The Impact of the Heptavalent Pneumococcal Conjugate Vaccine on Risk Factors for *Streptococcus pneumoniae* Carriage in Children

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Background: The aim of the study was to investigate whether the 7-valent pneumococcal conjugate vaccine (PCV7) alters common risk factors of nasopharyngeal carriage by *Streptococcus pneumoniae* in children.

Methods: From July 2005 through December 2010, we performed a cross-sectional study investigating risk factors associated with pneumococcal carriage in children. Parents of participating children completed questionnaires including whether or not the children received PCV7 vaccination.

Results: Among 9705 children, 20.2% of them received at least 1 dose of the PCV7 vaccine. Multivariate logistic regression models identified older age, having 1 sibling in a family, history of acute otitis media and household exposure to smoking as independent risk factors for pneumococcal carriage in the unvaccinated group, but not associated with pneumococcal carriage in the vaccinated group. The number of siblings ≥2 in a family, history of upper respiratory tract infection and child-care attendance were strong factors associated with pneumococcal carriage in children, regardless of vaccination. In vaccinated group, breast-feeding was associated with increased nonvaccine type pneumococcal carriage, mainly in children with upper respiratory tract infection.

Conclusions: PCV7 decreased the association between pneumococcal carriage and older age, 1 sibling in a family, history of acute otitis media and household exposure to smoking, but increased the association between pneumococcal carriage and breast-feeding.

Key Words: pneumococcal conjugate vaccine, risk factor, nasopharyngeal carriage

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Streptococcus pneumoniae is a leading extracellular Gram-positive pathogen that commonly colonizes the nasopharynx of children. Such carriage acts as a reservoir where adaptability provided through recombination enables *S. pneumoniae* to overcome various environmental challenges and continues to transmit in the community.[1] By residing on the mucosal surface of the upper respiratory tract, pneumococci can cause respiratory tract infections such as sinusitis, otitis media and pneumonia. If pneumococci spread beyond this niche into the blood or meninges, invasive disease of bacteremia, sepsis and meningitis occurs. A reduction of pneumococcal nasopharyngeal carriage would result in a decrease in respiratory infection and invasive disease caused by *S. pneumoniae*.

The mechanism of natural immunity to pneumococcal colonization has been studied. Malley et al[2] showed that passive transfer of serotype-specific antibodies protected against nasopharyngeal pneumococcal colonization in infant rats. However, colonization was shown to generate minimal anticapsular antibodies in a human carriage study,[3] and no correlation between naturally acquired IgG and carriage protection has been found.[3–5] In recent years, Toll-like receptor 2, $CD4^+$ T cells and IL-17A have been shown to mediate antibody-independent clearance of pneumococci in the airway.[6–8]

Pneumococcal conjugate vaccine has been shown to reduce vaccine serotype (VT) and cross-reacting serotype pneumococcal nasopharyngeal carriage among vaccinated children by preventing new acquisition[9] and by a consequent reduction in the transmission of *S. pneumoniae* from vaccinated children to unvaccinated children and adults.[10] Induction of serum serotype–specific pneumococcal anticapsular antibodies to reduce acquisition of certain *S. pneumoniae* serotypes has been demonstrated among recipients of pneumococcal conjugate vaccine.[4,11] Since October 2005, the 7-valent pneumococcal conjugate vaccine (PCV7) (Prevnar; Pfizer, New York, NY) has been available on the private market in Taiwan, but not included in the national immunization program, with a vaccination schedules of 2, 4, 6 and 13 months, and catch-up vaccination for children aged up to 5 years. To expand our insights into the ability of PCV7 to influence pneumococcal carriage in the community, we conducted a prospective, cross-sectional study to evaluate risk factors for pneumococcal carriage between vaccinated and unvaccinated children.

