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.
We aimed to

1) Investigate the changes in serotype distribution pre- and post PCV10 introduction,
2) Determine serotype coverage by pneumococcal conjugate vaccines,
3) Investigate the changes in antimicrobial resistance in pre- and post-vaccine era.

Methods

We whole-genome sequenced 190 pneumococcal isolates from pre- and post- PCV10 era. Of which:
a) 75 isolates were from carriage. Carriage isolates were majorly from children (74/75) and were from cohort studies and hospitals.
b) 113 isolates were from disease. disease isolates were collected from multiple diagnostic laboratories across the country.

In silico serotyping and GPSCs were determined using SeroBA and and PopPUNK, respectively. We report serotypes distribution, GPSCs, and antimicrobial susceptibility prediction from sequence data pre- (n= 80) and post-PCV10 (n=110) introduction.
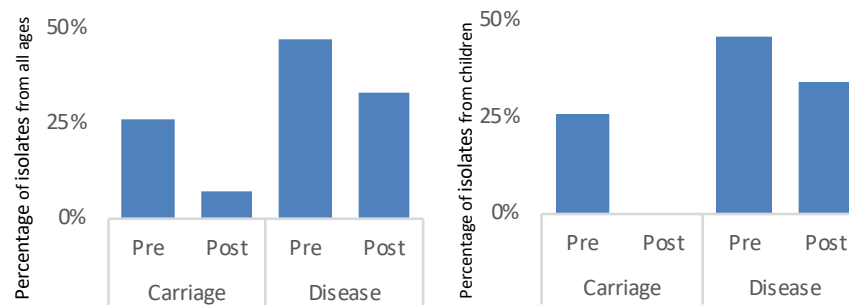
Results

1) High level of diversity in pneumococcal strains
From 190 isolates, we identified:
- 54 serotypes,
- 67 Global Pneumococcal Sequence Clusters (GPSCs), and
- 116 sequence types (23 novel STs)

### 2) Changes in the proportion of PCV10 serotypes following the introduction of PCV10 in Pakistan

3) Coverage rates by pneumococcal vaccines in carriage and disease isolates in children under 5 years

Vaccines	Carriage (n=74)	Disease (n=42)	Total (n=116)
PCV10	21.6% (16)	38.1% (16)	27.6% (32)
PCV13	33.8% (25)	54.8% (23)	41.4% (48)
PCV15	33.8% (25)	54.8% (23)	41.4% (48)
PCV20	52.7% (39)	64.3% (27)	56.9% (66)
PCV24	52.7% (39)	66.7% (28)	57.8% (67)
Pneumosil	24.3% (18)	47.6% (20)	32.8% (38)

4) Common serotypes in children under the age of 5 years

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.
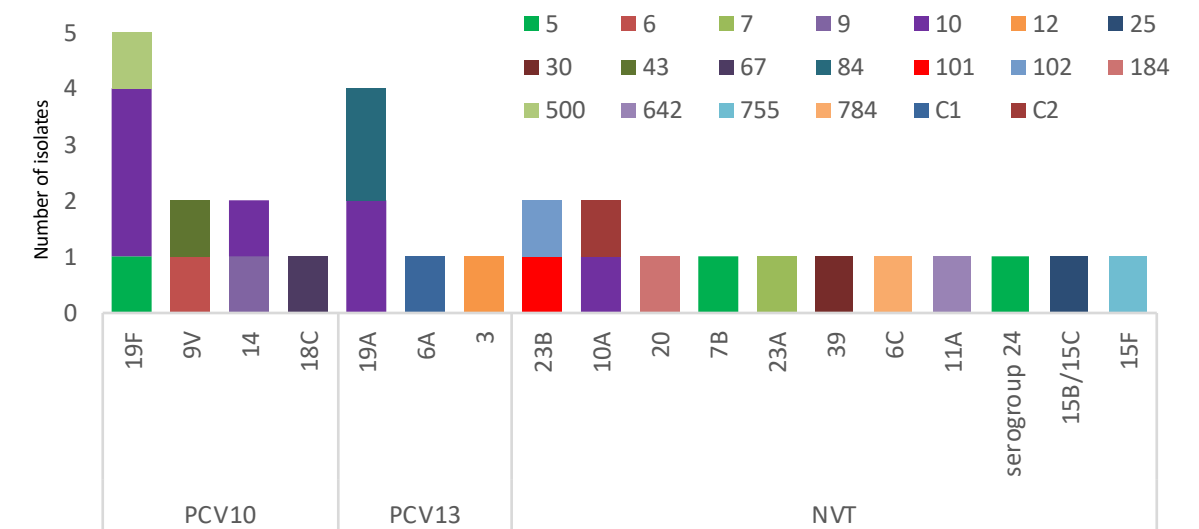
5) Changes in antimicrobial resistance in isolates from children under 5 years of age

Our results have shown a significant increase in resistance against penicillin and erythromycin in isolates from children.

Antibiotic (% (n/N))	pre-PCV10	post-PCV10	p for difference
Penicillin	47.3 %(35/74)	83.3 %(35/42)	<0.005
Erythromycin	8.1 %(6/74)	54.8 %(23/42)	<0.005
Cotrimoxazole	97.3 %(72/74)	95.2 %(40/42)	1
Tetracycline	37.8 %(28/74)	61.9 %(26/42)	0.078
Chloramphenicol	4.1 %(3/74)	2.4 %(1/42)	1

Conclusion

This study highlights that PCV10 has a limited coverage against pneumococcal strains in Pakistan. The sample size in post-vaccine period was small; continued surveillance 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.