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Multiple variants of phoP/Q and pmrAB TCRS conferring colistin resistance in XDR/MDR clinical isolates of *Klebsiella pneumoniae* in India

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Background: Several incidences worldwide have marked the emergence of colistin and carbapenem resistance in *K. pneumoniae* and increased morbidity and mortality associated with their infections. A retrospective observational study was conducted to study the prevalence and molecular events contributing colistin resistance among *K. pneumoniae* isolates at a tertiary hospital, New Delhi, India.

Methods and materials: Clinical samples were screened for susceptibility towards antibiotics. Colistin resistant *K. pneumoniae* isolates were analyzed by MLST to understand the clonal relation. The mechanism underlying colistin resistance was determined by sequence analysis of two component regulatory system genes. The phenotypic effect of amino acid substitutions were predicted using a combination of SIFT, PROVEAN and PolyPhen-2 based analysis. Gene expression of pmrC and pmrK was analyzed by qRT-PCR.

Results: Of the 335 *Klebsiella* spp. isolated, 11 (3.2%) were found colistin resistant. *K. pneumoniae* isolates belong to Clonal complex-11 with serotypes (ST): 14, 16, 43, 54, 147 and 395, four isolates had three novel ST profiles. High MIC-values were noted for colistin (>128 μg/ml), amoxyclav (>256 μg/ml), imipenum (>256 μg/ml), gentamycin (>256 μg/ml), ciprofloxacin (>256 μg/ml), Co-trimaxazole (>32 μg/ml), rifampicin (>128 μg/ml) and tetracycline (>128 μg/ml). Sequence analysis revealed non-synonymous deleterious mutations in phoP (T151A), phoQ (del87-90, del263-264, L30Q and A351D), pmrA (Q140L and G53S), pmrB (D150 V, T157P, L237R, G250C, A252G, R256G, R315P and Q331H) and mgrB (C28G and IS element) genes. mgrB gene in three strains were found to be disrupted by insertion sequences encoding glycosyl transferase-IS1-like and IS5/IS1182 family-like transposase genes and found to be with associated with high MIC. All isolates were negative for mcr-gene, while blaNDM-1, blaOXA-48 and blaCTX-M gene were positive in MRK-8, 5 and 9 isolate, respectively. All colistin resistant *K. pneumoniae* isolates showed an elevation in transcription level of pmrK and pmrC genes under colistin treated and untreated conditions.

Conclusion: All the colistin and carbapenem resistant *K. pneumoniae* isolates were distinct with no clonal relatedness and presents emergence of discrete resistance mechanisms.

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High rate of multidrug-resistant Enterobacteriaceae carrying ESBL and plasmid-borne AmpC ß-lactamase in a Malaysian community

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Background: Even though Southeast Asia is generally regarded as the hotspot for antibiotic resistance, there have been limited studies investigating the prevalence of antibiotic resistance among healthy people in the region. We aimed to investigate the prevalence of two ß-lactamase genes, ESBL and plasmid-borne AmpC (pAmpC) among Enterobacteriaceae in a healthy community in Malaysia.

Methods and materials: We collected stool samples and screened for ESBL and pAmpC-producing Enterobacteriaceae using phenotypic and genotypic methods. The susceptibility profile of the isolates towards 13 different antibiotics was observed. Plasmid replicon group, *E. coli* phylogenetic group and MLST analyses were also conducted to observe the spread pattern of these resistance genes. Risk factors associated with the carriage of ESBL or pAmpC-producing Enterobacteriaceae were then analysed.

Results: ESBL and pAmpC production was observed in 21.6% (95% CI 13.9–28.8%) and 32.1% (95% CI 24.5–38.9%) of the participants, respectively. A high proportion of the isolates (99.9%, 95% CI 98.6–99.9%) were multidrug-resistant regardless of the resistance genes carried. Although *E. coli* B2:ST131 was detected, there was no dominance of a specific clonal strain. Possession of multiple plasmid groups was common, with incFIB being the most frequently detected type. Mixed effect logistic regression analysis found that ESBL production was associated with having allergy ($p = 0.01$, OR 3.86, 95% CI 1.32–11.23) and consumption of chicken meat ($p = 0.02$, OR = 8.66, 95% CI = 1.40–53.29), while consumption of fermented food significantly lowers the risk of colonisation with pAmpC producing Enterobacteriaceae ($p = 0.02$, OR 0.23, 95% CI = 0.06–0.79).

Conclusion: The high prevalence of ß-lactamase and multidrug resistance suggests that antibiotic resistance is endemic among healthy people in Malaysia.

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