MATERIALS AND METHODS

Study Population and Data Collection

From July 2005 through December 2010, we enrolled children aged between 2 months and 5 years who were brought to primary care clinic because of acute illness or for regular vaccination at 3 tertiary teaching hospitals: Chang-Gung Memorial Hospital, Taoyuan (in northern Taiwan); Veterans General Hospital, Taichung (in central Taiwan); and Chang Gung Memorial Hospital, Kaohsiung (in southern Taiwan). Children with immunological, neoplastic, renal, cardiac or hematological disease; bronchopulmonary dysplasia or Down's syndrome were excluded from the study. Part of the study results (from 2005 to 2008) which did not discuss whether PCV7 influence the risk factor for pneumococcal carriage has been published.[12]

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Trained investigators obtained informed consent from the parents of participating children and conducted interviews using a standard questionnaire. Parents of participating children were asked about demographic information, attendance of group child care, numbers of siblings, smoking by family members and duration of breast-feeding. Parents of participating children also consented to a medical record review for information on PCV7 vaccination history, history of acute otitis media (AOM), history of upper respiratory tract infection (URI) in the previous 2 weeks, antibiotic use in the previous 2 weeks and symptoms and diagnoses at the time of the visit. Analyses of PCV7 vaccination divided the participants into those who received at least 1 dose and those who did not receive any dose. Respiratory tract infection included viral URI, bronchitis, pharyngitis and sinusitis. All study procedures were approved by the Institutional Review Board of the Chang Gung Memorial Hospital.

Bacteria Sampling and Serotyping (Including Serotype 6C and 6D Identification)

Trained study personnel collected the nasopharyngeal swabs from children by using a sterile swab (Transwab; Copan Italia, Brescia, Italy; Medical Wire & Equipment Co., Corsham, Wiltshire, England), which was introduced into the nostrils and was advanced until resistance was found. The swabs were inoculated into Amies transport medium (Copan) and were plated within 4 hours of sampling on blood agar plates with 5% sheep's blood to isolate *S. pneumoniae*.

Pneumococcal isolates was identified by standard methods. In brief, identification of *S. pneumoniae* was based on colony morphology and conventional methods of determination (optochin susceptibility and bile solubility assays). One *S. pneumoniae* colony per plate was then subcultured, harvested and kept frozen at −70°C for further testing. Pneumococcal serotyping was determined by the capsular swelling method (Quellung reaction) using antisera from the Statens Serum institut (Copenhagen, Denmark) at Chang Gung Children's Hospital**.** All isolates determined to be 6A by Quellung reaction were selected for testing to resolve serotypes 6A and 6C with the use of polymerase chain reaction–tested serotyping methods.[13] All isolates determined to be 6B by Quellung reaction were selected for testing to resolve serotypes 6B and 6D with the use of polymerase chain reaction–tested serotyping methods.[13]

Statistical Analysis

Children were divided into PCV7-vaccinated and unvaccinated groups. Statistical analyses were performed separately for the 2 groups. Differences between groups of categorical data were tested by the χ^2 test. Multivariate logistic regression models were then used to examine the effects of significant factors in the χ^2 test on *S. pneumoniae* colonization. Odds ratios with 95% confidence intervals were computed to assess the association between *S. pneumoniae* colonization and factors included in the univariate and multivariate logistic regression models. The χ^2 test or Fisher's exact test was used to evaluate differences in serotype prevalence rates. *P* value <0.05 was considered to be statistically significant. All statistical analyses were performed using SPSS software, version 15.0 (SPSS Inc., Chicago, IL).

RESULTS

Between July 2005 and December 2010, we enrolled a total of 9708 children, 3 of which were excluded because they did not complete the questionnaire form. In total, 9705 specimen were collected, of which 1225 (12.6%) were colonized with *S. pneumoniae*. Characteristics of the 9705 children are shown in Table 1. The PCV7 vaccination rate among participants increased from 0.2% in 2005 to 45.5% in 2010 (Fig. 1). During the study period, VT carriage rate among all participating children by year significantly decreased ($P < 0.001$) and serotype 15B ($P = 0.007$) and 19A ($P = 0.001$) carriage rates by year significantly increased (Fig. 1). The overall pneumococcal carriage rate was lower in vaccinated group compared with that in unvaccinated group (8.9% versus 13.6%; $P < 0.001$). In 2005, all types of pneumococcal carriage rates among each age group were different ($P < 0.001$) (Fig. 2). As the vaccination rate in each age group gradually increased over the study period, there was no significant variation in pneumococcal carriage rates among 3 age groups in 2010 ($P = 0.8$). One thousand nine hundred fifty-eight participants (20.2%) in this study received at least 1 dose of the PCV7 vaccine. In unvaccinated group, overall pneumococcal carriage rates were progressively lower only in the 24- to <60-month-old age group over the study period (18.6% in 2005 to 13.4% in 2010; $P = 0.001$).

