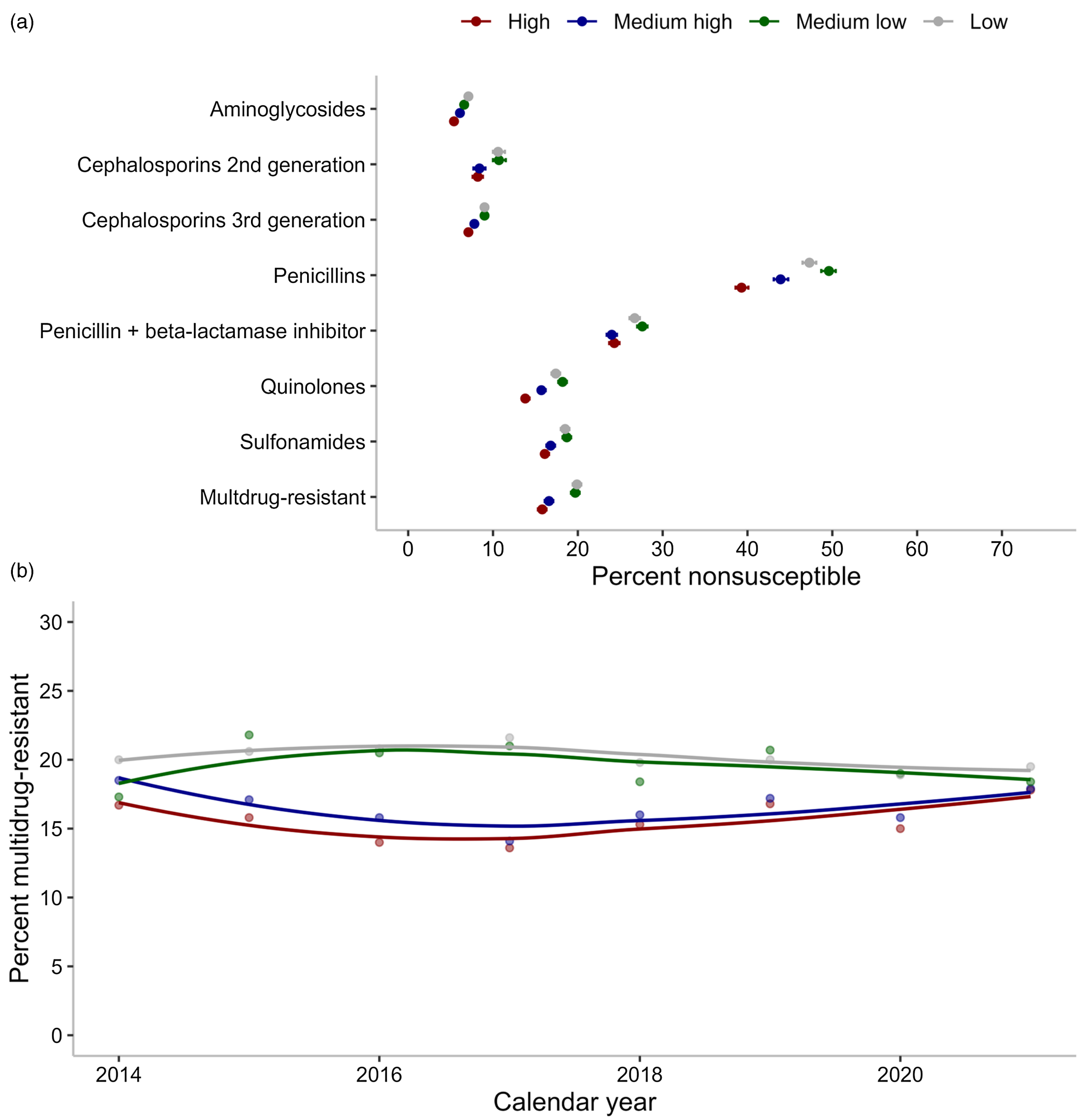

Figure 1. (a) Percentage of isolates that were reported as nonsusceptible to selected antibiotic classes or as multidrug resistant, sorted by socioeconomic status (SES) quartile. (b) Temporal trends in overall percentages of isolates reported as multidrug resistant.

