



PROJECT
REPORT

Study of Healthcare-Associated Infections and Multi-Drug Resistance in Brooklyn: An Integrative Approach

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Abstract

One SENCER ideal is to connect science education and civic engagement by student learning through complex, unresolved public issues. Using this approach, we established a collaborative interdisciplinary project involving faculty and undergraduate students at NYC College of Technology. Over several semesters, students conducted literature search and discovered the complex factors contributing to the occurrence and transmission of healthcare-associated infections (HAIs). Using microbiology data from 15 hospitals in Brooklyn, NY, they applied statistical analyses, studied the antibiotic resistance,

and developed a campaign to bring more awareness of this problem. The results of the project highlight the importance of immediate action in combating HAIs and support the need for a public health campaign. Undergraduate students were provided with the opportunity to conduct research, perform scientific and mathematical analyses, and present their results. They gained better understanding of the complex interactions among microbiology, epidemiology, and mathematics that is needed to develop preventative measures and combat HAIs.

Introduction

In April 2014, World Health Organization officials released a comprehensive report on antibiotic resistance, calling it a “major threat to public health” and seeking “improved collaboration around the world to track drug resistance, measure its health and economic impacts and design targeted solutions” (WHO, 2016). Using the SENCER ideals of connecting science education and civic engagement by teaching through complex, unresolved public issues, and inspired by the SENCER Summer Institute (SSI) in Chicago, we established a collaborative interdisciplinary project for undergraduate students at the NYC College of Technology, led by faculty from the Biological Sciences and Mathematics departments. By combining epidemiology and microbiology with mathematics, the project addressed the need for public education and awareness of two emerging health care problems: (a) healthcare-associated infections (HAIs), formerly known as nosocomial infections (NIs), and (b) antibiotic resistance. HAIs are infectious diseases, acquired during a hospital stay, with no evidence of being present at the time of admission to the hospital. HAIs affect 5–10% of hospitalized patients in the US per year. Approximately 1.7 million HAIs occur in U.S. hospitals each year, resulting in 99,000 deaths (CDC, 2015). Today the complications associated with HAIs may be responsible for an annual \$5–10 billion financial burden on our healthcare system (Cowan, Smith, and Lusk, 2019). Education and public awareness campaigns have been among the most effective tools used in many industries, including healthcare. HAIs are easily transmitted due to the numerous microbes in the hospital environment, the interaction of healthcare workers with multiple patients, the compromised immunity of patients, improper use of antibiotics, and inadequate antiseptic procedures. More than 70% of these infections are caused by multi-drug resistant (MDR) pathogens, which contribute to increased morbidity and mortality (Black and Hawks, 2009). Antibiotic resistance is the capability of particular microorganisms to grow in the presence of a given antibiotic. The acquired resistance results from spontaneous mutations or from the transfer of resistance genes from other microbes (Drlica & Perlin, 2011). Each year in the US, at least 2 million people are infected with antibiotic resistant bacteria, and at least 23,000 people die as a result

(CDC, 2018; Sifferlin, 2017). With the increased levels of antibiotic usage among humans, livestock, and crops, antibiotic resistant bacteria have increased dramatically in the past few decades (Foglia, Fraser, & Elward, 2007; Sedláková et al., 2014). If a bacterial cell carries several resistance genes, relating to more than just one antibiotic, it is termed MDR, for multiple drug-resistant. Today these organisms are known as superbugs (Sifferlin, 2017).

The rising rate of antimicrobial resistance demands research and development of entirely novel drugs and new therapeutic strategies, from small-molecule antibiotics to antimicrobial peptides, from enzymes to nucleic acid therapeutics, from metal-carbonyl complexes to phage therapy (Medina & Pieper, 2016; Brunetti et al., 2016; Betts, Nagel, Schatzschneider, Poole, & Ragione, 2017; Nayar et al., 2015; Phoenix, Harris, Dennison, & Ahmed, 2015).

