Neonatal invasive pneumococcal disease in NewZealand in the era of conjugate pneumococcal vaccination 2009 - 2013

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BACKGROUND

- *Streptococcus pneumoniae* is an uncommon but well-recognized cause of neonatal sepsis and can be associated with significant morbidity and mortality
- When invasive pneumococcal disease (IPD) occurs within the first 72 hours of life, the source is very likely the mother's genital tract
- IPD has been a notifiable disease in NZ since October 2008 and conjugate pneumococcal vaccine (PCV) was introduced in June that same year
- PCV is likely to reduce neonatal IPD through herd protection but some serotypes may not be covered even by PCV13

METHODS

- All cases of IPD in the first 7 days of life from the greater Auckland region [Auckland District Health Board (ADHB), Counties Manukau District Health Board (CMDHB) and Waitemata District Health Board (WDHB)] between January 2009 and December 2013 were identified
- Case finding was through Auckland Regional Public Health and Starship Paediatric Infectious Disease team consultations. Serotypes and national data for all infants aged <30 days was provided by the Institute of Environmental Science & Research (ESR)
- Ethics approval granted by Central Health and Disability Ethics Committee (ref 13/CEN/93)

RESULTS

9 cases of IPD in the first 7 days of life were identified; 5 cases from CMDHB, 2 from ADHB, and 2 from WDHB

Demographics

- 5 mothers were aged <24 years (range 15–34 years)
- 4 cases were NZ Maori, 3 were Indian and 2 were NZMaori/Samoan

Table 1: Exposure to identified and potential risk factors for neonatal (age <7 days) IPD in the Auckland region, 2009-2013

Case	1	2	3	4	5	6	7	8	9
Preterm <37w				X	X		X	X	
PROM >24h			X	X[a]	X[a]		X[a]		
LBW				X	X		X	X	
Mother unwell perinatally	X[b]	X[c]		X[d]	X[e]				
Mode of delivery	NVD	Em LCSC	NVD	Em LCSC	Em LCSC	NVD	Em LCSC	Em LCSC	NVD
NZ Deprivation Index Score[f]	8	10	10	6	8	10	8	3	8

PROM = Premature rupture of membranes; LBW = Low birth weight (<2500g); NVD = Normal vaginal delivery; Em LSCS = Emergency lower segment Caesarean section

a Received intrapartum antibiotic prophylaxis
b Maternal Streptococcus pneumoniae bacteraemia at delivery
c Wound infection
d Chorioamnionitis
e Maternal fever in labour
f Index measures relative socioeconomic deprivation in geographic areas (meshblocks) derived from census data. Scores range from 1 (least deprived) to 10 (most deprived).

Clinical features and management (Table 2)

- Meningitis and respiratory infection were frequent concurrent clinical presentations
- Median duration of hospitalisation: 20 days (range 1–41 days)
- All 9 cases required respiratory support (5 CPAP, 4 intubation and ventilation)

Table 2: Predominant clinical syndrome for neonatal IPD (age <7 days) IPD in Auckland region, 2009-2013

Case	1	2	3	4	5	6	7	8	9
Bacteraemia	X	X	X	X	X	X	X	X	X
Meningitis	X	X				X		X	
Pneumonia		X	X			X			X
Pleural empyema						X			

Outcomes and follow-up (Table 3)

- 1 baby died within 6 hours
- 3 had ongoing neurological or respiratory sequelae

Table 3: Outcome for neonatal IPD (age <7 days) in Auckland region, 2009-2013

Case	Outcome	Duration of follow up (months)
1	Complete resolution	8
2	Structural airway and parenchymal lung abnormalities	6
3	Complete resolution	11
4	Complete resolution	2
5	Complete resolution	26
6	Gross motor delay	>12
7	Death at 6 hours	N/A
8	Seizures - Global developmental delay	>12
9	Complete resolution	3

Serotypes (Figure 1and Table 4)

- Serotype 3 was most common
- 5 of 9 serotypes were not covered by conjugate pneumococcal vaccination in use at the time of infection
- 2 of 9 would not be covered by current PCV13

Figure 1: Serotypes of Auckland region neonatal IPD cases aged <7 days

Serotype of IPD isolates according to year and vaccination coverage.
Red serotypes were not covered by vaccination in that year.