To examine the relationship between SES and multidrug resistance, we fit generalized linear models to estimate prevalence ratios of multidrug resistance in each SES quartile, both overall and within specific classes of antibiotics. To examine the changes in multidrug resistance prevalence over time, we calculated the stratified yearly average of its prevalence among the isolates from each quartile.

Results

In total, 16,401 of 90,129 isolates met the criteria for multidrug resistance. Of 802 total ZIP codes in North Carolina, 686 had 1 or more Enterobacterales-positive cultures and could be included in the analysis.

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Our analysis revealed a statistically significant inverse relationship between multidrug resistance and calculated SES scores. The overall percentage of multidrug resistance was highest (19.9%; 95% CI, 19.4%–20.4%) in ZIP codes in the low SES quartile, and lowest (15.8%; 95% CI, 15.3%–16.3%) in the high SES quartile (Table 1). The intermediate quartiles matched this pattern (medium high: 16.6%; 95% CI, 16.1%–17.1%; medium low: 19.7%; 95% CI, 19.2%–20.2%) (Table 1).

Prevalence ratios for multidrug resistance by SES quartile show a similar association. The prevalence ratio was 1.05 (95% CI, 1.00–1.10) in the medium-high quartile, 1.24 (95% CI, 1.19–1.30) in the medium-low quartile, and 1.26 (95% CI, 1.20–1.31) in the lowest quartile, relative to the highest quartile (Table 1).

A similar pattern was observed in the relationship between SES and nonsusceptibility for individual antibiotic classes. In all classes analyzed, the percentage of nonsusceptible cultures was significantly higher in the low quartile than in the high quartile (Fig. 1a). The absolute difference was largest in penicillins: 39.2% (95% CI, 38.6%–40.1%) in the highest quartile and 47.3% (95% CI, 46.5%–48.1%) in the lowest quartile. The absolute difference was smallest in aminoglycosides: 5.4% (95% CI, 5.1%–5.7%) in the highest quartile and 7.1% (95% CI, 6.8%–7.5%) in the lowest quartile.

A consistent difference between the high and low quartiles was observed when temporally comparing the overall percentage of multidrug-resistant cultures over the years analyzed (Fig. 1b). This difference was greatest in 2017: (13.6% in the highest quartile and 21.6% in the lowest quartile. The difference was smallest in 2021: 17.8% in the highest quartile and 19.5% in the lowest quartile.

Discussion

In North Carolina during 2014–2021, measures of SES were persistently and significantly associated with prevalence of multidrug resistance in Enterobacterales at the population level. Enterobacterales-positive cultures taken from patients residing in the lowest SES quartile had a 26% higher prevalence of multidrug resistance relative to the highest SES quartile. This effect was observed across all studied years and antibiotic classes. Our findings are consistent with past research suggesting that socioeconomic disadvantage is associated with higher disease burden.[3]

The mechanisms underlying this association remain incompletely defined. Past data suggests some possibilities. Globally, low socioeconomic status has been linked to increased exposure to antibiotics[6] and to resistant pathogens,[7] as well as to a higher likelihood of suboptimal antibiotic use.[7] Additionally, waste from livestock treated with antibiotics can spread resistance in environmental bacteria.[8] This phenomenon has been observed in eastern North Carolina, where hog farming operations are heavily clustered in low-income regions, potentially contributing to the observed results.[9]

Although the prevalence of multidrug resistance in low SES-quartile areas remained higher than in high-SES quartile areas in all years analyzed, an apparent convergence was observed toward the end of the study period, though it is unclear whether this change is significant. The reason for this apparent convergence is unclear, but the upheaval of the healthcare system during the COVID-19 pandemic may have contributed.[10]

Our study had several limitations. First, we used data from a single healthcare center, potentially introducing a referral bias and restricting the geographic coverage of our analysis. Second, our analysis focused on Enterobacterales; because other pathogens may differ in transmission and carriage, their association with SES may differ as well. Third, testing was conducted according to clinical indication, which may have contributed to the reported observations. Although symptomatic carriage rates likely are reflected by rates of infection, important differences may exist. Fourth, socioeconomic and structural factors other than SES, such as systemic racism, may also play a role in the distribution of multidrug resistance.

In conclusion, markers of SES are associated with higher levels of multidrug resistance in Enterobacterales in North Carolina. These findings indicate a need for further investigation into the disparities associated with SES and infectious disease burden. These data may help inform preventative efforts to decrease the burden of these important public health threats.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/ice.2023.116

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