

PAEDIATRIC HOSPITAL VISIT WITH LABORATORY-CONFIRMED INFLUENZA IMPROVED FAMILY MEMBERS' INFLUENZA VACCINATION

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SUMMARY

Objectives: Vaccination is the primary intervention to prevent influenza infection, yet vaccine uptake remains low among children and other at-risk patients. The aim of the study is to investigate the impact of a paediatric hospital visit with laboratory-confirmed influenza on the influenza vaccination behaviour of participants and their family members in the subsequent influenza season.

Methods: This study compared the influenza vaccination coverage for participants < 18 years of age with a clinical suspicion of influenza in 2017–2018 during a hospital visit, in two subsequent influenza seasons. Data was retrieved from the hospital electronic medical record and a follow-up questionnaire (2018–2019) to ascertain the common reason(s) that families did not vaccinate their children the following year (2018–2019). The children were distributed into positive- (antigen and/or PCR) and negative-influenza groups.

Results: A total of 133 children were enrolled in our study. Participants' mean age was 4.6 years and 74 (55.6%) were males. Overall, 47 (35.3%) had confirmed influenza virus. A significant increase in influenza immunization was found among both positive- and negative-influenza participants between 2017–2018 and 2018–2019 (6.4% vs. 27.7%, $p < 0.001$; 8.1% vs. 29.1%, $p < 0.001$, respectively), as well as among family members of positive-influenza participants – siblings and parents (6.4% vs. 19.6%, $p = 0.003$; 0% vs. 17%, $p < 0.001$, respectively). Common reasons for failure to vaccinate included doubt in vaccine effectiveness, unlikely to get “flu”, busy, and side effects.

Conclusions: Our findings suggest that a paediatric hospital visit with laboratory-confirmed influenza increases vaccine uptake among families. Future studies should aim to evaluate evidence-based interventions to improve influenza vaccine uptake among children.

Key words: influenza, vaccine, vaccination, vaccine effectiveness

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<https://doi.org/10.21101/cejph.a7468>

INTRODUCTION

Influenza virus is associated with substantial hospitalization and morbidity particularly among risk groups including the elderly and young children (1). During the 2017–2018 influenza season in the United States, there were approximately 46,000 hospitalizations and 183 deaths among children < 18 years of age with laboratory-confirmed influenza (2). Vaccination is the primary strategy available to prevent influenza and reduce related complications (3, 4).

The Advisory Committee on Immunization Practices of the CDC recommends a routine annual influenza vaccination for all children > 6 months old who have no contraindications (5). Vaccination is associated with significantly reduced influenza-related deaths and decreased health care visits for children who are vaccinated, as well as their household members (3, 4, 6). Nevertheless, influenza vaccine uptake remains suboptimal in many parts of the world including sentinel sites in the United States (7, 8).

Since 2013, the Israeli Ministry of Health has recommended that children > 6 months receive an annual influenza vaccine and has offered the inactivated influenza vaccination at no cost (9). In the 2017–2018 influenza season, only 18.4% of children under 5 years of age were vaccinated against influenza in Israel (10), compared to 67.8% of children under 5 years in the United States (11). For children 5–18 years in the 2017–2018 influenza season, the rate of vaccine uptake in Israel was 13.9% compared to 54.8% among children in the United States (10, 11).

There are many factors that contribute to parents' decisions to vaccinate children against influenza or not. Psychological barriers surrounding perceived low vaccine effectiveness, perceived low risk of infection and concerns about vaccine safety contribute to vaccine hesitancy, whereas perceived social benefit and social norms promote uptake (12–14). It is important to evaluate parents' perceptions regarding the influenza vaccine to understand reasons for low uptake.

Individuals who have not previously suffered from influenza are less likely to vaccinate in subsequent seasons (14). However, the literature does not examine the effect of an emergency department (ED) visit or hospitalization due to influenza on the next season's vaccine coverage of both the index child and their family members. Therefore, this study aims to investigate the impact of a paediatric hospital visit with laboratory-confirmed influenza on the influenza vaccination behaviour of participants and their family members in the subsequent influenza season, as well as to ascertain the common reasons for failure to vaccinate.