TABLE 1. Characteristics of the 9705 Children at the Time of Enrollment

	N (%)
Age	
0 to <12 months	2733 (28.2)
12 to <24 months	2795 (28.8)
24 to <60 months	4177 (43)
Sex distribution	
Male	5276 (54.4)
Site	
North	3281 (33.8)
Central	3144 (32.4)
South	3280 (33.8)
Siblings	
0	3322 (34.2)
1 sibling	4298 (48.4)
2 siblings	1193 (12.3)
>2 siblings	492 (5.1)
Day-care attendance	1781 (18.3)
History of AOM	894 (9.2)
URI within 2 weeks	2940 (30.3)
Antibiotic usage within 2 weeks	571 (5.9)
Breast-feeding	
0	2705 (27.9)
1 month	960 (9.9)
2 months	1398 (14.4)
>2 month	4642 (47.8)
Household exposure to smoking	4546 (46.8)
PCV7 vaccination ≥1 dose	1958 (20.2)
2005	3 (0.2)
2006	150 (5.7)
2007	197 (17.1)
2008	404 (26.9)
2009	568 (37.5)
2010	636 (45.5)

With the univariate analysis, older age, having 1 sibling, history of AOM and household exposure to smoking were associated with an increased risk for pneumococcal colonization in the unvaccinated group, but not in the vaccinated group (Table 2). Number of siblings ≥2 in a family, day-care attendance, URI within 2 weeks and antibiotic usage within 2 weeks were significantly associated with pneumococcal carriage in both group. Of note, breast-feeding decreased the risk of pneumococcal carriage in the unvaccinated group, but increased the risk of pneumococcal carriage in the vaccinated group. In multivariate analysis, all factors except for antibiotic usage within 2 weeks had similar effects on pneumococcal colonization between unvaccinated and vaccinated group (Table 3).

