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Flu and pertussis vaccination during pregnancy in Geneva during the COVID-19 pandemic: A multicentric, prospective, survey-based study

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ABSTRACT

Objective: To determine pertussis and influenza vaccination coverage during pregnancy among women delivering in all the maternities of Geneva (Switzerland), during the COVID-19 pandemic.
Methods: All women delivering in all the maternity centres of the canton of Geneva from 1st November 2020 to 30th November 2020 (beginning of the flu vaccination season) and from 8th March 2021 to 7th April 2021 (end of the flu vaccination season) had their records checked upon admission to the labour ward regarding pertussis and influenza vaccination during pregnancy. Reasons for non-vaccination were recorded. Univariate and multivariate analyses were done to identify predictors of vaccine uptake.
Results: 951 women delivered in Geneva during the two study periods, of which 950 were included in the study. 86.2% were vaccinated against pertussis, with no significant difference between the study periods (87.5% vs 85% at the beginning and end of the flu vaccination season respectively). 49.8% were vaccinated against influenza, with no significant difference between the study periods (48.8% vs 50.7% beginning and end of the flu vaccination season respectively). The influenza vaccine was 5 times more likely not to be proposed (8.9% vs. 1.7%) and 3 times more likely to be refused (26.6% vs. 8%) than the pertussis vaccine. Main reason for refusal was a lack of maternal desire for both vaccines, but not vaccine fear. Maternal parity ≥ 1 was significantly associated with pertussis vaccine uptake at univariate analysis. Women were significantly more likely to accept the influenza vaccine if they had a university degree or if they did not deliver in a midwife-only run delivery unit in both univariate and multivariate analysis.
Conclusions: In Geneva, most gynaecologists offer pertussis immunization during antenatal care and uptake is high, but more efforts must be done to increase influenza vaccination coverage. Education level impacts maternal flu vaccination uptake, but other social disparities did not.

1. Introduction

In Switzerland, the Federal Office of Public Health (FOPH) recommends immunization during pregnancy against pertussis and influenza. Pertussis, caused by *Bordatella pertussis*, is transmitted by airborne droplets and causes recurrent outbreaks [1,2]. Although pertussis can occur at any age, it is more frequent and severe in infants < 6 months [3]. The rationale of antenatal pertussis immunization is to boost maternal antibody levels in order to maximise the amount transferred to the foetus, thus protecting the newborn by passive immunity during the early vulnerable months, until it generates its own active immunity via childhood vaccination. On the other hand, antenatal influenza immunization is recommended to protect both the mother and the infant, as the virus causing seasonal flu causes more severe disease in pregnant women [4,5], and increases the rate of miscarriage, intrauterine growth restriction (IUGR), prematurity and infant mortality [6].

Antenatal immunization against influenza and pertussis, recommended in Switzerland since 2010 and 2013 respectively, is

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both safe [7–14] and effective. Vaccine effectiveness (VE) for antenatal pertussis immunization is 91–95% [15,16], with maximum neonatal protection obtained when the vaccine is done during 2nd versus 3rd trimester [17,18]. This strategy is more effective than the "cocooning strategy", which is a complimentary strategy for close family members, but on its own only reduces the rate of neonatal pertussis by 6% [19]. VE for influenza antenatal immunization varies between 50 and 80% depending on the studies [20,21].

The current national recommendation is to vaccinate pregnant women against pertussis as of 13 gestational weeks (ideally between 13 and 26 gestational weeks), repeating vaccination at each pregnancy as maternal antibody levels decline significantly 1-year post-immunization. Antenatal influenza immunization is recommended during the entire epidemic season (from October until April) independent of gestational age [22].

Although pertussis and influenza antenatal immunization has been recommended in Switzerland for several years, there is no official data concerning vaccination coverage. Our study was designed at a cantonal level, including all maternity units of Geneva, and its primary objective was to determine the rate of antenatal vaccination coverage. Secondary objectives were to identify reasons for vaccine refusal and maternal predictors associated with vaccine uptake.

