Antimicrobial Resistance of S. pneumonia before and after introduction of a 10-valent pneumococcal conjugate vaccine in Kilifi, Kenya

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Introduction

• Antimicrobial resistance (AMR) is currently the most alarming issue for human health.

• AMR already causes 700,000 deaths/year. It is estimated that 10 million deaths due to AMR will occur every year after 2050.

• The importance of the likely utility of vaccines in the fight against AMR is increasingly being appreciated especially as the pipeline of new antibiotics is barely a trickle.

• Vaccines cause a much longer lasting control of infections while antibiotic resistance emerges rapidly desirable byproduct of vaccination
Incidence of IPD caused by penicillin-resistant isolates declined by 82% (95%CI, −85 to −78),

IPD caused by susceptible isolates declined by 47% (95%CI, −55 to −38)

Declines in the proportion of penicillin-resistant PCV7 serotypes, from 70% of isolates in 2009 to 47% in 2012 (P<0.001)

Introduction

• Kenya introduced a 10-valent pneumococcal conjugate vaccine (PCV10) into the routine childhood immunisation schedule in 2011, with a catch-up campaign in Kilifi for children <5 years

• We investigated the impact of the PCV10 immunisation on invasive pneumococcal disease (IPD) due to AMR of pneumococci in Kilifi, Kenya
Methods

- Hospital and laboratory-based laboratory IPD surveillance at the Kilifi County Hospital from 2000-2014.
• Electronic vaccination registry or Kilifi Vaccination Monitoring System (KiVMS)
Methods

• Data Analyses
  • We compared the incidence of AMR-IPD for the pre-vaccine era (2000-2010) and the vaccine era (2011-2014) in children under 5 years old resident in the area covered by the Kilifi Health and Demographic Surveillance System

• Serotypes were according to the frequency of AMR and classified them into vaccine- (VT) and non-vaccine types (NVT).
Results

• There were 1143 cases if IPD in all ages with 766 (67%) of them occurring in children under 5 years old.

• There was also a 61% reduction in incidence of all cause-IPD in <5 years

• Incidence of VT-IPD declined by 87% in <5 years in the vaccine era (see figure)
<table>
<thead>
<tr>
<th>Age group</th>
<th>Incidence Rate Ratio</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time (yrs)</td>
<td>0.96</td>
<td>0.84</td>
<td>1.09</td>
<td>0.51</td>
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<tr>
<td>2011-2014</td>
<td>0.13</td>
<td>0.05</td>
<td>0.35</td>
<td>&lt;0.0005</td>
</tr>
</tbody>
</table>

Incidence of VT-IPD in children <5 years
• VT-AMR also declined from 13.3 (95%CI: 10.2-17.1) in 2000-2010 to 3.1 (0.6-9.1) per 100,000 population in 2011-2014 (p=0.0073)

• Overall, NVT- AMR did not change significantly over time (6.0 [95%CI: 4.0-8.7]) vs. 4.1 [95%CI: 0.5-14.9] per 100,000 population, p=0.61)

• Penicillin-resistance was only seen in meningitis and 61.1% of penicillin-resistant isolates were VT serotypes.
• Penicillin resistance decreased from 4.8 [0.73-17.2] to 0 per 100,000 population.

• A few (9) Ceftriaxone-resistant pneumococci (meningitis and non-meningitis) were seen pre-PCV10 but all isolates were fully susceptible to Ceftriaxone in the post-PCV10 era.

• The top 10 serotypes with any AMR - 1, 14, 6B, 6A, 5, 23F, 19F, 19A, 18C and 4 – included 7 vaccine type (VT) serotypes.
Discussion and conclusions

• There is a relatively low incidence of pneumococci-AMR in this rural Kenyan setting.

• Regardless, a PCV10 immunisation programme dramatically reduced AMR-IPD in children <5 years and in particular Penicillin resistant pneumococci in meningitis.

• This change appears to be driven largely by a decrease in incidence of resistant serotype 14 IPD.
• In estimates of cost effectiveness, the impact of PCV on AMR is not typically taken into account suggesting it is a lot more cost effective than currently estimated

• Improving antibiotic stewardship and regulation of prescriptions are as important as developing novel antibiotic compounds in the fight against AMR

• It is also essential we ensure better utilization of PCV (high and timely coverage), and advocate for increased uptake of other existing vaccines like Hib and TCV
FIGURE 1 | Time to detection of resistance of human pathogens to antimicrobials (in red) and to vaccines (in green). Black X symbols indicate insurgence of resistance, with lines starting at product introduction (yellow stars; except for smallpox vaccination that began much earlier; with modifications from Ref. (1-4) with the permission of the publisher).

TABLE 1 | Comparison of the characteristics of vaccines and antibiotics in their capacity to fight pathogens.
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