AKADÉMIAI KIADÓ

Acta Microbiologica et Immunologica Hungarica

70 (2023) 4, 278–287

DOI:
10.1556/030.2023.02186


REVIEW ARTICLE

# Hypervirulent *Klebsiella pneumoniae*: An update on epidemiology, detection and antibiotic resistance

BÉLA KOCSIS*

Institute of Medical Microbiology, Semmelweis University, Budapest, Hungary

Received: November 10, 2023 • Accepted: November 20, 2023
Published online: December 4, 2023

**ABSTRACT**

*Klebsiella pneumoniae* is a major human pathogen as it is responsible for various infections. In the past years hypervirulent *K. pneumoniae* (hvKP) emerged and disseminated worldwide. In this review a summary will be given about epidemiology, detection and antibiotic resistance of hypervirulent *K. pneumoniae*. A common feature of hypervirulent *K. pneumoniae* is a combined expression of several virulence factors. A mucoviscosus phenotype, certain capsulare serotypes (e.g.: K1, K2, K28, K47, K63) together with additional genetic markers namely, *magA*, *rmpA* or *iucABCD,* are needed in combinations to achieve the hypervirulent pathotype. Plasmid coded virulence determinants are also detected, that indicates horizontal gene transfer of hypervirulence factors in *K. pneumoniae*.

Interestingly, infections caused by hypervirulent *K. pneumoniae* occur usually in the community in otherwise healthy people, and during these infections multiple infection sites are detected. Clinical pictures include both invasive infections and local abscess formation. Pyogenic liver abscess is the most frequently reported clinical manifestation and abscess formation in brain, spleen and lung are also diagnosed. Additionally, meningitis, endophthalmitis, trombophlebitis, pneumonia can also develop.

In the early reports, hypervirulent *K. pneumoniae* strains exhibited enhanced virulence but these were susceptible to commonly used antibiotics. However, recently KPC, VIM, NDM and OXA-48 carbapenemase producing hypervirulent *K. pneumoniae* strains are increasingly reported, furthermore, well-known high-risk *K. pneumoniae* clones (e.g.: ST11, ST147, ST307) can develop hypervirulent pathotype, that poses an even more alarming challenge.

**KEYWORDS**

*Klebsiella pneumoniae*, hypervirulence, hypermucoviscosity, antibiotic resistance, hvKP

## INTRODUCTION

*Klebsiella pneumoniae* is a member of the Enterobacteriaceae family and it is a normal inhabitant of human gastrointestinal tract, however, *K. pneumoniae* is also responsible for various human infections [1]. *K. pneumoniae* is divided into classical and hypervirulent pathotypes, based on phenotypic appearance and genetic markers. The classical *K. pneumoniae* pathotype occurs usually in healthcare settings, and it is a major nosocomial pathogen as it causes infections in hospitalized, older patients with certain level of immunosuppression. These infectious diseases include urinary tract infection, bloodstream infection, intra-abdominal infection and wound infection. By contrast, hypervirulent *K. pneumoniae* (hvKP) pathotype causes infections usually in the community, in otherwise healthy people, and multiple infection sites are typical for these infections. Interestingly, the main clinical appearance of these type of infections is abscess formation in liver, brain and spleen [2–4].

Genome of *K. pneumoniae* has a certain flexibility and variability to take up and to accumulate antibiotic resistance genes as well as virulence factor determinants [1]. Development of multiresistant strains has an ongoing tendency. It has been earlier

*Corresponding author.
E-mail: kocsis.bela@med.semmelweis-univ.hu

established that *K. pneumoniae* belongs to ESKAPE pathogens, and this group comprises well-known bacterial pathogens that are capable to develop multidrug-resistance and can cause high-number of difficult-to-treat infections [5, 6].

Hypervirulent *K. pneumoniae* was first reported in the 1980s and 1990s in Taiwan and in other Asian countries, however, recently a broader dissemination is seen [3, 4]. In the early reports hypervirulent *K. pneumoniae* demonstrated an enhanced virulence and it was isolated mainly from pyogenic liver abscess. Later on, hypervirulent *K. pneumoniae* was identified in different clinical manifestations namely, in spleen abscess, community acquired meningitis and bacteraemia [3].

A common feature of hypervirulent *K. pneumoniae* is a hypermucoviscosus phenotype that develops through production of different virulence determinants namely, *magA* and *rmpA*. Interestingly, in the early reports of hypervirulent *K. pneumoniae* the virulence determinants were located chromosomally however, recently virulence plasmids were detected that harbour different hypervirulence deteminants (e.g.: *rmpA*) [3]. This is an important feature, because hypervirulence determinants can spread through horizontal gene transfer, that results in further dissemination [3, 4].

Another interesting feature of hypervirulent *K. pneumoniae* is the antibiotic susceptibility. During the early reports hypervirulent *K. pneumoniae* strains were susceptible to commonly used antibiotics, but this has changed recently. The majority of currently isolated hypervirulent *K. pneumoniae* strains show multidrug resistance, that is explained mainly by acquired resistance determinants (e.g.: beta-lactamases) [2–4].

Generally, antibiotic resistance in *K. pneumoniae* is well described, as resistance to beta-lactams, fluoroquinolones and aminoglycosides are reported from all over the World [1]. Resistance to beta-lactams in *K. pneumoniae* is explained mainly by production of different beta-lactamases namely, extended-spectrum beta-lactamases (ESBLs) and carbapenemases. Among ESBLs the most frequently reported enzymes are TEM, SHV, CTX-M types, while among carbanemases *K. pneumoniae* carbapenemase (KPC) from Ambler class A, metallo-beta-lactamases (e.g.: VIM, NDM, IMP types) from Ambler class B and OXA types (e.g.: OXA-48, and OXA-48-like enzymes) from Ambler class D are detected in *K. pneumoniae* [7–11]. Fluoroquinolone resistance in *K. pneumoniae* is explained by chromosomal mutations in gyrase and topoismerase IV coding genes namely, in *gyrA*, *gyrB*, *parC* and *parE*. Additionally, plasmid-mediated quinolone resistance determinants (PMQRs) have been also reported, that enhance development of fluoroquinolone resistance. PMQRs include Qnr determinants, Aminoglycoside acetyltransferase (6′)-Ib-cr variant enzyme [AAC(6′)-Ib-cr], QepA and OqxAB efflux pumps [12–15]. Resistance to aminoglycosides develops mainly through enzymatic modifications by aminoglycoside acetyltransferase, aminoglycoside adenyltransferase, and aminoglycoside phosphotransferase. Another mechanism in aminoglycoside resistance is the modification of ribosomal binding site through 16s rRNA methylase [16].

The aim of this review is to summarize current epidemiology, detection, clinical features and antibiotic resistance of hypervirulent *K. pneumoniae*.

## VIRULENCE DETERMINANTS ASSOCIATED WITH HYPERVIRULENT *K. PNEUMONIAE*

Phenotypic and genetic markers are detected in hypermucoviscosus and hypervirulent *K. pneumoniae*. Hypermucoviscosity can be detected by string test however, a hypervirulent type requires additional markers [17].

### String test

The string test is a well-known test to detect mucoviscosus phenotype of *K. pneumoniae*. This routine method is performed on fresh colonies from an overnight culture on blood agar with a loop. Detection of viscous string greater than 5 mm in length, when the colony was taken with a loop wire is considered a positive result [17–19].

