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Original article

Factors associated with receipt of Tetanus, Diphtheria, and Acellular Pertussis Vaccine (Tdap) in mothers who deliver preterm

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Abstract

Background: Maternal Tetanus, Diphtheria, and Acellular Pertussis Vaccine (Tdap) vaccination is recommended to prevent pertussis in newborns. Preterm infants experience greater morbidity/mortality from pertussis. Data on Tdap receipt in mothers who deliver preterm is limited.

Objective: To assess characteristics associated with Tdap vaccination in mothers who delivery preterm.

Methods: Analysis of 2,778 mothers between $27^{0/7}$-$36^{6/7}$ weeks gestation from the 2012-15 Rhode Island Pregnancy Risk Assessment Monitoring System (PRAMS) database. Tdap vaccination status was based on an affirmative response to the PRAMS question, "Did you receive a Tdap vaccination before, during or after your most recent pregnancy?" Variables assessed included: race/ethnicity, language, age, income, toxic habits, education, insurance status, marital status, and antenatal comorbidities. Rao-Scott chi-square test and logistic regression used for analysis. Reasons for non-immunization were described.

Results: Among preterm infants, maternal Tdap immunization rate was 87% (2,414/2,778), of which 57% were white. Hispanic mothers exhibited

lower rates of immunization (23% vs. 39%, p < 0.03). Previous live birth was also associated with decreased Tdap vaccination (51% vs. 71%, p = 0.001). Immunization rate was higher in mothers who received influenza vaccine (73% vs. 48%, p < 0.001). In un-immunized mothers, 50% of providers did not offer vaccination. In adjusted analysis, receipt of influenza vaccine and the pregnancy being "wanted" were associated with higher odds of Tdap immunization in mothers who delivered preterm (odds ratio [OR], 95% confidence interval [CI]: 2.10 [1.05-4.24], 2.20 [1.16-4.18], respectively). Previous live birth (OR 0.46, 95% CI: 0.23-0.91) and marriage (OR 0.31, 95% CI: 0.11-0.87) were associated with decreased odds of Tdap vaccination.

Conclusion: Increased offering of Tdap may increase immunization rates. Among mothers who delivered preterm receipt of influenza vaccine and desired pregnancy are associated with increased odds of Tdap immunization. In this cohort, mothers with a previous live birth or who are married may represent unique risk for non-immunization and may require more targeted counseling related to Tdap immunization.

Keywords

Pertussis, vaccine, immunization, Tdap, pregnancy, preterm.

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Introduction

Newborns and infants exhibit high rates of morbidity and mortality from pertussis infection [1, 2]. Infants less than 2 months of age comprise ~70% of pertussis-associated mortality and up and greater than 740 hospitalizations annually [2, 3]. Rates of pertussis are increasing and waning immunity in adolescent and young adults who received childhood vaccination contributes to horizontal transmission to newborns and young infants, who remain less protected until completion of the primary immunization series [4].

Within the neonatal age group, preterm infants with pertussis demonstrate higher mortality, hospitalization rates and Intensive Care Unit admission than older children [5]. To facilitate transfer of IgG antibodies, particularly during the 3rd trimester, maternal immunization of pregnant women between 27-36 completed weeks of gestation during each pregnancy has been recommended since 2012 [6]. However maternal Tetanus, Diphtheria, and Acellular Pertussis Vaccine (Tdap) immunization rates are low, ranging from 13% to 67% [7-9].

Among mothers who deliver at term, education level, insurance status, access to vaccination, race/ethnicity and language have been associated with maternal Tdap during or after pregnancy [7-9]. However factors associated with maternal Tdap receipt among mothers who deliver high risk preterm infants are not well described. The purpose of this study was to evaluate the relationship between maternal demographic characteristics and Tdap vaccination status during or shortly after preterm delivery using a state-based dataset.

Methods

We analyzed maternal responses obtained from the 2012-15 Rhode Island Pregnancy Risk Assessment Monitoring System (PRAMS) database. PRAMS is a Centers for Disease Control (CDC)-sponsored surveillance tool which provides access to state-specific population-based maternal data on issues related to pregnancy [10]. Exclusion criteria consisted of infants born < $27^{0/7}$ weeks or > 37 weeks gestation, mothers with a primary language other than English or Spanish, and surveys missing data on receipt of Tdap vaccine. Data was extracted and analyzed from September 2019 to January 2020. Institutional Review Board exemption was obtained.

