INTERNATIONAL JOURNAL OF ADVANCE RESEARCH, IDEAS AND INNOVATIONS IN TECHNOLOGY

ISSN: 2454-132X
Impact Factor: 6.078
(Volume 10, Issue 1 - V10I1-1257)
Available online at: https://www.ijariit.com

The outbreak of Extensively Drug-resistant Pseudomonas aeruginosa associated with the use of Artificial Tears and Contraction in hospital settings – An Epidemiological Overview

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Public health concern in the US due to the outbreak of extensively drug-resistant pseudomonas aeruginosa bacterium present in certain eye drops. Introduction: Drug-resistant mechanisms are present in this bacteria. Common exposures to the bacterium. Characteristics of the bacterium including morphology, biochemical characteristics, pathogenicity, resistance, etc. biological classification of the bacterium. Common exposures to the bacteria. Cases of the bacteria, severity of the disease, symptoms. treatments, prevention, and limitations of the study.

Keywords: *Resistance, Antibiotics, Exposures, Ezricare Artificial Tears, Pathogenicity, VIM-GES-CRPA, Symptoms, Treatments, Prevention.*

I. INTRODUCTION

The United States is currently facing a significant public health concern as a result of a multistate outbreak of an extensively drug-resistant strain of Pseudomonas aeruginosa. This strain, referred to as carbapenem-resistant Pseudomonas aeruginosa (CRPA), possesses multiple mechanisms of resistance against β-lactam antibiotics, including carbapenems. The outbreak strain is characterized by the presence of Verona integron-mediated metallo-β-lactamase (VIM) and Guiana extended-spectrum-β-lactamase (GES), denoted as VIM-GES-CRPA, signifying a previously unseen level of resistance in the country.

1. Outbreak Overview

The outbreak of the extensively drug-resistant strain of Pseudomonas aeruginosa has spread across multiple states, in the United States, causing concerns within the healthcare community. This specific strain, which exhibits resistance to carbapenem antibiotics, such as penicillin, poses a significant challenge to treatment options, as carbapenems are often considered the last resort for treating severe infections caused by drug-resistant bacteria.

2. Resistance Mechanisms

The emergence of VIM-GES-CRPA proteins represents a critical development in antibiotic resistance. The combination of Verona integron-mediated metallo-β-lactamase and Guiana extended-spectrum-β-lactamase provides the bacterium with multiple mechanisms to confer resistance against β-lactam antibiotics, including carbapenems. This complex resistance profile greatly limits the effectiveness of commonly used antibiotics and poses a serious threat to patient care.

3. Unprecedented in the United States

Prior to this outbreak, the presence of VIM-GES-CRPA had never been reported in the United States. The introduction of this extensively drug-resistant strain represents a concerning shift in the epidemiology of antibiotic resistance within the country. The absence of previous exposure to such resistant strains has heightened the urgency of understanding and managing the outbreak effectively.

4. Diverse Range of Infections:
The outbreak has been associated with various types of infections, including eye infections, highlighting the ability of this extensively drug-resistant strain to cause infections across different body sites. The wide range of affected areas underscores the importance of implementing stringent infection control measures to prevent further transmission and address the associated morbidity and mortality.

5. Common Exposure: EzriCare Artificial Tears:
Through extensive investigation, a common exposure has been identified in relation to the outbreak. EzriCare artificial tears have been implicated as a potential source of infection. Artificial tears are commonly used to alleviate dryness and discomfort in the eyes, but their role in transmitting the outbreak strain raises concerns about product safety and highlights the need for robust quality control measures.

Image A: *Pseudomonas aeruginosa*
https://www.cdc.gov/hai/organisms/pseudomonas.html

II. CHARACTERISTICS

Pseudomonas aeruginosa is rod-shaped bacterium that belongs to the family Pseudomonadaceae. It is a pathogen and one of the most common causes of healthcare-associated infections, particularly in immunocompromised individuals and patients with chronic diseases. Here, we will classify Pseudomonas aeruginosa based on various aspects:

1. Morphology:
Pseudomonas aeruginosa appears as a non-spore forming, motile bacterium with a single flagellum. Under a microscope, it exhibits characteristic features with the presence of an outer membrane and a thin peptidoglycan layer.

2. Biochemical Characteristics:
Pseudomonas aeruginosa is capable of metabolizing a wide range of organic compounds and can grow under aerobic or anaerobic conditions. It produces both cytochrome oxidase and pigments, which contribute to its diverse colony colors, including green, blue, yellow, purple, etc.

