Clinical and pathogenesis overview of Enterobacter infections

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Enterobacter spp. is a gram-negative environmental bacterium, which belongs to the Enterobacteriaceae family and is found in water, sewage, soil, and plants. These bacteria are common among humans and animals, and the most frequently isolated species is Enterobacter cloacae. The species of this genus are often opportunistic pathogens with expanding significance in nosocomial infections, particularly in neonates, immunocompromised patients in intensive care units, emergency sections, skin and soft tissue infection wards, and urology wards. With the unexpected and rapid increase in antibiotic resistance in various bacterial species, there has been a new alarm for the health of the human community. Enterobacter species cause pneumonia, bacteremia, post-neurosurgical meningitis, neonatal meningitis, skin and soft tissue infections, and urinary tract infections. Some of the main risk factors for the occurrence and dissemination of Enterobacter spp. infections are poor hand hygiene, crowding, low birth weight, premature birth, intubation of patients, prolonged hospital stay, contaminated infant formula, intravenous feeding, use of extended-spectrum antibiotics and use of intravenous catheters.

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Literature Review

Enterobacter is a fermentative gram-negative bacterium, which belongs to the Enterobacteriaceae family. This genus was introduced by Hormaeche and Edwards (1960a) (1). The ability of the genus Enterobacter spp. to survive in a wide range of environmental conditions leads to the outbreak of various infections in medical settings (2). These pathogens are mostly members of the gastrointestinal microbiota and respiratory tract of humans and animals (3, 4). These bacteria are facultative, anaerobic rod-shaped, and motile by peritrichous flagella (4-6 in general), and their glucose fermentation occurs with acid and gas production. Most Enterobacteriaceae strains have been reported to have a positive Voges-Proskauer reaction and a negative methyl red test. The reduction of nitrate to nitrite and alkaline reaction in Simmons citrate and malonate broth are also positive. However, no selective media is available for Enterobacter species (5). Normally, they are associated with the contaminations caused by intravenous injection fluids, blood products, stethoscope, cotton swabs, and colonized hands of healthcare professionals (6).

Recently and mainly in the past decade, infectious episodes due to the resistance of several gram-negative bacteria (e.g., Enterobacter spp.) have been observed in various regions in the world (7, 8). An insignificant bacterium could threaten the health of the human community. Therefore,
it is essential to acquire more knowledge regarding this bacterium and review its taxonomy classification and properties. In this genus, classification was described after delineation via DNA-DNA hybridizations. To date, 22 species have been detected in this genus. Some of the more clinically significant species that have been identified recently or in the past in the genus Enterobacter include Enterobacter cloacae, Klebsiella aerogenes (E. aerogenes), E. amnigenus, Cronobacter sakazakii (E. sakazakii), E. gergoviae, E. intermedium, Pantoea agglomerans (E. agglomerans), E. cancerogenus (E. taylorae), E. asburiae, E. hormaechei, and E. dissolvens (1, 9).

Enterobacter spp. strains differ with each other in molecular methods, in which the 16SrRNA gene, oriC locus, and gyrB are used as targets. The sequencing of a fragment of hsp60 is considered to be a discriminator tool with 12 genomic clusters that are propagated by Hoffmann and Roggenkamp clusters I-XII. In 16SrRNA analysis, Enterobacter has been typed as a polyphyletic genus, and most of the species could not be determined (10). Furthermore, the typing method has been applied to determine the source and modes of transmission in the epidemic strains. Some of the approaches in this regard include biotyping, serotyping, phage typing, bacteriocin typing, plasmid profile, ribotyping, pulse-field gel electrophoresis, and multi-locus enzyme electrophoresis testing. Polymerase chain reaction (PCR)-based methods such as repetitive extragenic palindromic PCR and enterobacterial repetitive intergenic consensus PCR are considered to be effective methods for the detection of epidemic circulating strains during outbreaks on a day-to-day basis (11, 12).