The main goal of this research project was to study the complex factors that contribute to the occurrence and transmission of HAIs associated with antibiotic resistance in Brooklyn hospitals, to apply statistical analyses to the data, and to bring more awareness of this problem to our college community.

Student Involvement

Students enrolled in Microbiology (BIO3302) and Statistics (MAT1272) worked collaboratively on this project. Undergraduate researchers, with a greater time commitment, were also involved in the project, through the college’s Emerging Scholars program (New York City College of Technology, Undergraduate Research, 2019) or the Honors Scholars Program (New York City College of Technology, Academics, 2019) the former providing stipends to students and the latter providing honors credit in a course. Both programs require student professional development related to research, such as abstract writing, preparing a poster, and making oral presentations, and each provides the opportunity for undergraduate students to conduct research with a faculty mentor and gain a practical understanding of the material learned in courses. Undergraduate researchers included students majoring in nursing and other health sciences (for whom both BIO3302

and MAT₁₂₇₂ are required), applied mathematics, and computer engineering technology.

The specific objectives of the project were (a) to define the most common bacterial pathogens responsible for the spread of HAIs; (b) to identify risk factors and common infection sites; (c) to analyze microbial resistance to commonly used antibiotics, using data on multi-drug resistant bacterial isolates from hospitals in Brooklyn; (d) to study variations of resistance rates among different hospitals, using statistical analysis; (e) to study association among resistant isolates, using regression analysis; (f) to define the antibiotics with the highest bacterial resistance; (g) to raise awareness of preventative measures for reducing HAIs; and (h) to introduce students to an interdisciplinary practical field.

Over six semesters, students performed comprehensive literature search on scientific articles by using the following key words: healthcare-associated infections, hospital acquired infections, HAI, nosocomial infections, antibiotic resistance, multi-drug resistance, epidemiology, Brooklyn hospitals. Additionally, they obtained already published data on multi-drug resistant clinical isolates from 15 coded (unidentified) hospitals in Brooklyn, (kindly provided by Dr. J. Quale, Division of Infectious Diseases, State University of New York Downstate Health Sciences University) (Bratu, Landman, Gupta, Trehan, Panwar, & Quale, 2006; Manikal, Landman, Saurina, Oydna, Lal, & Quale, 2002; Landman et al., 2002; Landman et al., 2007). Using the data, students performed statistical analysis, using chi-squared tests on antibiotic resistance and regression analysis.

Results

Most Common Bacterial Pathogens and Risk Factors

As a result of extensive literature search, students defined twelve bacterial pathogens associated with HAIs. The most common ones in Brooklyn were *Staphylococcus aureus*, including methicillin-resistant *Staphylococcus aureus* (MRSA), *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Clostridium difficile*. Next, the specific bacterial characteristics and the most prevalent sites of infections (urinary tract, lower respiratory tract, surgical incisions, and bloodstream) were

described. Those at highest risk of contracting HAIs are patients with (a) a compromised immune system as a result of a transplant, HIV infection, malignant tumors, or possible prolonged treatment with antibiotics, cytostatics, or corticosteroids; (b) surgical procedures; (c) invasive procedures (e.g., urethral catheters, trachea ventilators, and/or intravenous therapy); (d) trauma and burn patients; (e) an underdeveloped immune system (e.g., newborns); and (f) diminished resistance (e.g. elderly); and (g) prolonged hospitalization, also a significant risk factor.

Statistical Analysis of Antibiotic Resistant Clinical Isolates

The next step of the project was to study the impact of multi-drug resistance on HAIs. One of the project participants established personal communication with Dr. J. Quale, who provided numerically coded data on clinical isolates collected from 15 Brooklyn hospitals. The percentage of resistance to the following most commonly used antibiotics was examined and compared: Amikacin (AK), Gentamicin (GEN), Cefotaxime (CAZ), Piperacillin-Tazobactam (Pip-Taz), Ciprofloxacin (Cip), and Imipenem (Imi).