3. Pathogenicity:
As an opportunistic pathogen, Pseudomonas aeruginosa targets immunocompromised individuals. It possesses numerous virulence factors that aid in colonization, invasion, and evasion of the host immune system. These factors include pili for adherence, flagella for motility and the production of extracellular enzymes and toxins such as elastase and exotoxin A.
4. Antibiotic Resistance:
Pseudomonas aeruginosa exhibits intrinsic resistance to many antibiotics due to its low permeability outer membrane, , and ability to produce β-lactamases. It is known for its ability to acquire additional resistance mechanisms through genetic mutations, making it highly adaptable and challenging to treat.

5. Environmental Resilience:
Pseudomonas aeruginosa thrives in various environments, including soil, water, and hospital settings. It has a remarkable ability to survive and persist in diverse ecological niches due to its resistance to harsh conditions, such as high temperatures, disinfectants, and antibiotics.

Biological Classification
Pseudomonas is a genus of gamma proteobacteria belonging to the larger family of pseudomonas. As a result the genus *Pseudomonas* includes strains formerly classified in the genera *Flavimonas*. Other strains previously classified in the genus *Pseudomonas* are now classified in the genus *Burkholderia* and *Ralstonia.*

Image B: Biological Classification of *Pseudomonas aeruginosa*
https://www.slideshare.net/MaiMamdouh3/pseudomonas-aeruginosa-69643274

Exposures
Exposures, in the context of health and safety, refer to situations, substances, or conditions that individuals come into contact with or are subjected to. It involves contact with various physical, chemical, biological, or psychosocial agents that have the potential to cause harm or affect well-being. Exposures can occur in different settings, such as the workplace, home, community, or natural environment. Exposures to Pseudomonas aeruginosa bacteria can occur through various routes and in different settings. Here are some notable exposures, including specific examples:

1. Hospital Settings:
a) Ventilators: Pseudomonas aeruginosa can colonize and infect ventilator equipment, leading to the risk of transmission to patients through respiratory support devices.
b) Oxygen Masks: Improper disinfection or inadequate cleaning of oxygen masks can result in contamination and potential exposure to Pseudomonas aeruginosa.
c) Catheters and Medical Devices: Pseudomonas aeruginosa can colonize catheters, intravenous lines, urinary catheters, and other medical devices, increasing the risk of infection if proper hygiene practices are not followed.
d) Surgical Procedures: Surgical sites, particularly in post-operative wounds, may be susceptible to Pseudomonas aeruginosa infections if proper sterilization techniques and wound care protocols are not implemented.

2. Water Sources:
a) Tap Water and Faucets: Pseudomonas aeruginosa is commonly found in water environments, including tap water. Contaminated faucets and water systems can serve as a potential source of exposure, particularly in healthcare facilities.
b) Showers and Jacuzzis: Inadequate cleaning and maintenance of showers, hot tubs, and whirlpools can lead to the colonization of Pseudomonas aeruginosa and subsequent exposure to individuals using these facilities.

3. Eyedrops - EzriCare Artificial Tears: The specific exposure related to Pseudomonas aeruginosa is the use of EzriCare artificial tears, which has been associated with an outbreak. Contaminated eyedrops can introduce the bacteria directly into the eyes, potentially leading to eye infections and related complications. As a result, the American Centre for Disease Control and Prevention (CDC) has banned the eye drops.

These include, but are not limited to Eye drops and artificial tears such as EzriCare, Delsam Pharma's Artificial Tears, and Delsam Pharma's Artificial Ointment.

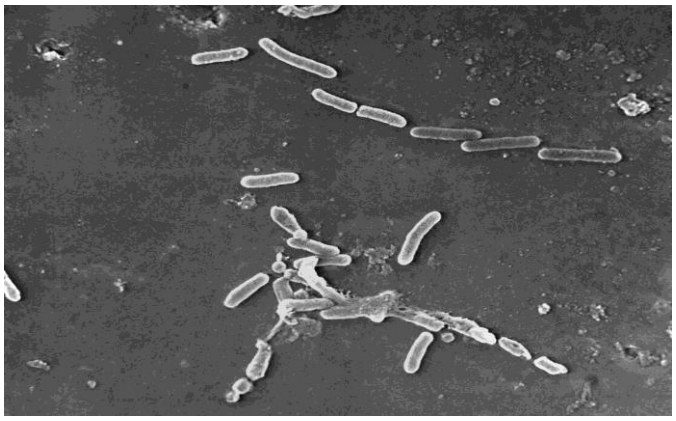
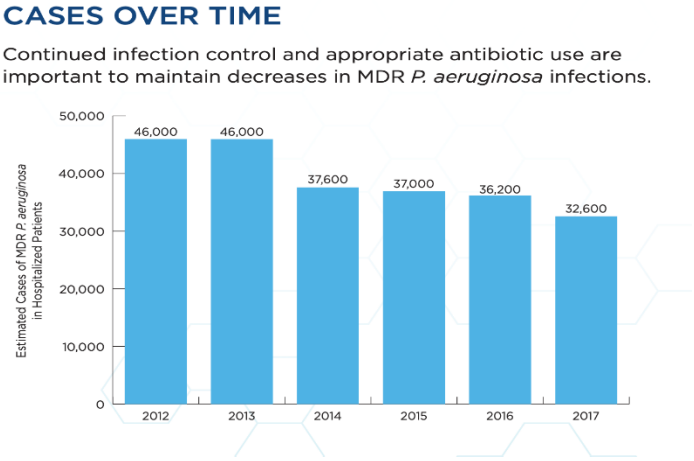