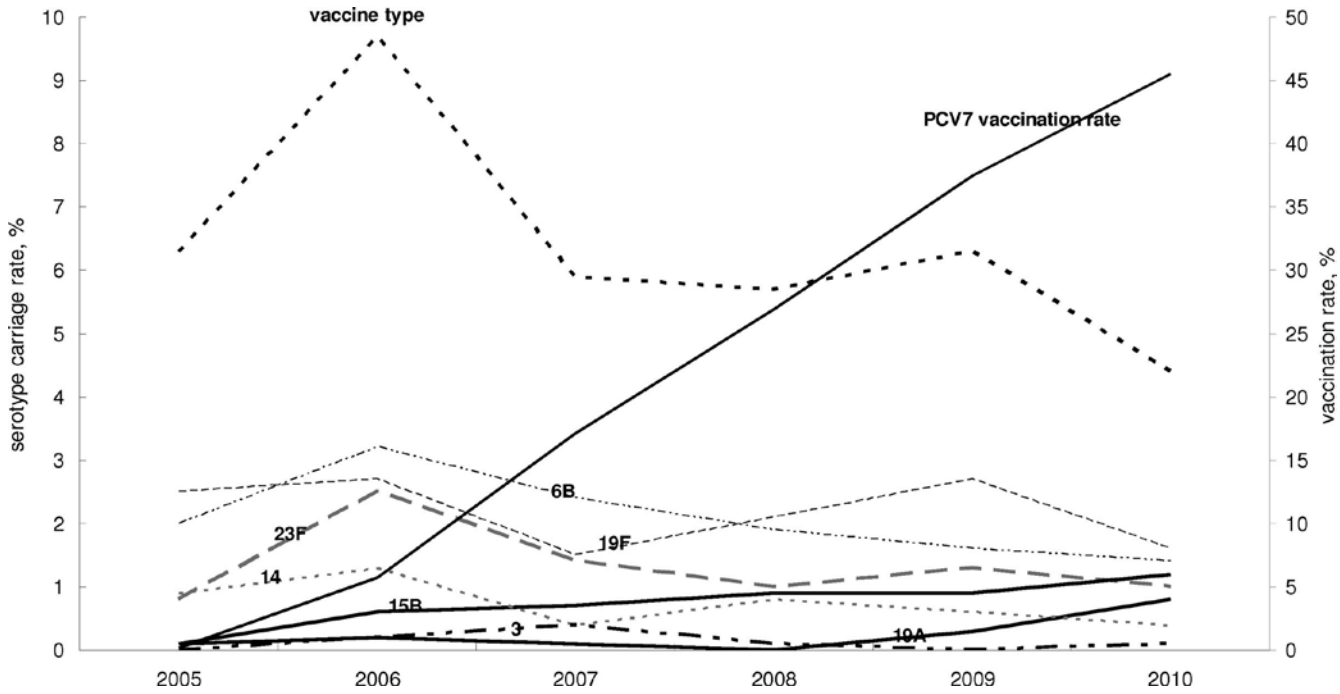

FIGURE 1. Serotype carriage rates and PCV7 vaccination rates (received at least 1 dose of PCV7) in children below the age of 60 months among the study population by year.