### Capsular polysaccharide serotype

Capsule polysaccharide is a virulence determinant of *K. pneumoniae* and at least 78 capsular serotypes are already described [20, 21]. Interestingly, serotype K1 and K2 are the most frequently associated with hypervirulent *K. pneumoniae*. Notebly, invasive infections like pyogenic liver abscess were associated with K2 serotype in 42.9% of cases while K1 serotype was present in 23.8% of cases [22]. K2 serotype was detected in 68.75% of *K. pneumoniae* strains exhibiting hypermucoviscosity in China [23]. In South Korea, *K. pneumoniae* strains showing hypermucoviscosity were commonly detected as serotype K1 and K2 [24].

Interestingly, K1 and K2 serotypes demonstrate more resistance to phagocytosis and intracellular killing by macrophages, compared to other serotypes of *K. pneumoniae*, that contribute to higher virulence [25–27]. During early detection of hypervirulent *K. pneumoniae* strains, the K1 and K2 serotypes were the most frequently reported however, recently the hypervirulent *K. pneumoniae* is associated with other capsular serotypes namely, K5, K16, K20, K28, K54, K57, K63 [3] (Table 1).

### RmpA (regulator of the mucoid phenotype A)

RmpA is a major regulator of capsule production, that leads to hypermucoviscosity and it is associated with enhanced virulence [28]. Altogether three *rmpA* genes were descibed in hypervirulent *K. pneumoniae* strains namely, *p-rmpA* and *p-rmpA2* (plasmid located) and c-rmpA (chromosomal located) [29, 30]. Based on whole genome sequence data, several reports demonstrated that hypervirulent *K. pneumoniae* strains commonly harbour *rmpA* gene. Interestingly, this feature was found in different countries and in different infection sites [31–34].

*Table 1.* Markers and virulence determinants associated with hypervirulent *K. pneumoniae*

| Virulence deteminants | Gene | Marker | Reference |
|---|---|---|---|
| **Hypermucoviscosity** | | capsular types: K1, K2, K5, K16, K20, K28, K54, K57, K63 | [3] |
| | | string test (>5 mm) | [17] |
| | *magA* | mucoviscosity associated gene A | [64] |
| | *rmpA* | regulator of the mucoid phenotype A gene | [64] |
| | *rmpA2* | | [64] |
| **Siderophores** | *iucABCD* | aerobactin siderophore biosynthesis | [64] |
| | *peg344* | putative transporter | [64] |
| | *peg-589* | putative carboxymuconolactone decarboxylase family | [64] |
| | *iroB* | salmochelin siderophore biosynthesis | [64] |
| | *irp2* | yersiniabactin siderophore biosynthesis | [64] |
| | *ybt* | yersiniabactin | [3] |
| **Other** | *terB* | tellurit resistance | [64] |

### MagA (mucoviscosity associated gene A)

MagA was described as a major factor in hypercapsular phenotype in *K. pneumoniae*, however, it has been clarified, that *magA* is a K1 serotype allele of *wzy* gene in *cps* gene cluster, therefore, *magA* is named as *wzy* K1 [17, 35]. A strong correlation (83% of detected *K. pneumoniae* strains) was found between *magA* gene positivity and hypervirulent *K. pneumoniae* strains obtained from pyogenic liver abscess [36]. Moreover, significant association was found between K1 capsular serotype and *magA* gene positivity in hypervirulent *K. pneumoniae* [22].

### Siderophores

*K. pneumoniae* produces several siderophores (aerobactin, salmochelin, enterobactin, and yersiniabactin) that take up iron from the environment. Iron is an important metal, that plays a cardinal role in growth and virulence of *K. pneumoniae* [37, 38]. It has been demonstrated that hypervirulent *K. pneumoniae* exhibits a 6-10 fold enhanced siderophore activity compared to that of classical *K. pneumoniae* strains [37, 39].

Aerobactin, salmochelin and yersinibactin are plasmid coded determinants and can be transferred through horizontal gene transfer [31, 40, 41].

Interestingly, hypervirulent *K. pneumoniae* mainly produces aerobactin, that was found in over 90% siderophore activity of investigated strains [37]. An *iucABCD* operon encodes aerobactin and this determinant was found in high prevalence among hypervirulent *K. pneumoniae* [22, 33, 34, 37, 42–47] (Table 1) (Fig. 1).

## ANTIBIOTIC RESISTANCE IN HYPERVIRULENT *K. PNEUMONIAE*

During early reports of hypervirulent *K. pneumoniae* antibiotic susceptible strains were isolated [3, 48]. However, recently several studies have detected antibiotic resistance in

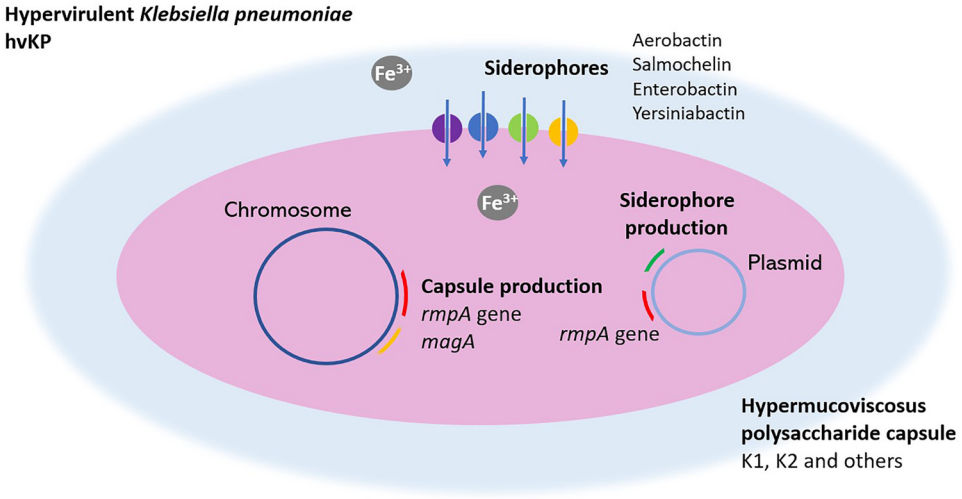


*Fig. 1.* Virulence determinants of hypervirulent *K. pneumoniae*

different sequence types (STs) of hypervirulent *K. pneumoniae*. The majority of multidrug-resistant and hypervirulent *K. pneumoniae* strains are identified in China however, in the past years a worldwide dissemination was seen [49, 50]. *K. pneumoniae* has several multidrug-resistant and high-risk clones that has been reported in the past decades namely, ST11, ST147, ST307. However, hypervirulent pathotype has just been recently detected in these high-risk clones [49]. Interestingly, the earlier detected hypervirulent and antibiotic susceptible *K. pneumoniae* STs (e.g. ST23, ST1265, ST1797) can take up resistance plasmids, therefore multidrug-resistant and hypervirulent strains can evolve also in this process [49] (Fig. 2).

ST11 is among the most frequently detected multidrug-resistant and hypervirulent *K. pneumoniae*. ST11 is a well-known antibiotic resistant high-risk clone and its expression of hypervirulence has been also reported. In a study in China colistin resistant hypervirulent *K. pneumoniae* ST11 strains were isolated. In these strains colistin resistance was mediated mainly by *mgrB* mutation (ISKpn26, or Q30Stop), *phoQ* mutation (D150G), *pmrD* mutation (D80G), *pmrB* mutations (R256G, D313N) [50].