Variables

Outcome was based on receipt of Tdap vaccine. Receipt of Tdap was defined as an affirmative response to the PRAMS question,

"Did you receive a Tdap vaccination before, during or after your most recent pregnancy?" Covariates included self-described race/ethnicity, maternal age, primary language, self-described marital status, maternal insurance status, years of maternal education, self-reported household income, presence of comorbid conditions receipt of influenza vaccination, desirability of pregnancy and experience with breastfeeding. Toxic habits included traditional cigarette smoking and alcohol use. For mothers who did not receive Tdap, reasons for non-vaccination were assessed, including the provider, "did not offer," or "did not have" vaccine, as well as safety concerns surrounding vaccination during pregnancy or nursing. These included "I don't like to get vaccinated," "I am worried about side effects," and concerns regarding vaccination safety "in pregnancy and nursing" [10].

Race/ethnicity was classified into Non-Hispanic White, Non-Hispanic Black, Hispanic or Non-Hispanic Other. Maternal age (in years) was divided into < 18 years, 18-24 years, 25-34 years and > 34 years at the time of delivery. Maternal insurance at time of delivery was classified as "Private/Military," "Medicaid," "Other," or "None" – with mothers insured under the Children's Health Insurance Program included in the "Medicaid" category. Education was divided as 0-11 years (less than high school graduation), 12 years (high school graduate), 13-15 years (partial post-high school education), and ≥ 16 years (at least college graduate.). Household income was categorized as ≤ $15,000, $15,001-$37,000, $37,001-$79,000 and > $79,000.

Diabetes, hypertension and depression were based on "Yes" responses to the question, "Before your got pregnant with your new baby, did a doctor, nurse or other healthcare worker tell you that you had any of the following conditions? Type 1 or type 2 diabetes, high blood pressure or hypertension, depression" [10]. Gestational diabetes was based on the responses to the question, "During your most recent pregnancy, were you told by a doctor, nurse or other healthcare worker that you had gestational diabetes (diabetes that started during this pregnancy)?" [10]. Breastfeeding experience was determined based on the self-reported response to, "Did you ever breastfeed or pump breastmilk to feed your new baby, even for a short period of time" [10].

Toxic habits included self-report of ever-smoking in the past 2 years, use of > 5 cigarettes smoked in an "average" day in the last 3 months of pregnancy and consumption of > 6 drinks in an "average" week during the last 3 months of pregnancy. Respondents who answered the question, "Thinking back to just before you got pregnant with your new baby, how did you feel about becoming pregnant?" with "I wanted to be pregnant then," were categorized as a "desired pregnancy." Influenza vaccination status was based on self-reported receipt of immunization in the 12 months before or during pregnancy.

Statistical analysis

All results are weighted in order to account for the survey sampling design. Tdap vaccination was compared with the above variables in bivariate analysis using the Rao-Scott chi-square test. Percentages were based on response to each question. Adjusted logistic regression modeling was used to determine the association between Tdap vaccination and demographic variables. Model 1 adjusted for covariates with a p-value of 0.1 or less in bivariate analysis and ultimately controlled for race, previous live birth and influenza immunization. Model 2 adjusted for all factors other than the exposure of interest. Odds ratios (OR) and 95% confidence intervals (95% CI) are reported. Statistical significance was determined by $p < 0.05$. Analysis was performed with Stata® version 16.0 (StatCorp 2019, College Station, TX, USA).

Results

Bivariate comparison of Tdap vaccination status and maternal characteristics are reported in **Tab. 1**. A total of 87% (2,414/2,778) of mothers who delivered preterm between $27^{0/7}$-$36^{6/7}$ weeks received Tdap. Recipients of Tdap vaccination were more likely to be Non-Hispanic White (57%) than other race/ethnicities, including Hispanic (23%), Non-Hispanic Black (10%) or Non-Hispanic Other (10%) ($p < 0.05$). Previous live birth was associated with a lower rate of Tdap immunization (51% vs. 71%, $p = 0.001$). However, receipt of influenza vaccine was associated with a higher rate of Tdap receipt (73% vs. 48%, $p < 0.001$). Maternal age, education level, annual income, primary language, insurance status, breastfeeding experience, comorbid conditions or toxic habits were not associated with maternal Tdap vaccination.