Analyses of the antibiotic resistance indicated that most of the clinical isolates were highly resistant to Ciprofloxacin, reaching 100% resistance among *Acinetobacter baumannii*. These results demonstrate that Ciprofloxacin should be used minimally for the tested HAI pathogens. Newer therapies such as Tigecycline and the combination of Polymyxine + Rifampin showed much better bacterial susceptibility.

Chi-squared tests (Table 1) revealed significant resistance variations of *Klebsiella* isolates to the antibiotics AK, CAZ, Cip, and Imi among the hospitals, that is, the variations of drug resistance of these isolates were too large to have occurred by chance alone. Significant resistance variations of *Pseudomonas* isolates to AK, Cip, and Imi were also observed. The underlying causes of these disparities are most likely the differences in the inpatient population. Elderly and sicker patients usually take in more antibiotics and thus harbor antibiotic resistant bacteria. Patients in trauma centers are also more likely to develop antibiotic resistance. Furthermore, overuse or repeated use of a specific antibiotic by a hospital would lead to a higher resistance rate for that particular antibiotic.

TABLE 1. Chi-Squared Tests on Resistance Variations Among Hospitals

Antibiotics/ Pathogens	Klebsiella	Pseudomonas	Acinetobacter
AK	$\chi^2 = 68.8155$ p-value < 0.001 (Null hypothesis rejected)	$\chi^2 = 25.5509$ p-value < 0.05 (Null hypothesis rejected)	$\chi^2 = 16.4532$ (Null hypothesis not rejected)
CAZ	$\chi^2 = 84.5723$ p-value < 0.001 (Null hypothesis rejected)	$\chi^2 = 9.7463$ (Null hypothesis not rejected)	$\chi^2 = 12.1614$ (Null hypothesis not rejected)
Cip	$\chi^2 = 81.8907$ p-value < 0.001 (Null hypothesis rejected)	$\chi^2 = 51.2586$ p-value < 0.001 (Null hypothesis rejected)	$\chi^2 = 5.758$ (Null hypothesis not rejected)
Imi	$\chi^2 = 91.8921$ p-value < 0.001 (Null hypothesis rejected)	$\chi^2 = 37.2784$ p-value < 0.001 (Null hypothesis rejected)	$\chi^2 = 41.1553$ p-value < 0.001 (Null hypothesis rejected)
Pip-Taz	$\chi^2 = 80.4947$ p-value < 0.001 (Null hypothesis rejected)	Not Applicable	Not Applicable

Interestingly, different scenarios were observed for *Acinetobacter* isolates. Variations of *Acinetobacter* resistance to the antibiotics AK, CAZ and Cip among the hospitals were not statistically significant; however, significant variations to Imi were observed. Patients with *Acinetobacter* infections are usually very ill and heavily exposed to antibiotics. *Acinetobacter* bacteria are resistant to most antibiotics, and thus for these isolates, variations of resistance to most antibiotics do not show statistically significant differences among the participating hospitals.

Regression analysis showed high correlation between the antibiotic resistance of different pathogens. The correlation coefficient between *Klebsiella* and *Pseudomonas* was 0.929, *Klebsiella* and *Acinetobacter* - 0.825 and between *Pseudomonas* and *Acinetobacter* - 0.859. The correlation between resistance of a specific organism to different antibiotics was also studied. Extremely strong positive correlation was found between Ceftriaxone and Ciprofloxacin ($R^2 = .9961$) in *K. pneumoniae* (Table 2), suggesting that these bacteria may carry the resistant genes for both antibiotics. Most hospital facilities nowadays use common antibiotics to treat infections. Within inpatient population there is a greater chance of contracting and spreading infections due to compromised or weakened immunity and the variety of pathogenic organisms present in such settings. Therefore, resistance to antibiotics that are prevalently used is higher.

