Multidrug resistant (MDR) *Klebsiella pneumoniae* is listed among the most urgent public health threats due to its virulence and susceptibility to a wide range of antimicrobial agents, leading to fatal outcomes, especially in low-income settings. Patan hospital is a 450-bed government hospital located within the Kathmandu Valley, Nepal. The hospital has previously witnessed multiple outbreaks caused by MDR *K. pneumoniae* in the neonatal intensive care unit (NICU). Particularly, a carbapenemase producing sequence type (ST) 15 *K. pneumoniae* clone was responsible for an outbreak with a mortality rate up to 75% in 2012. Recently in 2015, this same NICU suffered again from an MDR *K. pneumoniae* outbreak.

Aims

In this study, using whole genome sequencing (WGS) and the state-of-the-art analytic approaches, we aimed to define the nature of this recent outbreak and further investigate the correlation with the 2012 outbreak.

Results

From the sequences of 123 strains, 83/123 strains confirmed to be *K. pneumoniae* during the outbreak. After removing patient duplication from multiple blood cultures, we identified 57 individual *K. pneumoniae* strains, which were isolated from 54 patients, for further analysis. The MLST genes for these strains indicated that the dominant sequence type was ST15, which was represented by 22 of the 57 isolates, accounting for 38.6% of the *K. pneumoniae*, followed by ST43 which accounted for 10.5% and ST14 which accounted for 8.8%.

Conclusions

The 2015 outbreak in Patan Hospital was caused by the same MDR ST15 *K. pneumoniae* reported in 2012. Albeit genetically similar, these recent strains were susceptible to carbapenemases due to deletion of the blaNDM-1 cassette. Using Bayesian phylogenetic inference, we determined the outbreak strain was introduced to Patan Hospital in the late 2010 and subsequently caused major outbreaks in NICU in 2012 and again in 2015. This clone acquired four different plasmids encoding resistance to numerous therapeutic antimicrobials, and this may underlie its successful propagation and associated high mortality. This study demonstrates the viability of applying WGS in nosocomial outbreak investigation. Insights provided through this study are invaluable in tailoring infection control strategies as well as raising public awareness.

Acknowledgements & References