Table 1. Demographic comparison of mothers who delivered preterm by Tetanus, Diphtheria and Acellular Pertussis Vaccine (Tdap) vaccination status.

Variable		Tdap (n = 2,414)	No Tdap (n = 364)	p-value
Maternal age (years)	> 34	19%	24%	0.375
	25-34	54%	46%	
	18-24	24%	29%	
	< 18	2%	1%	
Maternal race	Hispanic	23%	39%	**0.028** [a]
	Non-Hispanic Black	10%	5%	
	Non-Hispanic White	57%	45%	
	Non-Hispanic Other	10%	11%	
Primary language	English	88%	88%	0.989
	Spanish	12%	12%	0.989
Insurance type	Private/Military	53%	51%	0.869
	Medicaid [b]	45%	47%	
	None	1%	1%	
Married		46%	50%	0.602
Maternal education (years)	0-11	17%	31%	0.095
	12	27%	22%	
	13-15	20%	21%	
	≥ 16	36%	25%	
Annual household income ($)	> $79,000	26%	15%	0.229
	$37,001-$79,000	20%	29%	
	$15,001-$37,000	25%	27%	
	≤ $15,000	30%	29%	
Diabetes		4%	3%	0.580
High blood pressure		7%	7%	0.924
Depression		17%	20%	0.473
Any health problem		22%	23%	0.850
Previous live birth		51%	71%	**0.001** [a]
Desired pregnancy		56%	52%	0.512
Flu vaccine before or during pregnancy		73%	48%	**< 0.001** [a]
Gestational diabetes		15%	17%	0.557
Smoked at all in the last 2 years		27%	29%	0.716
More than 5 cigarettes/day in the last 3 months		5%	5%	0.846
More than 6 drinks/week in the last 3 months		0%	0%	0.616
Ever breastfed		86%	79%	0.208

[a] Significant, $p < 0.05$ (Chi-square test).
[b] Mothers insured under the Children's Health Insurance Program were included in the "Medicaid" category.
Tdap: Tetanus, Diphtheria and Acellular Pertussis Vaccine.

Results of regression models are shown in **Tab. 2**. Model 1, which included maternal race, previous live birth and receipt of influenza vaccine, demonstrated lower odds of Tdap immunization (OR 0.47; 95% CI 0.28-0.76) among mothers with a history of previous live birth. Obtaining influenza vaccination before or during pregnancy and pre-existing diabetes were both associated with higher odds of maternal Tdap (OR 2.61; 95% CI 1.50-4.53; OR 7.50; 95% CI 1.37-40.95, respectively). A second model, adjusting for all other covariates, also demonstrated that previous live birth was associated with lower odds of maternal Tdap vaccination (OR 0.46; 95% CI 0.23-0.91). Lower odds of Tdap receipt were also seen among married mothers (OR 0.31; 95% CI 0.11-0.87). Again, in this model, mothers who previously received influenza vaccine exhibited higher odds of Tdap immunization (OR 2.10; 95% CI 1.05-4.24). Desiring the pregnancy also correlated with higher odds of maternal Tdap vaccination (OR 2.20; 95% CI 1.16-4.18).

Table 2. Logistic regression models of factors associated with increased odds of Tetanus, Diphtheria and Acellular Pertussis Vaccine (Tdap) receipt in mothers who delivered preterm.