In 2016 during an outbreak in China, hypervirulent carbapenem resistant *K. pneumoniae* caused ventilator-associated pneumonia. The detected five strains belonged to ST11 clone, and each carried aprox. 170 kbp pLVPK-like virulence plasmid [51].

In a study in China a hypervirulent carbepenem resistant *K. pneumoniae* ST23 was detected. It was isolated from a sputum sample of a chronic obstructive pulmonary disease patient. This *K. pneumoniae* strain harboured $bla_{\text{KPC-2}}$ on a plasmid [52].

A carbapenem resistant *K. pneumoniae* was isolated from bloodstream infection of a patient treated at an intensive care unit in Sichuan province, China. This *K. pneumoniae* strain was further investigated, and it carried $bla_{\text{KPC-2}}$ resistance gene and *rmpA* virulence determinant. According to multilocus sequence typing of this strain, it belonged to ST36 [53].

Altogether 163 *K. pneumoniae*-induced pyogenic liver abscess cases were investigated in China between 2016 and 2017. Twelve *K. pneumoniae* strains exhibited multidrug-resistance. K1 and K2 serotypes were detected in 40.5% and 19% of strains, whereas 30.7% of strains showed hypermucoviscosity. Diverse virulence determinants were detected in hypervirulent *K. pneumoniae* strains namely, *iroN* (24.5%), *magA* (45.4%), genes encoding for aerobactin, *rmpA*, *ybtA*, (68.7–100%). Among tested *K. pneumoniae* strains ST23 was the most frequently detected, however, additional STs (e.g.: ST3507, ST3508 and ST3509) were also reported [54].

A NDM-5 carbapenemase producing hypermucoviscosus *K. pneumoniae* was isolated from sputum sample in China. This *K. pneumoniae* harboured a pVir-SCNJ1 plasmid, that carried *rmpA* virulence gene, that determines hypervirulent pathotype. Interestingly, this strain belonged to ST29, and the $bla_{\text{NDM-5}}$ was located on a IncX3 conjugative plasmid [55].

Two carbapenem resistant IMP-4 producing hypervirulent *K. pneumoniae* were isolated from blood and sputum samples in an intensive care unit in China. Both *K. pneumoniae* strains belonged to ST65 and K2 capsular serotype. Virulence factors indicating hypervirulence pathotype, namely, *rmpA*/*rmpA2*, *iucA*, and *iroN* were also detected in these strains. One *K. pneumoniae* strain demonstrated tigecycline non-susceptibility, that was conffered by frameshift mutation in the TetR/AcrR transcriptional regulator [56].

A carbapenem resistant hypervirulent *K. pneumoniae* was recoved from a sputum sample of patient, who was treated in an intesive care unit in China. This *K. pneumoniae* strain belonged to ST592 and had K57 capsular serotype. Interestingly, this strain harboured a plasmid that was carrying $bla_{\text{KPC-2}}$. This carbapenem resistant *K. pneumoniae* strain harboured a virulence plasmid that possesed IncFIBK, IncHI1B replicons and carried *rmpADC*, *rmpA2*, *iucABCD-iutA* and *iroBCDN* virulence determinants [57].

A multidrug-resistant hypervirulent *K. pneumoniae* was isolated from a lung infection in China. This strain belonged to ST25 and K2 serotype. This *K. pneumoniae* strain harboured a plasmid carrying *iucABCD-iutA* operon, that codes

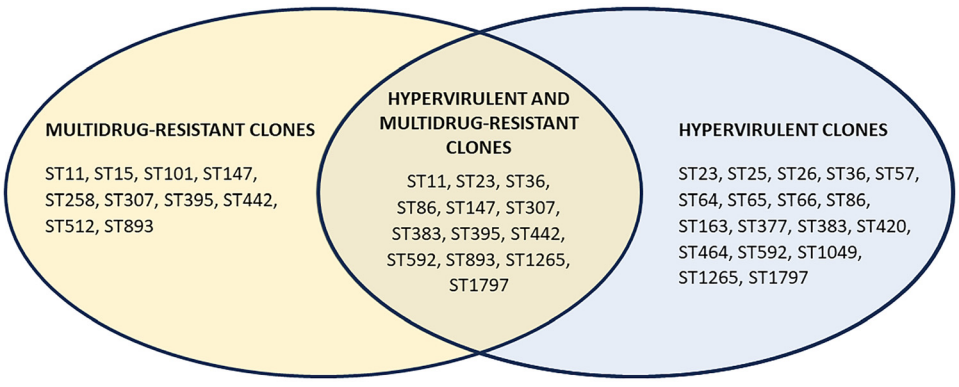


*Fig. 2.* Multidrug-resistant and hypervirulent *K. pneumoniae* clones

aerobactin virulence determinant. Interestingly, this strain harboured another plasmid, that was carrying $bla_{KPC-2}$. During conjugation assays it has been demonstrated that both plasmids can be transferred, indicating a possible joint horizontal genetranfer of $bla_{KPC-2}$ carbapenemase and hypervirulence determinant [58].

A multidrug-resistant *K. pneumoniae* was isolated from a blood sample of a haematological patient in China. This strain belonged to ST464 and co-produced NDM-1 and KPC-2 carbapenemases, and additionally it exhibited resistance to tetracyclin, fluoroquinolones, tigecycline and fosfomycin. Hypervirulent pathotype of this *K. pneumoniae* strain was confirmed by serum resistance, and in a *Galleria mellonella* infection model [59].

A hypermucoviscosus *K. pneumoniae* was isolated from a neck abscess in China. This strain belonged to ST1049 and exhibited resistance to ampicillin, however, it was susceptible to commonly used antibiotics. A virulence plasmid (pLVPK-like) was detected in this *K. pneumoniae* strain, indicating possible horizontal genetransfer of hypervirulence pathotype [60].

A survey in Qatar revealed carbapenem resistant and hypervirulent *K. pneumoniae*. Ten strains carried *rmpA* and/or truncated *rmpA2*. Strains carrying carbapenem resistance and hypervirulence determinants belonged to ST231 and ST383. A *K. pneumoniae* ST383 strain carried $bla_{NDM}$ on IncHI1B plasmid, that co-harboured *rmpA*, *rmpA2*, aerobactin (*iucABCD-iutA*) virulence determinants of hypervirulent pathotype [61].

A study in Germany detected two hypervirulent *K. pneumoniae* ST420 strains that were isolated from a swab and a bloodculture of a patient. In these strains a chromosomally integrated virulence plasmid was detected and increased siderophore production as well as hypermucoviscosity were also seen. Interestingly, both genomes of *K. pneumoniae* ST420 strains carried the "yersiniabactin lineage 9" that was associated with *K. pneumoniae* integrative conjugative element 3 (ICE*Kp3*). According to bioinformatic analysis insertion of the hypervirulence plasmid into *K. pneumoniae* chromosome was mediated by IS*5* family sub-group IS*903*, designated as IS*Kpn74* [62].

A 2 year survey in Ireland detected twenty-eight carbapenem resistant hypervirulent *K. pneumoniae* ST23 strains. All these *K. pneumoniae* strains were isolated from different clinical samples, including rectal swab, faeces (as colonizer) as well as from blood culture samples (from invasive infections). All hypervirulent *K. pneumoniae* strains produced OXA-48 and expressed different virulence markers indicating the hypervirulent pathotype namely, *rmpA2, iuc, iro, ybt* [63].

