On-time Vaccination Coverage in Premature Infants in Ontario, 2002-2009

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ABSTRACT

Objective: Premature children are at increased risk of complications from vaccine-preventable diseases and should be vaccinated with the routinely recommended childhood vaccines at the same chronological age as full-term infants with the exception of the hepatitis B vaccine for infants of HBsAg-positive mothers. We sought to compare on-time vaccination levels in premature children for recommended vaccinations to levels in children born at term.

Methods: Using linked health administrative databases, we compared the proportion of term (37+ wks), near term (33-36 wks), very premature (28-32 wks) and extremely premature (≤ 27 wks) children who received at least one vaccination during the 2-, 4- and 6-month vaccination visits within the recommended time period in the province of Ontario.

Results: When we excluded children who were hospitalized at any time during the vaccination window, we identified that vaccination rates were within 3% of each other in the 4 categories examined. However, when we included infants who may have been hospitalized at any point during the on-time window, we observed substantially lower rates in the extremely premature children at 2 and 4 months and in the very premature children at 2 months.

Conclusion: Our study identifies the need to confirm whether vaccinations are given while premature children are in hospital during the time of their scheduled vaccinations.

Key words: Vaccination; immunization; infant, premature; Ontario; health services research

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Premature and low birth weight (LBW) children are at increased risk of complications from vaccine-preventable diseases, including pertussis¹ and pneumococcal infection.² Consequently, the Public Health Agency of Canada and the American Academy of Pediatrics both recommend that premature and LBW children, if medically stable, should be vaccinated with the routinely recommended childhood vaccines at the same chronological age as full-term infants (i.e., no delay for degree of prematurity) with the exception of the hepatitis B vaccine for infants of HBsAg-positive mothers.³ Despite expert guidance concerning immunization of premature infants, previous studies have suggested that these infants in general continue to be vaccinated at lower levels when compared to infants born at term.⁴⁻⁶ Within the province of Ontario, Canada, publicly funded immunizations for children include the pentavalent diphtheria, pertussis, tetanus, polio, *Haemophilus influenzae* type b ([Hib]) (DaPT-IPV-Hib) vaccine along with Pneumococcal conjugate (Pneu-C-7) vaccine given at 2, 4 and 6 months of age. We sought to compare on-time vaccination levels in premature children for these recommended vaccinations to levels in children born at term.

METHODS

The purpose of this study was to compare the proportion of term (≥ 37 weeks gestational age), near term (33-36 weeks), very premature (28-32 weeks) and extremely premature (≤ 27 weeks) children who received at least one vaccination during the 2-, 4- and

6-month vaccination visits within the recommended time period based on established recommendations.⁷ As part of VISION (Vaccine and Immunization Surveillance in Ontario), we examined all children born in Ontario from April 1, 2002 to March 31, 2009 who were present in the Institute for Clinical Evaluative Sciences (ICES) Registered Persons Database (RPDB) – which provides basic demographic information about anyone who has ever received an Ontario health card number – and were eligible for the Ontario

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Health Insurance Plan (OHIP) until 7 months of age. If a child died or became ineligible for OHIP (e.g., moved out of Ontario) before reaching 7 months of age, they were excluded from the analysis as we were reliant on OHIP codes to ascertain vaccinations. Children with no well-baby visits or fewer than 4 primary care visits in the first year of life, according to OHIP data, were likely out of province during the study period or accessing health care services employing a non-fee-for-service funding model. These children were also excluded from the study cohort (Figure 1).⁸

Pediatric vaccinations were identified using billing codes for general vaccination in the OHIP claims database. To identify on-time 2-, 4- and 6-month vaccinations, we examined vaccinations occurring on the exact due date as well as any vaccinations occurring up to 4 days before or 30 days after the due date. Infants with at least one vaccination billing code occurring in the target window for the target vaccination were included in the numerator, and the total number of eligible children was included in the denominator. Based on admission and discharge dates available in the Canadian Institute for Health Information's (CIHI) Discharge Abstract Database (DAD), we determined whether a child was admitted to hospital at any time during each of the 2-, 4- and 6-month target vaccination windows. The DAD contains data for all inpatient visits to acute and non-acute hospitals. We used the DAD database to capture visits to acute care hospitals specifically. Some perinatal data, including gestational age, were available in the DAD. To determine whether infants were hospitalized during each target vaccination window, data on all acute admissions during the study period were obtained from the DAD.

