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Double infection by Multi-Drug Resistant *Escherichia coli* bacteria: A case report

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ABSTRACT

Introduction: Antimicrobial resistance (AMR) is a global issue causing multidrug-resistant bacterial infections, leading to higher morbidity and mortality rates. *Escherichia coli*, a Gram-negative Enterobacterales bacteria, is the predominant cause of common diseases. In 2018, *Escherichia coli ESBL* (beta-lactamase enzyme Extended-spectrum) bacterium had the highest antibiotic resistance in Surabaya, Indonesia. In 2022, 3rd generation cephalosporin-resistant *E. coli* and carbapenem-resistant *E. coli* were the top priority pathogens in Indonesia.

Case: A one-year-old girl was taken to the emergency room after vomiting seven times and vomiting. She had a fever for one week, and her nose was runny. The patient had kidney channels narrowed and had surgery to implant a DJ stent in her right kidney five months prior. Physical examination revealed anemia, jaundice, cyanosis, and dyspnea. Blood and urine cultures were conducted, and *Escherichia coli* bacteria were found in urine and blood samples. *Escherichia coli ESBL* was found to be sensitive to several drugs, while its blood showed it was carbapenem-resistant, only sensitive to Ceftazidim, Amikacin, Gentamicin, Tigecycline, and Cefoperazone Sulbactam.

Discussion: Pediatric patients often experience urinary infections from *Escherichia coli* (ESBL) and bloodstream infections from *Escherichia coli* (CRE). These bacteria colonize various sites in the human body, including the urinary tract, causing diarrhea and causing cystitis. ESBL, or Extended Spectrum b-lactamase, breaks down antibiotics, making them ineffective for treating infections. ESBL production is associated with a bacterium found in the bowel, and resistance genes are often transmitted through plasmids carrying other resistance genes. The emergence of carbapenem-resistant *Escherichia coli* isolates (CREC) has led to using polymyxin, tigecycline, fosfomycin, and aminoglycosides as effective antibiotics against CREC. CREC can lead to severe infections, including intra-abdominal infections, pneumonia, urinary tract infections, and device-associated infections.

Conclusions:
Escherichia coli, an MDRO bacteria, requires antibiotic sensitivity test results for effective treatment, with sensitive drugs often chosen in difficult cases, and requiring source control.

Introduction

The global issue of Antimicrobial resistance (AMR) is significant. (Huang et al., 2024; Leoni et al., 2023). Multi-drug-resistant bacterial infections are linked to higher morbidity and mortality rates in real-world environments (Kasanga et al., 2023; Saliba et al., 2023). With the usage of antimicrobial medications, AMR rises (Huang et al., 2024). Antibiotic resistance leads to fewer treatment options available, longer hospital stays, higher treatment costs, and higher death rates. The need for alternate treatment options is urgent due to the rise in antibiotic resistance and the ineffectiveness of antibiotic therapies (Nasrollahian et al., 2024). Multidrug-resistant organism (MDRO) infections are more common among elderly people confined to long-term care institutions (Rodríguez-Villodres et al., 2021).

Each continent has a different prevalence of MDROs in long-term care facilities (LTCF). Asia has the highest prevalence of extended-spectrum ß-lactamase (ESBL) Enterobacterales (71.6%), carbapenem-resistant (CRE) Enterobacterales (6.9%), and methicillin-resistant *Staphylococcus aureus* (MRSA) (25.6%) (Rodríguez-Villodres et al., 2021)

Escherichia coli belongs to the family Enterobacteriaceae and order Enterobacterales. Gram-negative Enterobacterales bacteria *Escherichia coli* is a facultative anaerobe that is not sporogenous (Nasrollahian et al., 2024; Vázquez-López et al., 2023). *Escherichia coli* is the predominant cause of several common bacterial diseases, such as gastroenteritis, urinary tract infections (UTIs), bloodstream infections (BSIs), septicemia, and newborn meningitis, even though it is a frequent member of the gut microbiota in both people and animals. It is also present in water, soil, and the vicinity of plants. Apart from the rising incidence of *Escherichia coli* infections, a significant problem is their ongoing drug resistance (Sora et al., 2021).