TABLE 2. Correlation of Resistance to Different Antibiotics in Isolates of *K. pneumoniae*

Klebsiella pneumoniae			
Caz and Pip-Taz	$R^2 = .9921$	Ak and Cip	$R^2 = .9208$
Caz and Cip	$R^2 = .9961$	Caz and Imi	$R^2 = .8904$
Piptaz and Cip	$R^2 = .9534$	Piptaz and Imi	$R^2 = .7593$
Piptaz and AZ	$R^2 = .8535$	Ak and Imi	$R^2 = .7531$
Ak and Caz	$R^2 = .8685$	Caz and Cip	$R^2 = .7264$
Cip and Imi	$R^2 = .8218$	Cip and Imi	$R^2 = .7184$

Preventative Measures

Another important objective of our study was to understand the need for proper preventative measures for reducing HAIs. In order to protect all individuals in the clinical setting—patients, healthcare workers, and public (visitors), CDC has laid down strict guidelines for handling patients and body specimens, termed Universal Precautions (CDC, 1998). All students, especially those majoring in health sciences, became acquainted with and learned these guidelines. The fight against the spread of MDR organisms begins with proper hand hygiene, correct use of personal protective equipment (PPE), and judicious use of pharmacologic treatment (Weinstein, 2001). Practicing proper frequent hand hygiene is essential to prevent the transmission of infections. It requires washing hands with soap and vigorous rubbing

under running water for at least twenty seconds. Alcohol-based sanitizers are also used on unsoiled hands and require less time than hand washing. However, sanitizers are not effective in killing bacterial spores, whereas hand washing is effective on all microbes. PPE includes gowns, goggles, or facial shields to protect skin and mucus membranes. Targeted pharmaceutical treatment, as a result of an antibiogram, should be prescribed instead of blind use of broad-spectrum antibiotics. Repeated bacterial cultures are necessary to assess the effectiveness of treatment. Additional preventative measures to reduce HAIs are (a) decreasing the number of skin punctures on a patient, since they provide opportunities for colonizing microflora; (b) following aseptic techniques when performing invasive procedures such as placing urethral and intravenous catheters; (c) reducing the duration of intravenous lipid use, since lipids are immunosuppressive, are easily contaminated, and support growth of fungi and bacteria; and (d) limiting the number of days for percutaneous deep lines.

Technology is also playing a role in preventing and improving effective patient care through sharing health information. The Health Information Technology for Economic and Clinical Health Act allows hospitals and providers to share patients' health information (ONC, 2019). In New York City many healthcare providers are taking advantage of programs like the Regional Health Information Organization, a network that contains a complete picture of patient's health history.

Assessment and Outcomes

The information gained in this project highlights the importance of immediate action in combating HAIs and supports the need for a public health campaign. The project provided students with the opportunity to conduct mentored interdisciplinary research, work as a team, perform scientific and mathematic analyses, participate in discussions, and exchange opinions. Students were enabled to better understand the complex interaction between microbiology, epidemiology, and statistics and to gain knowledge of the need for preventative measures to combat HAIs. Adding the research component to the Microbiology course has helped students connect

