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Case study of nursing home residents: The association between Carbapenemase-producing Enterobacteriaceae (CPE) and COVID-19

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Jordan Ranta – Epidemiology

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Abstract

The Multi-drug Resistant Organism (MDRO) Carbapenemase-producing Enterobacteriaceae (CPE) is a threat because of its degree of resistance to antibiotics and difficult treatment. Patients in long-term care may have worse outcomes when CPE is combined with COVID-19. This case study was designed to explore the association, if any, between CPE, COVID-19, and resident mortality in a nursing home. The data originated from previously collected datasets from the Nebraska Department of Health & Human Services (DHHS). The case-control study design included 40 nursing home residents that were screened for CPE. 15 of these residents were CPE-positive and 25 were CPE-undetected. Three of the 40 subjects died of

CPE infection. Following the CPE outbreak, 23 out of the remaining 37 residents from the original cohort were screened for COVID-19. This analysis describes the relationship between CPE and COVID-19 mortality in this outbreak. During the study period in the 40 resident cohort, 11 residents died. Three of the fatalities were CPE-positive and COVID-19 positive. Three were CPE-positive and COVID-19 negative. Five fatalities were COVID-19 positive and CPE negative (see Table 5). Preliminary evidence has been presented about CPE infection as it relates to health conditions, COVID-19, and mortality, however, no conclusions can be made. More research that is able to capture the potential relationship between CPE infection and COVID-19 is needed to understand if there is an association between CPE and COVID-19 mortality.

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Chapter 1 – Introduction

Research Question

Null hypothesis: There is no association between Carbapenemase-producing Enterobacteriaceae (CPE) and COVID-19 in a cohort of 40 residents in a Nebraska nursing home. Alternate hypothesis: There is an association between Carbapenemase-producing Enterobacteriaceae (CPE) and COVID-19 in a cohort of 40 residents in a Nebraska nursing home.

Specific Aims

The purpose of this analysis is to explain whether the presence of a Multi-drug Resistant Organism (MDRO) increased the possibility of a negative outcome from COVID-19. The specific MDRO examined is Carbapenemase-producing Enterobacteriaceae (CPE).

Significance

This case study will explores the potential associations between the CPE outbreak and the role of the outbreak in COVID-19 resident fatalities. The study population is a cohort of 40 residents screened for CPE in a Nebraska nursing home. The nursing home CPE outbreak began before the start of the COVID-19 pandemic, and therefore would be realistic to assume potential association between CPE infection and the COVID-19 positive resident outcomes.

Chapter 2 – Background and Literature Review

Description of the Health Problem

CPE is a type of Carbapenem-resistant Enterobacteriaceae (CRE) that also produces these resistant bacteria, enabling the transfer of the resistant gene to other bacterial organisms. CPE bacteria are becoming less rare as they increase their resistance to antibiotic treatments. These treatments typically involve last-resort antibiotics called carbapenems, which are used to fight the most severe infectious bacteria. CPE produces an enzyme that makes carbapenems not effective, and makes it very difficult to treat patients' infections. CPE is transmissible from

person-to-person, especially in high risk settings like long-term care facilities, unless strict contact precautions are enforced.

Scientific Background

Research has been done involving CPE in long-term care facilities, however, there is minimal research done on the association between CPE and COVID-19. The Centers for Disease Control and Prevention (CDC) defines the CRE organism as resistant to a majority of antibiotics which are a major risk for patients in most health care facilities. The resistant organisms make treatment of the bacteria less and less effective and lead to more severe treatments (CDC, 2019).

An article written by Gomes et al. from 2018, outlines a CRE outbreak investigation and describes the analysis of how person-to-person transmission happened throughout a residential group home. The outbreak investigation included residents, caregivers, and visiting healthcare personnel. Gomes et al. illustrated the chronological progression from index case to infection prevention and control measures that may have contributed to the spread of CRE bacteria and increase in positive CRE cases. The authors' conclusion states that resident and care practices may have increased the spread of antibiotic-resistant organisms like CRE (Gomes et al., 2018). The paper by Gomes et al. is relevant to this case study because the CRE investigations both occurred in a nursing home and describe trends in CRE infection.