Several other reports demonstrate multidrug-resistant and hypervirulent *K. pneumoniae* in different countries, namely, in India, France, Germany, Italy and Iran [70–76]. The most frequently reported antibiotic resistance determinants and STs of hypervirulent *K. pneumoniae* are summarized in Table 2.

## CHARACTERISTICS OF INFECTIONS CAUSED BY HYPERVIRULENT *K. PNEUMONIAE*

First infections caused by hypervirulent *K. pneumoniae* were reported in 1980s and 1990s in Southeast Asia [4]. These early reports described a special clinical picture that was dominated by community acquired pyogenic liver abscess, and it was associated with severe complications such as meningitis and endophthalmitis [3, 77–80]. Later on, several other reports from Asia described role of hypervirulent *K. pneumoniae* in different infections. A report from China demonstrated that 90.9% of the pathogens causing pyogenic liver abscesses were hypervirulent *K. pneumoniae* [43]. In different studies conducted in South Korea and Taiwan a high prevalence of hypermucoviscosus and hypervirulent *K. pneumoniae* strains were isolated from invasive infections, namely, 42.2% of *K. pneumoniae* strains isolated from bacteremia had hypermucoviscosity phenotype in South Korea [81], while 88.8% of *K. pneumoniae* isolates from community acquired extrahepatic abscesses exhibited hypermucoviscosity phenotype in Taiwan [82] and additionally, 41.5% of community acquired bacteriaemia caused by *K. pneumoniae* belonged to hypervirulent *K. pneumoniae* in Taiwan [83].

During infections caused by hypervirulent *K. pneumoniae* multiple infection sites and metastatic spread are detected [2, 84]. These interesting and specific features are characteristics of hypervirulent *K. pneumoniae,* that are normally not seen in infections of classical *K. pneumoniae.* Pathomechanism of multiple infection sites can be explained by the local invasion of hypervirulent *K. pneumoniae*, breaking into different tissues or another explantion can be a primary infection site in the human body that serves as a source for subsequent bacteriaemia and distant infections. This later type can be called as a metastatic spread [2].

The most frequently reported infection is pyogenic liver abscess that has been described mainly in Taiwan and China, however, recently several reports from USA, and from European countries have revealed its clinical significance [85–96].

Some specific features of pyogenic liver abscess caused by hypervirulent *K. pneumoniae* have been described: it is almost always monomicrobial infection, while in case of a non-hypervirulent *K. pneumoniae* infection a pyogenic liver abscess is almost always polymicrobial [97, 98]. During an infection caused by hypervirulent *K. pneumoniae* metastatic complications occur more frequently compared to that of other *K. pneumoniae* infections [45, 79]. Interestingly, pyogenic liver abscess through hypervirulent *K. pneumoniae* develops in patients with normal hepatic and biliary functions, by contrast, other liver infections are linked to hepatic imparement and to different pathological disorders. [45]. Regional thrombophlebitis is reported in aprox. 30% of pyogenic liver abscess infections. Additional intra-

*Table 2.* Sequence types, virulence determinants and antibiotic resistance associated with hypervirulent *K. pneumoniae*

| Country | Sequence type (ST) | Antibiotic resistance | Capsular types and virulence determinants | Reference |
|---|---|---|---|---|
| **China** | ST11 | KPC | K47, *rmpA, iucA, ybt* | [22] |
| | ST11, ST65, ST268, ST595, ST692 | KPC, SHV | K2, K20, *rmpA, iucA, ybtS* | [47] |
| | ST11, ST23, ST65, ST86, ST437 | ESBL | K1, K2, K20, *rmpA* | [45] |
| | ST11 | KPC | K1, *magA, rmpA, iro, iucA* | [65] |
| | ST23 | ESBL | K1, K2, K20, *rmpA, iro, iucA* | [66] |
| | ST23, ST1797 | KPC | K1, *magA, rmpA* | [67] |
| | ST65 | KPC | K2, *rmpA, iucA, entB* | [68] |
| | ST11, ST25, ST65 | KPC | K2, *rmpA, iucA, iro* | [69] |
| | ST23, ST1265 | ESBL | K1, K2, K20, K57, *rmpA* | [32] |
| | ST5253 | Colistin resistance | K28, *iroB, iucA* | [50] |
| | ST11 | Colistin resistance | K64, *iroB, iucA, rmpA* | [50] |
| | ST86 | Colistin resistance | K2, *iroB, iucA, rmpA, peg344* | [50] |
| | ST36 | KPC-2 | *rmpA* | [53] |
| | ST592 | KPC-2 | *rmpA, iroBCDN, iucA* | [57] |
| **Qatar** | ST383 | NDM | *rmpA, rmpA2, iucA* | [61] |
| **India** | ST15 | NDM-1 | *rmpA, rmpA2, iroB, iucA, peg-344* | [70] |
| | ST11 | NDM-1 | *rmpA, rmpA2, iroB, iucA, peg-344* | [70] |
| **France** | ST86 | ESBL | K2, *rmpA, iucA, ybtS, entB* | [71] |
| **Germany** | ST307 | OXA-48, NDM-1 | *rmpA, rmpA2, iucA, peg344* | [72] |
| **Italy** | ST395 | OXA-48 | *magA* | [73] |
| | ST383 | VIM, NDM, OXA-505 | *rmpA2* | [73] |
| | ST383 | NDM-5, OXA-48 | *rmpA, iucA* | [74] |
| **Ireland** | ST23 | OXA-48 | *rmpA2, iuc, ybt, iro* | [63] |
| **Iran** | ST442 | TEM, SHV | *iroB, iucA, peg-344* | [75] |
| | ST15 | TEM, SHV, OXA-48 | *iroB, peg-344, rmpA2* | [75] |
| | ST147 | TEM, SHV | *iroB, iucA, rmpA, rmpA2* | [75] |
| | ST377 | TEM, SHV | *iroB, iucA, rmpA, rmpA2* | [75] |
| | ST147 | TEM, SHV, CTX-M-15 | K20, *ybt, iroB* | [76] |
| | ST893 | CTX-M-15 | *ybt, magA* | [76] |
| | ST11 | TEM, SHV, CTX-M-15 | K20, *ybt, magA, rmpA, iroB* | [76] |

abdominal infection caused by hypervirulent *K. pneumoniae* includes splenic abscess [99].

Pneumonia is a typical infection caused by classical *K. pneumoniae* among hospitalized patients and it usually occurs as ventilator-associated pneumonia. However, recent reports demonstrated that hypervirulent *K. pneumoniae* is a major causative agent of community acquired pneumonia in Taiwan, and in these cases certain complications and clinical pictures develop namely, empyema, lung abscess, respiratory failuer, bilateral lobar involvement and septic schock [100].

Endogenous endophthalmitis develops in patients after a bacteraemia caused by hypervirulent *K. pneumoniae.* It is a very severe infection of eyes, and bilateral involvement can occur between 13 and 25% of cases. Furthermore, this infection can lead to irreversible blindness [101].

Among central nervous system infections, hypervirulent *K. pneumoniae* is a major pathogen in community acquired meningitis, and certain complications (e.g.: septic shock) can develop. Further central nervous system infections caused by hypervirulent *K. pneumoniae* include brain abscess, subdural empyema and epidural abscess [102].

