American Journal of Bioscience and Clinical Integrity
https://biojournals.us/index.php/AJBCI
ISSN: 2997-7347

Epidemiology, Risk Factors and Measures to Combat Diseases Caused by Klebsiella Bacteria

Muminova Madinakhon Abdulkhaq qizi
Assistant of the Department of Microbiology, Virology and Immunology of the Tashkent Medical Academy

Kalandarova Matluba Khuzhaniyoz qizi
Assistant of the Department of Microbiology, Virology and Immunology of the Urgench branch of the Tashkent Medical Academy

Nazarov Uktam Usmon ugli
Student of the 2nd Faculty of Medicine 2nd year of 207b group of the Tashkent Medical Academy

Received: 2024, 15, Oct
Accepted: 2024, 21, Oct
Published: 2024, 22, Nov

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Annotation: Infections caused by klebsiella species occur in various places such as the circulatory system, wounds or surgical incisions, lungs, urinary tract and brain. People with pre-existing diseases are more likely to be exposed to these infections. Due to the growing number of carbapenem-resistant and extremely virulent strains, K. pneumoniae has become a serious pathogen of international concern. It is extremely important to have an understanding of the risk factors, methods of prevention and methods of treatment of infections caused by klebsiella resistant to a variety of drugs. K. pneumoniae is a dangerous nosocomial pathogen that often causes nosocomial outbreaks and demonstrates varying virulence and sensitivity to antibiotics. Medical institutions must identify bacterial factors that are crucial during infection, due to the occurrence of many intractable infections caused by K. pneumoniae. We investigated the presence of virulence genes in several isolates obtained from urinary tract infections, respiratory tract infections, blood, wounds, and colonization of the digestive tract to

better understand this diverse pathogen. In this article, we review the epidemiology, risk factors, and methods of controlling infections caused by K. pneumoniae to highlight the serious threat posed by this pathogen, as well as existing treatments for diseases caused by klebsiella. Identification of virulence factors in K. isolates pneumoniae, especially in combination with antibiotic resistance, is very important because it allows you to assess the possible course and localization of infection in the human body and is necessary to develop a treatment strategy.

Keywords: Klebsiella pneumonia, Enterobacteriaceae family, hypervirulent K. pneumoniae, treatment strategy, respiratory tract infections.

Introduction. *Klebsiella pneumonia (K. pneumoniae)* is a gram-negative, encapsulated, immobile bacterium found in the environment that causes pneumonia in patients with alcohol dependence or diabetes. Carl Fridlender first described it in 1882 as an encapsulated rod that isolated a bacterium from the lungs of those who died from pneumonia; it was not until 1886 that the bacterium was renamed *Klebsiella*. Bacteria typically colonize the mucous membranes of the human throat and gastrointestinal tract, and once inside the body, they can show high virulence and antibiotic resistance. Today, *K. pneumoniae* is the most common cause of inpatient pneumonia in the United States, accounting for 3% to 8% of all inpatient bacterial infections [1,2,3,4]. *K. pneumoniae,* a gram-negative bacterium, is considered conditionally pathogenic and has the ability to cause a wide range of infections that can infect humans. *K. pneumoniae* is usually associated with bacteremia, pneumonia and urinary tract infections in people with weakened immune systems or those who often go to the hospital. In addition, *K. isolates pneumoniae* from the *Enterobacteriaceae* family, resistant to carbapenems, are part of a widespread class of broad-spectrum antibiotics. The World Health Organization has called these isolates "of serious concern," which means that new antibiotics are needed to combat this significant threat to human health. In fact, *K. pneumoniae* is the main cause of nosocomial pneumonia, and it is one of the few gram-negative microorganisms that can cause primary pneumonia. Nosocomial infections, usually caused by *K. pneumoniae,* most often occur in the elderly or people with insufficient immunity [5,6,7,8].

