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Routine immunizations during pregnancy, doctors' compliance and patient hesitancy: A two stage study on vaccination uptake



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ABSTRACT

Objective: To evaluate the compliance of healthcare professionals with national guidelines and the hesitancy of pregnant women to be immunized against influenza and pertussis.

Study design: We conducted a two-stage study. The first stage of our study included all women (n = 197) who gave birth in Alexandra Maternity Hospital in Athens, Greece during a 3-month period (April–June) 2018. They completed a questionnaire regarding their immunization status against influenza and pertussis. If pertinent, they detailed their reasons for not getting immunized. During the second stage of our study, we actively recommended both vaccines to the outpatients of Alexandra Maternity Hospital (n = 195) between September 2018 and January 2019.

Results: The majority of women (92.9%) were immunized during childhood according to Greek national immunization guidelines. Almost all the women (98%) stated that they will vaccinate their children. More than half (65.5%) responded that they would have been vaccinated during pregnancy if their doctor had recommended it, but in 73.6% of cases, their doctor did not do so. Only a small proportion of women (16.2%) were immunized against influenza during pregnancy while none of them (0%) received the Tdap vaccine. In most cases (65%), study participants stated they were not immunized because their doctor did not recommend vaccination. Additionally, 9.7% of participants feared possible side effects. During the second stage of our study 94.9% out of 195 women agreed to get vaccinated against influenza and 92.8% against pertussis.

Conclusions: It is apparent that the compliance with the immunization guidelines during pregnancy is surprisingly low. However, health professionals appear to be reluctant to recommend vaccination during pregnancy. Women appear to trust their doctors and usually agree with their recommendations.

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Introduction

Maternal immunization is beneficial for both the mother and the fetus. All women must be vaccinated according to the recommended adult immunization schedule. Completion of the immunization before pregnancy is ideal, however, vaccination

during pregnancy is considered in cases where the benefits of immunization outweigh the risks to the mother and the fetus. Consequently, where pregnant women are concerned, there are three categories of vaccines. Those that are safe and routinely recommended during pregnancy, those that are administered before possible exposure to certain pathogens, and those that must be avoided during pregnancy. Guidelines regarding immunizations during pregnancy have been issued by many scientific bodies such as the American College of Obstetricians and Gynecologists (ACOG) and the Advisory Committee on Immunization Practices (ACIP) of the Center for Disease Control (CDC) etc [1,2]. These guidelines recommend that all women must be vaccinated against Influenza during flu season and Tetanus, Diphtheria and Pertussis (Tdap) between weeks 27 and 36 of each pregnancy.

Seasonal Influenza during pregnancy has been associated with higher rates of hospitalization, intensive care unit admissions and death [3–5]. Pregnant women do not have higher infection rates

Abbreviations: ACOG, American College of Obstetricians and Gynecologists; ACIP, Advisory Committee on Immunization Practices; CDC, Center for Disease Control; Tdap, Tetanus, Diphtheria, Acellular Pertussis; WHO, World Health Organization; MHRA, Medicines and Healthcare products Regulatory Agency; UK, United Kingdom; Tdap-IPV, Tetanus, Diphtheria, acellular Pertussis, Inactivated polio vaccine.

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than the general population, however the course of the disease is more severe during pregnancy [6], especially if antiviral treatment is delayed. Concerning fetuses, maternal infection has been associated with increased incidence of congenital anomalies and congenital heart defects [7]. Moreover, influenza infection during pregnancy has been associated with first trimester miscarriages, preterm delivery, emergency cesarean delivery and low birth weight [3,4,8–10]. Fortunately, vaccination against influenza during pregnancy is effective in reducing maternal infection [11,12] and hospitalization [13], along with improving pregnancy outcomes [12,14,15] and providing passive protection for the infant [16,17]. Fear for fetal malformations is considered to be low as the vaccine does not seem to increase the risk compared to the incidence in the general population [18]. Moreover, the safety of the vaccine has been well established for both the mother and the fetus [11,19–24]. Hence, CDC recommends immunization of all pregnant women regardless of gestational age [25]. As far as breastfeeding women are concerned, inactivated influenza vaccines can be safely administered during lactation [26].

