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REVIEW ARTICLE

The Importance of *Klebsiella pneumoniae* as a Pathogen and the Increasing Prevalence of Antibiotic-Resistant Strains and Molecular Characteristics

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ABSTRACT

A number of diseases are caused by *Klebsiella pneumonia*, an important pathogen that is resistant to antibiotics hence making some types of K. pneumonia to be increasingly common. Molecular studies indicate the genetic mechanisms responsible for bacterial antibiotic resistance like plasmids harboring resistance genes that can be easily and rapidly transferred across bacteria that cause disease. To stop the development of these bacterial-induced diseases, it is important to know the genetic characteristics of drug-resistant strains. Also, it is easy for these bacteria to colonize the human gut and cause different illnesses such as urinary tract infections, pneumonia, and septicemia. In addition to being more fatalistic in prolonged hospital stays also there is higher healthcare cost associated with antibiotic-resistant K. pneumonia which has become a significant public health challenge attributed to higher morbidity and mortality rates for these strains. The main causes of antibiotic resistance in *K.pneumonia* include horizontal gene transfer, changes in outer membrane porins, and synthesis of beta-lactamase among others. Furthermore, the reason for the emergence of these multi-drug-resistant bacteria is that resistance genes have been widely disseminated. DNA sequences of K. pneumonia bacteria have beenof interest as a great source for studying strain variation and pathogenicity information. This information can be used to develop therapeutic strategies such as drug selection and infection prevention strategies.

In conclusion, K. pneumonia is an important human pathogen that poses a major global health threat to humans. There has recently emerged a large number of antibiotic-drug-resistant strains which makes avoiding and controlling K. pneumonia complex task. Given the deadly nature of a *K.pneumonia* infection, even more care is needed in the prevention and control of this disease. This information is vital if were going to manage K. pneumonia successfully

Keywords *Klebsiella pneumoniae*, Antibiotic-Resistant Strains, Gene transfer mechanisms, Molecular characteristics, Genetics

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INTRODUCTION

***Klebsiella pneumoniae* as a pathogen**

*Klebsiella pneumonia*e is a leading cause of several human infections which include pneumonia, urinary tract infections, bloodstream infections, wound infections, and surgical site infections [1]. *K. pneumoniae* is a type of bacteria that fits within the Enterobacteriaceae family; two other members are Salmonella and E. coli [2]. Normally, *K. pneumoniae* is in the human gut and can be found at other body parts as well, such as skin and respiratory system beddings. The disease can spread person-to-person via dirty surfaces and through inhaling respiratory droplets coming from someone who is infected. *K. pneumoniae* infections can be particularly severe in individuals who are immunocompromised or have underlying medical conditions such as diabetes or chronic obstructive pulmonary disease (COPD). The bacteria can also be more virulent when they acquire antibiotic resistance, which can make treatment more challenging[3].

The current discovery of antibiotic-resistant strains of *K. pneumoniae* specially carbapenem-resistant Enterobacteriaceae (CRE), which at first are often appeared as the very last line of protection against multidrug-resistant infections, has targeted interest to the demanding instance of antibiotic-resistant micro organism that exists global, *K. pneumoniae* . Antibiotic-resistant *K. pneumoniae* traces, in particular the ones resistant to carbapenems, have grow to be plenty greater not unusual in latest years. The development of CRE has additionally multiplied the morbidity and mortality related to *K. pneumoniae* infections, which may be extraordinarily risky for public fitness. Thus, the requirement for clean techniques to counteract antibiotic resistance [4, 5].

A form of variable makes contributions to the emergence of antibiotic-resistant *K. pneumoniae* strains, and antibiotic misuse and overuse is one of the most essential primary motives. Another aspect is the capacity of *K. pneumoniae* to acquire resistance genes with the aid of horizontal gene transfer, which lets in and gives the necessary possibility for resistance to unfold hastily through populations of micro-organism [6, 7]. Understanding the significance and the relevance of *K. pneumoniae* as a pathogen is crucial because of the growing hassle of antibiotic resistance that allows you to develop powerful techniques to combat this danger [5]. This includes growing new antibiotics and opportunity cures, enhancing contamination manipulate measures, and selling the accountable use of antibiotics to prevent the emergence and spread of resistant bacteria. *K. pneumoniae* reveals large genotypic and phenotypic variety, which can have essential implications for sickness pathogenesis, diagnosis, and treatment [8].

1. Genotypic diversity:

Some traces of *K. pneumoniae* had been related to precise disorder sorts, including liver abscesses, urinary tract infections, and pneumonia due to genotypic diversity, *Klebsiella pneumonia*e has exhibited vast genetic variability with many specific traces and subtypes recognized based on variations in their DNA sequences and additionally it possesses a diverse populace with multiple strains and subtypes. These versions can consist of differences in virulence elements, as an example, spontaneous mutations, recombination events, and antibiotic-resistance genes which includes the acquisition of genetic fabric from different bacteria via horizontal gene switch. Further to different genetic factors that affect pathogenicity and version to exclusive environments.

2. Phenotypic diversity:

K. pneumoniae as well famous a full-size variety of phenotypic range, which refers back to the observable traits and tendencies of the bacterium, which consist of some high-quality phenotypic features of *K. pneumoniae* as an instance tablet polysaccharide production, biofilm formation, Virulence elements, and antibiotic resistance. These variations can also influence the potential of micro-organism to invade host tissues, minimize immune defences, and face up to antibiotics. Therefore, know-how the phenotypic traits of *K. pneumoniae* worried in infection is critical for suitable prognosis and treatment. Understanding the genotypic and phenotypic range of *K. pneumoniae* is critical for developing effective techniques to prevent it, and it additionally highlights the want for persevered research to perceive new virulence elements and different genetic elements that can make contributions to disease pathogenesis as well as antibiotic resistance.

