Kozłowska Marta, Zaniuk Marcin, Wójcik Piotr, Rogowska Monika, Tomczyk Jan. Safety of anti-influenza vaccination during pregnancy. Journal of Education, Health and Sport. 2020;10(9):664-670. eISSN 2391-8306. DOI http://dx.doi.org/10.12775/JEHS.2020.10.09.080
https://apcz.umk.pl/czasopisma/index.php/JEHS/article/view/JEHS.2020.10.09.080
https://zenodo.org/record/4047725

The journal has had 5 points in Ministry of Science and Higher Education parametric evaluation. § 8. 2) and § 12. 1. 2) 22.02.2019.

Received: 20.09.2020. Revised: 24.09.2020. Accepted: 24.09.2020.

Safety of anti-influenza vaccination during pregnancy

Marta Kozłowska
ORCID iD https://orcid.org/0000-0001-7791-508X
Affiliation Medical University of Lublin
Country Poland
Bio Statement —
Principal contact for editorial correspondence.

Marcin Zaniuk
ORCID iD https://orcid.org/0000-0003-4643-0594
Affiliation Medical University of Lublin
Country Poland
Bio Statement —

Piotr Wójcik
ORCID iD https://orcid.org/0000-0002-9078-3701
Affiliation Medical University of Lublin
Country Poland
Bio Statement —

Monika Rogowska
ORCID iD https://orcid.org/0000-0002-9617-7307
Affiliation Medical University of Lublin
Country Poland
Bio Statement —

Jan Tomczyk
ORCID iD https://orcid.org/0000-0003-1034-3819
Affiliation Medical University of Lublin
Country Poland
Bio Statement —

Abstract

Flu, while seemingly harmless, is actually much more dangerous. These include ubiquity, high contagiousness and the possibility of serious complications. The flu is associated with serious complications, especially in pregnancy. It includes increased rates of miscarriage, stillbirths, neonatal deaths, premature births, and decreased birth weight. The flu vaccine is an effective and safe preventive measure.

According to WHO anti-flu vaccine is recommended to women in any trimester of the pregnancy. Research shows that vaccination during pregnancy is safe and does not cause foetal or maternal complications. Moreover, maternal antibodies cross the placenta and can protect infant against influenza up to 6 months.

The most common reasons for refusing vaccines by pregnant women are hesitations and fear of adverse pregnancy outcome. Due to that it is important to increase the society's awareness about flu complications during pregnancy as well for women and for children. Successful immunization of the society requires improving its vaccination behaviour and can benefit in reducing frequency of adverse pregnancy outcomes.

Key words: flu vaccination, pregnancy, influenza, safety.

1. Introduction

Vaccination has recently become a controversial topic among society. Decreasing levels of trust to healthcare workers leads to hesitations and fear. One of the most known issues is vaccination safety, especially during pregnancy [1].

Pregnant women, because of being immunocompromised can have more disease complications, affecting as well themselves and their unborn children [2] One of common illnesses that could lead to some serious complications and could be avoided thanks to vaccination is flu. However, there are a lot of hesitations about safety of vaccination during pregnancy.

According to WHO flu vaccination is recommended in any trimester of pregnancy, because pregnant women have been included as a group with a high-risk of serious diseases [3].

To achieve successful immunization of the population, it is required for the population to have confidence about vaccines and believe in their safety and their crucial meaning in society's health.

Studies show that pregnant women are mostly aware of contagiousness of flu, however only 34,6% believe that flu during pregnancy can have more serious complications, than flu in non-pregnant women. Only 5,8% of them know that flu vaccination is recommended during pregnancy and only 14,2% believe that flu vaccination is safe during pregnancy. [4]

Regular vaccination is important because influenza is a significant cause of morbidity and mortality in the society. Moreover prevention by vaccination is a cost-effective and minimally disruptive method of flu prevention. The influenza vaccine is also unique among vaccines because it requires annual readministration and providing brief immunity.