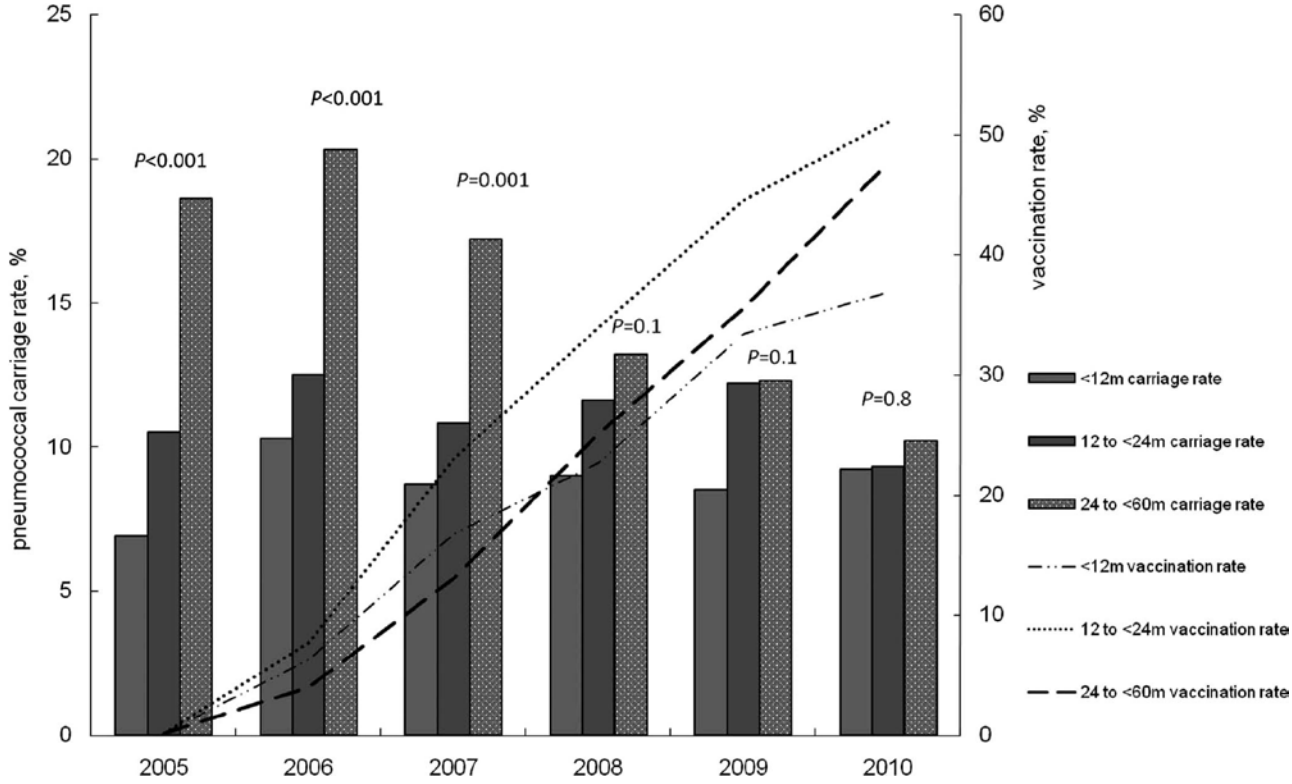

FIGURE 2. Pneumococcal carriage rates and PCV7 vaccination rates (received at least 1 dose of PCV7) in 3 age groups among the study population by year.

TABLE 2. Univariate Analysis of Factors for Pneumococcal Carriage Between Unvaccinated and Vaccinated Children

	Odds Ratio (95% Confidence Interval)					
	All		Health		URI Within 2 weeks	
	Unvaccinated (n = 7747)	Vaccinated (n = 1958)	Unvaccinated (n = 5311)	Vaccinated (n = 1454)	Unvaccinated (n = 2436)	Vaccinated (n = 504)
Sex						
Male	1.14 (0.9–1.3)	1.17 (0.85–1.6)	1.18 (0.98–1.4)	0.92 (0.61–1.39)	1.06 (0.87–1.29)	1.54 (0.92–2.55)
Age						
0 to <12 months	Reference group	Reference group	Reference group	Reference group	Reference group	Reference group
12 to <24 months	**1.43 (1.18–1.74)**†	0.92 (061–1.39)	**1.52 (1.18–1.96)**†	0.88 (0.52–1.5)	1.1 (0.81–1.52)	0.83 (0.43–1.62)
24 to <60 months	**2.16 (1.82–2.56)**†	1.04 (0.7–1.55)	**2.22 (1.78–2.78)**†	0.98 (0.59–1.63)	**1.53 (1.17–2.0)**†	0.95 (0.5–1.78)
Siblings						
0	Reference group	Reference group	Reference group	Reference group	Reference group	Reference group
1 sibling	**1.79 (1.51–2.11)**†	1.18 (0.82–1.7)	**1.65 (1.33–2.05)**†	1.1 (0.68–1.77)	**1.82 (1.4–2.36)**†	1.3 (0.73–2.32)
2 siblings	2.49 (2.02–3.07)†	2.62 (1.63–4.2)†	2.37 (1.79–3.13)†	2.47 (1.31–4.7)†	2.33 (1.68–3.22)†	2.48 (1.2–5.16)*
>2 siblings	2.89 (2.2–3.79)†	3.18 (1.73–5.87)†	2.32 (1.57–3.44)†	2.45 (1.1–5.58)*	3.03 (2.03–4.5)†	5.65 (2.05–15.6)†
Day-care attendance	3.05 (2.65–3.5)†	3.35 (2.38–4.72)†	3.2 (2.63–3.9)†	4.0 (2.54–6.28)†	2.3 (1.9–2.87)†	2.16 (1.27–3.67)†
History of AOM	**2.21 (1.8–2.68)**†	1.48 (0.93–2.37)	**2.07 (1.56–2.75)**†	0.87 (0.39–1.91)	**1.84 (1.43–2.38)**†	1.82 (0.98–3.38)
URI within 2 weeks	2.19 (1.92–2.49)†	2.56 (1.87–3.5)†	—	—	—	—
Antibiotic usage within 2 weeks	2.09 (1.67–2.62)†	2.1 (1.24–3.58)*	1.63 (0.95–2.8)	2.2 (0.75–6.44)	**1.45 (1.12–1.88)**†	1.19 (0.63–2.25)
Breast-feeding						
0	Reference group	Reference group	Reference group	Reference group	Reference group	Reference group
1 month	0.85 (0.67–1.08)	**2.77 (1.49–5.16)**†	1.02 (0.74–1.4)	**2.56 (1.13–5.8)***	**0.69 (0.48–0.99)***	**3.8 (1.43–10.14)**†
2 months	**0.81 (0.66–1.0)***	1.43 (0.73–2.8)	0.92 (0.69–1.21)	1.69 (0.73–3.92)	0.75 (0.54–1.03)	1.16 (0.37–3.64)
> 2 months	**0.85 (0.73–0.98)***	**1.97 (1.2–3.2)**†	0.85 (0.69–1.05)	1.65 (0.85–3.19)	0.98 (0.78–1.23)	**3 (1.43–6.29)**†
Household exposure to smoking	**1.22 (1.07–3.92)**†	1.07 (0.78–1.47)	**1.2 (1.0–1.43)***	1.04 (0.68–1.57)	1.13 (0.97–1.38)	1.05 (0.65–1.7)