## CONCLUSION

In the past years hypervirulent *K. pneumoniae* strains emerged and disseminated worldwide. Hypervirulent *K. pneumoniae* causes infections usually in healthy people and multiple infection sites are typical. The clinical picture is very diverse, however, the most frequent clinical presentation is abscess formation in liver, spleen and brain. Additionally, meningitis, endophthalmitis and other invasive infections (e.g.: bacteraemia, sepsis) can also develop. Noteworthy to mention, that classical infections of *K. pneumoniae* (e.g.: urinary tract infection, ventilator-associated pneumonia, catheter associated infections) are caused less frequently by hypervirulent *K. pneumoniae.*

During the early detection of hypervirulent *K. pneumoniae,* it has been demonstrated that these strains pose enhanced virulence alongside with an antibiotic susceptible feature. However, recently multidrug-resistant hypervirulent *K. pneumonaie* strains evolved through the acquisition of different resistance genes ($bla_{VIM}$, $bla_{NDM}$, $bla_{OXA-48}$, $bla_{CTX-M-15}$). Furthermore, multidrug-resistant high-risk *K. pneumoniae* clones, namely ST11, ST15, ST147, ST307, are also capable to take up virulence plasmids that carry *rmpA, ybt*

hypervirulence determinants, therefore development of hypervirulent pathotype is possible in these high-risk *K. pneumoniae* clones.

*Conflict of interest:* The author is a member of the Editorial Board of the journal. Therefore he did not take part in the review process in any capacity and the submission was handled by a different member of the editorial board.

## ACKNOWLEDGEMENT

B.K. was supported by Janos Bolyai Scholarship (BO/00286/22/5) of the Hungarian Academy of Sciences.

## REFERENCES

1. Navon-Venezia S, Kondratyeva K, Carattoli A. *Klebsiella pneumoniae:* a major worldwide source and shuttle for antibiotic resistance. FEMS Microbiol Rev 2017; 41(3): 252–75.
2. Russo TA, Marr CM. Hypervirulent *Klebsiella pneumoniae*. Clin Microbiol Rev 2019; 32(3): e00001–19.
3. Lee CR, Lee JH, Park KS, Jeon JH, Kim YB, Cha CJ, et al. Antimicrobial resistance of hypervirulent Klebsiella pneumoniae: epidemiology, hypervirulence-associated determinants, and resistance mechanisms. Front Cell Infect Microbiol 2017; 7: 483.
4. Shon AS, Bajwa RP, Russo TA. Hypervirulent (hypermucoviscous) *Klebsiella pneumoniae*: a new and dangerous breed. Virulence 2013; 4: 107–18.
5. De Oliveira DMP, Forde BM, Kidd TJ, Harris PNA, Schembri MA, Beatson SA, et al. Antimicrobial resistance in ESKAPE pathogens. Clin Microbiol Rev 2020; 33(3): e00181–19.
6. Orosz L, Lengyel G, Ánosi N, Lakatos L, Burián K. Changes in resistance pattern of ESKAPE pathogens between 2010 and 2020 in the clinical center of University of Szeged, Hungary. Acta Microbiol Immunol Hung 2022; 69: 27–34.
7. Antinori E, Unali I, Bertoncelli A, Mazzariol A. *Klebsiella pneumoniae* carbapenemase (KPC) producer resistant to ceftazidime-avibactam due to a deletion in the blaKPC3 gene. Clin Microbiol Infect 2020; 26(7): 946.e1–3.
8. de Barsy M, Mercuri PS, Oueslati S, Elisée E, Huang TD, Sacré P, et al. Detection and characterization of VIM-52, a new variant of VIM-1 from a *Klebsiella pneumoniae* clinical isolate. Antimicrob Agents Chemother 2021; 65(11): e0266020.
9. Biedrzycka M, Urbanowicz P, Guzek A, Brisse S, Gniadkowski M, Izdebski R. *Dissemination of Klebsiella pneumoniae* ST147 NDM-1 in Poland, 2015–19. J Antimicrob Chemother 2021; 76(10): 2538–45.
10. Jánvári L, Damjanova I, Lázár A, Rácz K, Kocsis B, Urbán E, et al. Emergence of OXA-162-producing *Klebsiella pneumoniae* in Hungary. Scand J Infect Dis 2014; 46(4): 320–4.
11. Seiffert SN, Marschall J, Perreten V, Carattoli A, Furrer H, Endimiani A. Emergence of Klebsiella pneumoniae co-producing NDM-1, OXA-48, CTX-M-15, CMY-16, QnrA and ArmA in Switzerland. Int J Antimicrob Agents 2014; 44(3): 260–2.
12. Ferreira S, Toleman M, Ramalheira E, Da Silva GJ, Walsh T, Mendo S. First description of *Klebsiella pneumoniae* clinical isolates carrying both *qnrA* and *qnrB* genes in Portugal. Int J Antimicrob Agents 2010; 35(6): 584–6.
13. Kocsis B, Kocsis E, Fontana R, Cornaglia G, Mazzariol A. Identification of $bla_{LAP-2}$ and *qnrS1* genes in the internationally successful *Klebsiella pneumoniae* ST147 clone. J Med Microbiol 2013; 62: 269–73.
14. Szabo O, Kocsis B, Szabo N, Kristof K, Szabo D. Contribution of OqxAB efflux pump in selection of fluoroquinolone-resistant *Klebsiella pneumoniae*. Can J Infect Dis Med Microbiol 2018; 2018: 4271638.
15. Bialek-Davenet S, Lavigne JP, Guyot K, Mayer N, Tournebize R, Brisse S, et al. Differential contribution of AcrAB and OqxAB efflux pumps to multidrug resistance and virulence in *Klebsiella pneumoniae*. J Antimicrob Chemother 2015; 70(1): 81–8.
16. Isler B, Falconer C, Vatansever C, Özer B, Çınar G, Aslan AT, et al. High prevalence of ArmA-16S rRNA methyltransferase among aminoglycoside-resistant Klebsiella pneumoniae bloodstream isolates. J Med Microbiol 2022; 71(12).
17. Fang CT, Chuang YP, Shun CT, Chang SC, Wang JT. A Novel virulence gene in *Klebsiella pneumoniae* strains causing primary liver abscess and septic metastatic complications. J Exp Med 2004; 199: 697–705.
18. Saki M, Amin M, Savari M, Hashemzadeh M, Seyedian SS. Beta-lactamase determinants and molecular typing of carbapenem-resistant classic and hypervirulent Klebsiella pneumoniae clinical isolates from southwest of Iran. Front Microbiol 2022; 13: 1029686.
19. Örsten S, Demirci-Duarte S, Ünalan-Altıntop T, Çakar A, Sancak B, Ergünay K, et al. Low prevalence of hypervirulent *Klebsiella pneumoniae* in Anatolia, screened via phenotypic and genotypic testing. Acta Microbiol Immunol Hung 2020; 67(2): 120–6.
20. Wyres KL, Wick RR, Gorrie C, Jenney A, Follador R, Thomson NR, et al. Identification of *Klebsiella* capsule synthesis loci from whole genome data. Microb Genom 2016; 2: e000102.
21. Pan YJ, Fang HC, Yang HC, Lin TL, Hsieh PF, Tsai FC, et al. Capsular polysaccharide synthesis regions in *Klebsiella pneumoniae* serotype K57 and a new capsular serotype. J Clin Microbiol 2008; 46: 2231–40.
22. Guo Y, Wang S, Zhan L, Jin Y, Duan J, Hao Z, et al. Microbiological and clinical characteristics of hypermucoviscous *Klebsiella pneumoniae* isolates associated with invasive infections in China. Front Cell Infect Microbiol 2017; 7: 24. https://doi.org/10.3389/fcimb.2017.00024.
23. Zhao J, Chen J, Zhao M, Qiu X, Chen X, Zhang W, et al. Multilocus sequence types and virulence determinants of hypermucoviscosity positive *Klebsiella pneumoniae* isolated from community-acquired infection cases in Harbin, North China. Jpn J Infect Dis 2016; 69: 357–60.
24. Kim YJ, Kim SI, Kim YR, Wie SH, Lee HK, Kim SY, et al. Virulence factors and clinical patterns of hypermucoviscous *Klebsiella pneumoniae* isolated from urine. Infect Dis (Lond) 2017; 49: 178–84. https://doi.org/10.1080/23744235.2016.1244611.
25. Kabha K, Nissimov L, Athamna A, Keisari Y, Parolis H, Parolis LA, et al. Relationships among capsular structure,