MATERIALS AND METHODS

Children aged 1 month to 18 years who were admitted to the emergency department of Bnai Zion Medical Centre, Israel, during the 2017–2018 influenza season with a clinical suspicion of influenza followed by influenza testing were eligible for inclusion. Recruitment season lasted from 10 October 2017 to 31 March 2018. Children with respiratory symptoms suspicious for influenza were initially tested using the rapid antigen test. If the antigen test was negative, but there was high clinical suspicion, or if a physician specifically requested the more sensitive test, Xpert® Xpress flu/respiratory syncytial virus (RSV) automated multiplex real-time polymerase chain reaction (PCR) test detecting influenza A, influenza B and RSV was conducted. Both antigen and/or PCR influenza testing were utilized to distribute study participants into positive-influenza and negative-influenza groups. Informed consent to participate in the study was obtained by all study participants or their legal representative. Given that some children were hospitalized following their ED visit, we use the term “hospital visit” to capture both.

Hospital electronic medical records of recruited study participants were reviewed for relevant health information and seasonal influenza vaccination status. A structured follow-up questionnaire to collect data on socio-demographic characteristics, seasonal influenza vaccination status of the child and their family members, sources of influenza vaccination recommendations, and reasons for not vaccinating was conducted via telephone one year following the hospital visit. The questionnaire was developed in Hebrew and Arabic by adapting numerous surveys that evaluate factors associated with influenza vaccine hesitancy (12–15) and piloted before administering it to the study population.

In order to be able to detect a 10% or more increase in the vaccination rate in the following year at $p=0.05$, a sample size of 130 was required, assuming a 10% vaccination rate in 2017–2018 and 80% power. Demographic and clinical factors were compared between the positive- and negative-influenza groups using the student t-test or Mann-Whitney test (for length of stay, white blood cells and C-reactive protein) for continuous data and χ^2 test or Fisher's exact test for categorical data, when appropriate. Demographic and clinical data was compared in the same manner between patients who were vaccinated in the subsequent season versus those who were not. Vaccination rate was compared to the age group population rate via binomial test for one sample proportion. The McNemar test was used to compare 2018–2019 vaccination rates to those of 2017–2018. Significance was set at $p<0.05$. All analyses were conducted using IBM SPSS Version 21.0. Principal component analysis (using varimax rotation) was

used to identify underlying components of the questionnaire. The resulting two factors had good internal consistency: demographic characteristics (age of the child, parents and youngest sibling), Cronbach's alpha 0.780; vaccination characteristics (parental education, vaccine status of parents and siblings prior to the child's influenza illness, clinic encouragement to get vaccinated, e.g., treating physician, and post-influenza vaccine status of the child and family), Cronbach's alpha 0.768.

RESULTS

Of the 173 children recruited, 133 completed the follow-up questionnaire, therefore, only 133 participants were finally enrolled for statistical analysis in our study. Participants' mean age was 4.6 years and 74 (55.6%) were males. Overall, 47 (35.3%) had a confirmed influenza virus, the other were influenza negative (64.7%). Among positive participants, 23 (49%) had positive PCR and 31 (66%) had positive antigen tests, seven had both tests positive.

While 130 (97.7%) of participants were up-to-date with their immunization according to the national recommendations schedule, only 10 (7.5%) received an influenza vaccine in 2017–2018 prior to their hospital visit.

There were no statistically significant differences in parental age or education between the positive- and negative-influenza participants, or between the parents of participants vaccinated in 2018–2019 and those not vaccinated (Table 1).

There was a statistically significant increase in the overall number of children immunized against influenza from 2017–2018 to 2018–2019 in both groups (positive-influenza 6.4% vs. 27.7%, $p<0.001$, negative-influenza 8.1% vs. 29.1%, $p<0.001$). The rates of vaccine uptake among participants' family members increased significantly in the positive-influenza group, both for one or more sibling (6.4% vs. 19.6%, $p=0.003$) and for one or more parent (0% vs. 17%, $p<0.001$). No significant increase was observed among the families of negative-influenza children, neither for one or more sibling (25.6% vs. 23.2%, $p>0.99$), nor for one or more parent (17.5% vs. 20.9%, $p>0.99$) (Table 2). Overall, vaccine uptake significantly increased in children under 5 years of age (6.7% vs. 32.2%, $p<0.001$), but not in children aged 5–18 years (Table 3).