Pertussis, commonly known as “whooping cough”, is a respiratory illness caused by the gram-negative aerobic coccobacillus *Bordetella Pertussis*. Pertussis is highly contagious infecting approximately one third of exposed individuals [27,28]. Vaccination against pertussis during pregnancy is recommended by many scientific bodies worldwide such as the World Health Organization (WHO) and the American College of Obstetricians and Gynecologist (ACOG) [29–31]. The safety of administering the pertussis vaccination in pregnancy was demonstrated by a study of 20,074 pregnant women conducted by the Medicines and Healthcare products Regulatory Agency (MHRA) in the United Kingdom (UK) [32]. Maternal immunization with the Tdap-IPV vaccine used in the UK was highly effective in protecting infants from pertussis [32,33]. Protection of the neonate is achieved via placental transfer of maternal antibodies to the fetus [34]. The optimal timing of immunization for maximum antibody transfer to the fetus is between 27 and 36 weeks of pregnancy [35], if immunization with Td is complete. In case of unknown or incomplete immunization against tetanus, diphtheria and pertussis, pregnant women should complete the series of 3 vaccinations, replacing one of Td doses with the Tdap [31]. Earlier administration is considered when a woman requires a tetanus booster for wound management or lives in an area with a pertussis epidemic [31]. Vaccination with the Tdap is safe during lactation [26]. Postpartum inoculation of women who have not received Tdap during pregnancy is recommended, as maternal antibodies are secreted in breast milk [26]. However, antibody response may not be sufficiently rapid to provide adequate protection for the infant [36].

The objective of our study is to evaluate the compliance of healthcare professionals with the Greek national guidelines and the hesitancy of pregnant women to be vaccinated against influenza and pertussis.

Materials and methods

The first, retrospective stage of our study was conducted in the First Department of Obstetrics and Gynecology of Alexandra Hospital, in Athens, Greece, between April and June 2018. All women who gave birth in Alexandra Hospital within that timeframe were included in the study. The timeframe was chosen in order to ensure the women would be pregnant during flu season. After delivery, the participating women completed a written questionnaire with multiple choice questions regarding their immunization status. They were asked whether they had been immunized as children, whether they were going to vaccinate their children, whether they would agree to get vaccinated during pregnancy if their doctor had recommended it, which vaccines

their doctor recommended during pregnancy. If the women chose not to be vaccinated, they were asked about the reasons.

During the second, prospective stage of our study we actively recommended vaccination of pregnant women through the outpatient clinic of our hospital. This stage of our study took place between September 2018 and January 2019. Flu vaccination commenced as soon as the vaccine was commercially available in October 2018. All pregnant women were counseled regarding their need to be immunized. Both the benefits of immunization and the possible side effects were thoroughly explained by their physician. The vaccines were prescribed and administered by our staff in order to ensure validity. Women with allergies to the ingredients of the vaccines or egg and women with serious infections at the time of their visit were not included in the study. All women were offered immunization against the flu regardless of the gestational age at the time of the visit. Tdap was offered to the same population between 27 and 36 weeks of gestation.

The results were analyzed via IBM SPSS Statistics for Windows, Version 25.0. We calculated the frequencies of the women's responses to the questions asked and the 95% confidence intervals (CI 95%). The critical alpha level to achieve statistical significance was 0.05. Chi-squared was used to compare immunization frequencies for the flu and Tdap vaccines, before and after our intervention. The mean age between the two groups was compared with independent samples *t*-test.

Results

Of all the women who took part in the first part of the study ($n = 197$), 92.89% (89.3–96.5) indicated that they had been immunized during childhood according to the national guidelines on children's immunization while 3.0% (0.6–5.4) had not been immunized and 4.1% (1.3–6.9) did not know (Table 1). Similarly, 98% (96–99.9) of the women declared that they planned to immunize their children according to the national immunization schedule while 0.5% (–0.5 – 1.5) would not and 1% (–0.4 – 2.4) did not know (Table 1). When asked if they would have been vaccinated during pregnancy if their doctor had recommended it, 65.5% (58.8–72.2) replied positively, 21.8% (16–27.6) were not certain and 12.2% (7.6–16.8) replied that they would not (Table 1). Furthermore, 24.9% (18.8–31) of women responded that their doctor had recommended immunization during pregnancy, while 73.6% (67.4–79.8) held that their doctors had not mentioned it, 1.5% (–0.2–3.2) did not respond (Table 1). All doctors that suggested vaccination during pregnancy recommended the vaccine against influenza. Only one of them recommended the Tdap vaccine. A significant proportion (65%, 52–78.6) of the women who had been prompted by their doctors to get the flu vaccine followed through (Table 1). The percentage of women who were immunized during pregnancy against influenza was 16.2% (11–21.4) while none of them received the pertussis vaccine during pregnancy (0%) (Table 1). Of those who did not receive the vaccine, 65.5% (58.8–72.1) indicated that they had not been informed by their physician, 7.6% (3.9–11.3) responded that they were concerned about possible side effects on the fetus, 2% (0.1–4) were worried about possible side effects on themselves and 6.1% (2.8–9.4) replied “for other reasons” (Table 1).