Image C: Drug Resistant *P. aeruginosa* suspended in medium of Ezri Care artificial tears.
https://www.npr.org/2023/03/22/1165268600/eyedrop-recall-bacteria-infection-cdc

The U.S. Centres for Disease Control and Prevention has reported another death and even more cases linked to Pseudomonas aeruginosa, a drug-resistant strain of bacteria, found in artificial tears or eyedrops. The bacteria strain has been found in 81 people — four of whom have died from infections, according to specimens collected between May 2022 and April 2023, according to the CDC's most recent update. Over 10 different brands of ophthalmic drugs were involved in these cases, the CDC said. But the most common was Ezri Care Artificial Tears

Cases
Prior to Drug Resistant Outbreak:

- In 2017, multidrug-resistant *Pseudomonas aeruginosa* caused an estimated 32,600 infections among **hospitalized patients** and 2,700 estimated deaths in the United States
- *P. aeruginosa* is most commonly contracted in the surgical setting, especially given its high antibiotc resistance.. It is estimated that *P. aeruginosa* has a prevalence of 7.1%–7.3% amongst all healthcare-associated infections.
- *P. aeruginosa* accounts for 10%–20% of isolates in cases of VAP (Ventilator Associated Phenomenon).



Graph 1: Cases *of P. aeruginosa* disease from 2012-2017
https://www.cdc.gov/drugresistance/pdf/threats-report/pseudomonas-aeruginosa-508.pdf

It is estimated that *P. aeruginosa* has a prevalence of 7.1%–7.3% amongst all healthcare-associated infections. The most common site of *P. aeruginosa* infection is pneumonia Prevalence has been increasing over the past decade . In intensive care unit (ICU) patients, *P. aeruginosa* is responsible for an even higher percentage of healthcare-associated infections. A large international observational point-prevalence study of infections in ICU patients found that *P. aeruginosa* represented 16.2% of patient infections and was the cause of 23% of all ICU-acquired infections, with a respiratory source being the most common site of *P. aeruginosa* infection

After Drug Resistant Outbreak

In 2022 and 2023, the infection mutated into a far more drug resistant strain and had new exposure; Artificial Eye drops. The new strain was classified as an Epidemic by the CDC due to contamination in certain eye drops. The CDC issued a warning after 55 patients in 12 states were identified with infections caused by a strain of the "extensively drug resistant" *Pseudomonas aeruginosa* bacteria between May and January. Most patients had used artificial tears before the onset of their condition, said the CDC, which is investigating the infections with the Food and Drug Administration.

As of May 15, 2023, CDC, in partnership with state and local health departments, identified 81 patients in 18 states (CA, CO, CT, DE, FL, IL, NC, NJ, NM, NV, NY, OH, PA, SD, TX, UT, WA, WI) with VIM-GES-CRPA, a rare strain of extensively drug-resistant *P. aeruginosa.* This represents an increase of 13 patients since the last update. Among these 13 patients, 6 (46%) had specimens collected prior to the February 2, 2023, manufacturer recall of products associated with this outbreak. These cases were confirmed after the recall date due to the time it takes for testing to confirm the outbreak strain and because of retrospective reporting of infections. Of the 7 patients who had specimens collected after the recall, most either resided in long-term care facilities with other known cases or reported use of a recalled brand of artificial tears.