Influenza is associated with serious complications, especially during pregnancy. It includes increased rates of miscarriage, stillbirths, neonatal deaths, preterm deliveries and

reduced birth weight. Pregnant women are also at increased risk of influenza complications, including hospitalization and admission to intensive care units [5]. Pregnant women also are more likely to experience severe pneumonia when infected with the seasonal influenza. Furthermore, historical data from previous pandemics (in 1918 and 1957) indicate an excess of deaths in pregnancy and an increased risk of premature delivery and stillbirth [6].

Increasing society's awareness of vaccinations' safety and benefits related to regular vaccination is important to achieve a satisfying level of society's immunization. Moreover, increasing the number of women accepting vaccination against flu during pregnancy could help reduce the amount of post-influenza complications as well among women and their children.

2. Research

A prospective cohort study conducted by Ohfuji et al. in the 2013/2014 flu season included 10 330 pregnant women. There were 6387 unvaccinated women and 3943 were vaccinated. Adverse birth outcomes were reported for 641 (10%) of the unvaccinated pregnant women and 356 (9%) of the vaccinated pregnant women. The results showed that vaccination during pregnancy is not related to the risk of adverse birth outcomes. Moreover, vaccination during the first or second trimester was not related to adverse birth outcomes, whereas vaccination during the third trimester was associated with a decreased risk of adverse birth outcomes [7].

The WHO Strategic Advisory Group of Experts stated that pregnant women should be the highest priority group for countries that are developing vaccination programmes for seasonal flu. Studies have shown that mortality associated with seasonal flu may be greater during pregnancy. Moreover, during the 2009 H1N1 pandemic increased maternal and foetal mortality was documented.
Research showed that the inactivated influenza vaccine (IIV) is immunogenic in pregnant women and produced antibodies cross the placenta and can offer protection to the infant for 6 months. Antibody transfer is the most efficient in the third trimester of pregnancy, however a clinical trial in Nepal showed that there was no difference in infant:mother ratio of antibodies or maternal seroconversion based on the time of vaccination.
Maternal antibodies passed to the infant protects infants against laboratory-confirmed influenza with 30-63% efficacy.
Safety of the vaccination is an important issue for society. A large number of studies have demonstrated that vaccination against flu during pregnancy is safe for both mother and infant. There is no increase in the risk of pregnancy complications, including pre-eclampsia and chorioamnionitis or adverse foetal outcomes, including stillbirth, preterm birth and foetal growth restriction [8].

Pregnant women are five times more likely to be hospitalised as a result of flu because of physiological and immunological changes that occur during pregnancy. Between 2009 and 2012, one in eleven maternal deaths were related to flu, making it an important public health concern. The metaanalysis by Parsons J. showed that there is a serious concern regarding knowledge about influenza and its complications among pregnant women. Although a programme of free vaccination was started in the UK in 2010, the uptake of the flu vaccine is still suboptimal. Interventions taken to improve society's awareness about vaccination showed no effect on intention to vaccinate and no effect on vaccination behaviour. The qualitative study showed a number of beliefs that were based on incorrect knowledge and may have had a negative effect on vaccination behaviour. The most important beliefs were that pregnancy

did not increase the severity of flu, that flu does not have any severe consequences either on pregnant women or their unborn baby, and that the vaccination involved the administering of a live vaccine [9].

In 2015-2016, during the annual vaccination season, a prospective observational study related to influenza vaccination in pregnant women was conducted.
In the first phase of the study, in 10 primary care clinics midwives were trained on influenza vaccination advice and established a registry to collect study variables. Research variables included sociodemographic data and obstetric characteristics of pregnant women, especially: health department (TV / EC), country of origin (Spain / not Spain); age (≤24, 25-29, 30-34, 35-39, ≥40); previous pregnancies (1, 2, ≥3); number of abortions (0, 1, 2), current trimester of pregnancy (1T, 2T, 3T), month of midwife's visit (October, November, December, January); and the intention or predisposition to vaccinate with an influenza vaccine.

After the selection of pregnant women who complied with the criteria of the study, the second phase of the study was started. This included a telephone interview, during which variable data were collected regarding their knowledge, sources of information, location and the reason for accepting or rejecting the vaccine.