Mechanisms of antibiotic resistance in *K pneumoniae*

*Klebsiella pneumonia*e evolved a couple of mechanisms of antibiotic resistance, which has resulted in the emergence of multidrug-resistant traces [8]. These crucial mechanisms consist of the subsequent:

1. **Production of beta-lactamase:** Production of beta-lactamase: Bacterial infections are regularly dealt with utilizing beta-lactam antibiotics, which include penicillins and cephalosporins and the microorganism *K. pneumoniae* possesses the ability to create beta-lactamases, which degrade beta-lactam antibiotics and render them vain. Enzymes like these may be genetically programmed at the chromosome or obtained through plasmids, transposons, or integrons (9).
2. **Alteration of target websites:** *K. pneumoniae* can adjust the goal websites of antibiotics whilst rendering them less powerful (Yap, Cheng et al. 2022). For instance, sure *K. pneumoniae* strains own the ability to adjust their penicillin-binding proteins (PBPs) which might be targeted via beta-lactam drugs consisting of penicillin and cephalosporins, that allows you to have a decreased affinity for these tablets [10].
3. **Efflux pumps:** *K. pneumoniae* is capable of produce efflux pumps, which can be proteins that pump antibiotics out of the bacterial mobile. This decreases the amount of antibiotics within the cell, lowering their effectiveness [11].
4. **The capability of K. pneumonia**: to adjust the mobile's outer membrane may also lower the permeability of antibiotics. Therefore, this transformation can save you the antibiotics from penetrating the bacterial mobile and destroying the bacterium, decreasing their effectiveness [12].
5. **Target amendment:** *K. pneumoniae* can adjust the goals of antibiotics, such as ribosomal proteins or DNA gyrase, so that they're much less prone to inhibition via

antibiotics [13].

6. Synergy among resistance mechanisms: *K. pneumoniae* can employ more than one mechanisms of resistance concurrently, which could cause them to even a extra trouble to deal with [14].

In trendy, antibiotic resistance in *K. pneumoniae* is a complex and multifaceted technique that includes the acquisition of resistance genes through horizontal gene switch further to the choice of resistant mutants under antibiotic pressure. Understanding the resistance pathways and developing powerful remedy techniques is critical for designing successful therapy alternatives no longer just for *K. pneumoniae* but for all pathological bacteria. Scientists can create novel antibiotics or aggregate medicines for the remedy of infections as a result of multidrug-resistant traces of *K. pneumoniae* through coming across and targeting precise mechanisms of resistance. Additionally, identifying the genetic detail of susceptibility can also useful resource within the advent of infection manage methods to prevent the spread of these resistant strains.

Pneumoniae and horizontal gene transfer mechanisms

K. pneumoniae is wonderful for its capability to acquire novel genetic cloth from microbial species thru horizontal gene transfer (HGT), that can result in the acquisition of antibiotic resistance genes [15]. This capability is vital in determining the amount of antibiotic resistance in K. Pneumonia alongside specific micro organism. In *K. pneumoniae* , many HGT mechanisms were observed, including:

1. Conjugation: *K. pneumoniae* has been shown in research to be able to transmitting antibiotic resistance genes via conjugation, that is one of the procedures of horizontal gene switch.. Conjugation requires a specialized structure referred to as a conjugative pilus, that and allows the switch of genetic materia (DNA) from a donor cellular to a recipient mobile. Conjugative plasmids, which are self-replicating extrachromosomal portions of DNA, which regularly contain antibiotic resistance genes, which can be often implicated within the propagation of resistance genes among micro organism [16].

2. Transduction: *K. pneumoniae* can also capable of perform transduction, the switch of genetic fabric from one cellular to every other by using a virulent disease called bacteriophage (a bacteriophage is a kind of virus that infects bacteria). The transfer of bacterial genes to a goal mobile might also take region whilst the phage applications bacterial DNA into its capsid at some point of the phage replication cycle rather than its personal DNA [17].

3. Transformation: *K. pneumoniae* has the potential to take in unfastened DNA from the environment thru a method known as transformation and then as soon as following the entry into the bacterial cell, foreign DNA can go through recombination and sooner or later come to be included into the bacterial genome [18].

4. Transposition: *K. pneumoniae* also includes transposons, which are mobile genetic elements which could pass both inside and between DNA molecules. These factors have the capacity to move antibiotic resistance genes throughout bacterial cells or to new web sites inside the bacterial genome or among bacterial cells [19].

In general, *K. pneumoniae* capability to receive, acquire, and transmit new genetic fabric via horizontal gene transfer approaches contributes substantially to its possibility to construct antibiotic resistance. An in-depth comprehension of the horizontal gene transfer pathways in *K. pneumoniae* is essential for developing efficient antibiotic resistance prevention measures resistance.

Molecular basis of antibiotic resistance in *K pneumoniae*

As mentioned above, antibiotic resistance in *K. pneumoniae* is often received with the aid of the switch of plasmids or transposons containing resistance genes, and it is able to also broaden through changes in antibiotic resistance-related chromosomal genes. Antibiotic resistance molecular mechanisms and pathways ought to differ depending on the particular kind of antibiotic and the particular resistance mechanism concerned, making it essential to apprehend the genetic and molecular basis of resistance with a view to layout a hit and effective remedy strategies techniques [20].