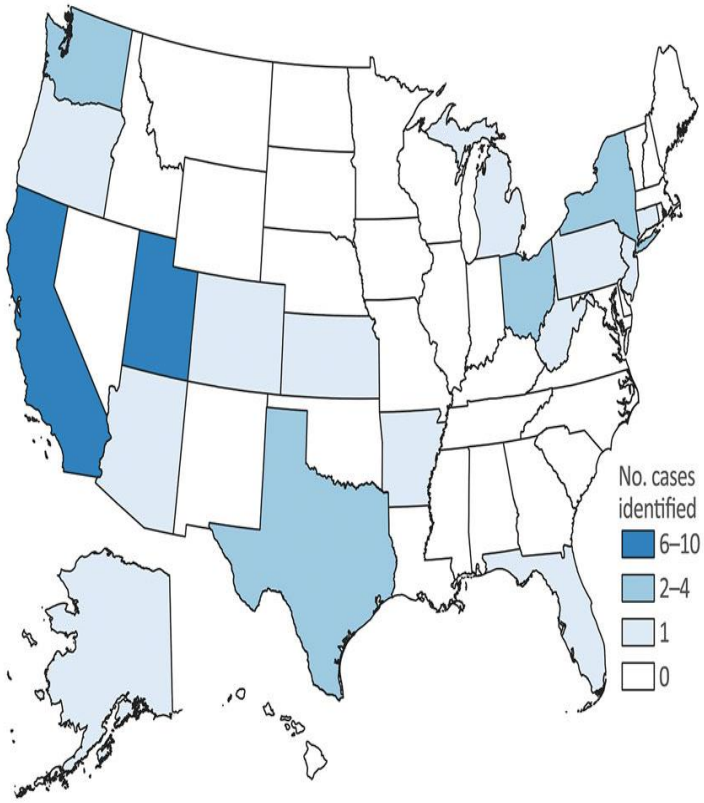
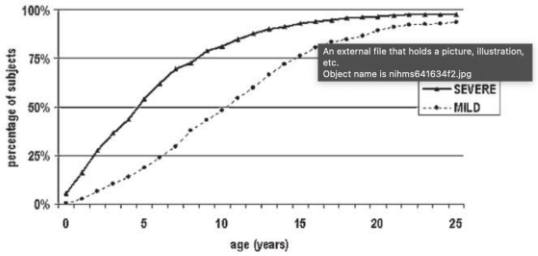


Image D: Cases of Drug Resistant *P. aeruginosa* per state on January 7th, 2023.
https://wwwnc.cdc.gov/eid/article/28/1/21-1880-f1

Person Characteristics- Age with Infection:
Age: age doesn't impact the acquisition of disease, but rather the severity. The given graph depicts the severity of disease and the percent of subject to infected from ages 0-25.

Fig. 2



Cumulative percentage of subjects ever reported positive for *Pseudomonas aeruginosa* (*Pa*) by age and lung disease severity. Subjects were considered *Pa* positive at a given age if they had a history of at least one culture positive for *Pa* by that age.

Graph 2: Cumulative percentage of subjects ever reported positive for Pseudomonas aeruginosa (Pa) by age and lung disease severity. Subjects were considered Pa positive at a given age if they had a history of at least one culture positive for Pa by that age.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4239995/

Symptoms
Symptoms of *P. aeruginosa* vary based on the type of infection. It may cause:

- Pneumonia
- Fever and chills
- Difficulty breathing
- Chest pain
- Tiredness
- Cough, sometimes with yellow, green, or bloody mucus

Infection in Urinary Tract:

- Strong urge to urinate frequently
- Painful Urination
- Unpleasant odour in urine
- Cloudy or bloody urine

Infection Through Wound

- Inflamed wound site
- Fluid leakage from wound

Infection Through Ear

- Ear Pain
- Decreased hearing
- Redness or swelling of outer ear
- Fever

Infection Through Eye

- Swelling of the Eye
- Temporary Blindness
- Yellowing of the Eye
- Eye Pain
- Inflammation of Blood Vessels in the Eye

Colonization

Colonization means that the organism is found in or on the body, but it is not causing any symptoms or disease. CRPA can colonize many body sites, including the respiratory tract, wounds, and digestive tract. Patients may remain colonized for months to years. Infections represent only a fraction of the burden of CRPA; many more patients are colonized. Patients colonized with CRPA can be a source of spread to other patients and develop CRPA infections. Because patients colonized with CRPA do not have signs or symptoms of infection, they can go undetected and

Treatments

Pseudomonas aeruginosa infections are generally treated with antibiotics. Unfortunately, in people exposed to healthcare settings like hospitals or nursing homes, *Pseudomonas aeruginosa* infections are becoming more difficult to treat because of increasing antibiotic resistance. To identify the best antibiotic to treat a specific infection, healthcare providers will send a specimen (often called a culture) to the laboratory and test any bacteria that grow against a set of antibiotics to determine which are active against the germ. The provider will then select an antibiotic based on the activity of the antibiotic and other factors, like potential side effects or interactions with other drugs. For some multidrug-resistant types of *Pseudomonas aeruginosa*, treatment options might be limited.
CDC tracks *Pseudomonas aeruginosa* and the infections this germ can cause, including antibiotic-resistant infections. Additionally, CDC works closely with partners, including public health departments, other federal agencies, healthcare providers, and patients, to prevent healthcare infections and to slow the spread of resistant germs.
Prevention

