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Hypervirulent Klebsiella pneumoniae: prevalence, clinical presentation and antibiotic resistance in a French tertiary care hospital.

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Introduction

Klebsiella pneumoniae (KP) is a Gram-negative bacillus of enteric origin responsible primarily for healthcare-associated infections and infections in debilitated settings (1,2). The hypervirulent pathotype of KP (hvKP) has characteristics such as hypermucoviscosity, unique serotypes with high pathogenicity mainly mediated by virulence plasmids (3). Previous molecular biology studies have demonstrated the polyclonal and non-subtype associated nature of hvKP infections (4).

Objective

To determine the prevalence in clinical isolates of the different virulence genes defining hvKp in association with clinical presentation and antibiotic resistance

Methods

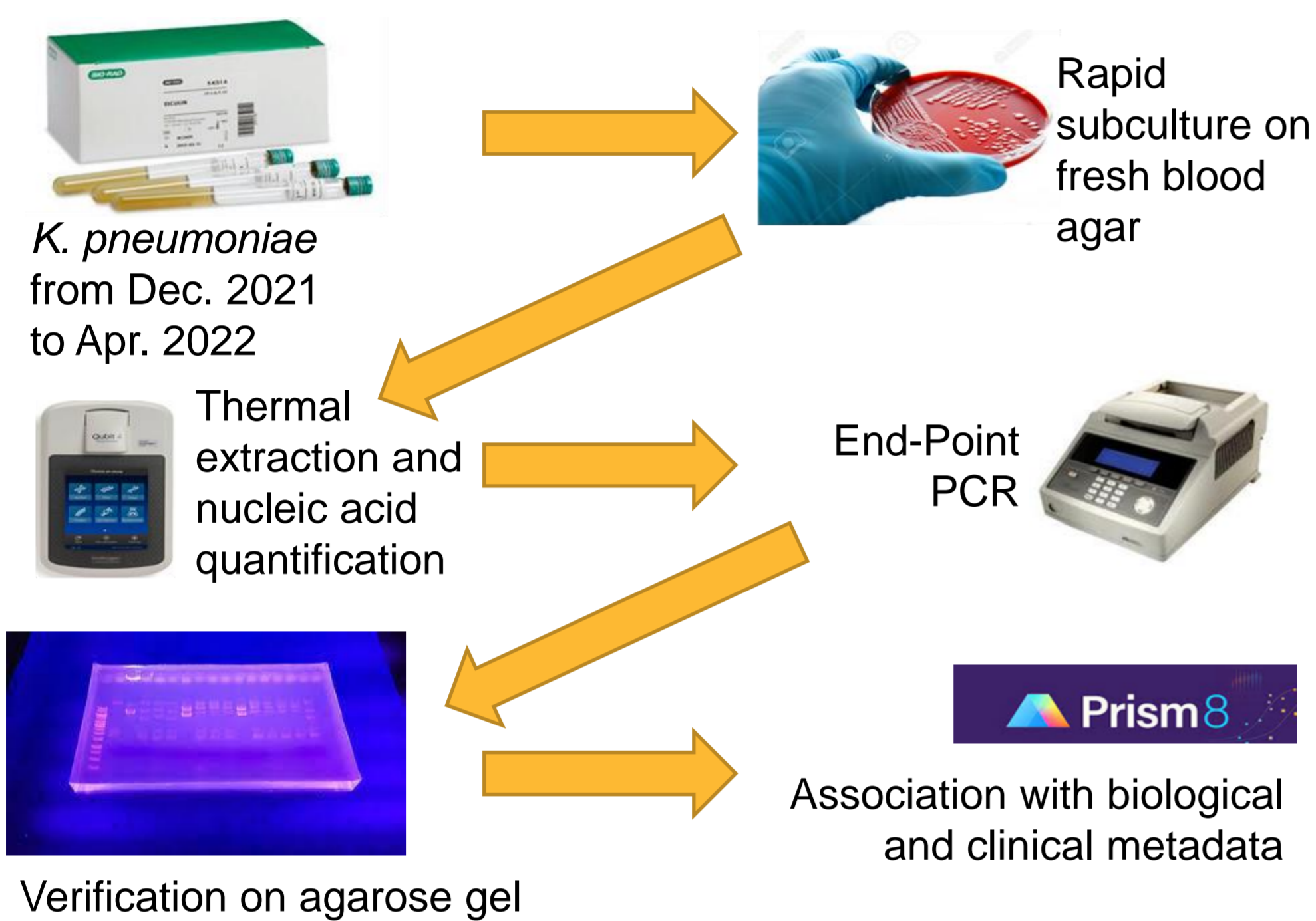


Figure 1. Analysis protocol. The strains studied (n=207) were identified consecutively from December 2021 to April 2022 in documented infections (samples received at the bacteriology laboratory of the infectious agent department of the University Hospital of Poitiers). Klebsiella pneumoniae were cultured on blood agar before extraction by heat shock (95°C 5 min). Extracts were then assayed/diluted (100 ng per reaction) before amplification and separation of PCR products on agarose gel.