phagocytosis, and mouse virulence in *Klebsiella pneumoniae*. Infect Immun 1995; 63: 847–52.
26. Lin JC, Chang FY, Fung CP, Xu JZ, Cheng HP, Wang JJ, et al. High prevalence of phagocytic-resistant capsular serotypes of *Klebsiella pneumoniae* in liver abscess. Microbes Infect 2004; 6: 1191–8. https://doi.org/10.1016/j.micinf.2004.06.003.
27. Yeh KM, Kurup A, Siu LK, Koh YL, Fung CP, Lin JC, et al. Capsular serotype K1 or K2, rather than magA and rmpA, is a major virulence determinant for *Klebsiella pneumoniae* liver abscess in Singapore and Taiwan. J Clin Microbiol 2007; 45: 466–71. https://doi.org/10.1128/JCM.01150-06.
28. Cheng HY, Chen YS, Wu CY, Chang HY, Lai YC, Peng HL. RmpA regulation of capsular polysaccharide biosynthesis in *Klebsiella pneumoniae* CG43. J Bacteriol 2010; 192: 3144–58.
29. Hsu CR, Lin TL, Chen YC, Chou HC, andWang JT. The role of *Klebsiella pneumoniae rmpA* in capsular polysaccharide synthesis and virulence revisited. Microbiology 2011; 157: 3446–57.
30. Wacharotayankun R, Arakawa Y, Ohta M, Tanaka K, Akashi T, Mori M, et al. Enhancement of extracapsular polysaccharide synthesis in *Klebsiella pneumoniae* by RmpA2, which shows homology to NtrC and FixJ. Infect Immun 1993; 61: 3164–74.
31. Struve C, Roe CC, Stegger M, Stahlhut SG, Hansen DS, Engelthaler DM, et al. Mapping the evolution of hypervirulent *Klebsiella pneumoniae*. MBio 2015; 6: e00630.
32. Liu YM, Li BB, Zhang YY, Zhang W, Shen H, Li H, et al. Clinical and molecular characteristics of emerging hypervirulent *Klebsiella pneumoniae* bloodstream infections in mainland China. Antimicrob Agents Chemother 2014; 58: 5379–85.
33. Sun Y, Wu H, Shen D. Clinical and molecular analysis of *Klebsiella pneumoniae* causing liver abscess in China. J Mol Microbiol Biotechnol 2016; 26: 245–51.
34. Wu H, Li D, Zhou H, Sun Y, Guo L, Shen D. Bacteremia and other body site infection caused by hypervirulent and classic *Klebsiella pneumoniae*. Microb Pathog 2017; 104: 254–62.
35. Yeh KM, Lin JC, Yin FY, Fung CP, Hung HC, Siu LK, et al. Revisiting the importance of virulence determinant *magA* and its surrounding genes in *Klebsiella pneumoniae* causing pyogenic liver abscesses: exact role in serotype K1 capsule formation. J Infect Dis 2010; 201: 1259–67.
36. Chuang YP, Fang CT, Lai SY, Chang SC, andWang JT. Genetic determinants of capsular serotype K1 of *Klebsiella pneumoniae* causing primary pyogenic liver abscess. J Infect Dis 2006; 193: 645–54.
37. Russo TA, Olson R, Macdonald U, Metzger D, Maltese LM, Drake EJ, et al. Aerobactin mediates virulence and accounts for increased siderophore production under iron-limiting conditions by hypervirulent (hypermucoviscous) *Klebsiella pneumoniae*. Infect Immun 2014; 82: 2356–67.
38. Hsieh PF, Lin TL, Lee CZ, Tsai SF, Wang JT. Serum-induced iron-acquisition systems and TonB contribute to virulence in *Klebsiella pneumoniae* causing primary pyogenic liver abscess. J Infect Dis 2008; 197: 1717–27.
39. Russo TA, Shon AS, Beanan JM, Olson R, MacDonald U, Pomakov AO, et al. Hypervirulent *K. pneumoniae* secretes more and more active iron-acquisition molecules than "classical" *K. pneumoniae* thereby enhancing its virulence. PLoS ONE 2011; 6: e26734.
40. Nassif X, Sansonetti PJ. Correlation of the virulence of *Klebsiella pneumoniae* K1 and K2 with the presence of a plasmid encoding aerobactin. Infect Immun 1986; 54: 603–8.
41. Bach S, de Almeida A, Carniel E. The Yersinia high-pathogenicity island is present in different members of the family Enterobacteriaceae. FEMS Microbiol Lett 2000; 183: 289–94.
42. Guo S, Xu J, Wei Y, Xu J, Li Y, Xue R. Clinical and molecular characteristics of *Klebsiella pneumoniae* ventilator-associated pneumonia in mainland China. BMC Infect Dis 2016; 16: 608.
43. Ye M, Tu J, Jiang J, Bi Y, You W, Zhang Y, et al. Clinical and genomic analysis of liver abscess-causing *Klebsiella pneumoniae* identifies new liver abscess-associated virulence genes. Front Cell Infect Microbiol 2016; 6: 165. https://doi.org/10.3389/fcimb.2016.00165.
44. Yan Q, Zhou M, Zou M, Liu WE. Hypervirulent *Klebsiella pneumoniae* induced ventilator-associated pneumonia in mechanically ventilated patients in China. Eur J Clin Microbiol Infect Dis 2016; 35: 387–96.
45. Zhang Y, Zhao C, Wang Q, Wang X, Chen H, Li H, et al. High prevalence of hypervirulent *Klebsiella pneumoniae* infection in China: geographic distribution, clinical characteristics, and antimicrobial resistance. Antimicrob Agents Chemother 2016; 60: 6115–20.
46. Zhao J, Chen J, Zhao M, Qiu X, Chen X, Zhang W, et al. Multilocus sequence types and virulence determinants of hypermucoviscosity positive *Klebsiella pneumoniae* isolated from community-acquired infection cases in Harbin, North China. Jpn J Infect Dis 2016; 69: 357–60.
47. Zhan L, Wang S, Guo Y, Jin Y, Duan J, Hao Z, et al. Outbreak by hypermucoviscous *Klebsiella pneumoniae* ST11 isolates with carbapenem resistance in a tertiary hospital in China. Front Cell Infect Microbiol 2017; 7: 182.
48. Klaper K, Wendt S, Lübbert C, Lippmann N, Pfeifer Y, Werner G. Hypervirulent *Klebsiella pneumoniae* of lineage ST66-K2 caused Tonsillopharyngitis in a German patient. Microorganisms 2021; 9(1): 133.
49. Arcari G, Carattoli A. Global spread and evolutionary convergence of multidrug-resistant and hypervirulent Klebsiella pneumoniae high-risk clones. Pathog Glob Health 2023; 117(4): 328–41.
50. Liu X, Wu Y, Zhu Y, Jia P, Li X, Jia X, et al. Emergence of colistin-resistant hypervirulent Klebsiella pneumoniae (CoR-HvKp) in China. Emerg Microbes Infect 2022; 11(1): 648–61.
51. Gu D, Dong N, Zheng Z, Lin D, Huang M, Wang L, et al. A fatal outbreak of ST11 carbapenem-resistant hypervirulent *Klebsiella pneumoniae* in a Chinese hospital: a molecular epidemiological study. Lancet Infect Dis 2018; 18(1): 37–46.
52. Yan R, Lu Y, Zhu Y, Lan P, Jiang S, Lu J, et al. A sequence type 23 hypervirulent *Klebsiella pneumoniae* strain presenting carbapenem resistance by acquiring an IncP1 $bla_{KPC-2}$ plasmid. Front Cell Infect Microbiol 2021; 11: 641830.
53. Feng Y, Lu Y, Yao Z, Zong Z. Carbapenem-resistant hypervirulent *Klebsiella pneumoniae* of sequence type 36. Antimicrob Agents Chemother 2018; 62(7): e02644–17.
54. Zhang S, Zhang X, Wu Q, Zheng X, Dong G, Fang R, et al. Clinical, microbiological, and molecular epidemiological characteristics of *Klebsiella pneumoniae*-induced pyogenic liver abscess in southeastern China. Antimicrob Resist Infect Control 2019; 8: 166.

