Researchers investigate diversity of E. coli bacteria in hospitalized patients

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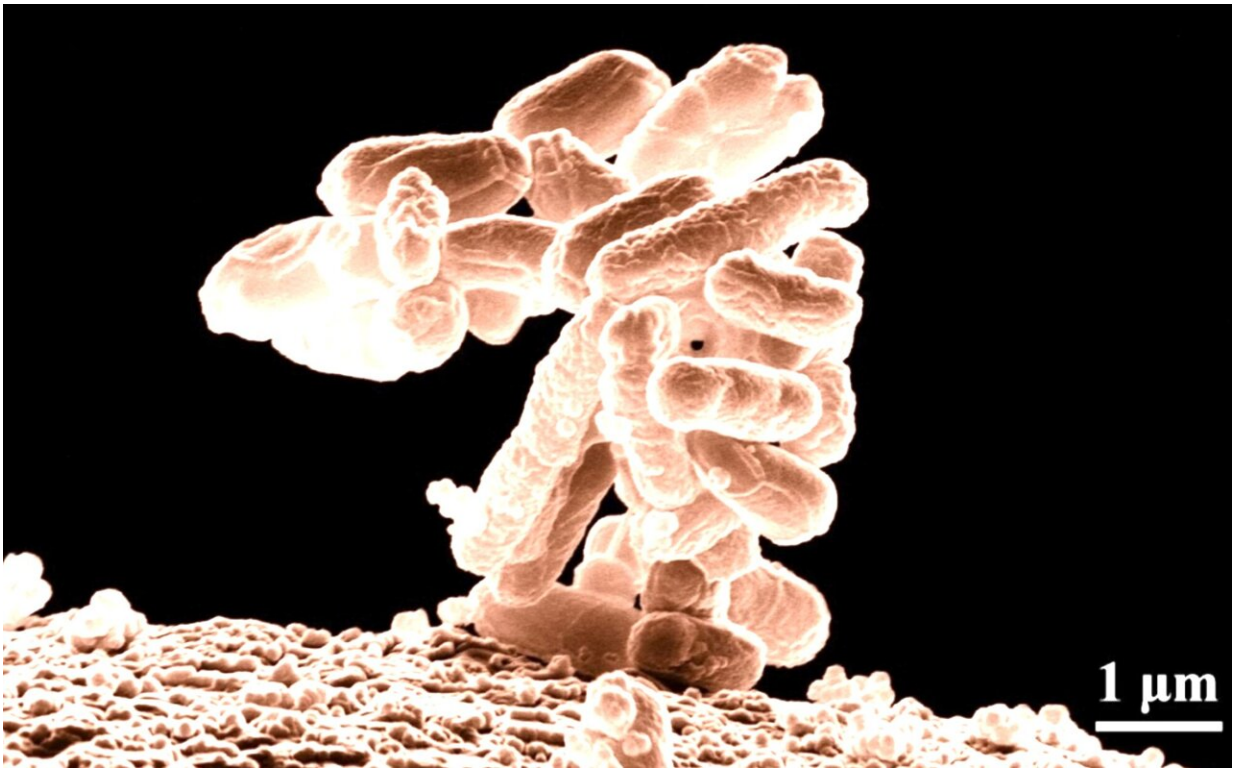

The aim of the study was to analyze the virulence and antimicrobial resistance profile of the main agent of urinary tract infections. Credit: Ericc Erbe, Christopher Pooley/Agricultural Research Service

The human intestine is an environment inhabited by many bacteria and other microorganisms collectively known as the gut microbiome, gut microbiota or intestinal flora. In most people, it contributes to wellness.

A healthy gut indicates a stronger immune system, improved metabolism, and a healthy brain and heart, among other functions.

Escherichia coli is one of the bacteria found in practically everyone's gut microbiota, where it performs important functions, such as producing certain vitamins. "But there's a vast amount of genetic diversity in the species. Some of its members are pathogenic and can cause diseases such as urinary tract infections," said Tânia Gomes do Amaral, head of the Experimental Enterobacterial Pathogenicity Laboratory (LEPE) at the Federal University of São Paulo's Medical School (EPM-UNIFESP) in Brazil.

"E. coli is the main agent of this type of infection among both healthy people and hospitalized patients or users of healthcare services."

Amaral is first author of an article published in the journal *Pathogens* on the virulence of these bacteria and their resistance to antibiotics in hospitalized patients.

"Our study focused on hospitalized patients because patients who stay in hospital for a long period are more likely to undergo various procedures, such as urine catheter insertion or venous access. Although these procedures are performed to assure life support, they may facilitate the entry of bacteria into the organism and cause an infection," Amaral explained.