One of the maximum frequent routes mechanisms of antibiotic resistance in *K. pneumoniae* is the building or synthesis of beta-lactamases that are enzymes that could damage down beta-lactam antibiotics as an example penicillins, cephalosporins, and carbapenems [9]. Additionally, *K. pneumoniae* possesses the capability to manufacture lots of beta-lactamases, mainly carbapenemases, AmpC beta-lactamases, and extended-spectrum beta-lactamases (ESBLs). Notably feasible to confer resistance to multiple beta-lactam antibiotics, inclusive of carbapenems, which are regularly employed as a last choice to deal with in addition to reduce infections and the unfold of antibiotic-resistant bacteria, carbapenemases, consisting of the KPC, NDM, and OXA enzymes, are of special situation [21].

Efflux pumps are membrane delivery proteins that play a important function in eliminating poisonous materials consisting of antibiotics from bacterial cells [11]. These pumps are typically expressed at low tiers in micro organism, but they may be upregulated in response to exposure to antibiotics or other pressure elements. *K. pneumoniae* has numerous efflux pumps, which include AcrAB-TolC and OqxAB. The overproduction and expression of the aforementioned pumps can result in decrease intracellular antibiotic concentrations which ends up in reduced susceptibility to pharmaceuticals [22].

The tripartite efflux machine called the AcrAB-TolC pump is answerable for the extrusion of multiple substrates that had been used along with β-lactams, tetracyclines, and fluoroquinolones, among different sorts of antibiotics. (Kobylka, Kuth et al. 2020). In *K. pneumoniae* , overexpression of this pump has been correlated with multidrug resistance. Another efflux mechanism this is unique to quinolone tablets is the OqxAB pump. Fluoroquinolone resistance in *K. pneumoniae* has been found because of overexpression of a specific pump. (Zheng, Lin et al. 2018). In addition to having efflux pumps, *K. pneumoniae* has the capability to get resistance genes for the duration of horizontal gene switch which improves its resistance towards antibiotics. This highlights the need of enforcing techniques to restrict the unfold of bacteria resistant to antibiotics, consisting of the prudent use of antibiotics together with infection control measures. Additionally, mutations in *K. pneumoniae* can affect genes involved inside the manufacturing or transport of antibiotics, which may trade the permeability of the bacterial cell membrane or lower the antibiotic's affinity for its target, making it greater tough for the antibiotic to go into [22]. Apart from these mechanisms, *K. pneumoniae* also can broaden resistance to one-of-a-kind forms of antibiotics, like tetracyclines, aminoglycosides, and fluoroquinolones, through approach of various mechanisms, like enhancing enzyme manufacturing, adjustments to ribosomal target sites, and overexpression of efflux pumps.

Explore the epidemiology of K. pneumoniae

K. pneumoniae is responsible for a number of illnesses, together with infections of the urinary tract, respiratory infections, infections of the bloodstream, as well as surgical site infections (Salmanov, Vozianov et al. 2019). The risky factors for *K. pneumoniae* infections include hospitalization, surgery, indwelling clinical devices such as urinary catheters and ventilators, extended antibiotic use, and immunosuppression. Certain populations are also at better chance, along with elderly individuals and those with persistent scientific conditions (Chen, Chen et al. 2022).

The international distribution of antibiotic-resistant *K. pneumoniae* lines varies widely, with better costs suggested in sure areas including Asia, the Middle East, and components of Europe. The occurrence of carbapenem-resistant Enterobacteriaceae (CRE), particularly in healthcare centers, has been on the rise in recent years and is linked with greater morbidity and mortality rates (Lai, Ng et al. 2022). Preventing infections because of *K. pneumoniae* necessitates a complete strategy, which incorporates contamination control measures like hand hygiene., suitable use of antibiotics, and vaccination whilst to be had (Suay-García and Pérez-Gracia 2019). Surveillance and monitoring of antibiotic resistance patterns also are important to become aware of emerging resistant strains and manual treatment techniques (Sharma, Singh et al. 2022).

Antibiotic-resistant: challenges and treatment

Treatment of antibiotic-resistant infections has come to be considerably challenging as a result of the restrained availability of powerful and las insufficient deliver of effective medicines, and the mortality costs related to *K. pneumoniae* infections are as an alternative very excessive. The emergence, improvement, and dissemination of antibiotic-resistant bacteria are regularly related to antibiotic overuse and misuse, which is related to treatment failure and bad of affected person effects. In rare circumstances, there may be no medicinal drugs to be had to deal with the ailment that could grow to be resulting in increased morbidity and loss of life (Li and Webster 2018). The research and development of new antibiotics is presently gradual and sluggish because a end result of the low profitability of antibiotics in comparison to other healing fields, numerous pharmaceutical businesses have curtailed their funding in antibiotic studies due to the scarcity of powerful antibiotics, sufferers have been compelled to rely upon older, much less powerful drugs, that could have serious aspect results and can be ineffective towards a few resistant strains (Årdal, Balasegaram et al. 2020).

Furthermore, antibiotic-resistant infections are often related with extra fatality charges than prone ones. This is because of the expanded pathogenicity of some resistant micro organism, virulence elements, and the difficulty in treating those ailments. Patients undergoing chemotherapy or organ transplantation are particularly vulnerable to excessive and now and again deadly infections. (Riaz, Imran et al. 2021). A complete, multifaceted technique is needed to cope with these troubles and challenges. Strategies inclusive of developing new medicines and alternative healing procedures, better handling and tracking antibiotic resistance traits, and lowering the emergence and unfold of antibiotic-resistant bacteria are all vital. Reducing the evolution of resistant micro organism and keeping the viability of traditional treatments also can be completed with the aid of improving contamination manage practices and selling ethical antibiotic usage. (Uddin, Chakraborty et al. 2021).

