Chapter 2

Rationale and objectives

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Klebsiella spp. are major group of pathogens in both community acquired and nosocomial infections. *Kp* is second only to *E. coli* in UTIs and nosocomial Gram-negative bacteremia. Numerous studies have reported pathogenesis of *Klebsiella* in liver abscess conditions. However, study of clinical isolates of *Klebsiella* from UTIs is lacking in literature.

The increasing number of hospital and community-acquired infections by *Klebsiella pneumoniae* (*Kp*), especially by extended-spectrum beta-lactamases (ESBL)- and carbapenemase-producing *Kp*, led to the declaration of *Kp* as an 'urgent threat' and 'priority pathogen' by public health agencies. The resistance has been developed for almost all the existing antibiotics and there is no new antibiotics at horizon; *Klebsiella* are also acknowledged as the reservoir of antibiotic resistant genes that have spread into other gram-negative pathogens. Further, the developing countries of Asia like India are reported to be the hub for emergence of MDR strains of *Kp*. Hence, strict and continuous surveillance of antibiotic resistance of *Klebsiella* spp. is warranted. Application of genomics approach enable us to understand the genomic epidemiology, evolution and dissemination of the high-risk clones. In-depth knowledge of genetic features of emerging resistant strains would help in prediction of future threats and find potential targets for effective drug discovery against the battle of emerging resistance. Investigation of the genomic features XDR and PDR strains is extremely crucial to design combat strategies.

Klebsiella is an extremely resilient bacterium, and cause complicated infections due to the actions of virulence factors. Despite of high prevalence of *Klebsiella* infections, very few reports on pathogenesis of *Klebsiella* has been reported from India. Study of CPS EPS and virulence gene such as *rmpA* are important virulence determinants of *Klebsiella.* To best of our knowledge, quantification of EPS and CPS only been done in typed strains and the same has not been reported in clinical isolates of UTIs. Study of *rmpA* is crucial since it's a virulent gene itself and, also it has a role in the increase of another virulence factor, CPS. Despite of many reports on *Kp* biofilms, studies on characterization and

quantification of *Kp* biofilms are lacking. *Klebsiella* biofilms are less studied as compared to other biofilm forming organisms such as *Pseudomonas* and *Candida* spp. Little is known about the nature of the mechanisms involved in strong biofilm formation by *Kp* on artificial surfaces like catheters. No study includes the comparative analysis of strong and weak biofilm matrix of different catheter material and media conditions. In-depth understanding about virulence factors and pathogenesis is a critical step towards the development of effective, either preventive or curative, approaches to minimize the impact of community and Healthcare Associated Infections (HAI).

Hence, in the present study, we have studied the clinical isolates of pathogenic *Klebsiella* spp. from UTIs and investigated antibiotic resistance and virulence factors of the clinical isolates.

Following are the objectives:

1. Collection, isolation and identification of clinical isolates of pathogenic *Klebsiella* spp.
2. To study antibiotic resistance.
3. To study the various virulence factors involved in the pathogenesis of *Klebsiella.*