We conducted 4 analyses. We calculated: 1) rates of hospitalization during the on-time vaccination coverage window for 2, 4 and 6 months according to level of prematurity; 2) on-time vaccination coverage at 2, 4 and 6 months for each level of prematurity excluding children who were admitted at any time during the coverage window; 3) on-time vaccination coverage including children who were admitted at any time during the coverage window; and 4) on-time vaccination coverage only for children who were hospitalized at any time during the coverage window. All analyses were conducted using SAS version 9.2 (SAS Institute, Cary, NC). Statistical significance was not reported since we examined the entire population. Furthermore, due to the size of this population of children, extremely small (<1%) differences, that would not be considered clinically significant, would have achieved statistical significance based on reporting of p-values.⁹

RESULTS

Study population

Data were available for 980,987 infants who were eligible for OHIP at 6 months of age from April 1, 2002 to March 31, 2009. We excluded data on 220 infants who died within the first 7 months of life. Gestational age at birth was available in 931,554 (95.0%) of eligible infants who were alive at age 7 months. After excluding infants with no well-baby visits and/or fewer than 4 primary care visits in the first year of life, 848,604 infants were available for study (see Figure 1).

Hospitalization data

Overall, our analysis showed that 1.9% of infants were hospitalized during the on-time vaccination coverage window for the

Figure 1. Flow diagram describing the derivation of the final study cohort

2-month visit, 0.9% for the 4-month visit and 0.7% for the 6-month visit. For infants born prematurely, 93.6% of the extremely premature infants and 24.0% of the very premature infants were hospitalized during the 2-month on-time vaccination window. At 4 months of age (second recommended vaccination event), the proportions were 26.0% and 4.4% respectively, and at 6 months of age, these numbers decreased to 8.3% and 2.8%, respectively (Table 1).

On-time vaccination levels excluding hospitalized children

After excluding children who were hospitalized during the on-time vaccination window, overall vaccination levels were similar in premature children versus term children at the 2-, 4- and 6-month vaccinations. On-time vaccination levels appeared to be slightly lower for the very premature and extremely premature children at 2 months of age (80.0% and 80.3%) compared to children born at term (82.7%), however these were the largest absolute differences observed (Table 1).

Table 1. Hospitalization Rates and Vaccination Coverage During On-time Vaccination Window

Total Infants	All Infants	Term (37+ wks)	Near Term (33-36 wks)	Very Premature (28-32 wks)	Extremely Premature (≤27 wks)
	N=848,604	N=782,917	N=54,361	N=9176	N=2150
2 months					
Infants admitted/not admitted during on-time window (%)	16,130 (1.9)/ 832,474 (98.1)	10,180 (1.3)/ 772,737 (98.7)	1738 (3.2)/ 52,623 (96.8)	2199 (24.0)/ 6977 (76.0)	2013 (93.6)/ 137 (6.4)
Infants vaccinated	687,177	638,705	42,779	5583	110
Excluding admitted (%)	(82.6)	(82.7)	(81.3)	(80.0)	(80.3)
Infants vaccinated	696,349	645,767	43,876	6393	313
Admitted + non-admitted (%)	(82.1)	(82.5)	(80.7)	(69.7)	(14.6)
Infants vaccinated	9172	7062	1097	810	203
Admitted only (%)	(56.9)	(69.4)	(63.1)	(36.8)	(10.1)
4 months					
Infants admitted/not admitted during on-time window (%)	7572 (0.9)/ 841,032 (99.1)	5778 (0.7)/ 777,139 (99.3)	833 (1.5)/ 53,528 (98.5)	402 (4.4)/ 8774 (95.6)	559 (26.0)/ 1591 (74.0)
Infants vaccinated	645,805	597,235	40,521	6837	1212
Excluding admitted (%)	(76.8)	(76.9)	(75.7)	(77.9)	(76.2)
Infants vaccinated	650,225	600,733	41,006	7077	1409
Admitted + non-admitted (%)	(76.6)	(76.7)	(75.4)	(77.1)	(65.5)
Infants vaccinated	4420	3498	485	240	197
Admitted only (%)	(58.4)	(60.5)	(58.2)	(59.7)	(35.2)
6 months					
Infants admitted/not admitted during on-time window (%)	5989 (0.7)/ 842,615 (99.3)	4875 (0.6)/ 778,042 (99.4)	676 (1.2)/ 53,685 (98.8)	259 (2.8)/ 8917 (97.2)	179 (8.3)/ 1971 (91.7)
Infants vaccinated	610,677	564,468	38,329	6468	1412
Excluding admitted (%)	(72.5)	(72.6)	(71.4)	(72.5)	(71.6)
Infants vaccinated	613,948	567,171	38,663	6619	1495
Admitted + non-admitted (%)	(72.4)	(72.4)	(71.1)	(72.1)	(69.5)
Infants vaccinated	3271	2703	334	151	83
Admitted only (%)	(54.6)	(55.5)	(49.4)	(58.3)	(46.4)

On-time vaccination levels including hospitalized children

When including children who were hospitalized at any time during the on-time vaccination window, we observed approximately similar levels of vaccination in the categories all infants, term infants and near-term infants at 2 months (82.1%, 82.5% and 80.7%, respectively). However, markedly lower levels were noted for the categories of very premature and extremely premature infants (69.7% and 14.6%, respectively). The differences were considerably less at 4 and 6 months (Table 1).

