 REVIEW ARTICLE
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A spotlight on *Raoultella ornithinolytica*: A newly emerging life-threatening zoonotic pathogen

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Abstract

The genus *Raoultella* contains *Raoultella ornithinolytica* (*R. ornithinolytica*), which was previously named as *Klebsiella ornithinolytica*. *R. ornithinolytica* is a Gram-negative bacillus that belongs to the family *Enterobacteriaceae*. This pathogen is normally present in aquaculture, and it has been isolated from fish, insects, and wild and domestic birds. Seafood and poultry products are incriminated as sources of *R. ornithinolytica* infection. Community-acquired human infection with *R. ornithinolytica* is common. This infection is commonly associated with sepsis, bacteremia, food poisoning, purities, and urinary and respiratory tracts' infections. Rapid acquired resistance of *R. ornithinolytica* strains is common, and it is related to the development of resistant genes. *R. ornithinolytica* is considered as a newly emerging life-threatening pathogen worldwide. Hence, it is very important to determine the role of animals and birds in the epidemiological situation of this pathogen as well as the detection of antibiotic resistance genes before treatment.

Keywords: Animals, antibiotic resistance, birds, human, *Raoultella*, susceptibility.

Introduction

Raoultella ornithinolytica (*R. ornithinolytica*) belongs to the family *Enterobacteriaceae* which is Gram-negative, non-motile, aerobic or facultative anaerobic, and encapsulated bacillus [1,2]. This pathogen is a member of *Raoultella* genus which was previously designated *Klebsiella* till differentiation through the phylogenetic analysis of the organism in 2001 [3-5]. The underreported incidence of *R. ornithinolytica* may be due to the inaccuracy of conventional identification methods causing uncertainties [6,7] as well as the similarities with species of *Klebsiella,* namely, *Klebsiella pneumoniae* and *Klebsiella oxytoca* [8].

R. ornithinolytica is commonly found in aquatic environments [9], and it could be isolated from fish and insect species such as ticks and termites [2,10,11]. The role of *R. ornithinolytica* in animal infection has not yet been well studied. Some reports showed isolation of this pathogen from wild and domestic birds [12-17]. Moreover, *R. ornithinolytica* is a potent histamine producer [18,19], so it became a pathogen of great importance in food products. The pathogen has also been isolated from poultry products [20] as well as seafood products [21,22]. It has been found that *Raoultella* species produced more than 1.000 mg histamine/kg in fresh tuna [19].

It is well known that *R. ornithinolytica* is an emerging, lethal and intermittent nosocomial pathogen and associated with community-acquired and/or hospital-acquired human infections [8,23,24]. The reported cases of *R. ornithinolytica* infections in humans included urinary, respiratory, and gastrointestinal tracts infections as well as wound, skin, and catheter-related blood-stream infections [25-27].

Although *R. ornithinolytica* can be treated easily, the development of resistant strains from natural environments and clinical material is common [28-30]. For example, a carbapenem-resistant *R. ornithinolytica* strain has been isolated from the urban river sediment in China [9].

Accordingly, this review article has been designed to spotlight on *R. ornithinolytica* pathogen, host susceptibility, and human infection as well as its treatment.

The Pathogen

The order Enterobacterales include genus *Raoultella* which is an aerobic, non-motile, Gram-negative, and encapsulated rods [3,31]. It is difficult to probably distinguish *Raoultella* from *Klebsiella* genus using conventional biochemical and phenotypic methods [32,33]. *Raoultella* was first classified in cluster II of *Klebsiella* genus and termed *Klebsiella ornithinolytica* [3,31,34]. Hence, ornithine decarboxylase has been used to differentiate between *Raoultella* and *Klebsiella* [28,35]. Based on sequence analysis of *16S rRNA, rpoB, gyrA,* and *gyrB* genes, the cluster II of the genus *Klebsiella* was renamed as a new genus *Raoultella* [3,36]. The genus *Raoultella* contains four species; *R. ornithinolytica*, *Raoultella planticola*, *Raoultella terrigena*, and *Raoultella electrica* [26,37]. The only way to achieve reliable identification of *R. ornithinolytica* and other species of *Raoultella* is by applying supplemental biochemical tests and/or using Analytical Profile Index E20 and Matrix-Assisted Laser-Desorption Ionization Time-of-Flight Mass Spectrometry [13,16,20,33,38,39]. It is oxidase-negative and catalase-positive and grows at low temperatures using sorbose as a source of carbon [3,6,31].

R. ornithinolytica is considered as an emerging pathogen that has some virulence factors such as capsule, and CFA/I and CFA/II colonization factors, in addition to the production of siderophores, histamine, and bacteriocins [8,40,41].

Host Susceptibility

R ornithinolytica is commonly present in water [9,33] and has been isolated from fish [2]. The pathogen has also been found naturally in soil, vegetables, and insects as ticks and mites [6,42-45].

The isolation of *R. ornithinolytica* from animals or birds is infrequent. For instance, it has been detected in the cloacal samples of apparent healthy vulture [14] and in a case of hepatitis in ring-neck [12]. In addition, *R. ornithinolytica* has been described during a routine evaluation of aerobic enterobacteria in cloacal microbiota of birds in Argentina [16]. Mallard ducks also have been found to harbor *R. ornithinolytica* in their intestines and could act as a reservoir for this bacterium [13]. Moreover, *R. ornithinolytica* isolate was found in the droppings of the migratory common crane in Slovakia [15]. Recently, in Spain, *R. ornithinolytica* has been isolated from wild Canarian Egyptian vultures after feeding on fish [17].