Of the 1,017 pregnant women who received telephone advice on influenza vaccination, 77.4% said they would be vaccinated. Following the recommendation, 61.6% of the declared pregnant women were vaccinated.
Moreover, a telephone interview with 67.2% of the women (n = 683) showed that the majority of women were aware of the vaccination recommendations and indicated the clinic and the midwife as the main source of information.

		Vaccinated	Non-Vaccinated	Total	CI (95%)
Overall (n/%)		(421/61.6%)	(262/38.4%)	(683/100%)	
Have you Heard about the flu vaccine? *					
Yes		402 (64.2%)	224 (35.8%)	626 (91.7%)	(89.5–93.8)
No		19 (33.3%)	38 (66.7%)	57 (8.3%)	(1.1–15.4)
Where did you obtain information about the flu vaccine during your pregnancy?					
Family–Friends		50 (60.2%)	33 (39.8%)	83 (12.2%)	(5.1–19.2)
Internet *		27 (74.4%)	12 (25.6%)	39 (5.7%)	(0.0–12.9)
Private Office		42 (80.8%)	10 (19.2%)	52 (7.6%)	(0.4–14.8)
Hospital		9 (81.8%)	2 (18.2%)	11 (1.6%)	(0.0–9.0)
Health Center		15 (75.0%)	5 (25.0%)	20 (2.9%)	(0.0–10.2)
No information *		285 (61.0%)	182 (39.0%)	467 (68.4%)	(64.2–72.6)
Media (press, radio, TV)		18 (36.7%)	31 (63.3%)	49 (7.2%)	(0.0–14.4)
		Vaccinated	Non-Vaccinated	Total	CI (95%)
Has anyone recommended vaccination to you? *					
Yes		409 (64.9%)	221 (35.1%)	630 (92.2%)	(90.1–94.3)
No		12 (22.6%)	41 (77.4%)	53 (7.8%)	(0.5–15.0)
Who	Family Doctor	31 (70.5%)	13 (29.5%)	44 (6.4%)	(0.0–13.6)
	Midwife *	391 (64.7%)	213 (35.1%)	604 (88.4%)	(85.8–90.9)
	Nurse	0 (0.0%)	1 (100%)	1 (0.1%)	(0.0–6.3)
	Gynecologist	6 (75.0%)	2 (25.0%)	8 (1.2%)	(0.0–8.7)
	Family/Friend	9 (42.9%)	12 (57.1%)	21 (3.1%)	(0.0–1.4)
	No one *	12 (23.1%)	40 (76.9%)	52 (7.6%)	(0.3–14.8)

* Statistically significant differences between the vaccinated and non-vaccinated ($p < 0.05$).

Table 1. Distribution of frequencies and percentages in women surveyed on the knowledge and sources of information about flu vaccine [10].

The main reason that pregnant women refused the flu vaccine was fear of advert effects and not being previously vaccinated, which accounts for more than half of the reasons put forth for its rejection. [10]