Over the past ten years, a special strain of *K. pneumoniae* has appeared, called hypervirulent (HvKP), which can infect both healthy people and people with weakened immune systems. Unlike cKP, the hypervirulent strain often affects healthy people and is mainly characterized by high pathogenicity and mortality. In addition to several infections such as pneumonia, meningitis and endophthalmitis, liver abscess in healthy people is the main clinical manifestation of HvKP infection. HvKP differs from cKP and other members of the *Enterobacteriaceae* family in that it has the ability to metastasize from an infection site in an immunocompetent host. So far, antibiotics have been effective for most HvKP strains. However, it seems that the antibiotic-resistant phenotypes HvKP and cKP have already begun to combine. Previous studies have shown that some HvKP strains have become capable of producing carbapenemases and broad-spectrum β-lactamases, which allowed the HvKP strain to become resistant to antibiotics [9,10,11]. *Klebsiella* often enters the nasal and digestive tracts of people who do not have symptoms of the disease.

However, colonization can develop into infection if the host's immunity fails to stop the spread of the pathogen. Diabetic patients receiving glucocorticoid therapy, as well as individuals who have received organ transplants, are examples. In this brief review, we will consider the main parts of the biology of *K. pneumoniae*, as well as its pathogenesis and control methods [4,7,11,12,13,14].

The bacterium *K.pneumoniae* is gram-negative, encapsulated, immobile and facultatively anaerobic. It was isolated for the first time from the respiratory tract of Edwin Klebs, a pneumonia patient, in 1875. In 1882, Carl Friedlander described it, and it was subsequently known as Friedlander's wand (Koehler and Mohmann, 1987*). Klebsiella pneumoniae, Klebsiella ozaenae* and *Klebsiella rhinoscleroma* are all *Klebsiella* species that cause serious clinical consequences. *Klebsiella* often enters the nasal and digestive tracts of people who do not have symptoms of the disease. However, colonization can develop into infection if the host's immunity fails to stop the spread of the pathogen. Diabetic patients receiving glucocorticoid therapy, as well as those who have received organ transplantation, are examples [1,2,8,9,13]. The gram-negative bacterial pathogen *K. pneumoniae* is becoming more common and can cause serious organ damage and even death. Currently, there are two pathotypes of *K. pneumoniae*: classic *K. pneumoniae* (cKp) and hypervirulent *K. pneumoniae* (HvKP). Doctors face each of these two types with different problems. Both pathotypes are common worldwide, but over the past three decades, the Asia-Pacific region has seen a steady increase in the number of infections caused by HvKP. In contrast, cKp has historically been the most common pathogen in Western countries, but infections caused by HvKP are becoming more common outside Asia. Capsules, siderophores, lipopolysaccharides, fimbriae, outer membrane proteins and type 6 secretion system are all virulence factors necessary for survival and pathogenicity. The first two of these factors are [13,14,15,16,17].

Epidemiology. Humans are the source of *K. pneumoniae*. From 5% to 38% of people in the general population carry this microorganism in their stools, and from 1% to 6% — in the nasopharynx. The patient's gastrointestinal tract and the hands of medical workers are the main sources of infection. This can lead to an outbreak in the hospital. However, people of Chinese descent and people suffering from chronic alcoholism showed higher rates of colonization. The incidence of *K. pneumoniae* in hospitalized patients is significantly higher than in the general population. In one study, the number of antibiotics prescribed to patients was associated with 77% of fecal carrier cases [11,14,17,18,19]. Community-acquired and nosocomial pneumonia are caused by *K. pneumoniae*. Community-acquired pneumonia is a fairly common diagnosis. However, *K. pneumoniae* infection is rare. In Western culture, it is generally believed that K. pneumoniae infection is responsible for about 3-5% of all community-acquired pneumonia cases; however, in developing countries such as Africa, this figure can reach 15% of all pneumonia cases. In general, *K. Pneumoniae* is responsible for approximately 11.8% of all pneumonia cases in hospitals worldwide. In patients who received artificial ventilation, from 8% to 12% of cases of pneumonia are caused by *K. pneumoniae*, while in patients who were not connected to a ventilator, this figure is only 7%. Mortality in patients with alcoholism and septicemia ranges from fifty percent to one hundred percent. In the same way, Gorrie et al. The relationship between colonization and susceptibility to *K. pneumoniae* infection was investigated in 498 patients in the intensive care unit. They found that among the patients who were colonized with *K. pneumoniae*, there were only 16%, and among those who were not carriers, there were only 3% [17,20,21,22]. According to genome-wide sequencing, the patients were infected with the same strain that was spread in the form of colonization. These studies have shown from the point of view of genomics that the microbiota of the gastrointestinal tract is the main source of nosocomial infections caused by *K. pneumoniae*. 80% of these infections are caused by strains of bacteria capable of self-colonization. Basically, diseases or immunosuppressive therapy weaken the body's defenses, which leads to a transition from colonization to infection [17,18,21,22,23].