2. Methods

This is a multicentric, prospective, survey-based study including women delivering in all five maternities in the canton of Geneva, Switzerland (Hôpitaux Universitaires de Genève [HUG], Clinique des Grangettes [CG], Clinique Générale Beaulieu [CGB], Hôpital de la Tour [HT], Maison de naissance la Roseraie [MNR]) during two periods during the COVID-19 pandemic: from 1st November 2020 to 30th November 2020 (beginning of the flu vaccination season) and from 8th March 2021 to 7th April 2021 (end of flu vaccination season). Inclusion criteria were women $\geq$ 18 years and live birth after 24 gestational weeks (GW). Women with pregnancy termination or miscarriage before 24 GW or unfollowed pregnancies were excluded. All data were recorded anonymously. The National Ethics Committee approved the research protocol (Swiss Ethics Committees on research involving humans).

Upon admission to the labor ward, all patients' records were checked by midwives and/or doctors for vaccination during pregnancy (pertussis and influenza). We recorded: implementation (yes/no); timing of vaccination; reason for non implementation (refusal; not proposed; reason unknown); reasons for refusal (fear of vaccination; not interested; other). We also gathered: maternal age, gestational age at delivery, ethnicity (Caucasian, African, Hispanic, other), gestity, parity, highest level of education (obligatory secondary school, high school [leading to Swiss baccalaureate or equivalent], university degree), residential postal code (France and Switzerland) and type of delivering maternity setting (university hospital, private clinic, midwife-led setting).

Statistical analyses were conducted using R (v.4.1.0). Continuous variables are reported as mean and standard deviation and categorical variables are reported as count and proportion. For women to whom the vaccine was proposed, univariate and multivariate logistic regressions were done to investigate the effect of maternal age, ethnicity, gestity, parity, country of residence (France vs Switzerland), education level and type of delivery maternity unit on vaccine uptake.

We also carried out a subgroup analysis for patients living in Geneva, for which income levels was deduced from their postal code, as per the data published by Vallarta-Robledo et al. [23], who obtained annual median neighborhood household income (only reported for married couples) between 2005 and 2016 from the Cantonal Office of Statistics (OCSTAT). Categories of these revenues (100′000-150′000 CHF/year, 150′000-250′000 CHF/year, $\geq$ 250′000 CHF/year) were compared between patients who accepted the vaccine and those who refused, using a chi-square test.

Comparisons between the 2 studies periods were also done. A p-value < 0.05 was considered significant.

3. Results

A total of 951 women delivered in Geneva during the two study periods. 450 delivered between 1st and 30th November 2020 (HUG: 322; other maternity units: 128 [CG: 56, CGB: 40, HT, 27, MNR: 5]; 501 delivered between 8th March 2021 and 7th April 2021 (HUG: 312; other maternity units: 189 [CG: 61, CGB: 73, HT, 47, MNR: 8]. Data from 1 patient who delivered in CG in November was excluded due to error in data collection. The characteristics of the 950 eligible participants are shown in Table 1. The mean (±standard deviation) maternal age and gestational weeks (GW) at delivery were 32.8 years (±5.1) and 39.3 GW (±1.7). Characteristics of women did not significantly differ between the two study periods, with the exception of the type of delivery unit, with significantly more patients delivering in private clinics in the second study period with respect to the first.

Antenatal vaccination coverage was higher for pertussis (86.2%) than for influenza (49.8%), with no significant differences in coverage between the two study periods. The influenza vaccine was more often not proposed (8.9% vs 1.7%), and more likely to be refused when proposed (26.6% vs 8.0%), than that against pertussis. In both cases, the main reason for vaccine refusal was reported to be a lack of interest from the mother, and not vaccine fear (Table 2). When carried out, pertussis immunization was more often done in the 3rd trimester of pregnancy (63.8%) than in the 2nd one (36.2%). Pertussis vaccine status was missing in one of the questionnaires.

Univariate logistic regression showed that the only independent variable significantly associated with pertussis vaccine uptake was maternal parity. Due to the low proportion of patients refusing this vaccine, no further analysis was carried out (Table 3).