This review aimed to introduce several important species of this bacterium from a clinical perspective as they are involved in hazardous human infections. Within a genetic complex group referred to as the Enterobacter cloacae complex, six genetically relevant and phenotypically similar species were intermixed, including Enterobacter cloacae, E. asburiae, E. dissolvens, E. hormaechei, E. kobei, and E. nimipressuralis. Several of these strains subscribe to a DNA fragment to affiliate with E. cloacae within the range of 61-67% (10,13). Furthermore, at least 12 genetic clusters have been phylogenetically defined within the complex (14, 15).

Clinical bacteriologists have recognized E. cloacae based on the biochemical attributes, demonstrating a large complex of at least 13 diverse species, subspecies, and genotypes (15, 16). These clusters are often recognized as E. cloacae using commercial biochemical kits, such as API20E. It is also notable that matrix-assisted laser desorption ionization-time of flight mass spectrometry and E. cloacae-specific duplex real-time PCR in combination are used to identify E. cloacae complex species (17). Among these members, E. hormaechei and E. cloacae are often isolated from human clinical specimens, especially from the patients admitted at intensive care units (ICUs). Therefore, E. cloacae have been one of the most usual Enterobacter spp. strains causing nosocomial infections in the past decade, and there have been numerous publications on the antibiotic resistance properties of these bacteria. Moreover, it has been remarked as an opportunistic pathogen involved in a wide array of infections, while the exact mechanism of pathogenicity remains unclear (18, 19).

This bacterium could form biofilms and contribute to the secretion of multiple cellular toxins, such as enterotoxins, hemolysins, and pore-forming toxins (10, 20, 21). Type III secretion system and curli fimbriae may contribute to its pathogenesis as well (22). The pathogenic strategies and agents that are involved in the diseases associated with the E. cloacae complex are not yet acknowledged, which could be due to the deficiency in the distribution of the available data in this regard (20). The Enterobacter cloacae complex is an opportunistic pathogen, which causes infections in wounds, the urinary tract, musculoskeletal (postoperatively), bloodstream, skin and soft tissues, respiratory tract, and postsurgical peritonitis (23). In addition, it may occasionally cause blood and brain infections, especially in immunocompromised persons (24, 25).

Drastic outbreaks of nosocomial and community infections are mostly caused by E. cloacae, E. asburiae, and E. hormaechei (10). E. amnigenus and E. asburiae strains have been isolated from human infections (4). Table 1 shows a summary of the biochemical properties of the important clinical Enterobacter species. Intrinsic resistance to aminopenicillins, amoxicillin-clavulanate, first-generation cephalosporins, and cefoxitin due to the production of constitutive AmpC β-lactamase (26). Aminoglycoside and carbapenem resistance have also been reported in this bacterium (10). The frequency of the clinical isolates of Enterobacter spp. producing extended-spectrum beta-lactamases (ESBL) highly varies in different countries. For instance, the rate has been estimated at 52.1% in Nigeria (27), 9% in Iran (28), 14.93% in Pakistan (29), 37.9% in France (30), 21.5% in Taiwan (31), 6.7% in Barcelona (32), 7.6% in the Netherlands (33), and 17.7% in Algeria (34). ESBL production in Enterobacter spp.
Table 1. Characteristics of the clinical common species of the genus Enterobacter.