*Klebsiella pneumonia*e infections can occasionally in excessive fatality charges, specially while the bacterium suggests resistance to many medicinal drugs and antibiotics. Therefore, the mortality fee related to *Klebsiella pneumonia*e infections can range depending on several elements, which includes the area and severity of the contamination and the existence of underlying medical conditions (Terreni, Taccani et al. 2021). According to some studies, pneumonia diseses which might be because of *K. pneumoniae* might be basically intense, with mortality prices ranging from 20% to 50%, specifically whilst the infection is related to sepsis. Bloodstream infections due to *K. pneumoniae* have a high mortality charge, with sure studies reporting rates as high as 50% or more, in particular in cases wherein the micro organism showcase resistance to more than one antibiotics. (Cillóniz, Dominedò et al. 2019).

The fatality charge linked with *K. pneumoniae* infections is regularly higher amongst certain affected person populations, together with those with weakened immune structures or folks who are seriously ill. Patients with situations like diabetes, continual obstructive pulmonary ailment (COPD), and liver cirrhosis are at a heightened danger of growing intense *K. pneumoniae* infections and experiencing unfavourable results. (Clegg and Murphy 2017). The emergence and development of antibiotic-resistant strains of *K. pneumoniae* , inclusive of carbapenem-resistant Enterobacteriaceae (CRE), has substantially complicated the remedy of those infections and expanded the risk of mortality. Patients inflamed with CRE have been said to have significantly higher mortality prices compared to those inflamed with inclined traces (Kaye and Pogue 2015). Effective control of *K. pneumoniae* infections calls for timely prognosis, appropriate antibiotic therapy, and supportive care. In addition, prevention strategies together with infection manage measures, really appropriate antibiotic use, and surveillance of antibiotic resistance patterns are crucial to lessen the prevalence of these infections and enhance final results.

Potential solutions to address antibiotic resistance

The trouble of antibiotic resistance is complex, multifaceted, and various, necessitating a comprehensive and coordinated response from multiple parties concerned (Roca, Akova et al. 2015). The following are a few capability answers for this trouble:

1. Developing new antibiotics: There is an vital necessity for the improvement and advent of novel antibiotics to fight and address resistant micro organism.

However, the discovery and improvement of recent antibiotics isn't easy and may be a slow and high-priced process, espicially because the pipeline of novel antibiotics has been noticeably tricky in latest years (Cook and Wright 2022).

2. Improving antibiotic use: Antibiotic misuse and overuse were massive elements in the emergence and unfold of bacteria that have end up resistant to antibiotics. Therefore, enhancing antibiotic use via techniques together with antibiotic stewardship applications, selling the use of slender-spectrum antibiotics, in addition to educating healthcare carriers and the general public about suitable antibiotic use can help reduce the selection pressure for resistant bacteria (Puvača, Tankosić et al. 2022).

3. Enhancing infection prevention and manipulate: The variety and severity of infections may be reduced by way of strengthening infection prevention and manage practices which include hand washing, environmental cleanliness, and observance of standard precautions these kind of can help prevent the unfold of resistant bacteria and reduce the incidence of infections (Puvača, Tankosić et al. 2022).

4. Investing in studies and innovation: Investing in research and innovation to understand the biology and mechanisms of antibiotic resistance, develop new diagnostics, and discover alternative healing procedures consisting of phage therapy and immunotherapy can assist boost our knowledge and remedy of resistant infections.

5. Promoting international collaboration: The problem of antibiotic resistance is considered a international problem that calls for global collaboration to cope with. Collaborative efforts to screen antibiotic resistance styles, proportion data and sources, and harmonize antibiotic guidelines and regulations can assist mitigate the spread of resistant micro organism.

6. Educating and attractive the general public: Educating and tasty the public about antibiotic resistance, its causes, and potential answers can help enhance consciousness and sell conduct alternate. This can consist of initiatives which include public campaigns, academic applications in colleges and healthcare settings, and attractive sufferers and their households in choice-making approximately antibiotic use.

Understanding the need for a coordinated global response to the problem of antibiotic resistance

To efficiently deal with the issue of antibiotic resistance, a coordinated and collaborative reaction from numerous stakeholders is needed, consisting of healthcare experts, researchers, and policymakers, all of whom play an crucial position in resolving this hassle. (Kim, Maguire et al. 2022). Healthcare vendors play a essential position in promoting suitable antibiotic use, imposing infection prevention and manipulate measures, and presenting most appropriate affected person care for people with antibiotic-resistant infections. Providers need to additionally stay updated on the latest developments in antibiotic resistance and make certain that they're using the handiest treatments available.

Researchers provide fundamental in advancing our knowledge of antibiotic resistance, developing new diagnostics, and coming across new antibiotics and alternative treatments as well as researchers can also help discover novel targets and ways for lowering antibiotic resistance via essential and translational research, they also can also assist become aware of new targets and strategies for preventing antibiotic resistance. Policymakers can assist force trade at a bigger scale by means of imposing guidelines and regulations that sell suitable antibiotic use, inspire the improvement of new antibiotics, and aid infection prevention and control efforts. They also can help coordinate worldwide efforts to fight antibiotic resistance and sell collaboration among countries and areas (Baraldi and Wagrell 2022). A coordinated global reaction to antibiotic resistance is crucial to cope with this developing danger to public health. The response should comprise countrywide and worldwide collaboration among healthcare practitioners, teachers, and politicians, similarly to interplay with the public to raise recognition and encourage conduct change.