During the second stage of our study, both vaccines were actively recommended to the pregnant women who visited Alexandra's Hospital Outpatient Clinic ($n = 195$). Of the 195 women who were approached by researchers, 185 agreed to be vaccinated against the flu (94.9%, 91.8–98) and 181 agreed to be vaccinated with one dose of the Tdap-IPV (92.8%, 89.1–96.5) (Table 1).

The comparison of the two groups of women (before and after our intervention) revealed that there was a statistically significant difference in vaccination percentages both for the flu and Tdap vaccines ($p < 0.001$) (Table 2). The mean age of pregnant women did not differ significantly between the two groups ($p = 0.2867$) (Table 2).

Table 1
Questionnaire regarding immunization status of pregnant women before and after an intervention.

Question	Answer	Frequency	Percent	CI 95%
Maternal immunization during childhood	YES	183	92.9	89.3 – 96.5
	NO	6	3.0	0.6 – 5.4
	DO NOT KNOW	8	4.1	1.3 – 6.9
	Total	197	100.0	
Maternal intention to vaccinate their children	NO ANSWER	1	.5	–0.5 – 1.5
	YES	193	98.0	96 – 99.9
	NO	1	.5	–0.5 – 1.5
	DO NOT KNOW	2	1.0	–0.4 – 2.4
	Total	197	100.0	
Would you get immunized during pregnancy if your doctor recommended it?	NO ANSWER	1	.5	–0.5 – 1.5
	YES	129	65.5	58.8 – 72.2
	NO	24	12.2	7.6 – 16.8
	DO NOT KNOW	43	21.8	16 – 27.6
	Total	197	100.0	
Did your doctor recommend any vaccines during pregnancy?	YES	49	24.9	18.8 – 31
	NO	145	73.6	67.4 – 79.8
	DO NOT KNOW	3	1.5	–0.2 – 3.2
	Total	197	100.0	
Which vaccine was recommended to you during pregnancy?	NON	146	74.1	67.9 – 80.3
	FLU VACCINE	48	24.4	18.3 – 30.5
	FLU AND Tdap VACCINES	1	.5	–0.5 – 1.5
	OTHER	2	1.0	–0.4 – 2.4
	Total	197	100.0	
Did you get vaccinated during pregnancy?	YES	32	16.2	11 – 21.4
	NO	164	83.2	77.9 – 88.5
	DO NOT KNOW	1	.5	–0.5 – 1.5
	Total	197	100.0	
Which vaccine did you receive during pregnancy?	NONE	162	82.2	76.8 – 87.6
	FLU VACCINE	32	16.2	11 – 21.4
	Tdap	0	0	0
	OTHER	3	1.5	–0.2 – 3.2
	Total	197	100.0	
Question	Answer	Frequency	Percent	CI 95%
Vaccination against the flu	NO	10	5.1	2 – 8.2
	YES	185	94.9	91.8 – 98
	Total	195	100.0	
Vaccination with Tdap	NO	14	7.2	3.5 – 10.9
	YES	181	92.8	89.1 – 96.5
	Total	195	100.0	

Discussion

Our findings underscore the high acceptance rate of children's vaccinations among the Greek population. Nearly all participating women had been vaccinated during their childhoods (92.9%) and an even higher percentage were willing to vaccinate their own

children (98%) (Table 1). This can be attributed both to the persistence of pediatricians in recommending vaccines, and the strict state policy regarding children's immunization. On the other hand, it is disappointing that the percentage of women who were immunized during pregnancy against influenza was only 16.2% and immunization against pertussis was virtually nonexistent in our

Table 2
Comparison of the groups before and after the intervention.

		Vaccination Status		Total	
		No	Yes		
Vaccination with the Tdap / Tdap IPV	Before the intervention	197	0	197	
	After the intervention	14	181	195	
	Total	211	181	392	
	Pearson Chi-Square	Value	df	Asymptotic Significance (2-sided)	
		245.157 ^a	1	.000	
Vaccination against the flu	Before the intervention	165	32	197	
	After the intervention	10	185	195	
	Total	175	217	392	
	Pearson Chi-Square	Value	df	Asymptotic Significance (2-sided)	
		245.157 ^a	1	.000	
Age	Before the intervention	N	Minimum	Maximum	Mean
	After the intervention	197	16	49	32.49
		195	21	46	33.0667
	Independent group t-test	t-statistic	Degrees of freedom	Two-tailed probability	
		1.067	390	0.2867	