Regarding the influenza vaccine, the level of maternal education and type of delivery setting were significant variables in both univariate and multivariate analysis, with women being significantly more likely to be vaccinated if they had a university degree and if they did not deliver in a midwife-lead delivery setting (Tables 4 and 5). There was no significant difference in influenza vaccine uptake based on income in the subgroup analysis done on patients living in Geneva (Table 4). The income level in patients living in Geneva was not included in the multivariate analysis to avoid multi-collinearity problems with other factors already included in the model (i.e. country of residence).

4. Discussion

To our knowledge, this is the first study in Switzerland to assess antenatal pertussis and influenza vaccination coverage during pregnancy, as well as factors influencing vaccine uptake. The study included all pregnant women delivering in all the maternity settings of the whole canton of Geneva.

We have seen that whereas the majority of women delivering in Geneva received pertussis immunization during pregnancy (86.2%), less than half received the influenza vaccine (49.8%). This disparity was not due to the seasonal nature of flu (one could think that patients delivering in November had little time to receive the vaccine), as no statistical difference was observed in rates of influenza vaccine uptake between the two study periods.

Table 1
Characteristics of women.

	Entire study N = 950 N (%)	November period N = 449, 47.3% N (%)	March-April period N = 501, 52.7% N (%)	p-value (chi^2)
Maternal age (years)				0.316
18–24	44 (4.7)	16 (3.6)	28 (5.7)	
25–34	544 (57.7)	262 (58.5)	282 (57.0)	
≥35	355 (37.6)	170 (37.9)	185 (37.4)	
Missing values	7 (0.7)	1	6	
Ethnicity				0.865
Caucasian	682 (72.1)	323 (72.4)	359 (71.8)	
African	114 (12.1)	56 (12.6)	58 (11.6)	
Hispanic	89 (9.4)	41 (9.2)	48 (9.6)	
Other	61 (6.4)	26 (5.8)	35 (7.0)	
Missing values	4 (0.4)	3	1	
Gestity				0.536
1	316 (33.3)	157 (35.0)	159 (31.7)	
2	315 (33.2)	141 (31.4)	174 (34.7)	
3	166 (17.5)	75 (16.7)	91 (18.2)	
≥4	153 (16.1)	76 (16.9)	77 (15.4)	
Parity				0.984
0	378 (39.8)	178 (39.6)	200 (39.9)	
≥1	572 (60.2)	271 (60.4)	301 (60.1)	
Highest level of education				0.086
University degree	378 (41.6)	173 (41.1)	205 (42.1)	
High school	268 (29.5)	138 (32.8)	130 (26.7)	
Secondary school	262 (28.9)	110 (26.1)	152 (31.2)	
Missing values	42 (4.4)	28	14	
Country of residence				0.606
Switzerland	894 (94.7)	422 (94.2)	472 (95.2)	
France	50 (5.3)	26 (5.8)	24 (4.8)	
Missing values	6 (0.6)	1	5	
Delivery unit				0.009
University hospital	634 (66.7)	322 (71.7)	312 (62.3)	
Private clinic	303 (31.9)	122 (27.2)	181 (36.1)	
Midwife only	13 (1.4)	5 (1.1)	8 (1.6)	

N = number.

Table 2
Vaccination coverage and reason for non vaccination.

Vaccine	Vaccinated N (%)	Non vaccinated N (%)	N total	p-value (chi^2)
Pertussis	**818 (86.2)**	**131 (13.8)**	**949**	
November period	392 (87.5)	56 (12.5)		0.314
March-April period	426 (85.0)	75 (15.0)		
Influenza	**473 (49.8)**	**477 (50.2)**	**950**	
November period	219 (48.8)	230 (51.2)		0.598
March-April period	254 (50.7)	247 (49.3)		
Reason for non vaccination	**N (%)**	**Reason for refusal N (%)**		
Pertussis				
Refusal	76 (8.0)			
Fear		3 (3.9)		
Not interested		37 (48.7)		
Other		36 (47.4)		
Not informed	16 (1.7)			
Unknown reason	39 (4.1)			
Influenza				
Refusal	253 (26.6)			
Fear		10 (4.0)		
Not interested		153 (60.5)		
Other		90 (35.6)		
Not informed	85 (8.9)			
Unknown reason	139 (14.6)			

N = number.