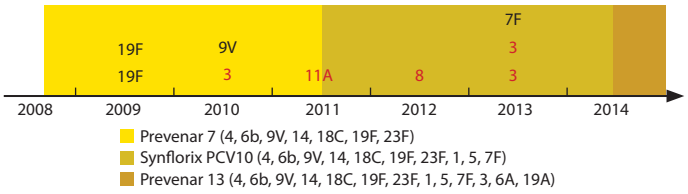

Table 4: National cases of IPD and serotype occurring infants aged <30 days

AGE < 30 days	DHB	2009	2010	2011	2012	2013	Total
Our cases series	Waitemata	(19F)				3	2
	Auckland		(9V)			3	2
	CMDHB	(19F)	3	11A	8	(7F)	5
	Northland	1		1	7NT 19A	38	5
	Waikato			19A			1
	Taranaki		(19F)				1
	Wairarapa				19A		1
	Canterbury	22A					1
	Southern					(19F)	1
Total		**4**	**3**	**3**	**4**	**5**	**19**

Serotypes highlighted in red indicate those not covered by vaccine in use at the time

Antibiotic treatment and susceptibility

- Initial antibiotic regimen
  - Beta-lactam and aminoglycoside (6/8)
  - Beta-lactam only (2/8)
- Total intravenous antibiotic duration: median 14 days (range 7–31 days)
- One infant died prior to receiving antibiotics; intrapartum beta-lactam and metronidazole were given for maternal sepsis
- 7/9 isolates were fully susceptible
- Both 19F serotypes were resistant to penicillin with intermediate susceptibility to cefotaxime. Both were multi-resistant (defined as resistance to penicillin and 3 other antibiotic classes)

Incidence rates of neonatal IPD[1]

- NZ infants aged <90 days: 9.1/100,000[2]
- NZ infants aged <30 days: 6.0/100,000
- UK infants aged <90 days: 10-13/100,000 (Ladhani et al. CID 2013)
- US infants aged <90 days: 5-11.8/100,000 (Olarte et al. Pediatrics 2013)
  <30 days: 2.0/100,000 post PCV7 (Poehling JAMA 2006)

1. Calculated with denominator live births for each year 2009-2012. No adjustment was made for deaths within the first 90 days. Live birth data for 2012 was used as denominator for 2013 data as this was not available at time of analysis.
2. Based on national IPD cases aged <90 days between 2009-2013, n= 29. Source ESR https://surv.esr.cri.nz/surveillance/IPD.php

DISCUSSION

- IPD is an uncommon but important disease in the neonatal period accounting for 1-10% of early onset sepsis. Cases occurring in the first 2 months of life account for 1-5% of all IPD.
- The rate of neonatal IPD (6.0/100,000 for infants aged <30 days) is low compared with rates of early onset group B streptococci (GBS) infection. GBS is the commonest early-onset pathogen and rates of GBS neonatal infections in infants <6 days old have been variously reported to range between 23 and 50/100,000.
- However, based on our results and those reported by other investigators both the case-fatality ratio and rate of meningitis are higher for neonatal IPD than for early onset GBS (meningitis in neonatal IPD 40% compared with 5-10% of early onset GBS).
- Genital colonisation in pregnancy with *S. pneumoniae* is very uncommon. Evidence of nonspecific maternal infection was present in in 3/9 of our cases plus 1 mother proven bacteraemic with *S. pneumoniae*. Therefore *S. pneumoniae* is a highly invasive infection for both mothers and newborns if present. This is important in considering treatment of any woman with antenatal swab positive for *S. pneumoniae*.
- Current PCV13 vaccination if used in pregnancy would cover 74% (14/19) of serotypes seen nationally since 2009 in infants less than <30 days. Polysaccharide 23-valent pneumococcal vaccine would cover 84% (16/19). Maternal vaccination is an interesting potential strategy to consider in view of our high early neonatal IPD rate for a disease with severe morbidity and mortality.
- Despite the first dose of PCV being scheduled at or after 6 weeks, use of PCV in infants and children <5 years since 2000 has resulted in a significant impact on neonatal IPD in the US. Although NZ numbers are small and not showing impact of PCV herd protection in neonates as yet, we may also see similar benefit for maternal/neonatal IPD with more time and broader PCV13 cover.

REFERENCES: 1. ESR website at https://surv.esr.cri.nz/surveillance/IPD.php; 2. Hoffman et al Pediatrics 2003;112;1095-1102; 3. Olarte et al. Pediatrics 2013;132:e17–e24; 4. Ladhani et al. Clin Infect Dis 2013;56(5):633–40 ; 5. Poehling et al JAMA 2006; 295:1668–74; 6. Grimwood et al. J Paed Child Health. 2002;38(3):272-7