<table>
<thead>
<tr>
<th>Test</th>
<th>E. cloacae complex</th>
<th>K. aerogenes</th>
<th>C. sakazakii</th>
<th>P. glomerans</th>
<th>Test</th>
<th>E. cloacae complex</th>
<th>K. aerogenes</th>
<th>C. saka-zakii</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Indole</td>
<td>-</td>
<td>-</td>
<td>D</td>
<td></td>
<td>20 Adonitol</td>
<td>d</td>
<td>+</td>
<td>-</td>
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<tr>
<td>2 Methyl Red</td>
<td>d</td>
<td>-</td>
<td>-</td>
<td>d</td>
<td>21 Raffinose</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>3 Voges-proskaufer</td>
<td>d</td>
<td>+</td>
<td>+</td>
<td>d</td>
<td>22 L-Rhamnose</td>
<td>d</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>4 Citrate</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>23 Malonate</td>
<td>d</td>
<td>d</td>
<td>+</td>
</tr>
<tr>
<td>5 Urease</td>
<td>+ (65%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>24 Maltose</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>6 H₂S Production</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>25 D-glucose production</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>7 Oxidase</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>26 ONPG</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>8 Motility(36°C)</td>
<td>d</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>27 Trehalose</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>9 Lysine de-carboxylase</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>28 Glycerol</td>
<td>d</td>
<td>+</td>
<td>-</td>
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<tr>
<td>10 Ornithine decarboxylase</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>29 D-mannitol</td>
<td>+</td>
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<tr>
<td>11 Arginine di-hydrolase</td>
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<td>-</td>
<td>+</td>
<td>-</td>
<td>30 Dulcitol</td>
<td>D</td>
<td>d</td>
<td>-</td>
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<tr>
<td>12 Esculin hydrolysis</td>
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<td>+</td>
<td>+</td>
<td>d</td>
<td>31 Catalase production</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>13 Sucrose</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>d</td>
<td>32 Deoxyribonuclease (25°C)</td>
<td>-</td>
<td>-</td>
<td>(+)</td>
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<tr>
<td>14 Melibiose</td>
<td>d</td>
<td>+</td>
<td>+</td>
<td>d</td>
<td>33 Lipase</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>15 D-sorbitol</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>d</td>
<td>34 Growth in KCN</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>16 Mucate</td>
<td>d</td>
<td>+</td>
<td>-</td>
<td>d</td>
<td>35 Phenylalanine deaminase</td>
<td>-</td>
<td>-</td>
<td>d</td>
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<tr>
<td>17 Lactose</td>
<td>d</td>
<td>+</td>
<td>+</td>
<td>d</td>
<td>36 Nitrate reductase</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>18 Gelatine hydrolysis (22°C)</td>
<td>(d)</td>
<td>+</td>
<td>-</td>
<td>+</td>
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<tr>
<td>19 Salicin</td>
<td>D</td>
<td>+</td>
<td>-</td>
<td>d</td>
<td></td>
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</table>

*a*: 90–100% strains positive in 1–2 days; (+): 90–100% strains positive in 1–4 days; d: positive or negative in 1–4 days; D: test used to differentiate species within a complex; (d): positive or negative in 3–4 days.

*b* The E. cloacae complex includes E. cloacae, E. dissolvens, E. hormaechei, and E. asburiae (1, 78, 79).
Carbapenem-resistant Enterobacteriaceae (CRE) has become a major public health concern worldwide. Carbapenemase enzymes are the major mechanism of carbapenem resistance in this family, while Klebsiella pneumoniae and Escherichia coli primarily represent the etiology of CRE infections, and carbapenem-resistant E. cloacae has occasionally been described due to its unique properties (38, 39).

New Delhi metallo-beta-lactamase (NDM)-producing E. cloacae was reported in various regions worldwide (39, 40). Fosfomycin is a bactericidal antibiotic that inhibits peptidoglycan synthesis, which has been used as a therapeutic solution for the management of invasive infections, including the infections caused by CRE strains (e.g., NDM-producing E. cloacae) (41). Moreover, VEB-producing Enterobacteriaceae (e.g., E. cloacae) are mostly found in Vietnam and Thailand (10). To date, tigecycline and colistin resistance has rarely been reported in the E. cloacae complex, which may indicate that effective therapeutic options against multidrug-resistant Enterobacter spp. (42-44). It is also notable that for many species of this genus, there have been no commercially available vaccines. It was originally known as Aerobacter aerogenes, while based on the most recent taxonomic modifications, the name was changed to Klebsiella aerogenes (45). Motility and urease activity tests have been reported to be negative, while ornithine decarboxylase activity has been shown to be positive for this bacterium (46). Enterobacter aerogenes and E. cloacae are the most frequent human pathogens in genus Enterobacter (47).