A 2019 article by Durante-Mangoni et al. reviews the most relevant clinical infection control data for CRE. The authors also discuss interpretation of this data from CRE treatment in randomized control trials and observational studies (Durante-Mangoni et al., 2019). Durante-Mangoni et al. focus on monotherapy instead of combination treatment. In another 2019 study by Lutgring, CRE and the role of microbiology laboratories is examined which is important to show results for the type of CRE. The CRE results discussed by Lutgring may also provide

information to make decisions about alternative treatment options for CRE types in the future, such as CPE in this case study.

The 2017 article by Richter et al. discusses the risk factors for those most susceptible to CRE infection, which includes an independent predictor of mortality for CRE infections as, "delay in initiation of appropriate antimicrobial therapy" (2017). The authors name immunosuppressed and aging individuals as independent predictors of CRE infection (Richter et al., 2017). Richter et al. state that these traits of aging or immunosuppressed are underreported risk factors since they are mostly seen to be confounders (2017). Similarly, Singhal reviews COVID-19, including the origin of disease, risk factors, and complications of immunosuppression and aging in "SARS-CoV-2" patients (2020). Singhal also describes the ease of COVID-19 transmission between infected individuals, whether they are symptomatic or asymptomatic.

Surie et al. published a 2021 article which outlines the infectious period of COVID-19 in nursing home residents as being shorter than symptom duration. This article utilized a cohort study that tested nursing home residents frequently to determine positive or negative culture (Surie et al., 2021). Surie et al. also determined that the infectivity duration is longer for the COVID-19 nursing home residents that are immunocompromised.

In another publication in 2020, McMichael et al. discuss the trends from a long-term care facility COVID-19 outbreak, including confirmed cases, hospitalization rate, and case fatality rate among residents. Risk factors of COVID-19 patients in the McMichael et al. study were stated as, "advanced age and frequent chronic underlying health conditions," and indicated the median age of residents was 83 years, with a range of 50 to 100 years (2020). McMichael et al. also stated hypertension as the only underlying condition present in patients that were positive

for COVID-19, however, not all residents were tested. It was concluded that residents with advanced age and multiple underlying health conditions were at higher risk of more severe outcomes and transmission of COVID-19 than other residents (McMichael et al., 2020).

In addition to individual risk factors for severe outcomes and infection, an article by Brown et al. from 2021 describes a cohort study of nursing home residents, and states there is an association between higher COVID-19 outbreak trends and residents that share bathrooms and bedrooms. The outbreak trends that are referenced in this study are higher mortality and larger outbreak numbers for COVID-19. These trends increase when residents had 2 or more roommates, which Brown et al. describes as high crowding (Brown et al., 2021). Brown et al. concludes that reducing the number of roommates, referred to as low crowding, would have decreased the number of COVID-19 cases and deaths in nursing home residents (2021).

Limitations and gaps in existing literature

Current literature provides numerous studies of CRE and numerous studies about COVID-19, but I could find none that explore the relationship between the two. It is possible that the reason is the rarity of CRE outbreaks. The current literature found does not particularly examine CPE, and only looks at the broader CRE terminology.

Chapter 3 – Data and Methods

Study Design

This case study utilizes a descriptive case-control study design to analyze existing datasets from the Nebraska Department of Health & Human Services (DHHS). The data contained dates of lab results, investigation reports, and death certificates. Data was examined to identify trends in a long-term care facility related to CPE and COVID-19. The data for the study population, a cohort of 40 residents, was manually organized into a case study based on

residents' diagnoses of CPE, COVID-19, or both. The case study also utilizes analytical approaches to describe, summarize, and interpret trends in the CPE and COVID-19 related DHHS data from the long-term care facility.

The information recorded for most resident CPE cases included medications, hospitalizations, and comorbidities. Additional information noted for some residents was bedroom number, bathroom use, and number of roommates, if any. Information collected briefly included resident's common usage of the bathroom and shower, as well as other recreational areas like the dining room and whirlpool. Residents also were allowed to have visitors at the time of the CPE outbreak.

Quantitative software was not used in this descriptive study, but numbers and basic epidemiological findings are represented in the results section of the report.