Table 1. Multiplexed PCR protocol. Table with columns: Primer name, DNA sequence (5' to 3'), Target gene product/function, EMBL accession no., Amplicon size (bp). Lists genes like ybtS, iutA, allS, kfu, k2, rmpA, entB, mrkD, ybtS.

Table 1. Multiplexed PCR protocol. Amplifications were enabled by primers published by Compain F. targeting nine genes at the same time (1). Verification on agarose gels have been performed at the same time. The gels were read blindly by two operators, with the advice of a third operator in case of discordance to allow classification.

Table 2. Distribution of strains analyzed according to the nature of the clinical specimen (n=207). Table with columns: Specimen type, Eye E, Blood B, Pneumonia P, Abdomen A, Cutaneous C, Urinary U, Multiple.

Table 2. Distribution of strains analyzed according to the nature of the clinical specimen (n=207).

Results

Table 3. Distribution of virulence genes according to the nature of the clinical isolation specimen. Table with columns: Gene (n;%), Eye E, Blood B, Pneumonia P, Abdomen A, Cutaneous C, Urinary U, Multiple.

Table 3. Distribution of virulence genes according to the nature of the clinical isolation specimen. Strains isolated from respiratory specimens had a significantly higher number of virulence genes compared to strains isolated from multiple sites (p<0.05) or urine (p<0.1).

Table 4. Individual distribution and association of virulence genes according to the nature of the clinical isolation specimen. Table with columns: Gene name, Pos, Neg, B/U, A/U, p-value.

Table 4. Individual distribution and association of virulence genes according to the nature of the clinical isolation specimen. mrkD was significantly more associated with iutA and magA (p<0.05 and p<0.1). entB and iutA were significantly more frequently found in strains isolated from blood or respiratory sources (p<0.05). rmpA tended to be found in strains isolated from abdominal or urinary samples (p<0.1).

Table 5. Distribution of virulence genes according to lethality. Table with columns: Gene name, Cure (n=184), death (n=23), p-value.

Table 5. Distribution of virulence genes according to lethality.

Table 6. Distribution of virulence genes according to the nosocomial or non-nosocomial origin of the strain studied. Table with columns: Number of gene per bacteria (mean; SEM), Community-acquired infection (n=160), Healthcare-associated infection (n=47), p-value.

Table 6. Distribution of virulence genes according to the nosocomial or non-nosocomial origin of the strain studied. Strains involved in community-acquired infections had significantly fewer virulence genes than healthcare-associated infection strains (p<0.05). The k2, rmpA and ybtS genes tended to be associated with nosocomial origin (p<0.1).

Table 7. Presentation of antibiotic resistance based on the presence of virulence genes. Table with columns: Antibiotic, R (n=34), S (n=175), p-value.

Table 7. Presentation of antibiotic resistance based on the presence of virulence genes. iutA was significantly associated with resistance to Amoxicillin-Clavulanic Acid, and Cotrimoxazole (p<0.05). iutA tended to be associated with cephalosporin susceptibility (p<0.1). Kfu tended to be associated with resistance to Amoxicillin-Clavulanic Acid and cotrimoxazole (p<0.1).

Discussion

Among the virulence arsenal of KP, two genes have been initially associated with invasive infections ie. magA (mucosity-associated gene A) and rmpA (regulator of mucoid phenotype A). (5). Epidemiological studies have shown that hypervirulent KP have iron acquisition systems encoded by entB whose receptors are encoded by iutA, are distinct from Yersiniabactin (encoded by ybtS) (6, 7, 8). allS (allantoin metabolism) is associated with strains involved in hepatic abscesses (16). mrkD is involved in adhesion to extracellular matrices (9)

Conclusion

This cohort performed on all strains consecutively isolated in a medical laboratory brings a new light on the genomic arsenal of virulence of KP. The high prevalence of certain genes (mrkD and entB) (already suggested in the literature) raises the need for new studies to deepen our knowledge of their pathophysiology and to allow an appropriate diagnosis.

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