Significant odds ratios and 95% confidence interval only in 1 group (vaccinated or unvaccinated) are shown in boldface.
*$P \leq 0.05$.
†$P \leq 0.005$.

TABLE 3. Multivariate Analysis of Risk Factors for Pneumococcal Carriage Between Unvaccinated and Vaccinated Children

	Odds Ratio (95% Confidence Interval)					
	All		Healthy		URI Within 2 Weeks	
	Unvaccinated (n = 7747)	Vaccinated (n = 1958)	Unvaccinated (n = 5311)	Vaccinated (n = 1454)	Unvaccinated (n = 2436)	Vaccinated (n = 504)
Age						
0 to <12 months	Reference group	Reference group	Reference group	Reference group	Reference group	Reference group
12 to <24 months	**1.29 (1.06–1.57)***	0.84 (0.55–1.29)	**1.43 (1.11–1.84)***	0.84 (0.49–1.46)	1.07 (0.78–1.48)	0.77 (0.38–1.55)
24 to <60 months	1.04 (0.85–1.27)	0.48 (0.3–0.79)†	1.18 (0.9–1.54)	**0.4 (0.21–0.78)***	0.84 (0.61–1.15)	0.57 (0.27–1.21)
Siblings						
0	Reference group	Reference group	Reference group	Reference group	Reference group	Reference group
1 sibling	**1.62 (1.36–1.92)**†	1.27 (0.87–1.85)	**1.51 (1.21–1.89)**†	1.2 (0.73–1.98)	**1.74 (1.33–2.28)**†	1.3 (0.72–2.37)
2 siblings	2.27 (1.83–2.81)†	2.71 (1.65–4.45)†	2.2 (1.65–2.93)†	2.88 (1.49–5.57)†	2.36 (1.69–3.28)†	2.45 (1.14–5.3)*
>2 siblings	2.68 (2.02–3.55)†	3.31 (1.75–6.27)†	2.22 (1.48–3.31)†	2.42 (1.02–5.71)*	3.2 (2.12–4.82)†	6.51 (2.3–18.9)†
Day-care attendance	2.77 (2.32–3.3)†	4.47 (2.85–7.0)†	3.01 (2.37–3.83)†	6.94 (3.77–12.8)†	2.56 (1.97–3.33)†	2.61 (1.32–5.2)*
History of AOM	**1.43 (1.17–1.75)**†	1.13 (0.68–1.9)	**1.38 (1.02–1.86)***	0.77 (0.34–1.78)	**1.5 (1.14–1.97)**†	1.58 (0.78–3.19)
URI within 2 weeks	1.74 (1.51–2.01)†	2.34 (1.66–3.3)†	—	—	—	—
Antibiotic usage within 2 weeks	1.18(0.92–1.51)	1.25 (0.69–2.26)	1.51 (0.86–2.64)	2.07 (0.68–6.29)	1.15 (0.87–1.52)	1.12 (0.55–2.27)
Breast-feeding						
0	Reference group	Reference group	Reference group	Reference group	Reference group	Reference group
1 month	0.91 (0.71–1.16)	**2.89 (1.51–5.5)**†	1.09 (0.79–1.5)	**2.33 (1.0–5.43)***	0.73 (0.51–1.06)	**4.1 (1.49–11.3)***
2 months	0.93 (0.75–1.15)	1.61 (0.81–3.21)	1.07 (0.81–1.43)	1.81 (0.76–4.28)	0.77 (0.56–1.08)	1.21 (0.37–4.0)
>2 months	1.02 (0.87–1.19)	**2.06 (1.24–3.42)**†	0.99 (0.8–1.23)	1.59 (0.8–3.13)	1.1 (0.85–1.35)	**2.95 (1.37–6.4)***
Household exposure to smoking	**1.18 (1.03–1.35)***	1.08 (0.77–1.5)	1.16 (0.97–1.39)	0.94 (0.6–1.47)	1.19 (0.97–1.47)	1.27 (0.75–2.14)

Significant odds ratios and 95% confidence interval only in 1 group (vaccinated or unvaccinated) are shown in boldface.
*$P \leq 0.05$.
†$P \leq 0.005$.