Setting and Study Population

The outbreak investigation used data from a Nebraska nursing home, that allows long and short term care durations for residents. The certified and licensed facility's medical staff is localized, and provides 24 hours, 7 days a week care for residents. The nursing home is considered a skilled nursing facility, and also employs other types of healthcare workers that provide different health services, such as physical and occupational therapy. The CPE outbreak occurred from December 2019 through the spring of 2020, while the COVID-19 outbreak occurred in the fall of 2020.

Caregiver IPC Practices

The caregivers at this nursing home are skilled nurses and healthcare personnel (HCP) that are local and provide care 24 hours a day, 7 days a week. Exact shift duration is unknown, but typically caregivers prepare meals and are involved with most of resident care and high risk activities. It is unknown whether HCP were trained to handle CPE infections, and what the exact

precautions and infection prevention and control (IPC) measures were during CPE and COVID-19 outbreaks. However, the only documentation of IPC measures was CPE-positive residents were placed into contact precautions upon confirmation of CPE detection. It is unknown whether HCP were separately tested for CPE or COVID-19 in this outbreak investigation.

Data Sources and Measurement

The CPE screening samples were taken to the Nebraska Public Health Laboratory (NPHL) for testing. Samples were obtained by rectal swabs if residents were tested at the facility. The methods for sample collection and testing in hospitals is unknown.

In the process of transporting samples from the third CPE screening, the contents of 6 samples leaked and therefore did not contain enough of the specimen to be tested.

According to the Centers for Disease Control and Prevention (CDC), COVID-19 testing can be done with a rapid antigen test or a polymerase chain reaction (PCR) test (CDC, 2021). Both of these tested respiratory specimen of residents by nasal or throat swab, and sometimes collecting saliva in a tube. Both tests can show if the patient is infected at that point in time, while the rapid antigen test gives faster results.

Chapter 4 – Results

Study Population

The mean and median age of case study residents was 82 years (range 59-102 years) (see Table 1). The median for CPE-positive residents was 82 years (range 64-99 years), and median for CPE-undetected residents was 86 years (range 59-102 years). The majority (70%) of case study residents were female (see Table 2). Approximately 47% of CPE-positive residents had recent hospitalizations and had recent wounds or infections. Of the 15 CPE-positive residents 73% had medication allergies, and 80% were on antibiotics in the last 6 months. 80% had

underlying health conditions or were unable to care for themselves. Twelve of 15 (80%) CPE-positive residents used the whirlpool frequently.

Table 1. Resident Age (N = 40)				
	Mean Age	Median Age	Age Range	N
CPE-positive Residents	80	82	(64 – 99)	15
CPE-undetected Residents	84	86	(59 – 102)	25
Total Residents Screened	82	82	(59 – 102)	40

Table 2. Resident Gender (N = 40)							
	Females	Column %	Row %	**Males**	Column %	Row %	N
CPE-positive Residents	9	32%	60%	6	50%	40%	15
CPE-undetected Residents	19	68%	76%	6	50%	24%	25
Total Residents Screened	28	100%	70%	12	100%	30%	40

Descriptive Data

The case definition was previously determined by the Nebraska Department of Health and Human Services (DHHS) and confirmed by NPHL. COVID-19 screenings were occurring as residents were symptomatic, but most testing, positive results, and investigations included in this case study occurred in the fall of 2020.

Common activities that may have put residents at higher risk of CPE infection involved using the whirlpool or shower seat, as well as sharing bathrooms or other living spaces. Some residents had wounds that were being soaked or washed on a daily or weekly basis because of medical treatment plans. These higher risk practices could have also increased the exposure to

COVID-19, although it was not noted at the time of the COVID-19 investigation. Sharing living spaces, bathrooms, and being in closer proximity puts residents at higher risk of COVID-19 exposure. Other activities that were not detailed but may have increased transmission were home cooked meals, visitors, and personal hygiene practices.

Exact number and type of antibiotics was not recorded for either CPE-positive or CPE-undetected residents. Number, type and duration of antibiotics would be helpful to understand treatment strategies and why residents are becoming resistant to these bacteria.

Main Results

The CPE outbreak started in early December 2019, when the index case sparked the outbreak investigation to monitor cases and understand the spread of CPE. Four screenings followed the index case, two of these screenings found 4 additional cases by the end of the month.

