

Effectiveness of influenza vaccination in preventing asthma exacerbations in children

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Abstract— Introduction: Bronchial asthma is the most common chronic disease and considered as major public health issue worldwide. Influenza infection can exacerbate asthma symptoms which increase the rate of hospitalization. Influenza infections precipitated about 80 % of asthma exacerbation. Different immunization programs recommended annual influenza vaccination as main prophylactic measure. Most children with asthma did not receive influenza vaccine despite these guidelines. **Purpose:** To determine the efficacy and safety of influenza vaccination in protecting against influenza-related asthma exacerbations among children with asthma in eastern region in Saudi Arabia. **Material and methods:** A prospective comparative cross-sectional study conducted among parents of children between the ages of 6-18 years with asthma in eastern region in Saudi Arabia. Study include Children with asthma whether they received annual influenza vaccination or not. Data collected from the parents by using self-administrated questionnaire. **Results:** Study included 362 asthmatic children of which 132 (36.5%) had received the seasonal influenza vaccine. As for effect of receiving the vaccine, only 21.2% were hospitalized for asthmatic attack after vaccination, 17.4% were hospitalized during last 2 weeks after vaccinations, asthma was controlled among 78% of vaccinated children, and 75% reported that frequency of asthmatic attacks reduced after vaccination. **Conclusion:** Immunization of influenza vaccine in children with asthma was effective and safe in decreasing respiratory illnesses and asthma-related events that leads to exacerbation and hospitalization. However, there is the need for an appropriate influenza vaccination strategy and program targeting high-risk children with a history of asthma in order to increase vaccination coverage.

Keywords— influenza vaccine, asthma control, asthma, children, Saudi Arabia

1. Introduction

Asthma is the most common chronic disease and is one of the leading causes of children's hospital admission. (1) Asthma is considered a major public health issue worldwide. The World Health Organization reported that around 300 million people currently suffering from asthma worldwide, and with current trends rising, it is expected to reach 400 million by 2025. Asthma is the most common chronic disorder among children, ranking among the top 20 conditions for disability-adjusted life years in children worldwide. (2) Prevalence rates of asthma diagnosed by physicians were 4%-33.7 among children in Saudi Arabia. The highest prevalence rates were found in Najran and Al-Hofuf while the lowest were in Abha and Jazan. (3)

Seasonal influenza results in substantial major global morbidity and mortality during winter months each year. In people with asthma despite effective controllers, influenza infection can exacerbate

asthma symptoms, which increase the rate of hospitalization. (4) Influenza infections precipitated about 80 % of asthma exacerbation. (5) The World Health Organization (WHO) and national immunization programs recommend annual influenza vaccination in asthmatic patients as the main prophylactic measure against influenza. (6) Most children with asthma will not receive influenza vaccines despite these guidelines. (7) One of the barriers to compliance is the uncertainty of parents and physicians about the efficacy of influenza vaccination in this population and the importance of immunization in preventing asthma exacerbations. (7) Influenza vaccine prevents influenza infection, subsequent illness, reduces systemic and respiratory illness. Influenza vaccination remains the cornerstone of defense and the evidence consistently shows the efficacy of influenza vaccinations in reducing overall hospitalization days, school absenteeism, and the loss of parental workdays among children at high risk. (8)

We conduct this study to extend our research knowledge regarding the effectiveness of influenza vaccination in prevention of asthma exacerbation. The effectiveness of influenza vaccination is still not well established as many researchers report different outcomes regarding the effectiveness of seasonal influenza vaccination. This study will evaluate the efficacy, effectiveness, and safety of influenza vaccination in protecting children against influenza-related asthma exacerbations and assess the rate of influenza vaccination among children with asthma.

Aim:

Our aim of this study is to investigate whether influenza vaccination in children with asthma is effective to prevent asthma exacerbations provoked by influenza infection. Whether influenza vaccination is more effective than placebo in.

OBJECTIVE:

First: Evaluate the effectiveness of influenza vaccine against influenza infection inducing asthma exacerbation.

Second: Evaluate the effectiveness of influenza vaccine of declining the asthma exacerbation in general.

Third: To assess the rate of influenza vaccination coverage among asthmatic patients.

STUDY METHODOLOGY:

Study design and population:

A comparative cross-sectional study conducted among parents of children between the ages of 6-18 years with asthma in eastern region in Saudi Arabia.