55. Yuan Y, Li Y, Wang G, Li C, Chang YF, Chen W, et al. $bla_{NDM-5}$ carried by a hypervirulent *Klebsiella pneumoniae* with sequence type 29. Antimicrob Resist Infect Control 2019; 8: 140.
56. Zhang Y, Wang X, Wang Q, Chen H, Li H, Wang S, et al. Emergence of tigecycline nonsusceptible and IMP-4 carbapenemase-producing K2-ST65 hypervirulent *Klebsiella pneumoniae* in China. Microbiol Spectr 2021; 9(2): e0130521.
57. Zhao Q, Feng Y, Zong Z. Conjugation of a hybrid plasmid encoding hypervirulence and carbapenem resistance in Klebsiella pneumoniae of sequence type 592. Front Microbiol 2022; 13: 852596.
58. Xia P, Yi M, Yuan Y, Huang J, Yang B, Liao J, et al. Coexistence of multidrug resistance and virulence in a single conjugative plasmid from a hypervirulent *Klebsiella pneumoniae* isolate of sequence type 25. mSphere 2022; 7(6): e0047722.
59. Hao J, Zhang B, Deng J, Wei Y, Xiao X, Liu J. Emergence of a hypervirulent tigecycline-resistant Klebsiella pneumoniae strain Co-producing $bla_{NDM-1}$ and $bla_{KPC-2}$ with an uncommon sequence type ST464 in southwestern China. Front Microbiol 2022; 13: 868705.
60. Lan P, Zhao D, Gu J, Shi Q, Yan R, Jiang Y, et al. Genome-based analysis of a sequence type 1049 hypervirulent *Klebsiella pneumoniae* causing bacteremic neck abscess. Front Microbiol 2021; 11: 617651.
61. Tsui CK, Ben Abid F, Al Ismail K, McElheny CL, Al Maslamani M, Omrani AS, et al. Genomic epidemiology of carbapenem-resistant *Klebsiella* in Qatar: emergence and dissemination of hypervirulent *Klebsiella pneumoniae* sequence type 383 strains. Antimicrob Agents Chemother 2023; 67(7): e0003023.
62. Eger E, Heiden SE, Becker K, Rau A, Geisenhainer K, Idelevich EA, et al. Hypervirulent Klebsiella pneumoniae sequence type 420 with a chromosomally inserted virulence plasmid. Int J Mol Sci 2021; 22(17): 9196.
63. Brennan C, DeLappe N, Cormican M, Tuohy A, Tobin A, Moran L, et al. A geographic cluster of healthcare-associated carbapenemase-producing hypervirulent *Klebsiella pneumoniae* sequence type 23. Eur J Clin Microbiol Infect Dis 2022. https://doi.org/10.1007/s10096-022-04535-z.
64. Russo TA, Olson R, Fang CT, Stoesser N, Miller M, MacDonald U, et al. Identification of biomarkers for differentiation of hypervirulent *Klebsiella pneumoniae* from classical *K. pneumoniae*. J Clin Microbiol 2018; 56: e00776–18.
65. Wei DD, Wan LG, Deng Q, Liu Y. Emergence of KPC-producing *Klebsiella pneumoniae* hypervirulent clone of capsular serotype K1 that belongs to sequence type 11 in Mainland China. Diagn Microbiol Infect Dis 2016; 85: 192–4.
66. Yan Q, Zhou M, Zou M, Liu WE. Hypervirulent *Klebsiella pneumoniae* induced ventilator-associated pneumonia in mechanically ventilated patients in China. Eur J Clin Microbiol Infect Dis 2016; 35: 387–96.
67. Zhang R, Lin D, Chan EW, Gu D, Chen GX, Chen S. Emergence of carbapenem-resistant serotype K1 hypervirulent *Klebsiella pneumoniae* strains in China. Antimicrob Agents Chemother 2015; 60: 709–11. https://doi.org/10.1128/AAC.02173-15.
68. Zhang Y, Zeng J, Liu W, Zhao F, Hu Z, Zhao C, et al. Emergence of a hypervirulent carbapenem-resistant *Klebsiella pneumoniae* isolate from clinical infections in China. J Infect 2015; 71: 553–60. https://doi.org/10.1016/j.jinf.2015.07.010.
69. Yao B, Xiao X, Wang F, Zhou L, Zhang X, Zhang J. Clinical and molecular characteristics of multi-clone carbapenem-resistant hypervirulent (hypermucoviscous) *Klebsiella pneumoniae* isolates in a tertiary hospital in Beijing, China. Int J Infect Dis 2015; 37: 107–12.
70. Mukherjee S, Bhadury P, Mitra S, Naha S, Saha B, Dutta S, et al. Hypervirulent *Klebsiella pneumoniae* causing neonatal bloodstream infections: emergence of NDM-1-producing hypervirulent ST11-K2 and ST15-K54 strains possessing pLVPK-associated markers. Microbiol Spectr 2023; 11(2): e0412122.
71. Surgers L, Boyd A, Girard PM, Arlet G, Decré D. ESBLProducing strain of hypervirulent *Klebsiella pneumoniae* K2, France. Emerging Infect Dis 2016; 22: 1687–8.
72. Heiden SE, Hübner NO, Bohnert JA, Heidecke CD, Kramer A, Balau V, et al. A *Klebsiella pneumoniae* ST307 outbreak clone from Germany demonstrates features of extensive drug resistance, hypermucoviscosity, and enhanced iron acquisition. Genome Med 2020; 12(1): 113.
73. Ventura A, Addis E, Bertoncelli A, Mazzariol A. Multiple detection of hypermucoviscous and hypervirulent strains of *Klebsiella pneumoniae*: an emergent health care threat. Acta Microbiol Immunol Hung 2022; 69(4): 297–302.
74. Lorenzin G, Gona F, Battaglia S, Spitaleri A, Saluzzo F, Trovato A, et al. Detection of NDM-1/5 and OXA-48 co-producing extensively drug-resistant hypervirulent *Klebsiella pneumoniae* in Northern Italy. J Glob Antimicrob Resist 2022; 28: 146–50.
75. Davoudabadi S, Goudarzi H, Goudarzi M, Ardebili A, Faghihloo E, Sharahi JY, et al. Detection of extensively drug-resistant and hypervirulent *Klebsiella pneumoniae* ST15, ST147, ST377 and ST442 in Iran. Acta Microbiol Immunol Hung 2021; 69(1): 77–86.
76. Talebzadeh H, Mellali H, Solgi H. Association of fluoroquinolone resistance and ESBL production in hypervirulent *Klebsiella pneumoniae* ST11 and ST893 in Iran. Acta Microbiol Immunol Hung 2022; 69(2): 135–43.
77. Liu YC, Cheng DL, Lin CL. *Klebsiella pneumoniae* liver abscess associated with septic endophthalmitis. Arch Intern Med 1986; 146(10): 1913–6.
78. Chiu CT, Lin DY, Liaw YF. Metastatic septic endophthalmitis in pyogenic liver abscess. J Clin Gastroenterol 1988; 10(5): 524–7.
79. Siu LK, Yeh KM, Lin JC, Fung CP, Chang FY. *Klebsiella pneumoniae* liver abscess: a new invasive syndrome. Lancet Infect Dis 2012; 12(11): 881–7.
80. Wang YF, Chang CC, Lee TC, Shih IL, Lien WC, Chen SJ, et al. Recent trend of pylephlebitis in Taiwan: *Klebsiella pneumoniae* liver abscess as an emerging etiology. Infection 2013; 41: 1137–43.
81. Jung SW, Chae HJ, Park YJ, Yu JK, Kim SY, Lee HK, et al. Microbiological and clinical characteristics of bacteraemia caused by the hypermucoviscosity phenotype of *Klebsiella pneumoniae* in Korea. Epidemiol Infect 2013; 141(2): 334–40.
82. Ku YH, Chuang YC, Yu WL. Clinical spectrum and molecular characteristics of *Klebsiella pneumoniae* causing community acquired extrahepatic abscess. J Microbiol Immunol Infect 2008; 41: 311–7.
83. Lee HC, Chuang YC, Yu WL, Lee NY, Chang CM, Ko NY, et al. Clinical implications of hypermucoviscosity phenotype in *Klebsiella pneumoniae* isolates: association with invasive syndrome in patients with community-acquired bacteraemia. J Intern Med 2006; 259: 606–14.