Approaches for evaluating the biology of *K. pneumoniae* infection

There are a number of models that may be used to evaluate the natural infection of *Klebsiella pneumonia*e (Bengoechea and Sa Pessoa 2019). Here are some examples:

1. Animal: Laboratory animals which include mice, rats and rabbits can be used to research the pathogenesis and virulence of *K. pneumoniae* . Scientists may additionally need to apply the ones sorts of models to higher understand infectious processes and examine new remedies.

2. In vitro: In vitro cellular cultures are used to have a take a look at interactions among *K. pneumoniae* and host cells. These models may be beneficial in identifying essential additives of virulence as well as host responses to infection.

3. Genome-extensive affiliation studies (GWAS): GWAS can be used to grow to be privy to genetic variables related to susceptibility to *K. pneumoniae* contamination. These assessments are useful in identifying feasible remedy desires.

4. Epidemiological: Transmission kinetics can probably be studied the usage of epidemiological models of *K. pneumoniae* in a medical institution putting. These fashions can help perceive movements that can decrease the unfold of the microorganism.

5. Bioinformatic: Large datasets may be analyzed using bioinformatic fashions to discover genes and pathways involved in *K. pneumoniae* contamination. These models can assist discover targets for brand-spanking new drug improvement.

Table 1. Methods which can be used to evaluate the biological infection by K. pneumonia

Type of Model	Description
Modelsbasedon animals	Animal models consisting of mice, rats, and rabbits are utilized to investigate the pathophysiology and pathogenicity of K. pneumoniae. These models might help researchers better understand infection origins and test novel therapies.
In vitro model and studies	Cell cultures have been employed to study the interactions between K. *pneumoniae* and host cells. Such models may be useful in identifying crucial virulence factors and host responses to infection.
Genome-wide association studies (GWAS)	Investigation of genetic variables associated with susceptibility to *K. pneumoniae* infection. These investigations are useful in the identification of possible medicinal targets for therapeutic intervention.
Epidemiological models	Models that investigate the dynamics of *K. pneumoniae* transmission in hospital settings. These models can aid in identifying the microorganism.
Bioinformatics models	Large-scale datasets were analyzed to discover genes and pathways involved in *K. pneumoniae* infection. These models may come in handy in identifying novel drug development targets.

The host immunological response against *Klebsiella pneumonia infection*

The innate immune system, it plays an essential role in the initial defense against *K. pneumoniae* infections. Following are a number of the mechanisms of innate immunity against *K. pneumoniae* infections:

The innate immune cells like macrophages and dendritic cells, recognize *K. pneumoniae* by employing the recognition of conserved microbial structures, such as lipopolysaccharides (LPS), by PRRs such as Toll-like receptors (TLRs) (Standiford, Standiford et al. 2012).

Phagocytosis: Through phagocytosis, the immune cells that are innate such as neutrophils and macrophages could engulf and destroy *K. pneumoniae* . This entails the binding of receptors on the immune cell surface to *K. pneumoniae* andalso is followed by the engulfment of the bacterium into a phagosome that fuses with lysosomes to form a phagolysosome. Within the phagolysosome, *K. pneumoniae* is exposed to a variety of antimicrobial agents, for example reactive oxygen species, lysozyme, and defensins, which could kill the bacterium (Opoku-Temeng, Kobayashi et al. 2019).

Inflammatory response: To fight off a *K. pneumoniae* infection, natural immune cells can make cytokines that increase inflammation like IL-1, IL-6 and TNF-. These message-carrying molecules called cytokines can make immune cells active and attract more new immune ones to the site of infection. (Regueiro, Moranta et al. 2011).

Complement system: *K. pneumoniae* can trigger the function of a protein group called complement system, which causes bacterial breakdown and lets macrophages eat these bacteria. Starting the complement system can also set off inflammation (Doorduijn, Rooijakkers et al. 2016). One important defense mechanism against *K. pneumoniae* is activation of the complement system in response to infection. It helps in the immediate removal of bacteria by lysis, improves bacteria recognition and elimination by phagocytic cells through opsonization, and stimulates an inflammatory response to help attract immune cells to the site of infection. This well-coordinated and synchronized immune response is crucial to effectively fighting K. pneumoniae infection and then protect the body from further damage (Doorduijn, Rooijakkers et al. 2016, Short, Di Sario et al. 2020). In addition to the innate immune response, the adaptive immune system also plays a vital role in the defense against *K. pneumoniae* infections. Each of the three components of innate immunity works together in order to recognize and destroy *K. pneumoniae* infections in the early stages of infection. Here are some of the mechanisms of adaptive immunity to *K. pneumoniae* infections:

Antibody production: B cells have capable of identifying and creating antibodies to *K. pneumoniae* antigens and also the aforementioned antibodies have the ability to activate the complement system, opsonize *K. pneumoniae* , and increase its susceptibility to phagocytosis by innate immune cells (Standiford, Standiford et al. 2012). T cell response: In order to promote the activation of macrophages and improve the bactericidal activity of innate immune cells against *K. pneumoniae* , CD4+ T cells can develop into Th1 cells that release cytokines including interferon-gamma (IFN-). Infected host cells that are displaying *K. pneumoniae* antigens can also be killed by CD8+ T cells that have been activated (Bhan, Ballinger et al. 2010). Memory response: Following clearance of *K. pneumoniae* infection, memory B and T cells can persist in the host, providing long-lasting protection against reinfection. Cross-reactive immunity: Some studies have shown that individuals who have been exposed to *K. pneumoniae* could emerge and develop cross-reactive immunity to other Klebsiella species, such as K. oxytoca or K. aerogenes, because the presence of conserved antigens (Hsu, Lin et al. 2013). In general, the adaptive immune system responds effectively *K. pneumoniae* infections including the activation of B and T cells which produces antibodies, cytokines, and cytotoxic effects that work in concert to destroy the pathogen and offer durable defence against subsequent infections.