Examining on-time vaccination only in infants who were hospitalized during the on-time vaccination window, we observed that levels were comparatively low at 2, 4 and 6 months (56.9%, 58.4% and 54.6%, respectively). The lowest rates were in extremely premature children and very premature children at 2 months (10.1% and 36.8%, respectively) and extremely premature children at 4 months (35.2%).

DISCUSSION

Our findings suggest that infants born prematurely in Ontario are vaccinated at levels consistent with the general population when excluding children who were hospitalized during the on-time vaccination window. We also identified that high proportions of very premature and extremely premature infants are hospitalized at the time of the 2-month vaccination (24.0% and 93.6%, respectively), and that a high proportion of extremely premature children (26.0%) are also in hospital at the time of the 4-month vaccination. We further observed lower levels of vaccination in hospitalized children in general, and in particular in very premature children at 2 months, and extremely premature children at both 2 and 4 months.

Previous studies have examined the impact of prematurity and low birth weight, which correlates with prematurity, on vaccina-

tion status. Prematurity has been previously identified to be correlated with delayed vaccination.^{5,6} One study concluded that delays in vaccination are greater the lower the gestational age.⁴ Other studies have suggested that the vaccination levels among extremely or very LBW infants at 2, 4 and 6 months continue to lag behind those of normal-weight full-term infants.^{7,10} Reported reasons for the inappropriate delay in vaccination include the beliefs of some physicians and parents that the level of prematurity, birth weight or weight at time of visit influences the initiation of vaccination.^{11,12}

Our study has certain limitations. First, we assumed that the vaccination events observed at 2, 4 and 6 months of age are consistent with the DTaP-IPV-Hib and Pneu-C-7 vaccine. There is a small possibility that some of the children could have received another type of vaccine at the event. Second, we could not be certain of the vaccination status of children who were hospitalized during the on-time vaccination window. These children may have been classified as not vaccinated because of potential limitations to the billing code data for in-hospital children, or vaccination may have been deferred for legitimate medical reasons. This had a significant impact on our ability to make conclusions about vaccination coverage for the extremely premature children at 2 months of age. However, our observation of lower rates of in-hospital vaccination in these children compared to the other groups does suggest that the vaccinations may be being deferred or missed rather than not being identified through billing data.¹³ Also, importantly, the levels we presented should not be interpreted as coverage rates but rather the proportion of individuals who received their vaccination on-time according to standard guidelines. Coverage rates would include proportion of children vaccinated at any time and not just the proportion vaccinated during the on-time vaccination window.

Our findings suggest that on-time vaccination levels of premature children are similar to those of term children if hospitalized patients are excluded. However, given the importance of protecting

premature children from vaccine-preventable diseases and the comparatively high rates of hospitalizations of these children during their scheduled vaccine visits, further effort should be made to ascertain whether vaccinations are being given in hospital. If vaccinations are not being given, whether the reason for deferring vaccination is appropriate should be determined. This would be particularly important for very premature and extremely premature infants.

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RÉSUMÉ

Objectif : Les enfants prématurés courent un risque accru de complications des maladies évitables par la vaccination; ils devraient donc recevoir les vaccins infantiles systématiquement recommandés au même âge chronologique que les nourrissons nés à terme, à l'exception du vaccin contre l'hépatite B pour les nourrissons de mères séropositives pour l'AgHBs. Nous avons voulu comparer, pour les vaccins recommandés, les niveaux de vaccination à temps des enfants prématurés à ceux des enfants nés à terme.

Méthode : À l'aide de bases de données sanitaires administratives liées, nous avons comparé la proportion d'enfants nés à terme (37+ sem.), légèrement prématurés (33-36 sem.), très prématurés (28-32 sem.) et extrêmement prématurés (≤ 27 sem.) ayant reçu au moins un vaccin durant leurs visites de vaccination à 2, 4 et 6 mois dans les délais recommandés dans la province de l'Ontario.

Résultats : En excluant les enfants hospitalisés à un moment donné durant la fenêtre de vaccination, nous avons constaté que les taux de vaccination se situaient dans une proportion de 3 % les uns des autres dans les quatre catégories examinées. Cependant, en incluant les nourrissons ayant pu être hospitalisés à un moment donné durant la fenêtre de vaccination, nous avons obtenu des taux considérablement plus faibles dans la catégorie des enfants extrêmement prématurés à 2 et à 4 mois, et dans celle des enfants très prématurés à 2 mois.

Conclusion : Notre étude souligne le besoin de confirmer si les vaccins sont administrés aux enfants prématurés lorsqu'ils sont hospitalisés au moment de recevoir les vaccins prévus.

Mots clés : vaccination; immunisation; nourrisson, prématuré; Ontario; recherche sur les services de santé