Invasive *Streptococcus pneumoniae* serotype 35B in South Africa, 2005-2016

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**Background**

Since PCV introduction in children in 2009 (PCV7) and 2011 (PCV13), vaccine-serotype invasive pneumococcal disease (IPD) has declined in South Africa, predominantly in children aged <2 years and adults aged 25-44 years.

In the USA, penicillin non-susceptible serotype 35B increased following PCV introduction, primarily due to expansion of sequence type (ST) 558.

Novel serotype 35D, non-reactive with factor serum 35a and harbouring a disrupted *wciG* gene, was recently described in Australia and the USA, although prevalence was low.

**Aim**

To describe serotype 35B disease and detect putative 35D in South Africa, pre- and post-PCV introduction

**Methods**

We reviewed IPD cases reported through national, laboratory-based surveillance from 2005-2016.

Incidence rates for non-vaccine-serotype IPD, per 100,000 population, were calculated for 2005-2006 (pre PCV) and 2016 (post PCV) using population denominators from Statistics SA.

249 serotype 35B isolates, spanning 2005-2014, originally serotyped by Quellung as part of routine IPD surveillance, were re-serotyped using Quellung (22 isolates were no longer viable) (Fig. 1).

A subset of 35B isolates was characterised by whole genome sequencing (Fig 1).

- MLST-defined genotypes were determined for 62 isolates
- In silico serotype was determined for 50 isolates and these genomes were also investigated for a disrupted *wciG* gene
- A population snapshot of serotype 35B sequence types was generated using eBURST v3 (eburst.mlst.net)

**Results**

Surveillance identified 45,852 IPD cases, of which 376/31,513 (1%) were originally 35B by Quellung and 57% (214/376) were non-susceptible to penicillin.

Non-vaccine-serotype IPD increased 29% (95% CI, +9%, +54%) in children aged <5 years and 15% in adults (≥25 years) (95% CI, +7%, +23%) (Fig 2a & b).

- Serotype 35B incidence increased 4.5-fold in children aged <5 years (95% CI, 2.25-9.04; rates: 0.08 to 0.36) (Fig. 2a).
- In adults (≥25 years), serotype 35B incidence rates doubled from 0.05 to 0.10 (95% CI 1.20-3.21) (Fig 2b).

Serotype 35B was predominantly penicillin non-susceptible ST361 and associated single-locus variants (31/62, 50%), or penicillin-susceptible ST9813 (18/62, 29%) (Fig. 3).

- Only one serotype 35B isolate was ST558.
- 22/249 (9%) serotype 35B isolates did not react with factor serum 35a (Fig. 1).
- Of these, 4/6 with genomic data had a disrupted *wciG* gene and were ST361 (n=1), ST558 (n=1) or ST9813 (n=2) (Fig. 1).

**Conclusions**

- Serotype 35B incidence increased post PCV in children and adults.
- Half of the 35B isolates (with known MLST data) belonged to penicillin non-susceptible ST361.
- Genetically confirmed 35D was detected in unrelated lineages, at low frequency.
- Phenotypic detection of 35D using Quellung is currently unreliable.

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**References**

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**Figure 1. Summary of *S. pneumoniae* serotype 35B phenotypic and genotypic characterisation, 2005-2016**

- **Serotype 35B incidence rate:** 72% (95% CI: 49%-94%); rate: 4.3 to 5.4
- **Serotype 35D** 3% (95% CI: 0%-5%); rates: 0.0 to 0.8

**Figure 2a. Incidence of invasive pneumococcal disease episodes with viable isolates caused by non-vaccine serotypes in individuals aged <5 years, 2005-2016, South Africa**

- **Non-vaccine serotypes:** 11% (95CI: 7%-12%); rates: 3.5 to 4.2
- **Serotype 35D** 6% (95CI: 2%-10%); rates: 0.8 to 0.9

**Figure 2b. Incidence of invasive pneumococcal disease episodes with viable isolates caused by non-vaccine serotypes in individuals ≥25 years, 2005-2016, South Africa**

- **Non-vaccine serotypes:** 21% (95CI: 17%-26%); rates: 1.1 to 1.4
- **Serotype 35D** 9% (95CI: 5%-14%); rate: 0.3 to 0.5

**Figure 3. eBURST population snapshot showing relationships among sequence types for *S. pneumoniae* serotype 35B, South Africa (n=62, green) compared to serotype 35B’s available in the global PubMLST database (N=855, black) [https://pubmlst.org/spneumoniae/].** Sequence types in pink were present in both data sets. Blue and yellow circles denote founding and co-ancestral single-locus variants (31/62, 50%), or penicillin-susceptible ST9813 (18/62, 29%).