Escherichia coli can manufacture the beta-lactamase enzyme Extended-spectrum (ESBL) and is carbapenem-resistant. Broad-spectrum cephalosporins, monobactams, and penicillins can all be hydrolyzed by bacteria that produce enzyme-specific beta-lactamases (ESBLs). On the other hand, an isolate of *Escherichia coli* that is carbapenem-resistant is resistant to imipenem, meropenem, ertapenem, or any other carbapenem-containing antibiotic (Endraswari et al., 2022). Within six months, *Escherichia coli* was the third rank of Gram-negative bacteria responsible for a bloodstream infection at Dr. Soetomo Hospital in Surabaya in 2018. Regarding the most dangerous UTIs, *Escherichia coli ESBL* bacterium had the highest level of antibiotic resistance (Ariana et al., 2020; Endraswari et al., 2022). Distribution of WHO priority pathogens based on specimens in all hospitals in 2022 in Indonesia, 3rd generation cephalosporin-resistant E. coli, and carbapenem-resistant E. coli are in first and third place compared to other MDRO bacteria (PAMKI, 2023).

Case

The patient's mother took a one-year-old girl to the Emergency room. Since this morning, the patient has puked seven times and made quite a bit of vomit. She appeared thirsty and was still drinking. There was a fever for one week, reaching a temperature of 39.5ºC. The temperature drops with paracetamol and then increases again. She hasn't had diarrhea or shortness of breath in the last four days but has been coughing up phlegm. Her nose is runny. Past medical background: The patient, who was eight months old, had both of his kidney channels narrowed. Five months prior, she had surgery to implant a DJ stent in his right kidney. Additionally, the catheter was withdrawn from the patient two months ago.

On physical examination, the Glasgow coma scale (GCS) was found to be 456, heart rate 140 times per minute, pulse strong, body temperature 36.6, SpO2 97% fa, respiratory rate 26 times per minute. Head and neck: Anemia (-), Jaundice (-), cyanosis (-), Dypsnea (-), droopy eyes, dry lips, abdomen: supple, flat, not distended, normal bowel sounds, extremities: pale warm acral, CRT < 2 seconds. Blood laboratory examination: Hb: 8.5, WBC: 21.92x10^3, PCT: 5.82, Neut: 71.2%, BUN: 12.5, SK 0.4. Urinalysis: Clear yellow, Specific gravity 1.003, Ph 5.5, glucose -, ketones -, Leukocytes 3+, Nitrites +, erythrocytes 2+, Protein 1+, bilirubin -, urobilinogen -, albumin 150, erythrocytes 1.16/hpf, leukocytes 57.15/hpf, non-squamous epithelium 14.21 per visual field, crystals -, bacteria 1982 per visual field.

Then, urine and blood cultures are carried out. From the results of culture in the media on urine samples, direct Gram staining was obtained: PMN -, Epithelium -, Bacteria -. Blood Agar Plate: Round, small, white colonies, non-hemolyzed, > 10^5. McConkey Agar Plate: Pink colonies, lactose fermenter. The blood specimen showed a Gram Bactec result: Gram-Negative Rods. Blood Agar Plate: Round, small, white colonies, non-hemolyzed. Chocolate agar plate: Colonies are round, small, white, non-hemolyzed—McConkey Agar Plate: Pink colonies, lactose fermenters.