Case Finding

A total of 40 residents were screened, but some residents were included in more than one screening (see Table 3). The number of residents first screened increased from 11 to 28 by screening three and four. Following the first CPE screening in December, 2 of 11 residents screened were positive. The second screening at the end of December 2019, 3 of 23 residents screened were positive. The third screening in early January found 1 of 28 residents screened were positive. However, the contents of 6 samples from the third screening leaked during transportation and could not be tested. Of the 6 leaked samples, 2 CPE-positive residents were detected in later screenings. Some of these leaked samples may have been missed cases, and residents with undetected samples may have proceeded to infect other residents.

The fourth screening at the end of January found 2 of 28 residents screened were positive. The final list of CPE-positive patients shows that some residents were included in multiple

screenings without being detected or had a negative result in one screening but a positive result in another. It is possible that screened samples did not detect present CPE bacteria, therefore non-positive residents are referred to as CPE-undetected. The undetected samples may have contributed to infection transmission in the periods between screenings. There are 7 confirmed CPE-positive cases that are not documented in any of the four screenings. It is unclear from the data I reviewed whether there were 5 or more screenings.

Table 3. Resident Screenings (N=40)

Screening	CPE-positive	CPE-undetected**	Total
Screening 1 (12/18/19)	2	9	11 (100%)
Screening 2 (12/26/19)	3	20	23 (100%)
Screening 3 (1/8/20)	1	27***	28 (100%)
Screening 4 (1/28/20)	2	26	28 (100%)
Total (Non-repetitive)	15*	25	40 (100%)

*Total of 15 CPE-positive cases. Remaining 7 are not confirmed which screening they were detected from.
**Some residents were tested more than once and CPE was not detected.
***6 of 27 CPE-undetected were leaked samples - were not tested.

Figure 1.

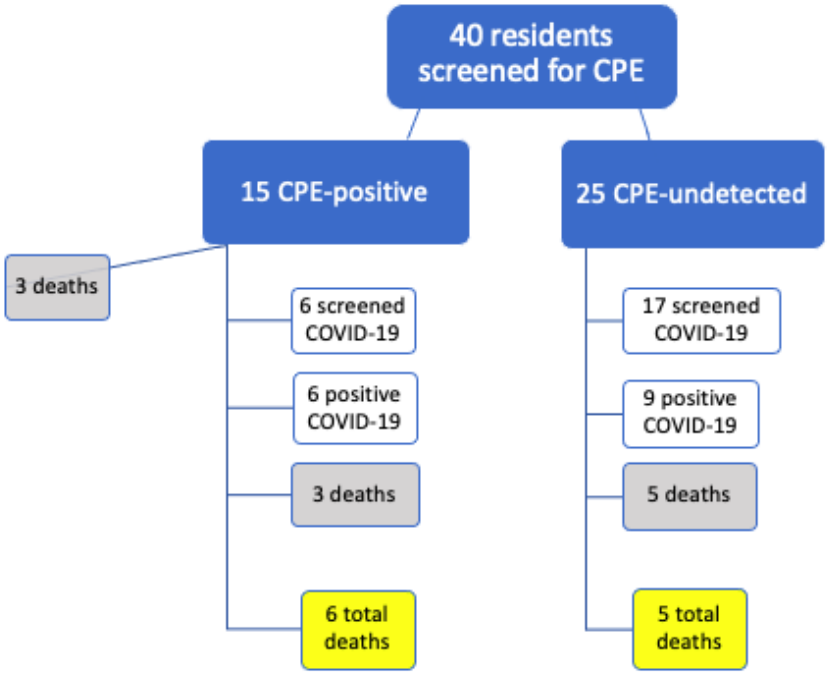

Figure 1 shows a total of 40 identified residents were screened for CPE over the course of the outbreak investigation. In total, 15 residents were CPE-positive patients, while 25 residents had samples that did not detect CPE. Of the 15 CPE-positive residents, 3 died in January 2020 after infection including the index case.