She earned a Ph.D. in microbiology from EPM-UNIFESP in 1988, conducting part of her research at New York University Medical School and the Center for Vaccine Development at the University of Maryland, Baltimore (UMB) in the United States.

The article reports the findings of a broader study led by Amaral, with 12 co-authors who are researchers and graduate students, on the

virulence and drug resistance of E. coli strains associated with urinary tract infections.

The main aim of this part of the study, described in the master's dissertation of José Francisco Santos Neto, was to evaluate the diversity and drug resistance of pathogenic E. coli strains isolated from the gut microbiota of inpatients, and to analyze the frequency of endogenous infection (caused by bacteria from the patient's own microbiota).

The UNIFESP group first investigated the genetic diversity and drug resistance of E. coli strains isolated from the gut microbiota of hospitalized patients, sequencing these strains as well as others isolated from their urine and comparing the results in order to evaluate dissemination of the bacteria in the hospital environment.

"We also compared the genomes of these strains with those of E. coli strains isolated in different parts of the world in order to see if any globally disseminated pathogenic bacteria were present in the study sample," said Ana Carolina de Mello Santos, a postdoctoral researcher working on the LEPE team.

Urinary tract infections proved to be endogenous for the vast majority of the patients in the study (more than 70%). The results also showed that the patients' gut microbiota contained at least two genetically different populations of E. coli and that about 30% were colonized by non-lactose-fermenting E. coli strains, which are less common, with some of the patients studied having only such strains in their gut microbiota.

"This finding is most interesting because previous research conducted in other countries to analyze the composition of human gut microbiota didn't investigate non-lactose-fermenting E. coli," Santos said.

The authors also note the presence of bacteria with all the genetic

markers required for classification as pathogenic and the detection of pathogenic bacteria in the gut microbiota of all patients that had not yet developed an infection. "Hospitalized patients are more susceptible to infection because by definition they are already unwell. Colonization by pathogens is the first step in the spread of hospital-acquired infections now so frequent worldwide," Santos said.

With regard to antibiotics and other antimicrobials, the authors stress that drug resistance is also a growing global problem, and enterobacterial resistance to third-generation cephalosporins as well as colistin is critical. In all patients whose gut microbiota was colonized by drug-resistant bacteria, the same bacteria also caused endogenous urinary tract infections. In other words, the multidrug-resistant bacteria colonized the gut and traveled to the urinary tract, where they caused an infection.

"In light of these findings, early assessment of gut microbiota in hospitalized patients, at least in cases of E. coli infection, can facilitate and guide their treatment, while also identifying patients who risk progressing to extra-intestinal diseases such as urinary tract infections, which were part of the focus for our study," Amaral said.

"We don't yet know whether the findings also apply to other bacteria found in gut microbiota, such as the genera Klebsiella, Enterobacter, Pseudomonas and others that can cause infections when they travel to extra-intestinal sites."

These bacterial genera tend to be even more drug-resistant than E. coli, representing a major public health problem in the hospital environment. As the researchers noted, the World Health Organization (WHO) considers E. coli strains resistant to cephalosporin and colistin to be a critical global health threat. "The presence in human gut microbiota of drug-resistant bacteria associated with severe infectious disease is a matter of great concern, not least because they could spread to people

outside the hospital environment," Amaral said.

Another point raised by the study is the importance of finding out when colonization of the patient's gut by drug-resistant virulent bacteria occurred. The authors of the article were unable to determine whether the bacteria resistant to cephalosporins and colistin colonized the patients before or after they were hospitalized.

By analyzing the genomes of the strains, however, the researchers were able to identify global risk clones that can cause severe disease and are associated with antimicrobial resistance. "One such clone found in the gut microbiota of two patients was identical to others isolated from urinary tract infections in Londrina, Paraná [a state in South Brazil], and in the United States, as well as European and Asian countries. This shows that some strains found in the study are clones generally associated with infections in all regions of the world," Amaral said.

This type of information is important when patients are hospitalized. Knowledge of bacterial virulence and drug resistance can be used to prevent infection in parts of the organism outside the intestine and stop the bacteria from spreading to other patients in the same hospital.

More information: José F. Santos-Neto et al, Virulence Profile, Antibiotic Resistance, and Phylogenetic Relationships among Escherichia coli Strains Isolated from the Feces and Urine of Hospitalized Patients, *Pathogens* (2022). DOI: 10.3390/pathogens11121528

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