Sample size and sampling strategy:

A sample size equal to 362 participants comparing two groups one group receive vaccination and the other did not receive vaccination. Including children between the age 6- 18 years by responding to an online questionnaire by their parents.

Methodology and Data collection:

The data collected from the parents and caregivers by using self-administrated questionnaire and an informed consent was obtained at the beginning. The questionnaire include the following section sociodemographic characteristics, receiving influenza vaccine or not and by whom advised and why taken or not. Also, the control of asthma was assessed by frequency of salbutamol use or reliever medication, the need for nebulized treatment, and hospitalization over the past 1 and 12 months.

Inclusion criteria:

- Child who is 6-18 years old with asthma and received annual influenza vaccination.
- Child who is 6-18 years old with asthma and not receive annual influenza vaccination.
- Current diagnosis of persistent asthma (mention its criteria)
- Children from eastern region in Saudi Arabia

Exclusion criteria:

Presence of other comorbidities other than asthma that influence the effectiveness of influenza vaccine including: hemoglobinopathies, cardiopulmonary diseases, neurodevelopmental diseases, chronic renal diseases, immunosuppression, autoimmune diseases, endocrinological and metabolic diseases.

Data analysis and statistics:

After data collection, it was modified, coded, and entered them to statistical software IBM SPSS version 22(SPSS, Inc. Chicago, IL). We did the statistical analysis using two tailed tests. We considered results statistically significant when P value less than 0.05. we did descriptive analysis based on frequency and percent distribution for all variables including demographic data, medical and family history, vaccination history, asthma clinical data, and vaccines frequency and effects. We used cross tabulation to test for the distribution of different demographic, clinical, and vaccination data among the study groups (vaccinated vs. non-vaccinated children). We used pearson chi-square test to test for relations significance. We used the exact tests to assess significant association due to small frequencies.

Data Management:

We stored data in a database on a safe computer within encrypted files, and was available only to the research team. Privacy and confidentiality was maintained under all circumstances.

Ethics approval and consent to participate:

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Finance and resource use:

This study is self-funded.

Result:

The study included 362 asthmatic children of which 132 (36.5%) had received the seasonal influenza vaccine (figure 1).

Table 1: Regarding children age 47.7% of the children who were vaccinated (group 1) aged 6-10 years compared to 41.7% of unvaccinated group (group 2) with no statistical significance (P=.076). A 68 (51.5%) of vaccinated children were males compared to 60.9% of unvaccinated children (P=.083). Most

of the child was diagnosed after the age of 5 years among 41.7% of vaccinated group in comparison to 34.3% of unvaccinated children ($P=.223$). As for mother education, university level of education was reported among 39.4% of the vaccinated children compared to 37.4% of unvaccinated group ($P=.0305$).

Table 2: shows clinical distribution of family and medical history among asthmatic children according to influenza vaccination history. Positive family history of asthma was detected among 41.7% of vaccinated children compared to 53% of non-vaccinated group with statistical significance, overall 48.9% of patient have positive family history of asthma. ($P=.037$). 25% of vaccinated children had other co-morbidities especially sickle cell disease (9.1%), and renal disorders (6.1%) in comparison to 15.2% of non-vaccinated group who had sickle cell disease (6.1%), and cardiac disorders (3%) with recorded statistical significance ($P=.005$). 17.4% of children who had the influenza vaccine had history of allergic disorder in comparison to 26.1% of non-vaccinated group ($P=.059$). Eczema was diagnosed among 25% of vaccinated children compared to 23% of the non-vaccinated group ($P=.0674$). Obesity was reported among 15.2% of vaccinated children compared to 17.1% of non-vaccinated children ($P=.340$).

Table 3: Demonstrates distribution of asthmatic attack severity among asthmatic children according to influenza vaccination history. 54.5% of vaccinated children needed ventilator during hospitalization compared to 35.1% of non-vaccinated group ($P=.081$). Daily need for bronchodilators was reported among 49.2% of vaccinated children in comparison to 53.9% of non-vaccinated group ($P=.797$). Also, regular intake of asthma treatment was reported by 76.5% of vaccinated children compared to 58.7% of non-vaccinated group ($P=.001$). Frequent doctor visits were reported among 65.9% of vaccinated group compared to 34.3% of non-vaccinated children ($P=.001$). Also, school absenteeism was reported among 60.6% of vaccinated children compared to 66.1% of non-vaccinated group ($P=.295$).