		Model 1			Model 2		
		OR	95% CI	p-value	OR	95% CI	p-value
Maternal race	Hispanic	0.54	0.284, 1.028	0.061	0.52	0.206, 1.311	0.166
	Non-Hispanic Black	1.79	0.813, 3.931	0.148	1.70	0.673, 4.303	0.261
	Non-Hispanic White	Ref	-	-	Ref	-	-
	Non-Hispanic Other	0.83	0.309, 2.234	0.713	0.85	0.232, 3.142	0.812
Previous live birth		0.47	0.283, 0.764	**0.002**	0.46	0.234, 0.911	**0.026**
Flu vaccine before or during pregnancy		2.61	1.499, 4.533	**0.001**	2.10	1.045, 4.238	**0.037**
Maternal age (years)	> 34	Ref	-	-	Ref	-	-
	25-34	1.53	0.741, 3.156	0.250	1.39	0.616, 3.148	0.426
	18-24	1.33	0.614, 2.872	0.471	0.75	0.199, 2.807	0.666
	< 18	2.12	0.369, 12.191	0.400	Omit	-	-
Language	English	Ref	-	-	Ref	-	-
	Spanish	1.68	0.624, 4.521	0.305	1.34	0.372, 4.787	0.657
Insurance type	Private/Military	Ref	-	-	Ref	-	-
	Medicaid	1.34	0.658, 2.716	0.422	0.86	0.335, 2.209	0.755
	None	1.76	0.390, 7.948	0.463	Omit	-	-
Married		0.64	0.358, 1.152	0.137	0.31	0.107, 0.867	**0.026**
Maternal education (years)	0-11	0.69	0.301, 1.556	0.366	0.35	0.080, 1.542	0.166
	12	1.24	0.550, 2.813	0.600	0.91	0.303, 2.706	0.860
	13-15	0.86	0.357, 2.078	0.739	0.99	0.344, 2.847	0.986
	≥ 16	Ref	-	-	Ref	-	-
Annual household income ($)	> $79,000	Ref	-	-	Ref	-	-
	$37,001-$79,000	0.51	0.206, 1.261	0.145	0.53	0.181, 1.567	0.252
	$15,001-$37,000	0.70	0.267, 1.814	0.458	0.78	0.190, 3.161	0.723
	≤ $15,000	1.03	0.407, 2.603	0.951	1.56	0.317, 7.621	0.586
Diabetes		7.50	1.373, 40.954	**0.020**	4.04	0.637, 25.558	0.138
High blood pressure		1.20	0.435, 3.289	0.729	0.90	0.110, 7.271	0.917
Depression		0.86	0.417, 1.755	0.670	0.98	0.119, 8.119	0.986
Any health problem		1.06	0.550, 2.041	0.863	0.89	0.114, 6.837	0.907
Desired pregnancy		1.20	0.664, 2.176	0.544	2.20	1.159, 4.180	**0.016**
Gestational diabetes		0.61	0.293, 1.262	0.182	0.45	0.176, 1.161	0.099
Smoked at all in the last 2 years		0.67	0.353, 1.279	0.227	0.76	0.282, 2.073	0.597
More than 5 cigarettes/day in the last 3 months		1.54	0.571, 4.139	0.395	2.29	0.452, 11.572	0.317
Ever breastfed		1.94	0.948, 3.990	0.070	1.57	0.585, 4.229	0.369

Model 1: adjusting for maternal race, previous live birth, and flu vaccine; Model 2: adjusting for all variables in list; OR: odds ratios; Ref: reference category; 95% CI: 95% confidence intervals. Omit indicates not enough numbers for regression modelling.

Reasons for non-immunization

Reasons for non-immunization are illustrated in **Fig. 1**. Respondents were able to select multiple answers to the survey question. Among the 364 mothers who were not vaccinated, 50% were not offered immunization from their physician. Issues of safety were also present, as 17% of mothers felt the vaccine was not safe in pregnancy and 13% expressed concern about side effects. Issues regarding immunization while nursing prevented 11% of mothers from immunization. Dislike of vaccination were the reasons for Tdap refusal in 12% of patients.

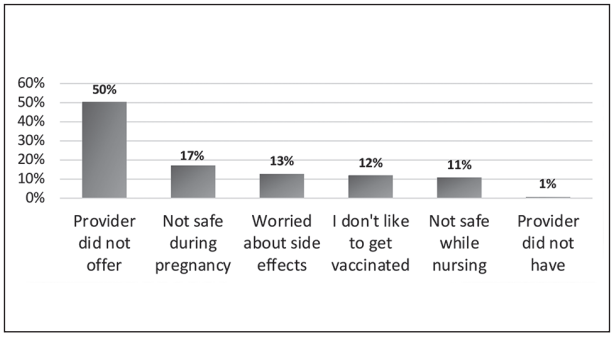

Figure 1. Reported reasons for non-receipt of Tetanus, Diphtheria and Acellular Pertussis Vaccine (Tdap) immunization in mothers of preterm infants ($27^{0/7}$-$36^{6/7}$ weeks), n = 364.

