J Trop Dis 2019, Volume 7
DOI: 10.4172/2329-891X-C1-003

Study of *OmpK*35 and *OmpK*36 Expression in Carbapenem Resistant ESBL Producing Clinical Isolates of Klebsiella pneumoniae

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Statement of the Problem: Carbapenem resistant extended spectrum *t*-lactamase (ESBL) producing *Klebsiella pneumoniae* (*K. pneumoniae*) is increasing worldwide. Carbapenem resistance (CR) has been attributed not only to production of carbapenemases but also to permeability barriers due to outer membrane proteins (*OmpK*35 and *OmpK*36) disruption.

Objective: Phenotypic detection of CR among ESBL producing *K. pneumoniae* isolates, followed by the evaluation of the role of *ompK*35 and omp*K*36 gene expression among carbapenem resistant *K. pneumoniae* (CR-KP) isolates.

Materials/Methods: 100 ESBL producing *K. pneumoniae* isolates were included in this study. Minimum inhibitory concentration (MIC) of imipenem was performed for all isolates by broth microdilution method. For CR-KP isolates, phenotypic detection of *K. pneumoniae* carbapenemase (*K*PC), metallo-β- lactamase (MBL) and AmpC enzymes was performed followed by Realtime qRT-PCR to detect and quantify *ompK*35 and *ompK36* gene expression.

Results: 42% of our isolates were carbapenem resistant, and all of them were KPC producers either singly or in combination with MBL and/or AmpC production. Reduced expression of both *ompK*35 and *ompK*36 was detected in (52.38%) of CR-KP isolates, while reduced expression of *ompK*36 or *ompK*35 alone was found in (2.38%) and (33.33%) respectively. Twenty of 42 CR-KP isolates (47.62%), showing reduced *ompK*35 and *ompK*36 expression, exhibited high level resistance (HLR) (>32 µg/ml) to imipenem. There was a significant correlation between reduced expression of *ompK*36 and increase MIC values ($p < 0.05$). The combined production of MBL or AmpC together with reduced expression of *ompK*35 and/or *ompK*36 resulted in significant increase in imipenem MIC ($p < 0.05$).

Conclusions: The combined *OmpK*35/*OmpK*36 loss resulted in HLR. However *OmpK*36 seems to play a major role in those strains. Imipenem MIC was markedly increased among *K. pneumoniae* showing carbapenemase and/or AmpC production together with loss of *OmpK*35 and/or *OmpK*36.