

Strain features of pneumococcal isolates in Pakistan in pre and post-PCV10 era

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Background: *Streptococcus pneumoniae* is a major human pathogen responsible for >317,000 deaths in children, annually. Pakistan is amongst the top four countries with the highest number of pneumococcal deaths. To lower the incidence of pneumococcal disease, PCV10 was introduced in Pakistan in 2013. However, studies reporting vaccine efficacy and dynamics of pneumococcal strains post-immunization remains scarce. In this study, we present strain features of pneumococcal isolates in Pakistan using whole-genome sequencing.

Methods: A total of 190 isolates (75 from carriage and 113 from disease), collected from individuals aged 1-week to 92 years old between 2006 and 2020 were included. Carriage isolates were majorly from children (74/75) and were from cohort studies and hospitals whereas disease isolates were from a nationwide network of diagnostic laboratories. We

report serotypes distribution and antimicrobial susceptibility prediction from sequence data pre- (n= 80) and post-PCV10 (n=110) introduction.

Results: A high diversity in serotype and genotypes of strains was observed. From 190 isolates, 54 serotypes, 67 Global Pneumococcal Sequence Clusters (GPSCs) and 116 sequence types (23 novel STs) were identified. A reduction in the proportion of PCV-10 serotypes from 26% (16/61) to 7% (1/14) in carriage and from 47% (9/19) to 33% (31/94) in disease isolates, was observed following the introduction of PCV10. Overall, PCV10 demonstrated limited coverage in carriage (21.6%, 16/74) and disease (38.1%, 16/42) isolates among children <5 years old. Introduction of higher valent vaccine PCV13 would only increase the coverage rates to 33.8% and 54.8% in carriage and disease, respectively. The most common disease-causing serotypes isolated from children <5 years old in post-vaccine era were 19F (17.2%, 5/29), 19A (13.4%, 4/29), 23B (6.9%, 2/29), 14 (6.9%, 2/29), 9V (6.9%, 2/29), and 10A (6.9%, 2/29%), which together accounted for 58.6% of the isolates in this group. Each common serotype was associated with 2-4 GPSCs. Among these GPSCs, eight GPSCs [GPSC10 (ST230), GPSC5 (ST13816 and ST162777), GPSC84 (ST12888 and ST16123), GPSC101 (ST16126) and GPSC43 (ST16164, ST280 and ST16087), GPSC9 (ST63, ST15321, and ST16265), GPSC6 (ST156), and a novel GPSC (ST16131)] were resistant to more than 3 antibiotic classes.

Conclusion: This study reports that PCV10 has a limited coverage against pneumococcal strains in Pakistan, although the sample size in post-vaccine period was small. Continued surveillance post-PCV introduction is needed for monitoring of serotypes to determine if a switch to a higher-valency PCV would be beneficial for further reduction of pneumococcal disease.