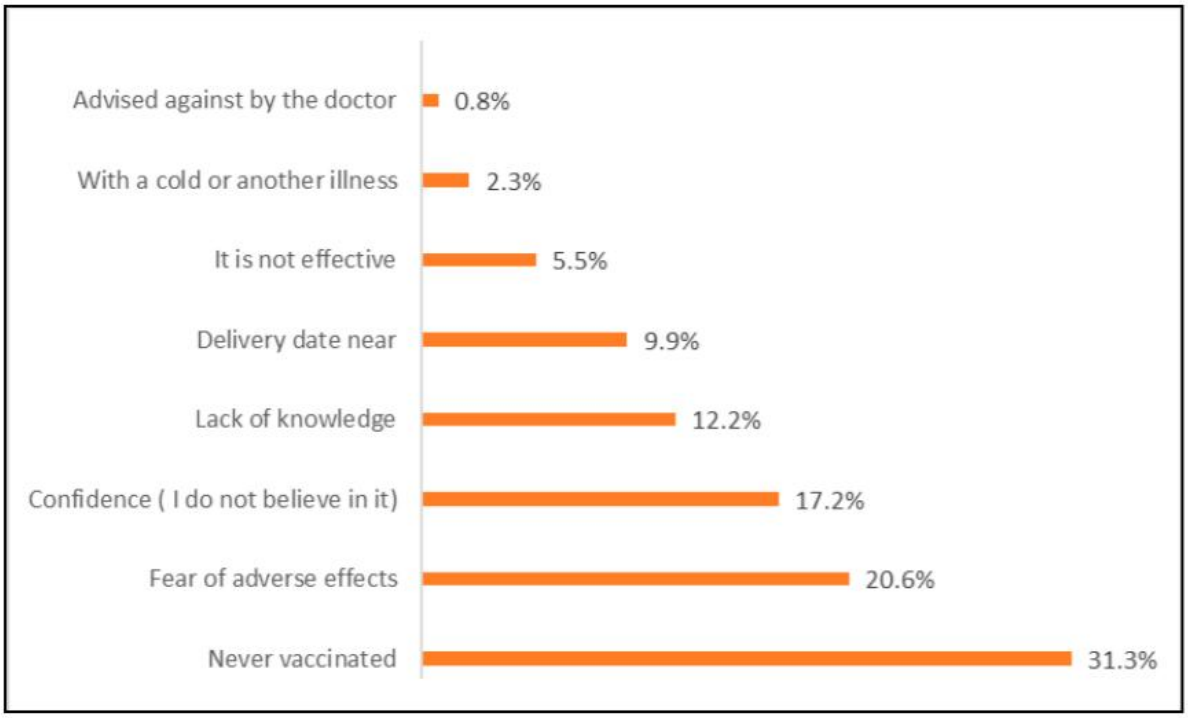

Figure 1. Reasons provided for not vaccinating [10].

In 2016-2018, Singh M. et al. conducted a retrospective study to evaluate the flu vaccine in pregnant women and infants up to 6 months of age. 346 pregnant women participated in the study, 58 of whom were unvaccinated and 288 vaccinated, including 117 receiving the vaccine in the first trimester. During pregnancy, the majority of vaccinated women did not show flu symptoms, comparing the results with the unvaccinated group is 92% vs 70.7%.

Similar results were observed after delivery, and a greater number of infants remained asymptomatic in the vaccinated group compared to the unvaccinated group (69.3% vs 25.9%). In addition, there were fewer premature deliveries in the vaccinated group compared to the unvaccinated group (8.6% vs 15.5%).

Studies have shown that influenza vaccination in pregnant women, regardless of the trimester, protects the mother and child up to 6 months of age from contracting seasonal flu without significant side effects [11].

3. Summary

Pregnant women are the group that is more likely to suffer from post-influenza complications. According to that, WHO recommends anti-flu vaccination in any trimester of the pregnancy. They are also five more times likely to be hospitalised because of the complications, including severe pneumonia.

Although that, most of the women have concerns about the safety of vaccination during pregnancy and not have enough knowledge about the flu and its complications. The main reason for refusing the vaccination was fear of adverse foetal outcomes or pregnancy

complications. Other reasons for refusing the vaccination are: lack of knowledge about increased severity of the influenza during pregnancy, lack of knowledge about post-flu complications and believe that anti-flu vaccine is live instead of inactivated.

Contrary to pregnant women's hesitations, a large number of researches showed that flu vaccination is safe during all trimesters of pregnancy. It does not increase the risk of complications including pre-eclampsia and chorioamnionitis or adverse foetal outcomes, including stillbirth, preterm birth and foetal growth restriction.

Moreover, the vaccination in any trimester leads to seroconversion and transferring antibodies through the placenta, which results in protecting an infant against flu up to 6 month of its life.

Anti-flu vaccine is effective and immunogenic in pregnant women. Vaccinated women did not show flu-like symptoms, when unvaccinated women show those symptoms more often (92 vs 70,7%). Anti-influenza vaccine is also beneficial for infants. Those, whose mothers were vaccinated did not have any flu symptoms more often, then those whose mothers were not vaccinated. Moreover, there were less premature deliveries in the group of vaccinated women and the anti-flu vaccination did not cause any significant complications regardless of the trimester.