1. Screening: Screening tests identify patients colonized with carbapenems-producing CRPA to prevent transmission to other patients through targeted interventions, like Transmission-Based Precautions.
2. Clean your hands immediately before touching a patient ,before performing an aseptic task (e.g., placing an indwelling device), before handling invasive medical devices, and before moving from work on a soiled body site to a clean body site on the same patient.
3. Perform hand hygiene after touching a patient or the patient's immediate environment; after contact with blood, body fluids, or contaminated surfaces; and immediately after glove removal.
4. CRPA can contaminate your hands and clothes while you care for a patient with CRPA or work in their environment. This puts the patients who you care for afterward at risk of acquiring CRPA. Protect your patients by wearing a gown and gloves for patient care according to the guidelines for your setting.
5. Follow your facility's cleaning and disinfection protocols. Ensure high-touch surfaces (e.g., bed rails, light switches, call buttons) are cleaned frequently. Dedicate non-critical medical equipment (e.g., stethoscopes, blood pressure cuffs) to CRPA patients whenever possible and always clean and disinfect between patients. Ensure shared medical equipment is cleaned and disinfected after each use.
6. CRPA can contaminate wastewater plumbing, especially sink drains, toilets, and hoppers. Water splashes from these sources has been associated with outbreaks of carbapenems-producing organisms. Clean and disinfect countertops, handles, faucets, and sink basins at least daily. Keep patient care items at least three feet away from sinks, toilets, and hoppers. Do not discard patient waste in sinks. Avoid discarding beverages or other sources of nutrients in sinks or toilets.

III. LIMITATIONS

This research paper has several limitations. For one, the study only focuses on the outbreak in North America. Specially emphasising the outbreak in the USA. This research paper is purely based on other studies. No first hand research, case studies and microbiological works were performed. This paper is not in line with the STROCSS and STROBE guideline published in 2022.
Conclusion

In conclusion, Pseudomonas aeruginosa remains a formidable pathogen with significant implications for human health. This research paper has provided an overview of its epidemiology, virulence factors, antibiotic resistance, and therapeutic approaches. Understanding P. aeruginosa's adaptability and multidrug resistance is crucial for effective treatment. Exploring its virulence factors and host interactions can guide targeted interventions. Genomic advancements offer potential drug targets, while alternative approaches like bacteriophage therapy and immunotherapy show promise. Collaboration between researchers, clinicians, and public health agencies is essential. Continued surveillance and antimicrobial stewardship are crucial to curb multidrug-resistant strains. Investment in research and development is needed for novel therapeutics. Addressing P. aeruginosa requires a multifaceted approach, promoting interdisciplinary collaboration, and innovative strategies to understand, prevent, and control its infections, thus improving patient outcomes and public health.

IV. REFERENCES

1. "Pseudomonas Aeruginosa Infection." *Centers for Disease Control and Prevention*, 13 Nov. 2019, www.cdc.gov/hai/organisms/pseudomonas.html#:~:text=Pseudomonas%20aeruginosa%20infections%20are%20generally,because%20of%20increasing%20antibiotic%20resistance.
2. "Pseudomonas Aeruginosa Infection." *Centers for Disease Control and Prevention*, 13 Nov. 2019, www.cdc.gov/hai/organisms/pseudomonas.html.

3. "Pseudomonas Aeruginosa." *Share and Discover Knowledge on SlideShare*, www.slideshare.net/MaiMamdouh3/pseudomonas-aeruginosa-69643274. Accessed 7
4. *Pseudomonas Aeruginosa - Statpearls - NCBI Bookshelf*, www.ncbi.nlm.nih.gov/books/NBK557831/. Accessed 6 July 2023.
5. "Pseudomonas Aeruginosa." *Wikipedia*, 21 June 2023, en.wikipedia.org/wiki/Pseudomonas_aeruginosa.
6. Bennington-Castro, Joseph, et al. "What Is Pseudomonas Aeruginosa? Symptoms, Causes, Diagnosis, Treatment, and Prevention." *EverydayHealth.Com*, www.everydayhealth.com/pseudomonas-aeruginosa/. Accessed 7 July 2023.
7. "Pseudomonas Aeruginosa: Bacterium Risk Factors and Symptoms." *WebMD*, www.webmd.com/a-to-z-guides/pseudomonas-infection. Accessed 7 July 2023.