Discussion

Years after the CDC recommendation, maternal Tdap immunization remains underutilized [2, 7, 8, 11-13]. While risk factors for maternal non-immunization in mothers who deliver at term have been previously identified, this study is among the first to recognize factors associated with non-immunization among mothers with preterm deliveries [7, 11-13]. Immunization of this population is of increased importance given the increased morbidity and mortality of premature infants to pertussis [14, 15]. Our results demonstrate, in 2 statistical models, that mothers with a previous live birth are at lower odds of Tdap vaccination. Further, married mothers were also at lower off begin unimmunized. These findings may have clinical implications in identifying parents who may require repeated counseling about the benefits of vaccination. Given that greater than 40% of unvaccinated mothers expressed concerns regarding side effects, counseling focused on immunization safety and tolerance may be beneficial for mothers who delivery preterm [16].

Parents who refuse standard childhood vaccinations are more likely to be white, college-educated, privately insured and of higher socio-economic status [14]. Unlike that demographic group, no economic, racial/ethnic or insurance factors associated with Tdap receipt were found. Further, our findings show that 50% of mothers who were not vaccinated cited "Provider did not offer" as a potential reason.

Barriers to offering immunization by obstetric providers have been well described and include lack of patient interest, cost and inadequate reimbursement, all of which may be magnified in suburban and rural populations [17]. Attempts to improve vaccine reimbursement via the Affordable Care Act and the 2021 payment increase for vaccination administration and storage may incentivize more providers of prenatal care to offer Tdap [18]. Further evaluation of the impact of these policy changes on reducing barrier to immunization is warranted.

As vaccine administration entails certain fixed costs, administering a greater number of vaccines in the practice setting may influence the financial impediment obstetric providers report as a disincentive to provide immunizations as part of routine care [3]. Obstetricians who provide both Tdap and influenza vaccine, for example, report fewer financial and practice barriers [3, 17]. Our finding that receipt of influenza vaccine increased odds of Tdap immunization may reinforce this notion. Use of evidenced-based measures to improve offering of Tdap, such as electronic support tools, immunization registries, and reminder/recall system are underutilized in obstetrics and may play a role in both increasing immunization opportunities and limiting cost impediments to antenatal vaccination [17, 19]. Greater adoption of resources such as the American College of Obstetrics and Gynecology immunization toolkit may also assist obstetric providers in overcoming these obstacles [3]. In one study, use of this toolkit increased the percentage of practice routinely administering Tdap from 59% to 77% [17].

A major hurdle toward improving immunization rates among pregnant women is perceived vaccine safety. Our data, similar to those of other studies, demonstrates ~40% of women refused vaccines due to concerns about side effects or worries about immunization in pregnancy or while nursing [18]. These aspects of vaccinations should remain a focus of both public health message and individual provider counseling. Maternal perception of vaccine safety is among the strongest influencers of vaccine receipt [11]. Further, healthcare workers providing a strong recommendation for vaccination is also a reliable predictor for maternal immunization [11, 17]. This may also explain the limited efficacy of public health education in immunization rates [20].

This study has several limitations. Data collection via survey is subject to recall bias. Further, use of state-based data from Rhode Island may not be nationally-representative. PRAMS data also does not capture information on type of obstetric practice, and since 50% of mothers who did not receive Tdap report the vaccine not being offered, practice characteristics or other factors associated with obstetric practices may confound results. For example, network-employed physicians are more likely to offer preventive care services than independent, private ones [8, 11]. Further study is required to better understand how to best improve Tdap vaccination rates in mothers who delivery preterm.

Abbreviations

CDC: Centers for Disease Control and Prevention

PRAMS: Pregnancy Risk Assessment Monitoring System

Tdap: Tetanus, Diphtheria, and Acellular Pertussis Vaccine

Declaration of interest

The Authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. Funding/support: none.

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