In the fall of 2020, residents were being tested for COVID-19. 3 of the CPE-positive residents that died were not included in COVID-19 screening. A total of 23 residents screened for CPE were also screened for COVID-19. The total number of COVID-19 positive residents was 15 of 23 (65%). Six residents that were initially CPE-positive were also COVID-19 positive, while 9 of 16 (56%) CPE-undetected residents were COVID-19 positive (see Table 4). There were 8 resident deaths from COVID-19; 3 CPE-positive residents died and 5 CPE-undetected residents died. In total, 11 residents died from December 2019 to December 2020; 6 residents that were CPE-positive died, and 5 CPE-undetected residents died (see Table 5).

Table 4. Resident Cases (N = 23)			
	COVID-19 Positive	COVID-19 Negative**	Total***
CPE-positive	6	0	6
CPE-undetected*	9	8	17
Total	15	8	23

*CPE-undetected represents lab results listed as "Not detected" – 6 samples were spilled during the 3rd screening and were not tested.
**COVID-19 Negative is a negative lab result.
***A total of 23 residents were screened for both CPE and COVID-19.

Table 5. Resident Death (N = 23)*			
	COVID-19 Positive	COVID-19 Negative	Total
CPE-positive	3	0	3
CPE-undetected	5	0	5
Total	8	0	8

*Deaths out of 23 residents screened for CPE and COVID-19.
**3 CPE fatalities prior to COVID-19 testing - not included in this table.

Chapter 5 – Discussion

Summary

This case study describes an outbreak of CPE and COVID-19 in a nursing home cohort of 40 residents. The case study illustrates that 28 percent (11 of 40) of total residents included in this investigation died during the study period. There were more deaths in residents that were CPE-positive and COVID-19 positive (50%) than deaths for those that were CPE-undetected and COVID-19 positive (31%). There were more residents in the sample that were CPE-undetected than CPE-positive after being screened.

Key results

Fifteen residents were CPE-positive, 3 of them died before COVID-19 screening was implemented (see Figure 1). Only 23 of 37 remaining residents that were screened for CPE were also screened for COVID-19. Six residents that were CPE-positive were also COVID-19

positive, while 9 of 17 (53%) CPE-undetected residents were COVID-19 positive. There were 8 resident deaths from COVID-19; 3 CPE-positive residents died and 5 CPE-undetected residents died. In total, 11 residents died from December 2019 to December 2020; 6 residents that were CPE-positive died, and 5 CPE-undetected residents died.

Strengths and limitations (gaps)

The strengths of the case study present a case-control design that is able to capture rare CPE bacteria transmission and the potential effect of COVID-19 on the health conditions of CPE-positive residents. This descriptive study describes the high risk setting and function of facilities where these infections occurred.

There are several limitations in this case study. The case study is a small and rare sample of nursing home residents and their conditions. Data for hospitalizations, comorbidities, medications, and notable high risk activities is incomplete for the CPE-undetected group. Only some CPE-undetected residents had this data recorded, and more data needs to be collected in order to compare to the CPE-positive residents. Information for type and number of antibiotics for both CPE-positive and CPE-undetected groups would be beneficial for implementation of effective treatments for CPE infection. Seven confirmed CPE-positive cases are not documented in any of the four screenings. It is unclear from the reviewed data whether there were 5 or more screenings. CPE-positive cases may have been missed because of leaked samples in one of the screenings. It is possible that some missed CPE cases were in the CPE-undetected group, and may have unknowingly contributed to COVID-19 deaths. Other limitations include undocumented details about COVID-19 restrictions for residents and other high risk activities in living spaces. It was also not noted whether residents were roommates of another, but some residents were documented to have roommates or room changes. An assessment of infection

prevention and control measures could help explore possible transmission of CPE and COVID-19 between residents and HCP.

Interpretation

Potential high risk activities and poor infection prevention and control measures that commonly lead to higher disease transmission were documented. These activities include shared living spaces, communal hot-tubs, shared bathrooms, etc. Additional CPE-positive cases could have been missed in this investigation, and may have contributed to increased transmission of CPE and COVID-19 mortality. However, in this population there is not enough evidence to conclude that CPE-positive residents that were also COVID-19 positive experienced higher mortality. There is not enough evidence to conclude whether there is or is not an association between CPE, COVID-19, and nursing home resident mortality.