84. Yu VL, Hansen DS, Ko WC, Sagnimeni A, Klugman KP, von Gottberg A, et al. Virulence characteristics of *Klebsiella* and clinical manifestations of *K. pneumoniae* bloodstream infections. Emerg Infect Dis 2007; 13: 986–93.
85. Chang Y, Chen JH, Chen WL, Chung JY. *Klebsiella pneumoniae* invasive syndrome with liver abscess and purulent meningitis presenting as acute hemiplegia: a case report. BMC Infect Dis 2023; 23(1): 397.
86. Rossi B, Gasperini ML, Leflon-Guibout V, Gioanni A, de Lastours V, Rossi G, et al. Hypervirulent *Klebsiella pneumoniae* in cryptogenic liver abscesses, Paris, France. Emerg Infect Dis 2018; 24: 221–9.
87. Lederman ER, Crum NF. Pyogenic liver abscess with a focus on *Klebsiella pneumoniae* as a primary pathogen: an emerging disease with unique clinical characteristics. Am J Gastroenterol 2005; 100: 322–31.
88. Pastagia M, Arumugam V. *Klebsiella pneumoniae* liver abscesses in a public hospital in Queens, New York. Trav Med Infect Dis 2008; 6: 228–33.
89. Pomakova DK, Hsiao CB, Beanan JM, Olson R, Macdonald U, Keynan Y, et al. Clinical and phenotypic differences between classic and hypervirulent *Klebsiella pneumonia*: an emerging and under-recognized pathogenic variant. Eur J Clin Microbiol Infect Dis 2012; 31: 981–9.
90. McCabe R, Lambert L, Frazee B. Invasive *Klebsiella pneumoniae* infections, California, USA. Emerg Infect Dis 2010; 16: 1490–1.
91. Keynan Y, Karlowsky JA, Walus T, Rubinstein E. Pyogenic liver abscess caused by hypermucoviscous *Klebsiella pneumoniae*. Scand J Infect Dis 2007; 39: 828–30.
92. Decre D, Verdet C, Emirian A, Le Gourrierec T, Petit JC, Offenstadt G, et al. Emerging severe and fatal infections due to *Klebsiella pneumoniae* in two university hospitals in France. J Clin Microbiol 2011; 49: 3012–4.
93. Sobirk SK, Struve C, Jacobsson SG. Primary *Klebsiella pneumoniae* liver abscess with metastatic spread to lung and eye, a North-European case report of an emerging syndrome. Open Microbiol J 2010; 4: 5–7.
94. Fierer J, Walls L, Chu P. Recurring *Klebsiella pneumoniae* pyogenic liver abscesses in a resident of San Diego, California, due to a K1 strain carrying the virulence plasmid. J Clin Microbiol 2011; 49: 4371–3.
95. Pope JV, Teich DL, Clardy P, McGillicuddy DC. *Klebsiella pneumoniae* liver abscess: an emerging problem in North America. J Emerg Med 2011; 41: e103–5.
96. Fazili T, Sharngoe C, Endy T, Kiska D, Javaid W, Polhemus M. *Klebsiella pneumoniae* liver abscess: an emerging disease. Am J Med Sci 2016; 351(3): 297–304.
97. Cheng DL, Liu YC, Yen MY, Liu CY, Wang RS. Septic metastatic lesions of pyogenic liver abscess. Their association with *Klebsiella pneumoniae* bacteremia in diabetic patients. Arch Intern Med 1991; 151: 1557–9.
98. Oikonomou KG, Aye M. *Klebsiella pneumoniae* liver abscess: a case series of six Asian patients. Am J Case Rep 2017; 18: 1028–33.
99. Kim SB, Je BK, Lee KY, Lee SH, Chung HH, Cha SH. Computed tomographic differences of pyogenic liver abscesses caused by *Klebsiella pneumoniae* and non-*Klebsiella pneumoniae*. J Comput Assist Tomogr 2007; 31: 59–65.
100. Lin YT, Chen TL, Siu LK, Hsu SF, Fung CP. Clinical and microbiological characteristics of community-acquired thoracic empyema or complicated parapneumonic effusion caused by *Klebsiella pneumoniae* in Taiwan. Eur J Clin Microbiol Infect Dis 2010; 29: 1003–10.
101. Yang CS, Tsai HY, Sung CS, Lin KH, Lee FL, Hsu WM. Endogenous *Klebsiella* endophthalmitis associated with pyogenic liver abscess. Ophthalmology 2007; 114: 876–80.
102. Yoon W A rare presentation of brain abscess and ventriculitis due to *Klebsiella pneumoniae*. J Neurol Sci 2013; 333: 1.