Table 4: Illustrates distribution of children asthma clinical data among asthmatic children according to influenza vaccination history. As for frequency of asthmatic attacks last year, it was few times among 46.2% of vaccinated children compared to 46.1% of unvaccinated group while 9.6% of vaccinated reported for many times compared to 14.3% of the non-vaccinated group with no statistical significance ($P=.422$). Considering frequency of asthmatic attacks last month, 46.2% of vaccinated children reported frequency of less than once per week compared to 48.3% of non-vaccinated group with no statistical significance ($P=.441$). Asthma control in last 2 weeks, good control to totally controlled were reported by 73.5% of vaccinated group compared to 69.4% of non-vaccinated children ($P=.116$). Asthmatic attacks were frequent at night among 65.9% of vaccinated children compared to 80.9% of non-vaccinated group with statically significant difference ($P=.001$). 68.9% of vaccinated children managed their asthmatic attacks at home in comparison to 74.8% of non-vaccinated group ($P=.230$).

Table 5: Considering vaccine frequency and its effect on asthma among asthmatic children who received the seasonal influenza vaccine, 68.9% of the children were vaccinated for 1-3 months before study time, 5.3% received the vaccine 1 year ago. As for number of received vaccine doses, 72.7% received the vaccine once and 15.9% had the vaccine twice. The most reported reasons behind having the vaccine where doctor advice (45.5%), followed by parents' decision to protect the child against influenza attacks, and to minimize asthmatic attacks (18.2%). As for reasons for not being vaccinated (group 2), feeling of being not important was the most common reason (35.2%) followed by indifference (22.6%), and not advised by the doctors (20.4%). The most reported side effects among vaccinated group were cough

(14.4%), followed by headache, fatigue, and tiredness (11.4% for each) while 41.7% did not had any side effects.

Table 6: As for effect of receiving the vaccine, only 21.2% were hospitalized for asthmatic attack after vaccination, 17.4% were hospitalized during last 2 weeks after vaccinations, asthma was controlled among 78% of vaccinated children, and 75% reported that frequency of asthmatic attacks reduced after vaccination.

Figure 2 shows parents intend to let their child getting an influenza vaccine in the upcoming flu season according to vaccination history. 73.5% of the vaccinated group parents intend to let their child getting an influenza vaccine in the upcoming flu season according to vaccination history compared to 22.6% of the others who never vaccinated their child ($P=.002$).

Discussion:

Influenza infections may cause life-threatening illnesses to a greater extent in young children as compared to adults. In asthmatic patients, despite effective controllers, asthma exacerbations may be triggered by respiratory tract infection. (9)

This study showed that most patients diagnosed after the age of 5 years and a higher level of education of mother had a significant relationship of accepting influenza vaccine assuming it reduces influenza infection rate. Around 17.4% of vaccinate children had history of allergic disorder comparing to 26.1% of non-vaccinated children. No significant difference was found between eczema and asthma in both groups (**Table 2**). This study showed similar finding of high prevalence of coexisting eczema and asthma which was 23.8% compared to the study conducted by Ali H. Ziyab 2017, who reported 20.2% of the coexistence. (10).

Prevalence of obesity was (19.1%) which is in accordance with a retrospective chart review by Neyer et al 2018 identified 188 cases of influenza complications, 29% of them diagnosed with asthma, showed that severe obesity in children and adolescents is not an independent high-risk condition for severe influenza complications. (11). Our study demonstrated high vaccination coverage among patient with other comorbidities, around 15.2% of the asthmatic children have co morbidities other than asthma (**Table 2**).

Vaccinated group reported frequent use of ventilator during the attack and frequent doctor visit before getting the vaccination. The daily need for bronchodilators was almost the same in both group. A possible explanation is that the vaccinated child received the vaccination due to high admission rate and frequent doctor visit in order to prevent asthma exacerbation. Asthmatic children who did not receive influenza vaccination were more likely to miss school. A study done by Bruce A. Ong et al 2009 showed that during asthma exacerbations, children are more likely to be hospitalized, miss school time, and are at higher risk for mortality.(12)

Our study showed that vaccinated children had less frequent attacks compared to the non-vaccinated during the last year as well as during last year as well as last month. Our findings demonstrated that vaccinated children experienced less attacks than non-vaccinated that emphasis the effectiveness of influenza vaccine. This study showed that most of the vaccinated children experienced good to total

control of their asthma during the last 2 weeks compared to non-vaccinated. We found a significance that vaccinated child experience less night symptoms in comparison to non-vaccinated. Furthermore, non-vaccinated children managed most of their attacks at home compared to vaccinated children in which they need hospitalization. (**Table 4**)

Most of the vaccinated asthmatic children receive the influenza vaccination in the last 1-3 months and most of them received only one dose (**Table 5**). Because the analysis focused on a single vaccination season the effectiveness of the vaccine assessed based on the outcomes of last month.