The 42 (31.6%) children with chronic diseases were not vaccinated at a significantly higher rate than healthy children in 2017–2018 (9.5% vs. 6.6%, $p=0.55$) or in 2018–2019 (33.3% vs. 26.4%, $p=0.41$). In 2018–2019, 11 more children with chronic diseases were vaccinated while 20 more healthy children were vaccinated, which was not statistically different (28.9% vs. 23.5%, $p=0.52$ respectively).

Among recruited children, 108 (81.2%) were hospitalised. Negative-influenza children were admitted to the hospital at a higher rate than positive-influenza children (88.4 vs. 68.1%, $p<0.004$, respectively). However, a hospital admission did not significantly impact parental decision to vaccinate in the following year, with 80.0% of those who did not vaccinate and 84.2% of those who did vaccinate having been admitted in 2017–2018 ($p=0.63$).

When comparing the source of influenza vaccine recommendation, community physicians versus hospital physicians, we found that physicians in community clinics recommended the vaccine to participants more than hospital doctors (54.9%

Table 1. Comparison of demographic variables between influenza positive and negative study participants (N = 133)

	Positive-influenza children N = 47 n (%)	Negative-influenza children N = 86 n (%)	p-value	OR (95% CI)
Age (years), mean (SD) (min–max)	6.8 (5.3) (0.10–17.00)	3.4 (4.3) (0.02–18.00)	0.001	1.15 (1.07–1.24)
Gender				
Male	24 (51.1)	50 (58.1)	0.43	1.00 (reference)
Female	23 (48.9)	36 (41.9)		0.75 (0.37–1.54)
Mothers age (years), mean (SD) (min–max) N = 130	36.6 (8.1) (23.0–56.0)	33.6 (7.6) (20.0–60.0)	0.04	1.05 (1.00–1.10)
Fathers age (years), mean (SD) (min–max) N = 128	39.4 (7.6) (25.0–56.0)	37.2 (7.5) (20.0–55.0)	0.12	1.04 (0.99–1.09)
Maternal education (N=131)				
None	3 (6.4)	5 (6.0)	0.49	1.53 (0.26–7.73)
High school	33 (70.2)	51 (60.7)		1.65 (0.72–3.86)
Academic	11(23.4)	28 (33.3)		1.00 (reference)
Paternal education (N=129)				
None	2 (4.4)	6 (7.2)	0.19	1.10 (0.13–6.63)
High school	37 (80.4)	54 (65.1)		2.25 (0.89–5.79)
Academic	7 (15.2)	23 (27.7)		1.00 (reference)
Length of stay (days), median (1st Qu–3rd Qu)	2.0 (1.0–3.0)	3.0 (2.0–4.0)	0.001	N/A

Table 2. Vaccination of participants and their family members in 2017–2018 and 2018–2019 (N = 133)

	Positive-influenza children (N = 47)		p-value	Negative-influenza children (N = 86)		p-value
	n (%)	95% CI		n (%)	95% CI	
2017–2018	3 (6.4)	2.2–17.2	0.001	7 (8.1)	4.0–15.9	0.001
2018–2019	13 (27.7)	16.9–41.8		25 (29.1)	20.5–39.4	
Sibling						
2017–2018	3 (6.4)	2.2–17.2	0.003	22 (25.6)	17.5–35.7	> 0.99
2018–2019	9 (19.6)	10.4–32.5		20 (23.2)	15.6–33.2	
Parent						
2017–2018	0 (0.0)	0.0–7.6	0.001	15 (17.4)	10.9–26.8	> 0.99
2018–2019	8 (17.0)	8.9–30.1		18 (20.9)	13.7–30.7	

Table 3. Comparison of vaccine uptake proportions in 2017–2018 and 2018–2019 seasons by age group (N = 133)