The protective effect of breast-feeding on pneumococcal colonization in the unvaccinated group was not seen, but remained associated with increased pneumococcal colonization in the vaccinated group. All participants were divided into healthy children and children having URI within 2 weeks for analysis as *S. pneumoniae* colonization among these 2 populations may be different (Tables 2 and 3). With multivariate analysis, PCV7 decreased the association between pneumococcal carriage and having 1 sibling and history of AOM in children, regardless of URI (Table 3). Breast-feeding increased a higher risk of pneumococcal carriage mainly in vaccinated children with URI (Table 3). Further analysis on VT and nonvaccine serotype (NVT) carriage showed that breast-feeding significantly increased NVT pneumococcal carriage in vaccinated children with URI ($P < 0.05$) (data not shown). However, the overall pneumococcal carriage rate was lower in vaccinated group compared with that in unvaccinated group among children with URI (15.5 % versus 20.3 %; $P = 0.01$).

Children having received the PCV7 vaccine had a significantly lower rate of carrying VT ($P < 0.001$) and NVT ($P = 0.008$) pneumococci than the unvaccinated children (Table 4). Only 4 isolates were identified as serotype 6C. One isolate was identified as serotype 6D. The vaccinated group had a higher rate of carrying serotype 15B ($P = 0.006$) and a lower rate of carrying serotype 6A ($P = 0.02$). The vaccinated group did not have a higher rate of carrying serotype 19A, 3, 6C and 6D. Among the children exposed to household smoking, those who received the PCV7 vaccine had a significantly lower rate of VT pneumococcal carriage ($P < 0.001$) (Table 5).

DISCUSSION

The primary finding of this study was that PCV7 vaccination decreased the association between pneumococcal carriage and older age, 1 sibling in a family, history of AOM and household exposure. In the United States where PCV7 has been used routinely since 2000, the presence of a sibling, history of URI and child-care attendance remain common predictors of pneumococcal carriage.[14] Similarly, number of siblings ≥2, history of URI and child-care attendance were strong factors associated with pneumococcal carriage in children, regardless of vaccination in our study.

Age and the presence of siblings influence the carriage of *S. pneumoniae* in children.[14] In the current study, we found that PCV7 vaccination decreases the risk for pneumococcal carriage that is associated with older age, and the presence of a sibling. *S. pneumoniae* is one of the most common pathogens that cause AOM, and there is a direct relationship between the frequency of colonization and episodes of AOM.[15] Studies have shown that PCV7 immunization reduces the rate of nasopharyngeal carriage of vaccine-type *S. pneumoniae*, reduces the incidence of AOM and alters the microbiology of AOM.[16,17] In the current study, we observed that the history of AOM was a risk factor for *S. pneumoniae* carriage among unvaccinated children, whereas the history of AOM was not associated with *S. pneumoniae* carriage among vaccinated children. The reason for this disparity is likely that PCV7 vaccination reduced nasopharyngeal colonization of *S. pneumoniae* and decreased the occurrence of AOM among the vaccinated children. This finding-implicated *S. pneumoniae* is an important pathogen causing AOM in children in Taiwan.

Cigarette smoking impairs mucociliary clearance and induces inflammation of the respiratory epithelium predisposing individuals to bacterial adherence and colonization.[18–20] Studies have shown that children exposed to household smoking have a higher rate of *S. pneumoniae* carriage.[21–23] Likewise, our study observed that household exposure to smoking was significantly associated with pneumococcal carriage among unvaccinated children. Among vaccinated children, exposure to smoking was not associated with a higher rate of pneumococcal carriage than children not exposed to household smoking. For the first time, we have demonstrated that PCV7 vaccination can decrease the influence of exposure to smoking for *S. pneumoniae* carriage among children, which may further reduce pneumococcal transmission and pneumococcal disease in adults as a result of smoking exposure.