The main reason of parental refusal of influenza vaccine was no recommendations were provided by their doctor, our finding is similar to a study conducted by A. Kaya et al 2016.(13) So, the doctor's opinion about flu vaccination is significantly associated with the parent's decision. While others reported that fearing of possible side effects and some of children has egg allergy. In recent years some vaccinations, such as the influenza vaccine are perceived as unsafe and unnecessary by a growing number of persons (14) and anti-vaccination ideas have spread over time with the contribution of misleading Internet sites and television programs. Overall influenza vaccination coverage among asthmatic child was very low.

Regarding the safety of vaccine, near half of vaccinated children 41.7% not experience any symptoms and the remaining of them had flue like symptoms fatiguability, tiredness and cough (**Table 5**). Overall, influenza vaccine appeared to be safe and well-tolerated in most of the patients.

Study showed that vaccinated group had significantly reduced hospitalization rate and rate of asthma attacks was lower in the vaccinated group. Furthermore, Asthma was well controlled during the last month in vaccinated group. (**Table 6**) A study done by C Christy et al 2004 goes against our finding which showed that the vaccinated group had a significantly increased risk of asthma related clinic visits and ED visits. (15) On a another hand, a study conducted by Charoen Jaiwong et al 2015 2015 showed similar results study showed that vaccinated children had significantly decrease acute respiratory tract illnesses, asthma exacerbations, ER visits and bronchodilator usage. Also, they found that the duration of hospitalizations reduced in the vaccinated group. (5) Also, Our results were comparable with a recent systematic review and meta-analysis by Vasileiou E et al 2017, which showed similar results in which influenza vaccine prevented 59%–78% of asthma attacks leading to emergency visits and/or hospitalizations. For persons with asthma, influenza vaccination may be effective in both reducing influenza infection and asthma attacks. (16) Vaccinated children were more adhere to the treatment which can provide another reason for the good control of asthma. This study suggests influenza vaccination is associated with fewer asthma exacerbations. This results provides evidence supporting the current public health recommendations for routine influenza vaccination of asthmatic children.

All over the hospitalization rate of vaccinated children was dramatically decreased as well as the frequency of asthmatic attacks were reduced. As a result of decreasing the rate of hospitalization and frequency of attack that was reflecting on having well-controlled asthma and low burden on the country and family. Almost all of the parents are planning to give their children influenza vaccine in the next season due to the good outcomes that experienced. (**Figure 2**) All of these findings supporting the purpose of this study that influenza vaccine has good efficacy and safety among asthmatic children.

There are some limitations in this study, the study designed as cross-sectional that there was no prospective follow-up with our subjects. In addition, small sample size may have insufficient power to

detect other relationships between influenza vaccination and other outcomes of interest. We acknowledge that it is possible that a portion of asthma exacerbations was attributable to causes other than influenza infection such as other viral infections. More detailed studies would be necessary to further understand these relationships. Because some number of both vaccinated and unvaccinated children may have factors other than influenza as a cause for their exacerbation, these children could reasonably be expected to be afforded no protection by the vaccine and require hospitalization. Although a potential limitation of our study is that it was conducted during only one influenza season with just one vaccine, the results are consistent with those obtained in a large prospective study. Lastly, it should be noted that in such a heterogeneous disease, many other factors such as individual immune response to infection, level of asthma severity, and level of symptom control all of these factors could influence children with a respiratory tract infection to develop a severe exacerbation leading to hospitalization. Therefore, it is possible that children who received the vaccine were afforded some level of protection, but not enough to prevent the hospitalization if the child had enough factors present to lead to a severe exacerbation.

Hence, the question remains whether or not it is worth the effort to promote vaccination of all asthmatic children. Therefore, to justify routine influenza vaccination in asthmatic children, we strongly recommend that randomized clinical trials studies to be carried out to assess the clinical effectiveness as well as the cost-effectiveness of influenza vaccination in children with asthma.