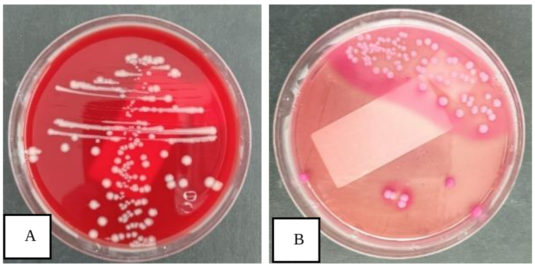

Figure 1. Colony growth in (A) Blood Agar, (B). McConkey Agar after incubation 1x24 hours, at temperature 37ºC

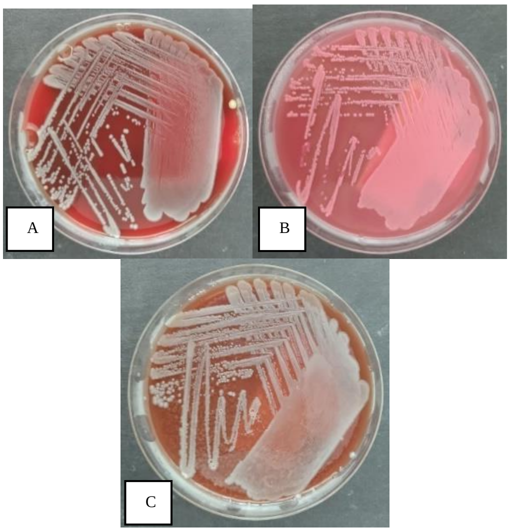

Figure 2. Colony growth in (A) Blood Agar, (B). McConkey Agar, (C) Chocolate Agar after incubation 1x24 hours, at temperature 37ºC

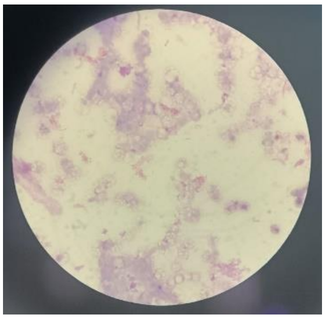

Figure 3. Direct gram stain from bacteria, Time to Positivity 1x24 hours, gram-negative rods in high power field

Table 1. Results of bacterial identification and antibiotic sensitivity testing

Specimens	Urine	Blood
Bacteria	*Escherichia coli ESBL*	*Escherichia coli CRE*
Antibiotic Sensitivity Test	Sensitive = Amikacin, Ceftazidime, Gentamicin, Imipenem, Meropenem, Tigecycline, Cefoperazone Sulbactam, Fosfomycin	Sensitive = Ceftazidime, Amikacin, Gentamicin, Tigecycline, Cefoperazone Sulbactam

Escherichia coli bacteria were found in urine and blood specimens with different bacterial sensitivity test results. In the urine specimen (*Escherichia coli ESBL)*, some drugs were still sensitive, namely Amikacin, Ceftazidim, Gentamicin, Imipenem, Meropenem, Tigecycline, Cefoperazone Sulbactam, and Fosfomycin. Meanwhile, the blood specimen results showed that *Escherichia coli* was carbapenem-resistant, which was only sensitive to the drugs Ceftazidim, Amikacin, Gentamicin, Tigecycline, and Cefoperazone Sulbactam.

On the 3rd day of hospitalization, urine and blood cultures came out, and the patient was given the antibiotic Cefoperazone Sulbactam.

Discussion

From the results above, it was found that these pediatric patients experienced infections in two different places. *Escherichia coli ESBL* in patients is called a urinary infection, and *Escherichia coli CRE* obtained in the blood is called a bloodstream infection. The urinary tract is the most often colonized extra-intestinal location by these bacteria, and these bacteria frequently cause bloodstream infections. The site of infection (e.g., uropathogenic *Escherichia coli*, named for their impact on the urinary system, and also extraintestinal pathogenic *Escherichia coli*, or ExPEC) are among the characteristics used to classify pathogenic *Escherichia coli* into "pathotypes" or "pathovars." (Foster-Nyarko & Pallen, 2022; Zhou et al., 2023)