Klebsiella aerogenes has been recognized as an opportunistic pathogen appearing as a nosocomial pathogen in patients admitted to the ICU (20). K. aerogenes is often disseminated through cross-contamination due to surgery or constant therapy in hospitals in the patients using catheters. Moreover, K. aerogenes may mostly cause wound, respiratory, urinary tract, skin and soft tissues, gastrointestinal tract, and septic infections, as well as the fulminant form of necrotizing meningitis in infants (48-51). Lysine decarboxylase and arginine decarboxylase activity tests are used for the biochemical differentiation between E. cloacae and K. aerogenes, in which K. aerogenes (unlike E. cloacae) has positive and negative reactions, respectively (52). The clinical significance of this bacterium is largely due to its high antibiotic resistance rather than the self-bacterial virulence. It has progressively introduced for resistance against various antimicrobials, leading to the appearance of multidrug-resistant clinical strains (53). Inherent resistance against aminopenicillins among the recent isolates of K. aerogenes has frequently displayed resistance against β-lactams antibiotics, and enzymatic degradation by plasmid-mediated, broad-spectrum β-lactamases has been recognized as the most common resistance mechanism (54).

The unnecessary use of the extended-spectrum cephalosorins and carbapenems in the antibiotic therapy of Enterobacter spp. infections leads to the emergence of pan-drug-resistant K. aerogenes isolates with resistance to carbapenems and colistin, for which no therapeutic selection has been accessible. The most effective approach to tackle K. aerogenes might involve proactive prevention practices. The adaptive evolution in K. aerogenes is mostly due to porin mutations and the efflux mechanism (55).

Cronobacter sakazakii was referred to as yellow-pigmented E. cloacae and determined as an inimitable species almost 40 years ago (56, 57). This bacterium was identified from E. cloacae based on biochemical test results (e.g., malonate utilization, sorbitol fermentation, urea hydrolysis, and presence of α-glucosidase), molecular methods (e.g., DNA-DNA hybridization and rRNA 16S sequencing), antibiotic susceptibility, and pigment production (58).

Among the five species of the Cronobacter genus (C. sakazakii, C. malonaticus, C. dublinensis, C. muytjensii, and C. universalis), C. sakazakii has more frequently been isolated from human infections (59, 60). However, C. sakazakii has been recovered from all age groups, while the most high-risk population has been reported to be neonates aged less than one year (61). This strain has been shown to cause bacteremia and meningitis first in infants and is associated with the use of powdered milk formula (47).

The isolation of C. sakazakii has also been accomplished from dairy products, infant foods, sausage meat, and raw herbal foods (62).

Cronobacter bacteria could survive in the food products that are not heated adequately or have not been pasteurized (63). In addition, contaminated powdered infant formula is considered to be the main source of C. sakazakii infections in infants (64). Recent reports have also highlighted the risk posed to immunocompromised adults, especially the elderly (65).
The infectious dose of Cronobacter spp. requires further investigation. In a study, Iversen and Forsythe primarily predicted that the infectious dose may be approximately 1,000 CFU (66). It has also been suggested that the infectious dose of Cronobacter spp. might be 10,000 CFU [65]. Cronobacter spp. have been clinically isolated from a wide range of samples, including the cerebrospinal fluid, bone marrow, blood, intestinal and respiratory tracts, urine, ear and eye swabs, and skin wounds (65).

Clinical personnel should be informed of the feasible risk of the infections caused by the utilization of nonsterile formula in neonatal healthcare settings. Necrotizing enterocolitis, neonatal sepsis, and meningitis are the most common manifestations of C. sakazakii infections in infants and children, with the mortality rate estimated at 40-80%, while diarrhea, urinary tract infection, and septicemia have also been reported in this regard. The manifestations in neonatal meningitis are often severe and include seizures, brain abscess, hydrocephalus, developmental delay, and death in 40-80% of the patients (67).

Low-birth-weight and premature birth (neonates aged of 28 days) are presumed to be at the higher risk of infections compared to normal infants (62, 68). Until recently, C. sakazakii pathogenesis was unclear (56). Biofilm formation, production of capsular materials in some strains, surface endotoxin, specific bacterial adhesins, and siderophores to acquire iron and thermo-tolerance are among the other properties facilitating the survival and pathogenicity of this bacterial strain (62). In cell culture, it has been reported to exhibit clustered adhesion [56], while surviving in macrophages and penetrating diverse cells (e.g., endothelial cells) (69).