Generalizability

The evidence presented in this case study may not be generalizable to all nursing homes. CPE of this nature is rare and, possibly rare to this instance in which the CPE outbreak was concurrent with a COVID-19 outbreak.

Conclusion

This case study of nursing home residents outlines the need for more understanding of CPE in the nursing home setting. Understanding of CPE will promote better HCP and resident infection prevention and control measures in high risk facilities. A larger sample and detailed documentation of residents would help to explore transmission of both CPE and COVID-19. More research that is able to capture the potential relationship between CPE infection and COVID-19 is needed to understand if there is an association between CPE and COVID-19 mortality.

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Appendix: Biography & CV

Jordan Ranta is a Master of Public Health student in the Department of Epidemiology at the University of Nebraska Medical Center (UNMC). She is currently employed as a Student Research Assistant through UNMC's College of Public Health, where she aids coordination of cancer-related projects and management of logistics for cancer focus groups. Additionally, Jordan is employed as a Patient Attendant at Nebraska Medicine where she works to ensure patient safety. Infectious Disease, Chronic Disease, and Environmental Epidemiology are among her top research interests. She holds integrity and respect as indispensable values throughout her academic and professional pursuits. Jordan received her Bachelor of Science degree in Public Health with a minor in Emergency Management from the University of Nebraska Omaha.

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EDUCATION

University of Nebraska Medical Center – Omaha, NE Current - May 2021
Master of Public Health: Epidemiology

Research Interests: Infectious Disease Epidemiology, Chronic Disease Epidemiology, Environmental Epidemiology

Relevant Coursework

Introduction to SAS Programming	Fall 2019
Biostatistics I & II	Fall 2019-Spring 2020
Epidemiologic Methods	Spring 2020
Applied Epidemiology	Fall 2020
Infectious Disease Epidemiology	Fall 2020

University of Nebraska at Omaha – Omaha, NE May 2019
Bachelor of Science: Public Health
Minor: Emergency Management
3.79/4.0 GPA

- **Dean's List**, every fall and spring semester
- **Chancellor's List**, spring 2018, fall 2018

PROFESSIONAL EXPERIENCE

Research Assistant 10/2020 to Current
University of Nebraska Medical Center – Omaha, NE

- Assist coordination of cancer-related projects and manage logistics of cancer focus group research
- Collaborate with to share and draft ideas with partners
- Create REDCap surveys to recruit participants and gather cancer focus group eligibility data

Patient Attendant 07/2019 to Current
Nebraska Medicine – Omaha, NE

- Effectively communicate with and support nursing staff to maintain patient safety
- Sit one-on-one with patients to reassure and redirect them based on individual needs to ensure their safety
- Monitor patients on video monitor systems and promptly communicate with nursing staff about their patients

Student Response Team Member 08/2019 to Current
University of Nebraska Medical Center – Omaha, NE

- Assist in COVID-19 response, fulfilling duties at local health departments as requested such as contact tracing interviews and data entry
- Actively participate in emergency response training and opportunities

Capstone Experience 12/2020 to Current
Nebraska Department of Health and Human Services – Lincoln, NE
- Organize and analyze data to chronologically interpret the story of infectious disease outbreak
- Produce a descriptive analysis report of the outbreak that will be sharable within the department

Applied Practice Experience
Douglas County Health Department, 05/2020 to 08/2020
Communicable Disease Epidemiology – Omaha, NE
- Produce Tuberculosis investigation written report, shared within the organization and the public
- Use SAS software to analyze and chart Tuberculosis investigation data results

Internship 01/2019 to 05/2019
Douglas County Health Department,
Communicable Disease Epidemiology – Omaha, NE
- Collaborate with various health professionals to work on unique tasks and understand new concepts
- Observe different collection methods of epidemiology data and disease case investigations
- Support department operations by preparing and updating documents: worked on Communicable Disease Epidemiology Manual chapters
- Complete long-term care facility project by representing data in an infographic and writing

PROFESSIONAL MEMBERSHIPS
Member, **Public Health Association of Nebraska** (Student) 01/2020 to Current
Member, **UNMC Student Response Team** 09/2019 to Current
Member, **Eta Sigma Gamma Student Honorary** 2019
Member, **International Association of Emergency Managers Student Chapter** 2018 to 2019