In Gram-negative bacteria, β-lactamase enzymes that hydrolyze the amide bond of the four-membered β-lactam ring are the primary resistance mechanism, with multiple enzymes disseminating on mobile genetic elements across opportunistic pathogens such as Enterobacteriaceae (e.g., *Escherichia coli*) (Tooke et al., 2019). ESBL stands for Extended Spectrum β-Lactamase. β-lactamase enzymes break down and destroy some commonly used antibiotics, including penicillin and cephalosporins, and make these drugs ineffective for treating infections. ESBL production is associated with a bacterium usually found in the bowel. Particularly in Enterobacteriaceae, genes that produce ESBL and carbapenemase frequently have a high transmission rate through plasmids that carry other resistance genes. Both resistances in the same strain are often on different plasmids since ESBL and carbapenemases are connected with various plasmids. This has a significant impact on the use of antibiotics, the price of treatment, patient outcomes, and the range of available treatments. *Escherichia coli* were treated by cephalosporin and carbapenem; nevertheless, following the emergence of carbapenem-resistant *Escherichia coli* isolates (CREC) and the global spread of these variants, polymyxin, tigecycline, fosfomycin, and aminoglycosides, either alone or in conjunction with other antibiotics, are the antibiotics that continue to be efficacious against CREC. CREC can lead to severe infections, including intra-abdominal infections, pneumonia, urinary tract infections, and device-associated infections (Huang et al., 2024; Nasrollahian et al., 2024). Various mechanisms of resistance are exhibited by *Escherichia coli* strains, including the production of different β-lactamase enzymes, lowered permeability of the membrane, formation of capsule and biofilm, employment of efflux pumps, and enzymatic modification (Nasrollahian et al., 2024). Through the release of antimicrobial compounds, food competition, maintenance of the integrity of the epithelial barrier, bacteriophage deployment, and immunological stimulation, the gut microbiota can offer resistance against colonization. Nevertheless, nothing is now known about the connection between MDRO colonization and the microbiome (Ducarmon et al., 2021)

Conclusion

Escherichia coli is an Enterobacteriaceae which is often listed as MDRO bacteria. Reporting of antibiotic sensitivity test results will be highly anticipated when treating patients. Treatment will choose culture results with still-sensitive drugs in difficult cases with *Escherichia coli* bacterial infections with different genotypes. However, source control management is still important to do while waiting for the drug to be administered.

References

Ariana, N., Pestariati, P., Sasongkowati, R., & Kusumaningrum, D. (2020). RESISTANCE PATTERN OF Escherichia Coli AGAINTS ANTIBIOTICS IN URINARY TRACT INFECTION PATIENTS IN RSUD DR. SOETOMO SURABAYA. *Journal of Community Medicine and Public Health Research*, *1*(2), 53. https://doi.org/10.20473/jcmphr.v1i2.21693

Ducarmon, Q. R., Terveer, E. M., Nooij, S., Bloem, M. N., Vendrik, K. E. W., Caljouw, M. A. A., Sanders, I. M. J. G., van Dorp, S. M., Wong, M. C., Zwittink, R. D., & Kuijper, E. J. (2021). Microbiota-associated risk factors for asymptomatic gut colonisation with multi-drug-resistant organisms in a Dutch nursing home. *Genome Medicine*, *13*(1), 1–17. https://doi.org/10.1186/s13073-021-00869-z

Endraswari, P. D., Setiawan, F., Paramita, A. L., & Mertaniasih, N. M. (2022). Epidemiology of Escherichia coli as a Critical Pathogen of Bloodstream Infection Patients in Dr . Soetomo General Hospital , Surabaya , Indonesia. *Indonesian Journal of Tropical and Infectious Disease*, *10*(3).

Foster-Nyarko, E., & Pallen, M. J. (2022). The microbial ecology of Escherichia coli in the vertebrate gut. *FEMS Microbiology Reviews*, *46*(3), 1–22. https://doi.org/10.1093/femsre/fuac008

Huang, J., Lv, C., Li, M., Rahman, T., Chang, Y. F., Guo, X., Song, Z., Zhao, Y., Li, Q., Ni, P., & Zhu, Y. (2024). Carbapenem-resistant Escherichia coli exhibit diverse spatiotemporal epidemiological characteristics across the globe. *Communications Biology*, *7*(1), 1–13. https://doi.org/10.1038/s42003-023-05745-7

