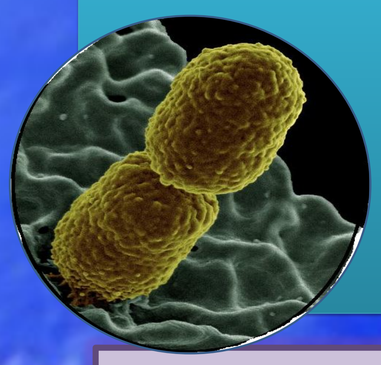
RESISTANCES AND VIRULENCE FORMS FOR *Klebsiella pneumoniae* IN HOSPITAL ENVIRONMENTS



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INTRODUCTION

- *Klebsiella pneumoniae* is a saprophytic bacteria that lives in a gastrointestinal tract, skin and nasopharynx of humans.
- It's the causing of infections of urinary tract and biliary tract, osteomyelitis and bacteriemia. This pathogen acts using different virulence factors.
- The formation of biofilms is a big problem to consider in hospital environment.
- This capacity is due to the proteins MrkA and MrkD.[1] Different studies have demonstrated that biofilms of *K. pneumoniae* are resistant to ciprofloxacin, tetracycline and chloramphenicol.

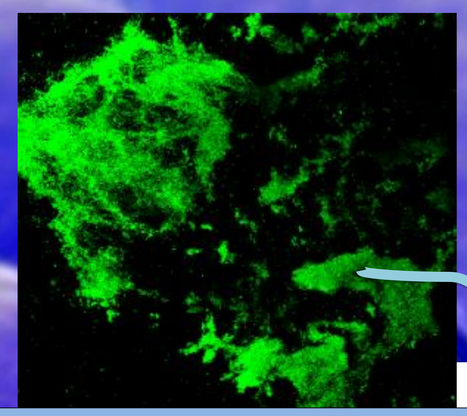


Fig.1: *K. pneumoniae in vitro* biofilm obtained by Confocal Laser Scanning Microscopy (CLSM).

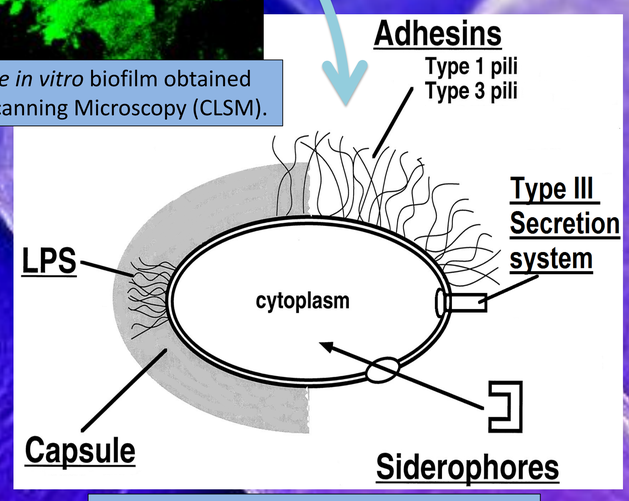
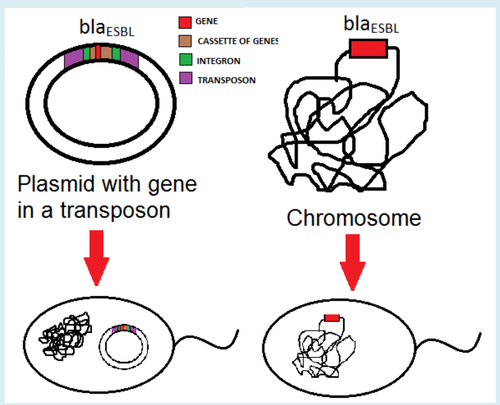


Fig. 2: Virulence factors of *K. pneumoniae*.

❖ Extended spectrum beta-lactamase (ESBL):

Extended spectrum beta-lactamases are enzymes with the ability to hydrolyze different types of drugs. High amount of these enzymes are included in chromosome and probably are related with penicillin-binding proteins.[2]



Inhibited by: clavulanic acid, sulbactam, tazobactam and carbapenems.

Resistance to: Penicillins, Aztreonam, Cephalosporins (except cefepime), Monobactams

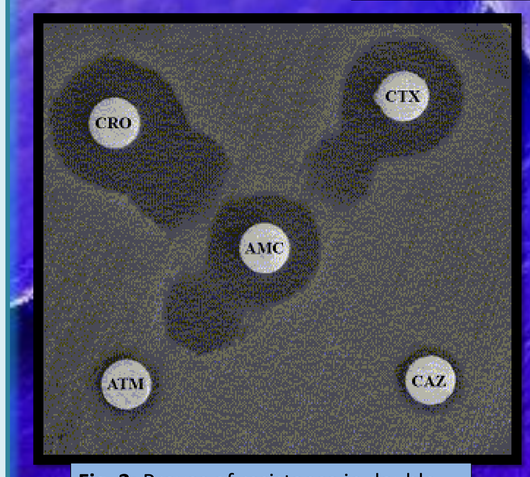
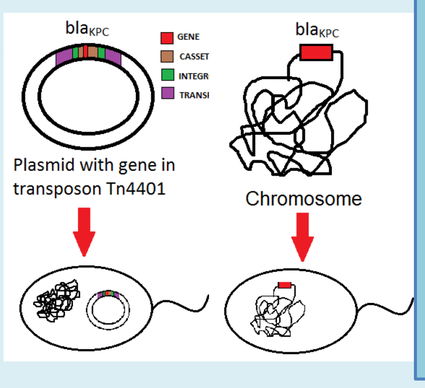


Fig. 3: Proves of resistance in double-disc synergism for detect ESBLs.