3. Conclusion

Our study showed that influenza vaccine immunization is beneficial for children with asthma as it can prevent acute respiratory tract infections, decrease asthma exacerbations and hospitalizations. To maximize influenza immunization in the high-risk population, including asthmatic patients, an annual, well-organized, computerized multi-component strategy should be introduced to increase the current low vaccine uptake in people with asthma. Further evaluation of the relationship between influenza vaccination and pediatric asthma exacerbations through the use of a large prospective study that tests all children with asthma exacerbations for influenza infection during the winter months is recommended.

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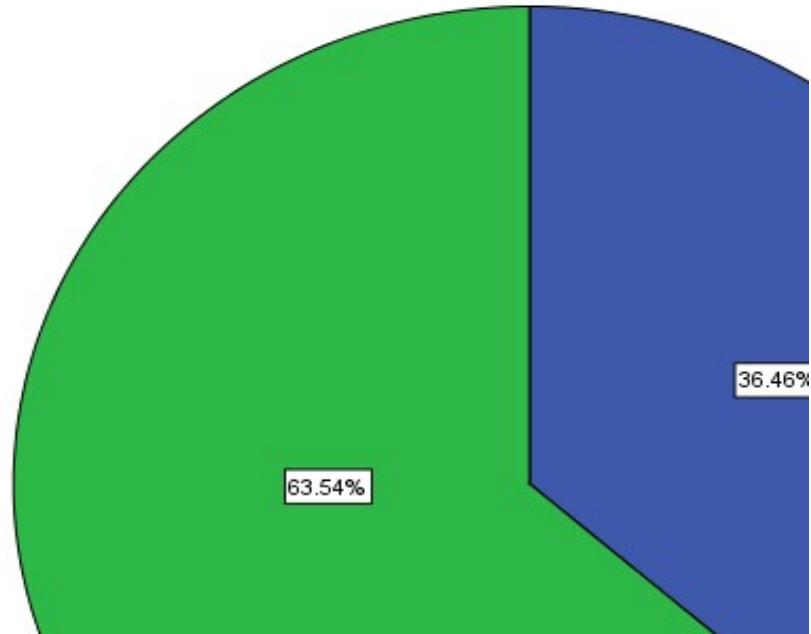


Figure 1. Prevalence of having seasonal influenza vaccine among asthmatic children in Eastern region, Saudi Arabia

Table 1. Demographic data of the asthmatic children according to influenza vaccination history

Personal data	Total		Child had influenza vaccine				P-value
			Yes		No		
	No	%	No	%	No	%	
Age in years							
Total (6-18)	362						
<i>6-10</i>	159	43.9%	63	47.7%	96	41.7%	.076
<i>11-14</i>	89	24.6%	37	28.0%	52	22.6%	
<i>15-18</i>	114	31.5%	32	24.2%	82	35.7%	
Gender							
Total	362						
<i>Male</i>	208	57.5%	68	51.5%	140	60.9%	.083
<i>Female</i>	154	42.5%	64	48.5%	90	39.1%	
Age of first diagnosis of asthma							
<i>First year</i>	80	22.1%	22	16.7%	58	25.2%	.223
<i>2nd - 3rd year</i>	72	19.9%	25	18.9%	47	20.4%	

<i>4th - 5th year</i>	76	21.0%	30	22.7%	46	20.0%	
<i>After 5th year</i>	134	37.0%	55	41.7%	79	34.3%	
Mother education							
<i>Below secondary</i>	58	16.0%	16	12.1%	42	18.3%	.305
<i>Secondary</i>	166	45.9%	64	48.5%	102	44.3%	
<i>University/ above</i>	138	38.1%	52	39.4%	86	37.4%	
Monthly income							
<i>< 5000 SR</i>	79	21.8%	30	22.7%	49	21.3%	
<i>5000-10000 SR</i>	154	42.5%	52	39.4%	102	44.3%	.074
<i>11000-20000 SR</i>	93	25.7%	30	22.7%	63	27.4%	
<i>> 20000 SR</i>	36	9.9%	20	15.2%	16	7.0%	
<i>P: Pearson χ^2 test</i>							

Table 2. Distribution of medical and family history among asthmatic children according to influenza vaccination history