Higher acceptance of pertussis versus influenza vaccine has also been found in studies in England (72.6% vs 44.8% in 2017)[24], Australia (71% vs 61% in 2015)[25] and the USA [26]. One of the reasons for this may be that antenatal pertussis vaccination benefits the newborn, whereas the flu vaccine is often portrayed as protecting the mother [27,28]. Since mothers value protecting their newborn more highly than protecting themselves [29], framing influenza vaccine information towards neonatal benefit may help

Table 3
Pertussis vaccination uptake based on maternal independent variables (univariate analysis).

	Vaccinated N = 818, 91.5% N (%)	Non vaccinated N = 76, 8.5% N (%)	p-value (chi^2)
Age (years)			0.051[1]
18–24	33 (4.1)	7 (9.2)	
25–34	478 (58.4)	36 (47.4)	
≥35	301 (36.7)	32 (42.1)	
Missing values	6 (0.7)	1 (1.3)	
Ethnicity			0.342[1]
Caucasian	584 (71.4)	58 (76.3)	
African	97 (11.9)	11 (14.5)	
Hispanic	81 (9.9)	3 (3.9)	
Other	52 (6.4)	4 (5.3)	
Missing values	4 (0.5)	0	
Gestity			0.054
1	284 (34.7)	18 (23.7)	
2	268 (32.8)	27 (35.5)	
3	137 (16.7)	21 (27.6)	
≥4	129 (15.8)	10 (13.2)	
Parity			0.026
0	339 (41.4)	21 (27.6)	
≥1	479 (58.6)	55 (72.4)	
University degree			0.057
Yes	338 (41.3)	23 (30.3)	
No	443 (54.2)	51 (67.1)	
Missing values	37 (4.5)	2 (2.6)	
Country of residence			0.597[1]
Switzerland	769 (94.0)	70 (92.1)	
France	44 (5.4)	5 (6.6)	
Missing values	5 (0.6)	1 (1.3)	
Delivery setting			0.169[1]
University hospital	546 (66.7)	54 (71.1)	
Private clinic	264 (32.3)	20 (26.3)	
Midwife only	8 (1.0)	2 (2.6)	
Subgroup analysis	**N = 713, 92.2%**	**N = 60, 7.8%**	
Income levels (CHF/year)			0.383[1]
100′000 – 150′000	484 (67.9)	38 (63.3)	
150′000 – 200′000	178 (25.0)	15 (25.0)	
≥200′000	51 (7.2)	7 (11.7)	

N = number, [1] Fisher's exact.

Table 4
Influenza vaccination uptake based on maternal independent variables (univariate analysis).

	Vaccinated N = 473, 65.2% N (%)	Non vaccinated N = 253, 34.8% N (%)	p-value (chi^2)
Age (years)			0.522[1]
18–24	21 (4.5)	15 (5.9)	
25–34	271 (57.8)	151 (59.7)	
≥35	177 (37.7)	87 (34.4)	
Missing values	4	0	
Ethnicity			0.237
Caucasian	333 (70.4)	189 (75.3)	
African	56 (11.8)	32 (12.7)	
Hispanic	50 (10.6)	17 (6.8)	
Other	34 (7.2)	13 (5.2)	
Missing values	0	2	
Gestity			0.054
1	165 (34.9)	79 (31.2)	
2	145 (30.7)	93 (36.8)	
3	76 (16.1)	50 (19.8)	
≥4	87 (18.4)	31 (12.3)	
Parity			0.152
0	205 (43.3)	95 (37.5)	
≥1	268 (56.7)	158 (62.5)	
University degree			0.009
Yes	212 (46.8)	88 (36.2)	
No	241 (53.2)	155 (63.8)	
Missing values	20	10	
Country of residence			0.282
Switzerland	447 (95.1)	234 (92.9)	
France	23 (4.9)	18 (7.1)	
Missing values	3	1	
Delivery unit			0.006[1]
University hospital	310 (65.5)	165 (65.2)	
Private clinic	161 (34.0)	79 (31.2)	
Midwife only	2 (0.4)	9 (3.6)	
Subgroup analysis	**N = 409, 65.5%**	**N = 215, 34.5%**	
Income levels (CHF/year)			0.801
100′000 – 150′000	274 (67.0)	149 (69.3)	
150′000 – 200′000	103 (25.2)	49 (22.8)	
≥200′000	32 (7.8)	17 (7.9)	