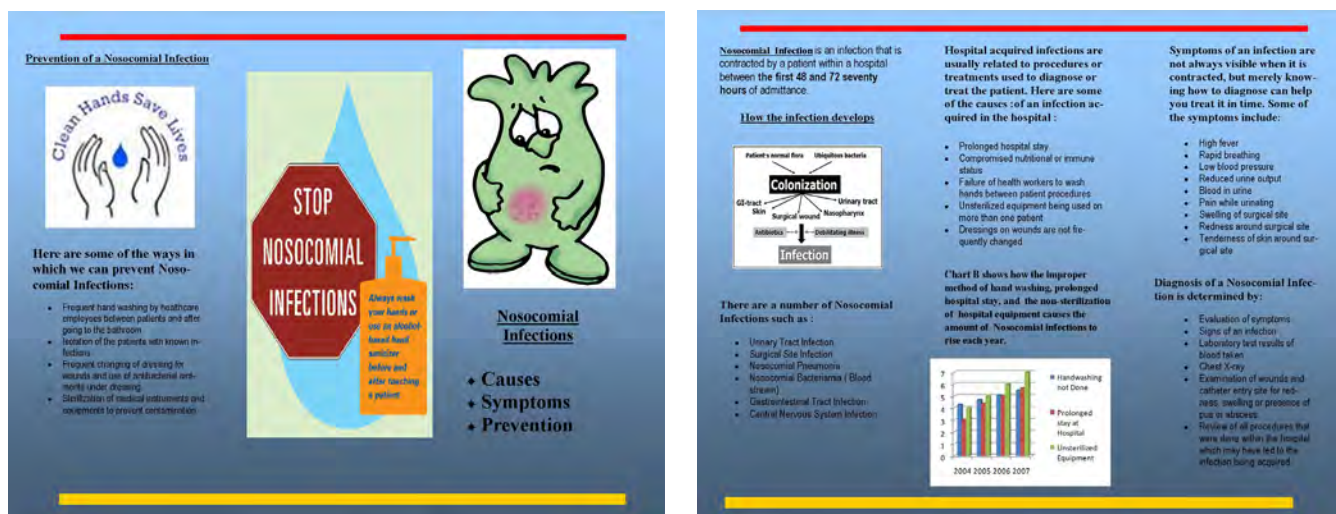
the information learned in class to the real world and to recognize the importance of HAIs and MDR as a threat to public health. Throughout the project, in a creative environment, students defined the most common bacterial species responsible for the spread of HAIs in Brooklyn and identified the risk factors and common infection sites. Using the data on multi-drug resistant isolates, they performed statistical analysis to study the correlation between two different antibiotic resistances and variability among Brooklyn hospitals. Their work was disseminated by publishing flyers (Figures 1 and 2) for distribution in local hospitals and clubs. Currently, the information from the project continues to be used by the participating faculty in MAT1272 for "hand washing habits" assignments, which also leads to a discussion on antibacterial soaps, sanitizers, and the occurrence of superbugs.

Furthermore, different phases of the project were presented at the end of each semester at the Semi-Annual Poster Sessions for Honors and Emerging Scholars at the New York City College of Technology. Several undergraduate students presented their research at regional and national conferences such as NYSMATYC (NYSMATYC, 2011), MAA Regional Meetings, Math Fest (Ghosh-dastidar, 2010), the 13th Annual CUNY Pipeline Honors Conference, and the Annual Biomedical Research Conference for Minority Students (ABRCMS). The project was also presented at the SENCER Washington Symposium and Capitol Hill Poster Session in Washington DC. The work was also reflected in MAA Focus magazine (Baron, 2011), and in the NY Daily News.

FIGURE 1. Flyer with Information about Nosocomial Infection (Courtesy of Gillian Persue)



FIGURE 2. Flyer with Information about Nosocomial Infection (Courtesy of Michell Cadore)



In conclusion, we consider the research project very successful. Our main goal was achieved: to combine different subject areas, to address serious public health issues, such as HAIs and antibiotic resistance, and to bring more awareness in our community. The students were very enthusiastic and eager to learn and interacted very efficiently among themselves as a team. The success of the project is best conveyed by the students' reflections on their research work:

"This was my first research project and it was challenging. I never thought I could do pathology research, but it opened a door to a new area. The experience was especially important for me, since health care workers can spread nosocomial infections. We're supposed to help patients, but we can harm

them. I would encourage everyone to do a research project in college. It's definitely worth it."

"The most significant part of this project for me was working as an interdisciplinary team. I am proud to say that the results of our research were later presented on a state level at Cornell University in Ithaca, New York."

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