Risk factors. Pathogen changes (e.g. virulence and antibiotic resistance), internal host factors (e.g. genetics, age and immune status) and external factors (e.g. antibiotic use, environmental exposure, nutrition and alcoholism) determine susceptibility to *K. pneumoniae* infection. Scientists have

found that many virulence factors contribute to the spread of *K. pneumoniae* infection. Capsule, lipopolysaccharide, adhesin and siderophores are virulence factors that are more common in CRKP/HvKP. This leads to various immune reactions and related phenotypes observed in HvKP strains [3,13,23,24]. Bacteria receive food and shelter from the host organism. At the same time, an effective immune system prevents infection by controlling the reproduction of bacteria. Heredity, age and concomitant diseases can increase the susceptibility of the host organism. Vered et al. investigated host susceptibility to *K. pneumoniae* using quantitative trait mapping and mouse crossing. Their study found candidate host genes for *K. pneumoniae* infection, such as Ctnnal1, Actl7a, Actl7b and Bag4. Due to an underdeveloped immune system and immature mucous membranes of the gastrointestinal tract, newborns, especially those born prematurely or in the intensive care unit, are more vulnerable. However, the risk of death from *K. pneumoniae* is highest in the elderly [9,10,11,12].

It is estimated that *K. pneumoniae* infections cause 30% of mortality among the elderly after hospitalization, mainly due to aspiration of the oropharyngeal microflora. Studies conducted on patients over the age of 60 showed that *K. pneumoniae* was the cause of 17.2% of all cases of community–acquired pneumonia and 6.5-11.6% of all cases of hospital-acquired pneumonia. Additional risk factors often associated with aging and increasing susceptibility are diabetes, malignant neoplasms, liver and gallbladder diseases, chronic obstructive pulmonary disease, kidney failure and nutritional status [14,17,18,21,23]. External factors include antibiotics, glucocorticoids, chemotherapy, transplantation, dialysis, hospital or intensive care unit stays, personal habits, invasive medical procedures such as endoscopy, subcutaneous injections, percutaneous surgery and implantation. Many of these procedures can either give the pathogen direct access to areas of the body, such as intubation, or destroy the mucous membrane of the colonization site, which allows the pathogen to spread infection [21,24,26,27,28].

Mortality, morbidity and control measures against K. pneumonia. A systematic review and meta-analysis conducted by Lee et al. showed that mortality from *K. pneumoniae* bacteremia was 17% for 7 days, 24% for 14 days, 29% for 30 days, 34% for 90 days and 29% in hospitals. More than 50% of *K. pneumoniae* cases detected by inpatient patients were accompanied by extended-spectrum beta-lactamase, carbapenem resistance and were in the intensive care unit, were associated with a noticeably higher mortality rate within 30 days [1, 8, 11, 14]. Numerous studies have shown that diabetes, cancer, and chronic liver and biliary tract diseases increase the risk of developing *K. pneumoniae* bacteremia. Since the probability of developing *K. pneumoniae* pneumonia decreases, more attention should be paid to secondary *K. pneumoniae* infection of the bloodstream (KP-BSI) [22, 24]. The treatment of one patient infected with *K. pneumoniae*, carbepemase, costs approximately more than $4,000 according to conservative estimates, with approximately 60% of the cost occurring during the illness. Carbepemase poses an economic risk for the entire healthcare sector. These microorganisms are becoming more common all over the world, and it is becoming increasingly difficult for most health systems to cope with their numbers. The redistribution of resources and the improvement of the effectiveness of medical care require the development of new antimicrobial drugs and treatment methods to combat CCP [21,22,24,26].