In Thailand, previous studies demonstrated that *R. ornithinolytica* and *R. terrigena* could form a biofilm during seafood processing [21,22,46]. For the first time in Egypt, strains of *R. ornithinolytica* have been detected in chicken products including nuggets, strips, burgers, luncheon meats, pane, frankfurters, and minced chicken meat. Thirty-three bacterial isolates out of forty samples (82.50%) were *Enterobacteriaceae* and three isolates out of 33 (9.09%) were regarded as *R. ornithinolytica* [20].

Human Infection

The different clinical pictures of human infection with *R. ornithinolytica* are shown in Figure-1. It was documented that *R. ornithinolytica* can change histidine to histamine causing poisoning and skin flushing and this is called scombroid syndrome associated with fish poisoning [25,26,40,47,48]. As a result of increasing histamine level, patients with this syndrome showed diarrhea, vomiting, and pruritus [11,42,49]. Infection with *R. ornithinolytica* may induce both systemic and localized diseases' conditions especially after the abdominal surgery of cancer patients [2]. In addition, *R. ornithinolytica* was implicated in joint infection in an immunocompetent patient [1,50], and it was isolated from sepsis in patients with acute lymphocytic leukemia [51]. *R. ornithinolytica* infection is associated with food poisoning [8], sepsis [11,52-54], bacteremia [25-27,39,55-57], peritonitis [58], enteric fever [10,59], and immune deficiency conditions [40,60]. It has been reported that human infection with *R. ornithinolytica* results in pneumonia [61], urinary tract infection [24,49,62-64], and biliary tract disease [7,26,39,65]. Moreover, *R. ornithinolytica* has been isolated from patients with arthritis [66] and mandibular osteomyelitis [36]. Some reports showed *R. ornithinolytica* infection with sepsis in neonates [11,23,53,55].

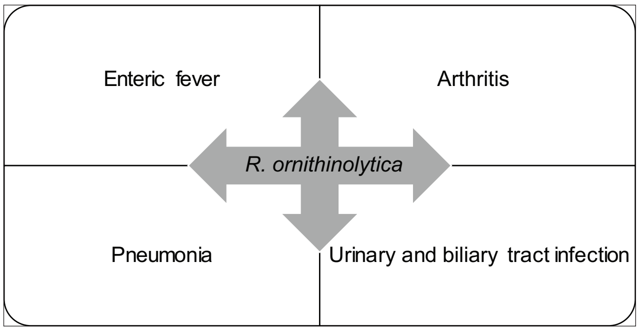

Figure-1: Clinical pictures of human infection with *R. ornithinolytica.*

Most *R. ornithinolytica* patients showed recovery after antibiotic treatment, but some revealed fatal consequences, especially in immunocompromised persons [25,56]. Among the 69 reported cases of *R. ornithinolytica*, the mortality rate was about 20%, but increased (34-44%), especially in cases of bacteremia [26,27,39,55-57].

Antibiotic Treatment and Resistance

Although *R. ornithinolytica* is not a very virulent pathogen and sensitive to antibiotics, it acquires resistance rapidly [8]. Strains of *R. ornithinolytica* were found to be sensitive to amikacin and gentamycin in USA [29], to amikacin, gentamycin, ciprofloxacin, and levofloxacin in Brazil [51], and to other carbapenemases in China [67]. The sensitivity of strains to piperacillin-tazobactam has been reported several times [7,8,26,56,58,67]. For 10-14 days treatment course, tigecycline, amoxicillin-clavulanic acid, levofloxacin, and cefmetazole can be used for *R. ornithinolytica* [25,47,56].

To obtain good results after the treatment of *R. ornithinolytica* infection, the antimicrobial resistance of the isolates should be detected. The multidrug resistance of *R. ornithinolytica* against some antimicrobials as quinolones, cephalosporins, and carbapenems has been recorded [68,69]. This type of resistance is primarily associated with the development of the resistance genes [70]. The first reported case of *R. ornithinolytica* resistance was in India, where metallo-β-lactamase-1 producing *R. ornithinolytica* was isolated from the wound in a patient with urethral injury [30]. Later, *R. ornithinolytica* antibiotic resistance has been reported in many countries like China [67], India [71] and Brazil [72].

The resistance of *Raoultella* strains to ampicillin [10,56] that is related to the expression of chromosomal resistance genes encoded the production of Class A β-lactamase [28]. There was low susceptibility to β-lactam antimicrobials [7,8,10,27,51,55,63]. It has been recorded that *R. ornithinolytica* strains carry bla_{NDM-1} resistant gene which is the key for the mechanism of β-lactam resistance displayed by the pathogen's strains [28,30,73,74]. The other carbapenem-resistant gene (bla_{KPC-2}) was also described in *R. ornithinolytica* isolates [29,67]. However, the coexistence of both genes in *R. ornithinolytica* has been recently detected [9]. A single ampicillin-resistant *R. ornithinolytica* isolate, carrying the bla_{KPC} gene was detected in the droppings of a common crane [15]. Colistin-resistant genes including *mcr*-1 [43], and *mc*r-8 and its variant (*mcr*-8.4) were also demonstrated in *R. ornithinolytica* [69]. Some resistance of *R. ornithinolytica* to ciprofloxacin and cotrimoxazole [63] has been detected.

Conclusion

R. ornithinolytica is considered a newly emerging life-threatening pathogen world-wide. Hence, it is very important to determine the role of animals and birds in the epidemiological situation of this pathogen as well as the detection of antibiotic resistance genes before treatment.

Author's Contributions

WAA has collected and drafted the manuscript, formatted it, and approved the final manuscript.

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Competing Interests

The author declares that she has no competing interests.

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