It is crucial to increase society's awareness about vaccination and its positive effects on public health. Some interventions, such as educational programmes should be introduced to increase the level of knowledge about vaccines and in effect, to reduce the fear and hesitations among pregnant women.

References:

1. Sweeney JF The eroding trust between patients and physicians; Medical Economics; 2018
2. Parsons J, Atherton H How effective are digital interventions in increasing flu vaccination amongst pregnant women? A systematic review protocol. Syst Rev 9, 117 (2020). https://doi.org/10.1186/s13643-020-01372-z
3. World Health Organization. Vaccine Position Papers (November 2012). Available online: https://www.who. int/wer/2012/wer8747.pdf?ua=1 (accessed on 20 October 2018).
4. Maurici M, Dugo V, Zaratti L, Paulon L, Pellegrini MG, Baiocco E, Rizzo G, Franco E (2016) Knowledge and attitude of pregnant women toward flu vaccination: a cross-sectional survey, The Journal of Maternal-Fetal & Neonatal Medicine, 29:19, 3147-p3150, DOI: 10.3109/14767058.2015.1118033
5. Prospero E Galmozzi S, Paris V, Felici G, Barbadoro P, D'Alleva A, Zocco G, Ciavattini A; Factors influencing refusing of flu vaccination among pregnant women in Italy: Healthcare workers' role; Influenza and other respiratory viruses; 2018
6. Elliott JE, Pregnancy and Pandemic Flu, Clinical Infectious Diseases, Volume 50, Issue 5, 1 March 2010, Pages 691–692, https://doi.org/10.1086/650461
7. Satoko Ohfuji et al; Safety of influenza vaccination on adverse birth outcomes among pregnant women: A prospective cohort study in Japan; International Journal of Infectious Diseases; Volume 93, April 2020, Pages 68-76
8. Sulivan GS, Price OH, Regan AK; Burden, effectiveness and safety of influenza vaccines in elderly, paediatric and pregnant populations; Therapeutic Advances in Vaccines and Immunotherapy; https://doi.org/10.1177/2515135519826481
9. Parsons J Changing risk and efficacy appraisals for flu vaccination amongst pregnant women; EThOS; 2020; https://ethos.bl.uk/OrderDetails.do?uin=uk.bl.ethos.810198

10. Rodríguez-Blanco N, Tuells J (2019). Knowledge and Attitudes about the Flu Vaccine among Pregnant Women in the Valencian Community (Spain). Medicina, 55(8), 467. doi:10.3390/medicina55080467
11. Singh M, Tanvir T, Nagoji D, Madan A, Gattem S, Singh H (2019). Influenza Vaccine ÷ A viable Option to Protect Pregnant women and Infant from Seasonal Flu: a retrospective Hospital based study in India. International Journal of Clinical Practice, e13361. doi:10.1111/ijcp.13361
12. Munoz, FM. Safety of influenza vaccines in pregnant women. Am J Obstet Gynecol 2012; 207: S33–S37
13. Centers for Disease Control and Prevention . Maternal and infant outcomes among severely ill pregnant and postpartum women with 2009 pandemic influenza A (H1N1) – United States, April 2009–August 2010. MMWR Morb Mortal Wkly Rep 2011; 60: 1193–1196.
14. Dabrera, G, Zhao, H, Andrews, N. Effectiveness of seasonal influenza vaccination during pregnancy in preventing influenza infection in infants, England, 2013/14. Euro Surveill 2014; 19: 20959.
15. Fell, D, Platt, R, Lanes, A. Fetal death and preterm birth associated with maternal influenza vaccination: systematic review. BJOG 2015; 122: 17–26.
16. Madhi, SA, Nunes, MC, Cutland, CL. Influenza vaccination of pregnant women and protection of their infants. N Engl J Med 2014; 371: 2340.