Family & medical history	Total		Child had influenza vaccine				P-value
			Yes		No		
	No	%	No	%	No	%	
Family history of asthma							
<i>Yes</i>	177	48.9%	55	41.7%	122	53.0%	.037*
<i>No</i>	185	51.1%	77	58.3%	108	47.0%	
Child had other type of allergy							
<i>Yes</i>	83	22.9%	23	17.4%	60	26.1%	.059
<i>No</i>	279	77.1%	109	82.6%	170	73.9%	
Child had eczema							.674

<i>One time daily</i>	101	27.9%	33	25.0%	68	29.6%	
<i>> 1 time daily</i>	88	24.3%	32	24.2%	56	24.3%	
<i>> 2 times weekly</i>	51	14.1%	20	15.2%	31	13.5%	
<i>< 2 times weekly</i>	122	33.7%	47	35.6%	75	32.6%	
Child had asthma treatment regularly							
<i>Yes</i>	236	65.2%	101	76.5%	135	58.7%	.001*
<i>No</i>	126	34.8%	31	23.5%	95	41.3%	
Frequent doctor visits							
<i>Yes</i>	166	45.9%	87	65.9%	79	34.3%	.001*
<i>No</i>	196	54.1%	45	34.1%	151	65.7%	
School absenteeism due to asthma							
<i>Yes</i>	232	64.1%	80	60.6%	152	66.1%	.295
<i>No</i>	130	35.9%	52	39.4%	78	33.9%	

P: Pearson X^2 test

** $P < 0.05$ (significant)*

Table 4. Distribution of children asthma clinical data among asthmatic children according to influenza vaccination history

Asthma clinical data after vaccination	Total		Child had influenza vaccine				
			Yes		No		
	No	%	No	%	No	%	
Frequency of asthmatic attacks last year							
<i>Few times</i>	167	46.1%	61	46.2%	106	46.1%	.422
<i>Seasonal</i>	149	41.2%	58	43.9%	91	39.6%	
<i>Many times</i>	46	12.7%	13	9.8%	33	14.3%	
Frequency of asthmatic attacks last month							.441

<i>< 1 time / week</i>	172	47.5%	61	46.2%	111	48.3%	
<i>1-2 times /week</i>	127	35.1%	43	32.6%	84	36.5%	
<i>3-4 times / week</i>	39	10.8%	16	12.1%	23	10.0%	
<i>5-7 times / week</i>	24	6.6%	12	9.1%	12	5.2%	
Asthma control dusting last 2 weeks							
<i>Totally uncontrolled</i>	16	4.4%	6	4.5%	10	4.3%	
<i>Poor control</i>	87	24.0%	29	22.0%	58	25.2%	.116
<i>Good control</i>	112	30.9%	33	25.0%	79	34.3%	
<i>Totally controlled</i>	147	40.6%	64	48.5%	83	36.1%	
Most reported time for asthmatic attacks							
<i>At morning</i>	89	24.6%	45	34.1%	44	19.1%	.001*
<i>At night</i>	273	75.4%	87	65.9%	186	80.9%	
Setting for management of asthmatic attacks							
<i>At home</i>	263	72.7%	91	68.9%	172	74.8%	.230
<i>At hospital</i>	99	27.3%	41	31.1%	58	25.2%	

P: Pearson χ^2 test

* $P < 0.05$ (significant)

Table 5. Distribution of vaccine frequency among asthmatic children in Eastern region, Saudi Arabia

Vaccine frequency and its effect	No (132)	%
Duration since having the vaccine		
<i>1-3 months</i>	91	68.9%
<i>3-6 months</i>	10	7.6%
<i>6-9 months</i>	18	13.6%
<i>9-12 months</i>	6	4.5%
<i>> 12 months</i>	7	5.3%
Number of received vaccine doses		
<i>Once</i>	96	72.7%
<i>2 times</i>	21	15.9%
<i>3 times</i>	13	9.8%
<i>4+</i>	2	1.5%