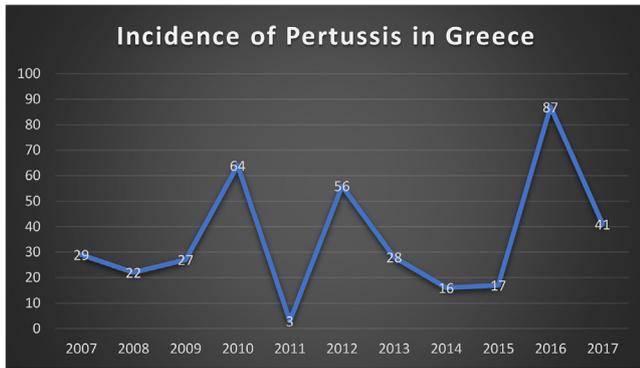


Fig. 1. Pertussis incidence in Greece in the last 11 years [38].

study (0%) (Table 1). Despite the relatively small number of women included in our study, the fact that immunization of pregnant women against pertussis has been seriously neglected is apparent. Only one of the 34 participants' physicians recommended Tdap. Finally, the impressive increase in vaccination rates in the second stage of our study (94.9% and 92.8 for the flu and Tdap vaccines, respectively), highlights the importance of proper patient consultation by their obstetrician.

The interpretation of these results shows the sensitive role of healthcare professionals regarding the enforcement of vaccination recommendations. Patients may be skeptical regarding the use of vaccines, especially considering the media attention around the anti-vaccine movement and the rumors regarding autism. However, patients appear to have faith in their physicians' opinions. On the other hand, skepticism among healthcare professionals regarding the value of immunization during pregnancy or otherwise is unacceptable. The physicians who do not recommend the routine immunizations during pregnancy may be held accountable both legally and scientifically.

The current dearth of pregnant women being vaccinated against pertussis becomes even more worrisome when considering the epidemiology of pertussis in Greece. Pertussis cases are on the rise in the last decade both in the United States of America [37] and in Europe [38]. In 2016, 48,446 new cases of pertussis were reported in Europe resulting in 26 deaths [38]. Pertussis incidence in Greece is rising as 87 cases were reported in 2016 (Fig. 1), 64.4% of which were infants less than one year old [38]. 73.1% of deaths from pertussis in Europe were infants, while Greece reported one death from pertussis which was an infant as well. Incidence of pertussis is rising in the less than one-year old group, with 3270 reported cases in Europe and 56 cases in Greece [38]. It is important to point out that while in Europe 6.75% of cases concern infants, in Greece 64.37% of cases concern infants [38]. The second important point is that 71.4% of the reported cases of pertussis in neonates in Greece concerns neonates who have not been vaccinated [38]. Considering the high percentage of vaccination coverage of children in Greece, it is reasonable to assume that the majority of these cases occur before the initiation of vaccination during the first 6 weeks of life, when the infant is protected passively by the antibodies it has received from its mother. Hence, immunizing pregnant women in Greece against pertussis has the potential to minimize the incidence of pertussis in the most susceptible part of the population.

Our study has limitations. For instance, the written questionnaire that was used in the first stage of the study was based on women's recollections of their childhood immunization status and their physicians' suggestions rather than formal documentation of these variables. This could have an impact on the precision of our estimate regarding the vaccine uptake during women's childhood

and doctors' recommendations for immunization during pregnancy. However, as the percentages of both these variables are overwhelming, we doubt that this could significantly alter our results. Furthermore, we did not make a direct comparison of the socio-demographic characteristics of the pre and post intervention groups (apart from age) before comparing vaccine uptake in the two groups. However, we would not anticipate any significant differences between the two groups as all women were recruited sequentially from the outpatient clinic of our hospital within a limited time frame. As for the strengths of our study, despite the small sample size, the differences in vaccine uptake are statistically significant. Hence, it is our belief that we can safely assume that consulting pregnant women regarding the need for vaccination during pregnancy is the determining factor in increasing vaccine uptake.

Conclusions

It is evident that increasing the rate of vaccination during pregnancy is entirely up to the physicians. Despite the anti-vaccination movement and the rumors surrounding immunization, it appears that women have confidence in the opinions of healthcare professionals. Hence, it is the responsibility of the caregivers to promote routine immunization during pregnancy. The increasing reports of pertussis outbreaks worldwide as well as the increased incidence of flu complications during pregnancy reinforce the necessity of immediate action. The adoption of national guidelines for vaccination during pregnancy in accordance with the recommendations of scientific bodies such as ACOG, CDC and others may help encourage physicians to follow the right path and lead to better perinatal outcomes.

Declaration of Competing Interest

The authors have no conflict of interest to declare.

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