The treatment of this infection is best carried out by a group of professionals consisting of infectious diseases specialists, pharmacists, nurses, intensive care specialists, nutritionists, pulmonologists and respiratory therapists. To stop the spread of the pathogen, nurses who care for such patients must follow strict infection control protocols. Hand washing is vital for both visitors and medical professionals. To prevent the spread of infection, nurses should ensure that the devices are used only once. The pharmacist should make sure that broad-spectrum antibiotics are not prescribed, because this can lead to the development of drug resistance. Since many of these patients are weakened, they should consult with a nutritionist to make their calorie intake optimal. Finally, since most of these patients are in bed, a physiotherapist should be consulted to improve mobility and avoid joint stiffness [24,25,26,27,28].

Discussion. *K. pneumoniae* causes infections of wounds, bloodstream, urinary tract and

respiratory tract. Infections caused by *K. pneumoniae* increase mortality and the duration of hospitalization and treatment. Nosocomial infections caused by *K. pneumoniae* have been reported in up to 10%. In the treatment of these infections, the widespread use of antimicrobials has led to a high level of resistance to *K. pneumoniae*. MDR *K. pneumoniae* was first reported in the United States of America, followed by Europe, South America and Asia. *K. pneumoniae* is an important pathogen that causes respiratory tract infections, which often cause severe pneumonia and infections of other organs. In addition, it can cause urinary tract infections, meningitis, sepsis, and biliary tract infections in patients in the hospital. These infections can also be caused by self-infection by bacteria that have entered the human body. It can also enter the human body through a contaminated respirator, nebulizer, or catheters. The emergence of HvKP and CRKP strains has become a big problem in clinical practice in recent years [1,5,7,9,11,17].

Further studies of virulence and resistance factors, genetic information on origin, mechanisms of spread, effective diagnostic methods, potential antibacterial agents and preventive measures are necessary to reduce the incidence and spread of *K. pneumoniae* infection, as well as related morbidity and mortality. Doctors face the problem of antimicrobial resistance in MDR-CCP patients due to a lack of effective antibiotics, which leads to higher mortality rates, longer hospitalizations and higher treatment costs [18,21,22]. Since *K. pneumoniae* does not spread in society, the treatment of pneumonia should be carried out in accordance with standard recommendations for antibiotic therapy. Antibiotic treatment should be determined based on local antibiotic sensitivity after confirmation or suspicion of *K. pneumoniae* infection. Treatment of community-acquired pneumonia caused by *K. pneumoniae* currently includes 14 days of treatment with third- or fourth-generation cephalosporins as a single therapy, respiratory quinolones as a single therapy, or any of the previously described methods in combination with aminoglycoside. The patient should be prescribed a course of aztreonam or respiratory quinolone if he is allergic to penicillin. Carbapene can be used as a single therapy for nosocomial infections until the results of sensitivity analysis are obtained [21,22,23,24,25].

Due to the high sensitivity of ESBL worldwide, carbapenem therapy should be initiated as soon as they have been diagnosed. If *Enterobacteriaceae* CRE resistant to carbapenems have been diagnosed, an infectious disease specialist should be consulted to receive treatment. Antibiotics such as polymyxins, tigecycline, fosfomycin, aminoglycosides, or carbapenems can be used to treat CRE. These antibiotics can also be used in combination with other drugs. As mentioned earlier, combination therapy with two or more drugs can reduce mortality compared to monotherapy [11,14,19,21,25,26].

Conclusions. Thus, *K. pneumoniae* is a dangerous nosocomial pathogen that often causes nosocomial outbreaks and demonstrates various virulence and sensitivity to antibiotics. Due to the occurrence of many intractable infections caused by *K. pneumoniae*, medical institutions must identify bacterial factors that are crucial during infection. We investigated the presence of virulence genes in several isolates obtained during infections.

Pneumonia caused by klebsiella usually leads to adverse results. Mortality from this lung infection ranges from thirty to fifty percent, even with the most effective therapy. Diabetics, the elderly, and people with weakened immune systems usually have worse prognoses. Lung dysfunction often remains even in survivors, and recovery can take months.

Further studies of virulence and resistance factors, genetic information on origin, mechanisms of spread, effective diagnostic methods, potential antibacterial agents and preventive strategies are necessary to reduce the incidence and spread of *K. pneumoniae* infection, as well as related morbidity and mortality.

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