Several biochemical full automatic and semi-automatic systems have been endorsed to identify Cronobacter spp., including Api20E, ID32E, BIOLOG microarray, and Vitek 2 system, while they could only be used for possible identification with relatively low accuracy (43%) (70, 71). According to the protocol of the Food and Drug Administration (FDA), violet red bile glucose agar medium could be used for the isolation of Cronobacter spp. from food products (65). It is also notable that among various biochemical tests, 100% of C. sakazakii have been reported to be positive for α-glucose oxidase compared to 0% of other Enterobacter species although some other members of the Enterobacteriaceae family are also positive for this enzyme (72).

Diverse chromogenic agars that are based on the alpha-glucosidase possessed by Cronobacter spp. are available (69). Similar to C. sakazakii, E. hormaechei has been isolated from enteric feeding and other infant products (57, 73). The misidentification of E. hormaechei as C. sakazakii could lead to substantial consequences (74). The production of acid from raffinose occurs by Cronobacter spp., while E. hormaechei has no such function, and there is key biochemical difference between these strains in this regard (75). C. sakazakii is inherently resistant to all macrolides, lincosymycin, clindamycin, streptogramins, rifampicin, fusidic acid, and fosfomycin. It is susceptible to numerous β-lactams, chloramphenicol, tetracyclines, aminoglycosides, antifolates, and quinolones (76).

Ampicillin-gentamicin and ampicillin-chloramphenicol have been traditionally used for the treatment of C. sakazakii infections. However, due to the emergence of resistance to ampicillin following the production of β-lactamase enzymes, it is recommended that combination therapy with carbapenems or newer cephalosporins be applied, along with a second agent (e.g., aminoglycosides) (77).

P. agglomerans is an environmental and agricultural bacterium of the genus Pantoea, which was reclassified into the genus from Enterobacter in 1989. The species of this genus include P. ananatis, P. citrea, P. dispersa, P. punctata, P. stewartii, and P. agglomerans, which are the type species of the genus Pantoea. All Pantoea species could be isolated from food, water, soil, and plants, where they may either be harmful or commensals (80, 81). Furthermore, it could be found among the normal hand flora in humans (82). The properties of this strain could be identified based on the produced yellow pigment on blood agar, as well as oxidase- and urease-negative and negative H2S. P. agglomerans is the most commonly isolated species in humans, which is often a causative factor for occupational diseases and human infections (81). This opportunistic human pathogen causes human infections, especially in children. Moreover, it is a potential candidate as a powdered infant milk formula-borne opportunistic pathogen. Nosocomial infections may also occur due to the contamination of medical equipment and fluids (80, 83, 84).

P. agglomerans could be obtained from both community and healthcare settings. However, no actual evidence has identified a separate evolutionary connection between plant-associated and clinical P. agglomerans isolates (85). P. agglomerans may cause soft tissue or bone/joint infections following penetrating trauma through vegetation, spondylodiscitis, tibial osteitis, bloodstream infections, urinary tract infection, pneumonia, and wound infections (80, 82).
According to the findings of Gonçalves et al., P. agglomerans is a permanent constituent of the flora in chronic periodontitis lesions, posing the risk of generalized infections, especially in immunocompromised and hospitalized hosts (75). The lipopolysaccharide from E. agglomerans is often found in cotton dust and has a high affinity for binding to the pulmonary surfactant (lipid-proteinaceous underlying matters), thereby converting its surface tension traits. Binding in the lungs may change the physiological properties of surfactant, acting as a feasible mechanism for pathogenesis by sinesuses, which is a professional respiratory untindness caused by the inhalation of cotton dust (86). P. agglomerans strains could also express extended-spectrum β-lactamase and carbapenemases, which highlights the clinical importance of this bacterium. However, the extensive majority of Enterobacter infections are the result of E. cloacae, E. aerogenes, and E. agglomerans, and other species may occasionally occur in distinct human infections.

Enterobacter cancerogenus (formerly E. taylorae) is another species that has rarely been isolated from human infections. It is more associated with wound infections and osteomyelitis and has intrinsic resistance to aminopenicillins (i.e., amoxicillin and amoxicillin-clavulanic acid) and/or cephalosporins (87, 88). The E. cloacae complex has been shown to have 18 clades (A-R). Clade R (Hoffmann cluster IX) has recently been defined to be E. bugandensis (3) as identified from E. cloacae based on biochemical tests (e.g., D-arabinose fermentation and ornithine decarboxylase test) (88). In addition, E. bugandensis has recently been recognized as a species of Enterobacter and is highly pathogenic in this genus (3). It could cause neonatal sepsis and other infections in infants, as well as severe infections in immunocompromised patients (3, 89).

