B-Lactamase-Mediated Resistance in Enterobacterales Uropathogens and Bench Tests to Detect B-Lactamase Production

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The World Health Organization (WHO) has declared antimicrobial resistance (AMR) as one of the top 10 global public health threats facing humanity. The aims of this study were to report currently Scarce data on AMR mechanism: β-lactamase production, in uropathogenic Enterobacteriales in Sri Lanka and to identify bench tests to detect β-lactamase production in low-income settings. A total of 422 Enterobacterales uropathogens from community-acquired urinary tract infections (CA-UTI) and hospital acquired UTI (HA-UTI) were studied. β-lactamase types: Extended spectrum β-lactamase (ESBL), AmpC β-lactamase and carbapenemase production and the bla genes that encodes them, identified by phenotypic tests followed by PCR and Sanger sequencing. Nine isolates were further analysed by whole genome sequencing. Common uropathogens identified were Escherichia coli, Klebsiella pneumoniae and Enterobacter sp. The prevalence of ESBL (50%), AmpC β-lactamase (19%) and carbapenemase (11%) was high and was greater in HA-UTI (75%) than CA-UTI (42%). The related genes: bla_{TEM-1}, bla_{SHV-1}, bla_{SHV-2}, bla_{SHV-11}, bla_{SHV-28} and bla_{OXA-1}; $bla_{CTX-M-15}$, bla_{CMY-42}, bla_{CMY-2}, bla_{DHA-1}, bla_{ACT-1}, bla_{ACT-7}, bla_{NDM-1}, bla_{NDM-4}, $bla_{OXA-181}$ and $bla_{OXA-232}$ were identified. Bla_{ACT-7} and $bla_{OXA-232}$ were novel genes to the country. Co-occurrence of multiple bla genes (25%) was a concerning phenomena. Omp mutations leading to carbapenem resistance even without producing carbapenemase enzymes were detected. K. pneumoniae ST16, and E.hormaechei subsp. Steigerwalt ST93 were described for the first time in the country. Virulence genes associated with AMR genes and mobile genetic elements were identified that lead to spread of more pathogenic antimicrobial resistant strains. Screening with cefotaxime or ceftriaxone, cefoxitin and meropenem, followed by the modified double disc synergy test, AmpC disc test and the modified carbapenem inhibition method were identified as suitable bench tests to detect β-lactamase production in Enterobacterales in the local setting. The findings of this study will contribute to the local and global strategies in controling AMR dissemination.

Keywords: *β-lactamase resistance, Enterobacterale, AMR genes, Virulence genes, Bench tests*