Breast-feeding has been shown to be protective against respiratory tract infection and invasive pneumococcal disease.[24,25] However, the association between breast-feeding and pneumococcal carriage was inconclusive.[26–28] In this study, we found breast-feeding significantly increased the risk of NVT pneumococcal carriage, mainly in vaccinated children with URI. Pneumococcal colonization is higher during URI than during health.[29] In vaccinated children with URI, NVT pneumococci should increase to occupy the niche. The reason for the association between breast-feeding and NVT pneumococcal carriage is not clear. Further well-designed, longitudinal studies to control socioeconomic factors, survey adult carriage and investigate the interaction between *S. pneumoniae* and other bacterial species that commonly colonize the nasopharynx among the vaccinated group with breast-feeding can be carried out.

TABLE 4. Serotype Distribution Between Unvaccinated and Vaccinated Children

	Unvaccinated (n = 7747), % (n)	Vaccinated (n = 1958), % (n)	*P*
Vaccine type	7.4 (576)	4.4 (86)	<0.001
6B	2.4 (189)	1.6 (32)	0.03
19F	2.4 (188)	1.3 (26)	0.003
23F	1.6 (126)	0.8 (16)	0.008
14	0.9 (66)	0.6 (12)	0.29
Others	0.1 (7)	0.1 (1)	1.0
Nonvaccine type	6.1 (474)	4.5 (89)	0.008
15B	0.6 (46)	1.2 (23)	0.006
6A	0.7 (51)	0.2 (2)	0.02
19A	0.2 (17)	0.3 (6)	0.44
3	0.1 (11)	0.1 (1)	0.48
6C	0 (3)	0.1 (1)	1.0
6D	0 (0)	0.1 (1)	0.2
1	0	0	—
5	0	0	—
7F	0	0	—
Others	4.5 (346)	2.8 (54)	0.001

TABLE 5. Serotype Distribution Between Unvaccinated and Vaccinated Children Exposed to Household Smoking

Smoking Exposure	Unvaccinated (n = 3737), % (n)	Vaccinated (n = 809), % (n)	*P*
Vaccine type	8.1 (301)	4.4 (24)	<0.001
19F	2.7 (102)	0.9 (5)	0.001
23F	1.8 (68)	0.7 (4)	0.03
6B	2.4 (88)	1.6 (9)	0.08
14	1.0 (38)	1.1 (6)	1.0
Others	0.1 (5)	0 (0)	0.6
Nonvaccine type	6.7 (251)	5.4 (44)	0.21
15B	0.7 (28)	1.5 (12)	0.06
6A	0.7 (25)	0.2 (2)	0.21
19A	0.2 (9)	0.5 (4)	0.27
Others	5.1 (189)	3.2 (26)	0.03

During the study period, the evolution of vaccine-type serotypes since vaccination does not appear as substantially reduction compared with the evolution of PCV7 vaccination rate: 6% in 2005, then 10%, then back to 5–6% in 2009–2010. The results may be due to low PCV7 vaccination rate. However, an increase in the colonization rates with serotypes 15B (initial) and 19 A (later) was observed. Currently, there are another 2 vaccines available in the market: PCV10 and PCV13. In the study, the rates of serotypes covered by PCV7 and PCV10 were the same because serotypes 1, 5 and 7F were not found. Serotypes 1, 5 and 7F are not common in nasopharyngeal isolates, as well as invasive isolates in Taiwan.[30] Serotypes 6A, 19A and 3 not covered by PCV7, but covered by PCV13 accounted for 4.3%, 1.9% and 1% of total pneumococcal isolates, respectively. Continued surveillance is warranted. Children with selected risk factors that could significantly benefit from vaccination of pneumococcal conjugate vaccine to decrease pneumococcal carriage should aggressively receive the new generation pneumococcal conjugate vaccine with broader serotype coverage to reduce pneumococcal spread and evolution.

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