Vaccination status		Age 6–59 months		p-value	Age 5–18 years		p-value
		% (n/N)	95% CI		% (n/N)	95% CI	
Influenza positive group	2017–2018	4.8 (1/21)	0.8–22.7	0.08	7.7 (2/26)	2.1–24.1	0.18
	2018–2019	33.3 (7/21)	17.2–54.6		23.1 (6/26)	11.0–42.0	
Influenza negative group	2017–2018	7.2 (5/69)	3.1–15.9	0.004	11.8 (2/17)	3.3–34.3	0.65
	2018–2019	31.9 (22/69)	22.1–43.7		17.6 (3/17)	6.2–41.0	
All	2017–2018	6.7 (6/90)	3.1–13.8	0.001	9.3 (4/43)	3.7–21.6	0.18
	2018–2019	32.2 (29/90)	23.5–42.4		20.9 (9/43)	11.4–35.2	

vs. 33.1%, $p=0.004$, respectively). Moreover, a significantly higher percentage of positive-influenza children were encouraged to vaccinate by the hospital physician (48.9% vs. 24.4%, $p=0.004$). Although, vaccine uptake was not statistically different between positive- and negative-influenza children who received a recommendation in the hospital (39.1% vs. 42.9%, $p=0.80$, respectively). Similarly, of the 19 (40.4%) positive-influenza children who received a recommendation in a community clinic, 10 (52.6%) were subsequently vaccinated, whereas of the 54 (63.5%) negative-influenza children who were encouraged, 21 (38.3%) were subsequently vaccinated ($p=0.30$).

Among participants who did not receive the influenza vaccine in the 2018–2019 season, the most frequent reasons provided by parents were: doubt in the vaccine's effectiveness (42.9%), unlikely to get the "flu" (17.0%), too busy (16.1%), and side effects (15.2%) (Fig. 1). There were no significant differences in the reasons for failure to vaccinate between the positive- and negative-influenza groups ($p>0.05$).

DISCUSSION

In this study, we compared the vaccination coverage and demographic factors between positive-influenza and negative-influenza children during a hospital visit in 2017–2018, examined the family's subsequent influenza vaccine uptake in 2018–2019, and explored factors shaping parental decision-making. Our study is the first in Israel to assess the relationship between a paediatric hospital visit for influenza and subsequent family influenza vaccination uptake.

Despite long-standing worldwide recommendations, many children in Israel remain unvaccinated against seasonal influenza. A study among six hospitals in Israel from 2015–2018 concluded that the influenza vaccine reduced hospitalizations associated with influenza by 54% among children 6 months to 8 years, evidencing the importance of vaccine promotion among this population (16).

We found that there was no significant difference in influenza vaccine uptake in the subsequent influenza season between positive-influenza and negative-influenza participants. Yet, the

siblings and parents of positive-influenza children significantly increased vaccine uptake in the subsequent season. Given that rates of influenza vaccination increased significantly among children with and without influenza, it appears that a hospital visit due to respiratory illness was associated with higher vaccination uptake. Perhaps the high severity of the 2017–2018 influenza season influenced this increase, however, vaccination coverage in Israel in 2018–2019 remained constant at 20% for the total population and 18% for children aged 6–59 months (17).

In this study, we found that physicians at community clinics recommended the influenza vaccination more than hospital physicians, yet recommendations in both medical settings may positively influence the decision to vaccinate. To improve uptake, healthcare providers in community clinics and hospitals must implement evidence-based vaccine communication strategies (18) and increase awareness of the effectiveness and safety of influenza vaccination, particularly for children with chronic conditions (19). Paediatricians play a crucial role in offering a strong recommendation, inquiring about children's vaccination status, and extending invitations and reminders to vaccinate (19).

Influenza vaccination uptake remains low, specifically among young children 6 months through 8 years old getting their flu vaccine for the first time, who are required to have a two-dose vaccine (7). Closing the gap between influenza vaccination recommendations and current vaccination rates in children in Israel requires addressing the factors that shape parents' decision-making (20). Given that coverage for routine childhood vaccinations is over 90% in Israel, parents appear to have different considerations towards the influenza vaccine (21). Our findings are consistent with many studies reporting influenza vaccine refusal stemming from perceived low effectiveness, perceived limited risk of infection, and concerns about vaccine safety (12–15). Social norms also play a large role in the decision to vaccinate (14), thus, given that only 20% of the overall Israeli population received the influenza vaccine in 2017–2018, strategies to improve influenza vaccine uptake in the adult population may lead more parents to decide to vaccinate their children (10, 12).