Reasons of having the vaccine (n=132)		
<i>Doctors advise</i>	60	45.5%
<i>My decision for child sake</i>	39	29.5%
<i>To minimize asthmatic attacks</i>	24	18.2%
<i>Social media effect</i>	9	6.8%
Reason for not having the vaccine (n=230)		
<i>Not important</i>	81	35.2%
<i>Not advised by physicians</i>	47	20.4%
<i>Don't care (forget)</i>	52	22.6%
<i>Fear of side effects</i>	39	17.0%
<i>Child has egg allergy</i>	11	4.8%
Side effects after having the vaccine		
<i>None</i>	55	41.7%
<i>Fever</i>	9	6.8%
<i>Sore throat</i>	13	9.8%
<i>Joint and bone ache</i>	6	4.5%
<i>Headache</i>	15	11.4%
<i>Cough</i>	19	14.4%
<i>Fatigue and tiredness</i>	15	11.4%

Table 6: Effect of vaccine on the clinical course of asthma of asthma among asthmatic children in Eastern region, Saudi Arabia:

Vaccine effect	No (132)	%
Hospitalization for asthmatic attack after vaccination		
<i>Yes</i>	28	21.2%
<i>No</i>	104	78.8%
Hospitalization during last month after vaccinations		
<i>Yes</i>	23	17.4%
<i>No</i>	109	82.6%
Asthma controlled well during last month after vaccination		
<i>Yes</i>	103	78.0%
<i>No</i>	29	22.0%
Child use respirometer after vaccination		
<i>Yes</i>	50	37.9%
<i>No</i>	82	62.1%
Frequency of asthmatic attacks reduced after vaccination		
<i>Yes</i>	99	75.0%
<i>No</i>	33	25.0%

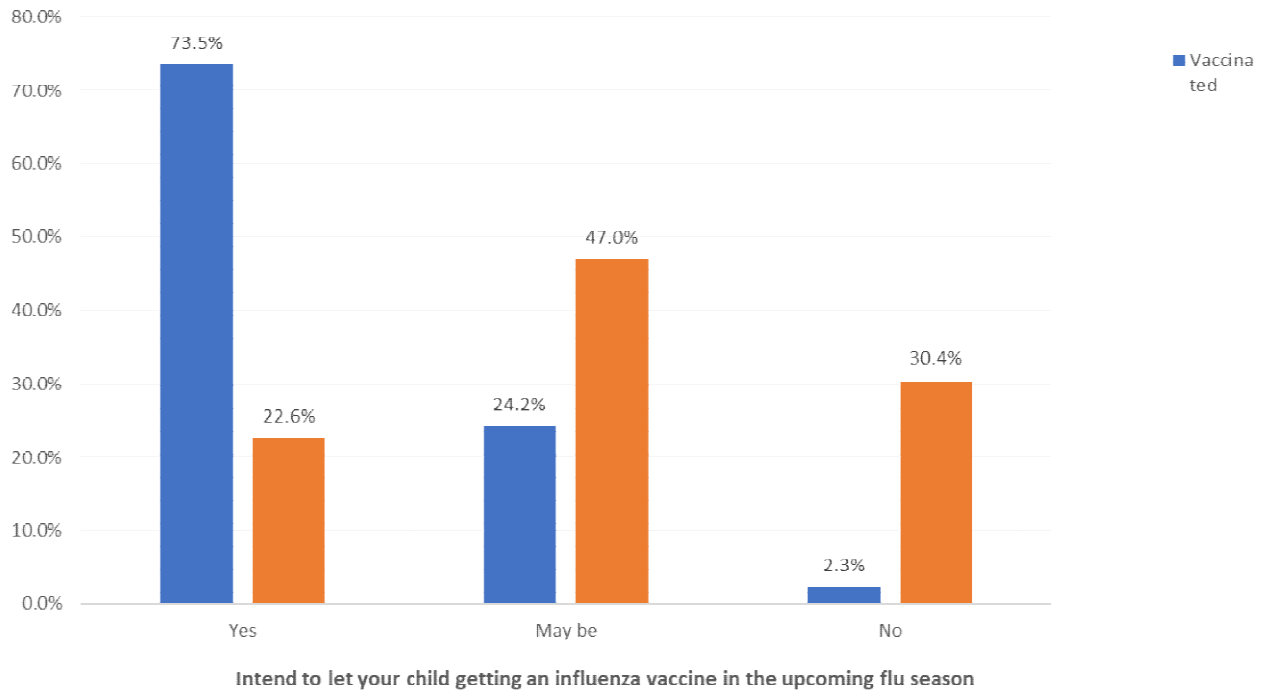


Figure 2. Parent's intention to let their child getting an influenza vaccine in the upcoming flu season according to vaccination history



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