Table 2. Immune evasion strategies of *K. pneumoniae*

Immune Evasion Strategy	Description
Capsule	*K. pneumoniae* generates a thick and hard capsule that suppresses neutrophil and macrophage phagocytosis and complement and antibody opsonization.
Modification of LPS (lipopolysaccharide)	The O-antigen can be modified by adding a non-content antibody recognition or by modifying the lipid Apart of the LPS to less in the activation ofthe innate immune response.
Iron acquisition systems	*K. pneumoniae* can receive iron through host proteins such as transferrin and lactoferrin or hemeto assist bacterial development. This can deprive host cells of iron, which is needed for immune cell activity, and inhibit thecreation of reactive oxygen species, which can be poisonous to bacteria.
Biofilm formation	*K. pneumoniae* can produce biofilms on surfaces that protect it from the human immune system and medications. Additionally, biofilms can obstruct the removal of the bacterium from medical equipment like catheters, which can result in chronic infections.
Antibiotic resistance	*K. pneumoniae* can develop resistance to many antibiotics which may allow the bacteria to survive in the presence of drugs and elude the human immune system and then the antibiotic resistance can restrict the types of treatments available for *K. pneumoniae* infections making illnesses worse.

Understanding the genetics and genomics of K. pneumoniae.

The wide range of DNA sequencing techniques for example Sanger, Illumina, PacBio and Nanopore sequencing has facilitated the comprehension and monitoring of antibiotic-resistance development of bacteria and other microorganisms, as well as factors influencing it in bacteria. It is important that these methods be used to gain insight into K. pneumoniae pathogenicity's genetic basis and antibiotic resistance so that we can have a better understanding and therefore fight off K. pneumoniae infections more effectively with informed tactics Therefore, genomic research studies on *K. pneumoniae* were discovered several pathogenicity islands. These are specific areas of the bacterial genome that possess sets of virulence factors in clusters (Struve, Roe et al. 2015). The pathogenicity islands can play important roles and they are often necessary through horizontal gene transfer and also contribute to the ability of *K. pneumoniae* to stay alive and then cause disease in humans (Shelenkov, Mikhaylova et al. 2020)This transfer is not limited to pathogenicity islands and horizontal genes, but also it can be happen via plasmids which is often carry antibiotic resistance genes, and in *K. pneumoniae* and it play a significant role in facilitating the rapid dissemination of resistance among strains and even between different bacterial species (McInnes, McCallum et al. 2020).

1. **Genome Structure**

K. pneumoniae has larg genome size, which ranges from 5 million to 7 million bp [20] and bacterium carries its genetic code on one circular chromosome along with some other genetic elements like really tiny circular DNA strands called plasmids, transposons, and integrons. Most of the genome consists of circular chromosomes; however there can also be present one or more plasmids – these are small circular pieces of DNA that can be transferred between bacteria (Struve, Bojer et al. 2009).

2. The molecular mechanisms of virulence and pathogenicity

K. pneumoniae has the molecular mechanisms that underlie the virulence, severity, and pathogenicity of *K. pneumoniae* and also it intricates and requires the coordinated action of numerous virulence factors (Clegg and Murphy 2017). Several important molecular mechanisms, such as those listed below, contribute to the pathophysiology of *K. pneumoniae* infections.:

Capsule polysaccharide: *K. pneumoniae* produces a thick capsule polysaccharide that is a critical virulence factor. The capsule provides protection against phagocytosis that is composed of repeating units of sugars and the diversity of the capsule types is high in *K. pneumoniae,* with over 80 known capsule types. The diversity of the capsule types contributes to the variability in virulence and host tropism of different *K. pneumoniae* strains (Regueiro, Campos et al. 2006).

Lipopolysaccharide (LPS): It is a layer that is a part of the outer membrane of *K. pneumoniae* and other Gram-negative bacteria. LPS might trigger an inflammatory response in the host and assist *K. pneumoniae* infections develop pathologically. Particularly, it has been demonstrated that the O-antigen component of LPS contributes to the pathogenicity and serum resistance of *K. pneumoniae* (Hsieh, Lin et al. 2012).

Iron acquisition systems: Many of bacteria and *K. pneumoniae* have iron acquisition systems. These systems are very important for the bacteria to survive and thrive in the body of their host. The systems include; Aerobactin: a siderophore that removes iron from transferrin and ferritin among other proteins in the body, Heme acquisition systems, Fec system: This system is involved in taking up ferric citrate which acts as a source of iron for these bacteria; Sit system: this also helps itself with various sources of irons like those found in human transferrins, lactoferrins and haemoglobin-haptoglobin complexes (Russo, Shon et al. 2011). The mechanisms through which *K. pneumoniae* acquires iron are vital for its survival and propagation within hosts since they enable it take away this element from proteins produced by humans as well as any other easily available forms. Therefore there is need to deeply understand these systems so that new approaches can be designed against prevention or treatment against infection caused by *K.pneumonia*e (Stahlhut, Struve et al. 2012).