Kasanga, M., Kwenda, G., Wu, J., Kasanga, M., Mwikisa, M. J., Chanda, R., Mupila, Z., Yankonde, B., Sikazwe, M., Mwila, E., Shempela, D. M., Solochi, B. B., Phiri, C., Mudenda, S., & Chanda, D. (2023). Antimicrobial Resistance Patterns and Risk Factors Associated with ESBL-Producing and MDR Escherichia coli in Hospital and Environmental Settings in Lusaka, Zambia: Implications for One Health, Antimicrobial Stewardship and Surveillance Systems. *Microorganisms*, *11*(8), 1–21. https://doi.org/10.3390/microorganisms11081951

Leoni, F., Sacchini, L., Pieralisi, S., Angelico, G., Magistrali, C. F., Cucco, L., Massacci, F. R., Albini, E., Duranti, A., Cammà, C., Secondini, B., Rinaldi, A., & Barchiesi, F. (2023). Occurrence and temporal distribution of extended-spectrum β-lactamase-producing Escherichia coli in clams from the Central Adriatic, Italy. *Frontiers in Microbiology*, *14*(November), 1–13. https://doi.org/10.3389/fmicb.2023.1219008

Nasrollahian, S., Graham, J. P., & Halaji, M. (2024). A review of the mechanisms that confer antibiotic resistance in pathotypes of E. coli. *Frontiers in Cellular and Infection Microbiology*, *14*(April), 1–28. https://doi.org/10.3389/fcimb.2024.1387497

PAMKI. (2023). *Pola Patogen dan Antibiogram di Indonesia Tahun 2022*. 1–103.

Rodríguez-Villodres, Á., Martín-Gandul, C., Peñalva, G., Guisado-Gil, A. B., Crespo-Rivas, J. C., Pachón-Ibáñez, M. E., Lepe, J. A., & Cisneros, J. M. (2021). Prevalence and risk factors for multidrug-resistant organisms colonization in long-term care facilities around the world: A review. *Antibiotics*, *10*(6). https://doi.org/10.3390/antibiotics10060680

Saliba, R., Zahar, J. R., Dabar, G., Riachy, M., Karam-Sarkis, D., & Husni, R. (2023). Limiting the Spread of Multidrug-Resistant Bacteria in Low-to-Middle-Income Countries: One Size Does Not Fit All. *Pathogens*, *12*(1). https://doi.org/10.3390/pathogens12010144

Sora, V. M., Meroni, G., Martino, P. A., Soggiu, A., Bonizzi, L., & Zecconi, A. (2021). Extraintestinal pathogenic escherichia coli: Virulence factors and antibiotic resistance. *Pathogens*, *10*(11). https://doi.org/10.3390/pathogens10111355

Tooke, C. L., Hinchliffe, P., Bragginton, E. C., Colenso, C. K., Hirvonen, V. H.

A., Takebayashi, Y., & Spencer, J. (2019). β-Lactamases and β-Lactamase Inhibitors in the 21st Century. *Journal of Molecular Biology*, *431*(18), 3472–3500. https://doi.org/10.1016/j.jmb.2019.04.002

Vázquez-López, R., Hernández-Martínez, T., Larios-Fernández, S. I., Piña-Leyva, C., Lara-Lozano, M., Guerrero-González, T., Martínez-Bautista, J., Gómez-Conde, E., & González-Barrios, J. A. (2023). Characterization of Beta-Lactam Resistome of Escherichia coli Causing Nosocomial Infections. *Antibiotics*, *12*(9), 1–22. https://doi.org/10.3390/antibiotics12091355

Zhou, Y., Zhou, Z., Zheng, L., Gong, Z., Li, Y., Jin, Y., Huang, Y., & Chi, M. (2023). Urinary Tract Infections Caused by Uropathogenic Escherichia coli: Mechanisms of Infection and Treatment Options. *International Journal of Molecular Sciences*, *24*(13). https://doi.org/10.3390/ijms241310537