

Providencial Progression: Time to be Intolerant

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Our already heavily burdened healthcare system can ill afford emergence of one more multidrug-resistant hospital-acquired pathogen. The evolution and eventual onslaught of organisms such as *Klebsiella* and *Acinetobacter* are continuing to place more than enough strain on our institutions. The reportage of increasing incidence of *Providencia* infections from an Indian city and its decremental susceptibility to common antibiotics is quite worrying to state the least.¹ *Klebsiella pneumoniae*, which originally was quite a susceptible organism, was first reported to acquire carbapenem resistance (carbapenem-resistant *K. pneumoniae*, CRKP) and cause an outbreak in Israel in 2006.² *Acinetobacter baumannii*, which was sensitive to many common antibiotics, has progressively developed resistance since the 1970s. By 2007, up to 70% of isolates in various settings were multidrug-resistant, including carbapenems and polymyxins.³ These progressions exemplify the possible futuristic and sinister scenario for hitherto susceptible organisms such as *Providencia*. Can we retard, if not halt, this sinister progression?

Providencia is a urease-producing gram-negative bacilli, from Enterobacteriaceae family, detected by Rettger in 1904 and studied by Stuart's et al. at Brown University in Providence, Rhode Island, USA. The five species currently in the genus *Providencia*, in descending order of prevalence, include *Providencia stuartii*, *Providencia rettgeri*, *Providencia alcalifaciens*, *Providencia rustigianii*, and *Providencia heimbachae*. Naturally found in several animal reservoirs, soil, water, and sewage, they are also isolated from human saliva, urine, stools, skin, and blood. *Providencia* species most often cause complicated urinary tract infections with chronic indwelling urinary catheters or condom catheters. They are also implicated in foodborne gastroenteritis and bacteraemia.⁴ Though the prevalence of *Providencia* infections is generally low, it is gradually increasing, especially those associated with antimicrobial resistance. An Italian university hospital study in 2003 found that the prevalence of ESBL-producing *P. stuartii* increased from 31% in 1999 to 62% in 2002.⁵ The mortality rate among patients with *Providencia* bloodstream infection ranged from 6 to 33% in various studies.⁶ *Providencia* species are usually resistant to tetracyclines, older penicillins, older cephalosporins, and polymyxins, with susceptibility to recent cephalosporins, aztreonam, and carbapenems. Carbapenem-resistant *Providencia* species are increasingly being recovered from adult, critically ill, and/or immunocompromised patients. The most common isolated carbapenemase of *Providencia* is NDM-1.⁷ Korea has even reported a yearlong outbreak from carbapenemase and ESBL producing *P. rettgeri*.⁸ These kinds of *Providencia* infections are certain to impact patients' treatment, morbidity, and mortality, critically depleting healthcare resources further. This trend of providencial progression is a reminiscent of rise of *Klebsiella* and *Acinetobacter* as MDR

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hospital-acquired infections and demands urgent attention and enhanced deterrence action.

Ekadashi Rajni et al. conducted a retrospective observational study in a major teaching tertiary care referral hospital in north India, where they studied all *Providencia* isolates over a 3-month period.¹ Their findings align broadly with other international works, but are noteworthy from the perspective that this study is one of the few Indian studies to throw light on this rather alarming trend of *Providencia*. Among 1,261 urine samples cultured, *Providencia* was the fourth commonest gram-negative bacterium, and they were all from intensive care unit (ICU). The authors hypothesized that this phenomenon is due to the complex trilogy of urinary catheterization⁹ (100%), comorbid conditions (mainly diabetes, 67%), and a prolonged ICU stay (100%). The subjects in this study had a providencial escape, as none of them developed bacteremia due to UTI! But an alarming proportion of 33.0 and 53.0% isolates have been found to be XDR and PDR, respectively. Worryingly, carbapenem and BL-BLI resistance was observed in 93% of resistant isolates. If the Ekadashi Rajni and coworkers' reportage is any indication of things to come, we are in for deep trouble ahead of us.

What could be the reasons that the hitherto sensitive microorganisms are developing antibiotic resistance and how can we treat and, more importantly, prevent these phenomena? While Carbapenems remain the drug of choice for hospital-acquired *Providencia* infection, Fosfomycin was also tried. The fact that *Providencia* is inherently resistant to reserved antibiotics such as colistin and tigecycline, coupled with emerging resistance to carbapenems and even Fosfomycin, makes therapeutic choice very challenging.^{8,10} Hykawa et al. hypothesize that overuse of colistin, especially during the coronavirus disease-2019 (COVID-19) pandemic, might have given rise to further rise in the prevalence of *Providencia*.¹¹ Initiation of early treatment along with antimicrobial stewardship is the only way out of this difficult situation. Diabetic, paraplegic, elderly, and immunocompromised patients deserve focused attention, both for prevention and treatment of

Providencia infection. Since we realize that long-standing urinary catheterization, suprapubic cystostomy catheters, presence of pathological obstructions in the urinary tract (stones, strictures, and tumors), urinary functional disorder (neurogenic bladder and vesicoureteral reflux) are the nodoses of *Providencia* colonization and ensuing infection, one has to focus on prompt resolution of these factors. As a proportion of these cases emanate from nursing homes and elderly care homes, our infection prevention and control radar has to be extended to these otherwise often neglected sources of infection.

Needless to say, infection control practices, their implementation, quality control, and course correction have to be repeatedly and religiously reinforced. Issue in focus here is catheter care, the preventive tool for which is “catheter-associated urinary tract infections (CAUTI) Bundle.” Along with strictly following all the elements of CAUTI Bundle scrupulously, one must constantly evaluate the necessity of the urinary catheter in every case and every day. In fact, this should become a dictum for every device inserted in the patient. A healthy intolerant attitude should be inculcated in healthcare workers’ minds toward artificial devices and accesses. I would christen this attitude as “Device Intolerance.”

Coming back to the increasing menace of *Providencia*, identification of vulnerable patient population, rigid infection control practices along with “device intolerance,” prudent antimicrobial stewardship and prompt disease and infection management are the mool mantras to mitigate this menace. The data provided by Ekadashi Rajni and coworkers¹ come in very handy in creating a narrative of emerging hospital-acquired infections in parts of our country. On a wider basis, a national database, such as Centre For Disease Dynamics, Economics and Policy (CDDEP)¹² for various important infections will go a long way in monitoring, alerting, and evolving strategies for handling not only *Providencia* but also various other organisms that are emerging threats.

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