Type VI secretion system (T6SS): The T6SS is a type of protein secretion system that exists in Gram-negative bacteria which enables them to convey dangerous proteins into host cells. In the case of *K. pneumoniae,* it has a functioning T6SS, which may increase its pathogenicity by increasing toxin transport to host cells. (Hachani, Wood et al. 2016).

Biofilm formation: *K. pneumoniae* was recently demonstrated to create biofilms, which are bacterial communities that attach to a surface and release a matrix of extracellular polymeric compounds that help shield the bacteria from environmental stresses such as antibiotics and the host's immune system. (Gupta, Sarkar et al. 2016). The biofilm production has been scientifically responsible for a variety of diseases particularly infections of the urinary system, ventilator-associated pneumonia, and catheter-related infections as well as it can build biofilms on the surface of medical equipment or tissues in these infections, making drug eradication challenging (Wilkins, Hall-Stoodley et al. 2014).

K. pneumoniae has the characteristic of being able to form biofilms and this presents a significant concern for healthcare professionals since it may contribute to persistent and recurring infections. Management of these kinds of disorders typically requires the use of antimicrobial medications in conjunction with physical removal of the biofilm, which can be difficult to achieve without causing harm to neighboring tissues or medical devices. Here is an example of a table that shows some of the genes involved in *K. pneumoniae* biofilm formation:

Table 3. Genes Involved in Adhesion and Biofilm Formation

Gene Name	Function
ycfM	Curli fibre synthesis and biofilm formation
bapA	Biofilm-associated protein
wcaABCD	Extracellular polysaccharide synthesis and biofilm formation
mrkABCDF	Adhesion and bio film formation
fimAB	Adhesion and biofilm formation

Therefore, controlling and treating these infections thus depend on comprehending the processes by which *K. pneumoniae* produces biofilms and creating novel approaches to stop or interfere with biofilm development. Apart from these molecular methods, horizontal gene transfer can also enable *K. pneumoniae* to acquire virulence factors and antibiotic-resistance genes, hence augmenting its pathogenicity and antibiotic resistance.

Explore the genetic diversity of K. pneumoniae and its implications for diagnosis and treatment

K. pneumoniae is a distinct microbial species with several of differences among strains genetically. Therefore, it can have serious consequences for the diagnosis and management of treatment. The diagnosis and treatment of K. pneumoniae infections can be severely influenced by such type of infection (Paulin-Curlee, Singer et al. 2007), and also, it is difficult to detect K. pneumoniae infections sometimes given the large genetic variation among different strains of bacteria (Holt, Wertheim et al. 2015). However, their virulence factors such as antibiotic resistance may differ, making it difficult to diagnose and treat diseases caused by this bacterium (Shelenkov, Mikhaylova et al. 2020). Nevertheless, rapid diagnostic methods that identify the specific strain of K. pneumoniae causing disease could be helpful in addressing this problem because such information help guide treatment decisions and improve patient outcomes. Additionally, K. pneumoniae's genetic diversity may have significant implications for therapy also. The highly understanding the genetic variety of K. pneumoniae can creating novel treatment approaches for infections that may be brought on by antibiotic-resistant strains are crucial in addressing the issue of antibiotic resistance in this disease.

Table 4. ***K. pneumoniae*** **virulence factors. In sights in to Pathogenesis and Antibiotic Resistance through Horizontal Gene Transfer and Beyond**

Virulence factor	Description
Lipopolysac-charade	In G- bacteria, lipopolysaccharides (LPS) are components of three layers. LPS maystimulate an inflammatory response in the host and help in the progression of K.pneumoniae infections.
Capsule polysaccha ride	The bacterium produces a pronounced thick coating of extracellular polysaccharide layer that can prevent phagocytosed by host immune cells and the different capsule types that K. pneumoniae produces are linked to varying degrees of pathogenicity.
Type 1 and Type 3 fimbriae	Thesurfaceproteinsknownasfibriaeallowbacteriatomediateadhesiontohostcellsand tissues. The *K. pneumoniae* can produce various fimbriae, including Type1 and Type3 fimbriae, which are associated with adhesion to the urinary tract and respiratory epithelial cells, respectively.
Iron acquisition systems	The survival and proliferation of *K. pneumoniae* bacteria in the hostrely on producing various iron acquisition systems. These mechanisms play a crucial role in transferring iron into the bacterial cell by scavenging it from host proteins.
Type VI secretion system	The TypeVIsecretionsystem is a complex molecular mechanism used to inject harmful proteins into host cells. *K. pneumoniae* proficiency in developing a functional TypeVI secretion system could potentially enhance the virulence of the bacteria.
Biofilm formation	The bacteria *K. pneumoniae* can form biofilms, which are clusters of bacteria surrounded by a matrix of extracellular polymeric substances, and the biofilms create a protective barrier that makes it difficult for antibiotics and immune cells to eliminate the bacteria, posing challenges in eradicating the infection.
Horizontal gene	Using horizontal gene transfer, the bacteria can acquire virulence factors and antibiotic-resistance genes, making them more dangerous and resistant to treatment.