The type of strain EB-247 is resistant to ampicillin, amoxicillin/clavulanic acid, piperacillin-sulbactam, piperacillin-tazobactam, cefalotin, cefuroxime, cefuroxime-axetil, cefoxitin, cefpodoxime, cefotaxime, ceftazidime, gentamicin, tobramycin, ciprofloxacin, norfloxacin, tetracycline, and trimethoprim/sulfamethoxazole. However, it is sensitive to imipenem, meropenem, and nitrofurantoin (89). Enterobacter dissolvens and E. nimipressuralis have only been isolated from the environment and not observed in clinical specimens (1). Among various gram-negative pathogens that are emerging as nosocomial pathogens (e.g., P. aeruginosa, Klebsiella, and Enterobacter spp.) that refuge intrinsic (chromosomal) or acquired (plasmid) antimicrobial resistance determinants, Enterobacter spp. infections have gained significance, especially in recent years (90). A wide range of clinical syndromes have also been attributed to Enterobacter spp., the rate of which is on the rise in ICUs and neonatal ICUs, mainly affecting patients with prolonged hospital stay. Infection could be acquired from endogenous or environmental sources. Contaminated medications or distilled water in mechanical ventilators and solutions used for parenteral nutrition in neonatal units are common transition sources of Enterobacter in these wards. Colonization of Enterobacter spp. in severely ill patients could occur in the gastrointestinal tract and other human body organs, thereby easily transmitting among patients. Furthermore, the presence of a foreign device, low birth weight in neonates, prematurity, and immunocompromised patients are among the other risk factors for the acquisition of Enterobacter infections.

Some of the main infections in the human body include bacteremia, skin and soft tissue infections, respiratory tract infection, severe septic arthritis, osteomyelitis, urinary tract infection, bone and joint infections, gastrointestinal tract infection, central nervous system infections. Most of the findings regarding bacteremia are not noteworthy (range: 56-100%). In most series, E. cloacae (range: 46-91%) is followed by E. aerogenes (range: 9-43%) E. agglomerans, C. sakazakii, and the range of 14-53% has been reported for other bacteremia types, which may occur incidentally, involving Enterobacter spp. as a polymicrobial condition (11, 91).

In the United States, Enterobacter spp. have recently outstripped Klebsiella spp. to become the third most common cause of nosocomial respiratory tract infections (25). In lung transplant recipients, Enterobacter spp. have also been recognized as the most frequent pathogens (11).

Conclusion

In general, immunization with the development of new vaccines and improved hygiene (particularly hand hygiene by hand washing in hospitals and care centers for patients and the elderly) are considered to the most common control strategies for nosocomial infections. Among gram-negative pathogens, the infections caused by Enterobacter spp. are emerging as nosocomial pathogens; such examples are Paeruginosa and Klebsiella, which harbors intrinsic (chromosomal) or acquired (plasmid) antimicrobial resistance determinants and have gained significance, especially in recent years. E. cloacae, K. aerogenes, C. sakazakii, and P. agglomerans are often isolated from human
clinical specimens. Enterobacter infections include bacteremia, skin and soft tissue infections, respiratory tract infections, severe septic arthritis, osteomyelitis, urinary tract infection, bone and joint infections, gastrointestinal tract infection, and central nervous system infections. Some of the main predisposing factors for the acquisition of Enterobacter infections include the presence of a foreign device, low birth weight in neonates, premature birth, and immunocompromised patients due to any causes. Moreover, the unnecessary use of the extended-spectrum cephalosporins and carbapenems in the antibiotic treatment of Enterobacter spp. infections has led to the emergence of resistant strains among Enterobacter spp. The effective control strategies for nosocomial infections are immunization with the development of new vaccines and improved hygiene, particularly hand hygiene (e.g., hand washing in hospitals and care centers for patients and the elderly).

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Conflict of Interest
The authors declare no conflict of interest.

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