❖ Carbapenemase-producing *K. pneumoniae* (KPC):

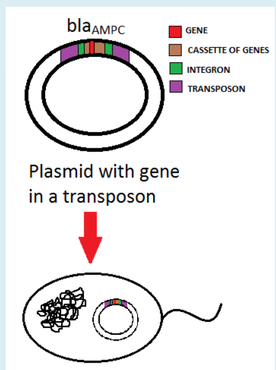
Many of the carbapenemases are present in chromosomes, but the most of them are encoded on mobile genetic elements, what allows their dissemination. For example, the transposon Tn4401 (found on plasmids) contains the gene bla_{KPC}, the KPC-encoding gene.[3]



Resistance to: Imipenem, Meropenem, Cephalosporins, Gentamicin, Tigecycline, Fosfomicine, Colistin, Polymyxin B

❖ AmpC beta-lactamase:

A mutation on genes ampA and ampB has resulted in an increased resistance. The ampC gene has been suggested as the structural gen for the beta-lactamase, after the observation of that a mutation in this gen led to the down-expression of this enzyme on the mutant strains.[4]

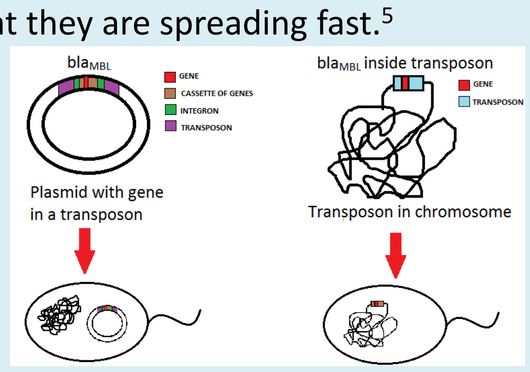


Inhibited by: fluoroquinolones, tigecycline and in occasions tazobactam and sulbactam.

Resistance to: Penicillins, Cephalosporins, Monobactams, Imipenem, Meropenem, Temociline, Amdinocillin, Clavulanic acid, Sulbactam, Tazobactam

❖ Metallo-beta-lactamase (MBL):

As the rest of beta–lactamases, MBLs can be encoded in mobile genetic elements and plasmids or normally chromosomally encoded. However, in the past 3 to 4 years many new transferable types of MBLs have been studied and it's thought that they are spreading fast.[5]



Beta-lactams, Aminoglicosids, Kanamycine,, Amikacin, Streptomycin.

Inhibited by: polymyxin, but the combinations as aztreonam, meropenem and colistin are too.

ACTUAL VISION

- New molecules are in development to face resistant *K. pneumoniae*, especially carbapenemase producers.
- The antibiotics that are the most important and potentially active against *K. pneumoniae* are new carbapenems, the combination of avibactam with ceftazidime, and plazomicin among others.
- Due to the promising antibiotics are in this moment in development, we need to approve these new molecules during the next years considering that are an important point for the future.[6]

Table 1: Activity of new antibiotics against ESBLs, KPCs and MBLs pathogens.

DRUG	ANTIBIOTIC CLASS	SPECTRUM
Ceftaroline	Cephalosporin	AmpC beta-lactamaseproducers
Ceftazidime/avibactam	Beta-lactam+beta-lactamase inhibitor	ESBLs, KPC, ampC beta-lactamase producers
Ceftobiprole	Cephalosporin	AmpC beta-lactamases producers
Delafloxacin	Quinolone	MDR (multi-drug resistant) Gram-negative
Doripenem	Carbapenem	ESBLs, MBLs, ampC beta-lactamase producers
Eravacycline	Tetracycline	ESBLs and KPCs producers
Finafloxacin	Quinolone	MDR Gram-negative
MK-7655	Beta-lactamase inhibitor	KPC producers
Omadacycline	Tetracycline	ESBLs and KPCs producers
Panipenem	Carbapenem	ESBLs, MBLs, ampC beta-lactamase producers
Plazomicin	Aminoglycoside	MDR gram-negative including metallo-beta-lactamase
Razupenem	Carbapenem	ESBLs and KPCs producers
Tebipenem	Carbapenem	ESBLs producers
Tomopenem	Carbapenem	ESBLs and ampC beta-lactamase producers

CONCLUSIONS

The emergency of multiresistent strain of *K. pneumoniae* is increasing constantly, so we need to create more novel antibiotics, combine different types of antibiotics to provide at patients and have under control the infections for these microorganisms.

REFERENCES

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[6] Bassetti, M., & Righi, E. (2015). Development of novel antibacterial drugs to combat multiple resistant organisms. *Langenbeck's Archives of Surgery*, *400*(2), 153-165.