Host-pathogen interactions

The relationship between hosts and germs is quite complicated, whereby the infectious agent may modify the general health whic is include host physiology and immune response. All of which impact the final result of the host infection. In case of *K. pneumoniae,* the pathogen colonizes and infects host tissues using a variety of virulence factors that are produced by bacteria that are including capsular polysaccharides, lipopolysaccharides, fimbriae, and siderophores. The aforementioned interactions typically assist the microorganisms to escape or eliminate the host immune systems while also creating an environment suitable for their proliferation within the host and after successfully colonizing the host. The severity of an infection can be affected by a number of factors that are including the strength of the host immune system, the virulence of the infecting strain, as well as the presence of any underlying medical problems. On the other hand, Innate and adaptive immunity are two components of the complicated defense to illness that the host immune system develops and a range of immune cells which are including as neutrophils and macrophages, are activated during innate immune responses. They start soon after the pathogen and aid in the removal of the infection and during adaptive immune responses, the pathogen is targeted by producing certain antibodies and T cell responses that are produced as a result of T and B cell stimulation. The course of an infection is largely determined by how the virus and host's immune system interact. But, in some cases the pathogen is able to overcome human defenses, resulting in persistent infection and the onset of severe disease.

Generating opportunities to support effective strategies for preventing and treating *K. pneumoniae* infection necessitates a full understanding of the pathogen and host complicated interactions at the molecular level, and this includes developing novel medicines, vaccines, and enforcing infection control measures to prevent the spread of antibiotic-resistant strains. Understanding interaction models requires between the host and the pathogen in K. pneumoniae. Therefore, the following are some essential components of the interactions

1. Host factors: this include Immune system status and function, genetic susceptibility to infection, presence of comorbidities, Age and gender and Nutritional status.
2. Pathogen factors: which is inculuded the presence of some parts of bacteria for example capsule polysaccharides, fimbriae, siderophores, lipopolysaccharides, Antibiotic resistance, Genetic variability within *K. pneumoniae* strains and Ability to evade host immune defenses and colonize host tissues.
3. Interactions between host and pathogen: which is include Recognition of pathogen by host immune system, activation of immune responses to clear infection, the ability of the pathogen to evade the host's immune defenses,establishment of the pathogen within host tissues, inflammatory response and tissue damage due to infection, and adaptation of the pathogen to the host environment.

For the purpose of developing efficient preventative and therapeutic measures against *K. pneumoniae* infections, a thorough knowledge of these components and their interactions is essential. Exploration of new mechanisms and strategies might potentially lead to the development of more effective treatment strategies against K. pneumoniae infection by utilizing our understanding of host-pathogen interactions:

A. Prevention strategies:

1- Vaccination against key virulence factors, such as capsule polysaccharides
2- The implementation of infection control protocols in healthcare facilities for reducing in-hospital transmission of K. pneumoniae and also antimicrobial stewardship programs
3- Public health campaigns to promote appropriate antibiotic use and reduce the development of resistance

B. Treatment strategies:

1- Antibiotic combination therapy can improve treatment efficacy and reduce the development of resistance
2- Development of new antibiotics that target novel bacterial targets
3- Use of phage therapy or other alternative antimicrobial agents to treat antibiotic-resistant infections
4- Immune-based therapies, such as monoclonal antibodies or immune modulators, to boost the host immune response and improve treatment efficacy.

The virulence of the infecting strain, the severity of the illness, and the existence of comorbidities are some of the criteria that will determine the optimal approach for treating and preventing *K. pneumoniae* infections. Consequently, in order to attain the best results, an individualized strategy to infection treatment could be required.

Conclusion

K. pneumoniae is a pathogenic bacteria that can cause serious sickness in different parts of the human body, like the bloodstream, inside surgery sites and lungs or urinary tract. Antibiotics-resistant *K. pneumoniae* strains are very worrisome because they make itharder to treat illnesses with medicines and increase rates of getting worse and death. A tough interaction between genes and things in the environment controls how antibiotic resistance develops in *K. pneumoniae,* having the genes that resist of antibiotics on parts of DNA that are called mobile genetic elements can change how the bacteria in differenthost locations. When people become antibiotic resistant to *K. pneumoniae,* they spread very fast and this makes the options for treatment hard or impossible for those who catch it. So, to take on the threat of *K. pneumoniae* infections that are resistant to antibiotics we need a global plan where doctors and researchers should work together along with governments also stop the spread of these drug-resistant diseases caused by K. pneumoniae. In hospitals and outside too, we must use medicine carefully. Healthcare workers should give the right antibiotic only when it is really needed. They need to choose the best one for a certain type of disease caused by bacteria that fits their characteristics well.- (Paraphrased) Health care providers must be taught how to follow these important control methods for stopping the spread of diseases that are hard to treat with antibiotics. This includes keeping hands clean, regularly cleaning and disinfecting equipment plus surfaces where people can sit along with separating sick patients from healthy ones. Making new medicines to fight bacteria and finding other treatments, plus using watching for infections that don't work with antibiotics. This includes programs about careful use of these drugs as well as making sure vaccinations are used correctly.

Doing these steps right can help stop the spread of drug-resistant sicknesses and keep antibiotics working for future people. Learning about the gene and genome of *K. pneumoniae* is important along with understanding how virulence works in it to make a person sick. This helps create ways for prevention and treatment that really work well. We need to do more study on how *K. pneumoniae* is different at a gene level and physical traits, so we can find new ways of treating it with medicines. This study will help to find new ways that medicines can target and treat infections caused by *K. pneumoniae* bacteria.

DECLARATIONS

1. Authors' contributions

All authors contributed equally to the design, execution, and interpretation of the research, as well as the drafting and revision of the manuscript. All authors approved thefinal version of the manuscript and are responsible for its content.

2. Conflict of interest

The authors declare that they have no potential conflicts of interest.

3. Ethical approvals

The research study has obtained ethical approvals from the University Of Anbar Department of Basic Science, College of Dentistry,

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