We found that overall vaccine uptake did not increase among participants aged 5–18 years, despite a hospital visit. Increasing

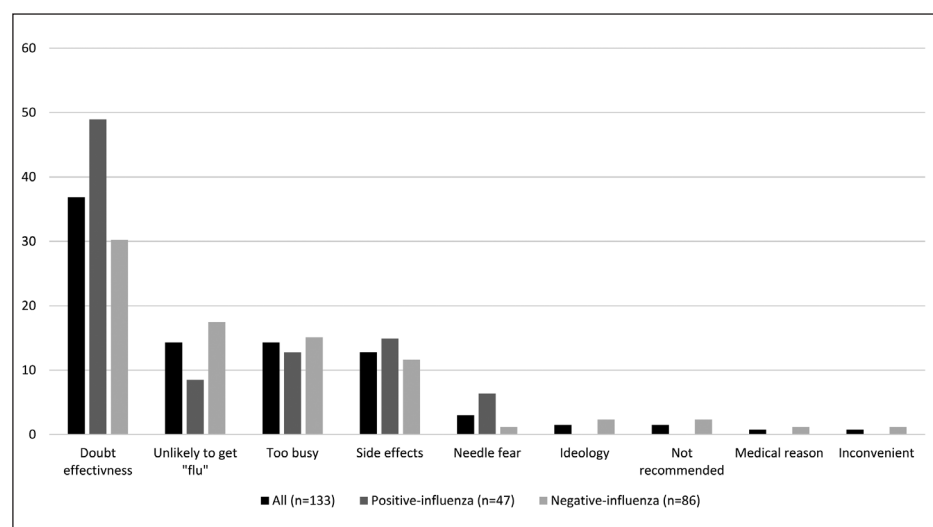


Fig. 1. Reasons for failure to vaccinate against influenza among Israeli children in the 2018–2019 season.

influenza vaccine uptake among adolescents requires targeted outreach efforts different than those aimed at young children. Internet- and texting-based marketing campaigns, as well as school-based interventions, could improve influenza vaccination uptake among adolescents (22). Israel's school-based vaccination programme, which has included the influenza vaccination since 2016, increased coverage among second graders who are typically 7–8 years of age from 13.4–13.9% in previous two years to about 50% in 2017–2018 (10). This indicates that school-based outreach is effective, yet additional outreach should also be implemented (9, 10).

A respiratory hospital visit led to increased influenza vaccination uptake among children, and an influenza-related hospital visit led to increased vaccine uptake among siblings and family members. Coupled with increased awareness campaigns and in-patient interventions, these findings can help to improve influenza vaccination rates among children in Israel, reducing morbidity and mortality among the paediatric population.

This study has some limitations, it was conducted at a single centre in northern Israel, which may not be generalizable nationally. We did not assess parental knowledge of the influenza virus or reasons for choosing to vaccinate. The children with influenza disease were older than the children without influenza disease. Moreover, our study included children < 6 months in 2017–2018, however, they were eligible for vaccination in the subsequent season. Also, family members' vaccination status was based on retrospective self-report, which may have led to a recall bias. However, parents accurately reported their child's previous season vaccination status, as verified with the electronic medical records. Using parental reporting in this study is supported by findings of a previous study that examined the reliability of parental reports in vaccine administration compared to the national immunization registry and found a high sensitivity of up to 97% and a specificity of 75% (23).

CONCLUSIONS

For conclusion, a paediatric hospital visit with laboratory-confirmed influenza did not increase participants' subsequent influenza vaccine coverage relative to a paediatric hospital visit without influenza, yet did increase vaccine uptake among family members. Interventions that promote the importance of annual influenza vaccination, improve healthcare provider communication regarding the influenza vaccine and address parental attitudes must be more widely implemented in Israel. Future studies should aim to evaluate evidence-based interventions to improve influenza vaccine uptake among children.

Conflict of Interests

None declared

Adherence to Ethical Standards

The questionnaire and methodology for this study were approved by the Institutional Review Board (approval number 0167-18 BNZ).

Electronic Supplementary Material

This article contains supplementary material (Study Questionnaire) available at <https://doi.org/10.21101/cejph.a7468>.

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Received May 11, 2022
Accepted in revised form April 22, 2023