N = number, [1] Fisher's exact.

improve its uptake [30]. Other barriers to influenza vaccination is lack of knowledge about the severity of influenza disease [31], concerns regarding the safety for the foetus, its lower effectiveness versus pertussis vaccine [32] and opinions of family and friends [33]. Another factor that may explain the success of pertussis vaccination in Geneva, was the tragic death of a young infant in the near canton of Vaud in 2015 from whooping cough, whose mother was not offered the vaccine during her pregnancy. This case was well publicized by media, informing the public of the severity of the disease and reminding them that it remains a current problem.

This study was carried out during the COVID-19 pandemic, where social distancing and hygiene measures greatly reduced the seasonal flu epidemic in Switzerland [34]. Since these exceptional circumstances could have impacted vaccine uptake, we carried out an analysis to determine antenatal vaccine uptake before the pandemic. In 2019, the rates of antenatal vaccination in the University Hospitals of Geneva, were 84% for pertussis and 37% for flu. Therefore during the Covid-19 pandemic, the rates of antenatal immunization were similar for pertussis but much higher for flu. The latter might indicate that pregnant women and care-givers were more aware about the potential higher risk of pregnancy complications due to two on-going respiratory viral diseases which might have increased both proposal and vaccine uptake. Since the FOPH now also recommends the COVID-19 vaccine in all pregnant women since April 2021 [35], it will be interesting to see if these new guidelines impact the uptake of the other vaccines during

Table 5
Variables affecting influenza vaccination based on multivariate analysis.

Variables	Odds ratio	95% CI
Age - continuous (years)	1.009	0.974 – 1.045
Ethnicity		
Caucasian	reference	
African	0.941	0.572–1.568
Hispanic	2.076	1.121–4.082
Other	1.432	0.730–2.986
Gestity		
1	reference	
2	0.938	0.540 – 1.648
3	0.967	0.511 – 1.849
≥4	1.952	0.970 – 4.004
Parity		
0	reference	
≥1	1.394	0.833 – 2.367
University degree		
No	reference	
Yes	1.637	1.144 – 2.353
Country of residence		
France	reference	
Switzerland	1.495	0.745–2.961
Delivery setting		
University hospital	reference	
Private clinic	0.928	0.640–1.348
Midwife only	0.108	0.016–0.437

CI = confidence interval.
An odds ratio > 1 represents a higher chance of being vaccinated.

antenatal care, as some patients may find having to receive 3 different types of vaccine during pregnancy a little excessive.

Safety concerns have often been cited as a major reason for vaccine rejection [26]. However, our study found that maternal lack of interest was the main cause for vaccine refusal for both vaccines. Unfortunately, specific details regarding the reasons for this lack of interest were not recorded, but 32% of the women that had mentioned a lack of interest for pertussis antenatal immunization cited as a reason having already been immunized in the past. Only a few women that chose "other" as a reason for vaccine rejection cited plans to do so in the post-partum. Although vaccines are systematically offered in the post partum at the University Hospitals in Geneva, no data was collected regarding catch-up immunization after birth, since the questionnaire was filled out in the labor suite and post partum catch-up immunization was not the purpose of the study. In order to protect pregnant woman against flu and the newborn against flu and pertussis, the vaccines should be given during the pregnancy.

Our logistic regression model showed that the maternal education was a significant predictor of influenza vaccine uptake during pregnancy. Higher levels of maternal education have already been associated with vaccine uptake during pregnancy in previous studies [33,36], underlining the importance of providing adapted information to patients, which should begin early in antenatal care to give them enough time to reflect and take an informed decision. The other factor that significantly reduced influenza vaccine uptake in univariate and multivariate analysis was delivering in a midwife-lead setting. Recommendations from healthcare professionals play a key role in encouraging vaccination during pregnancy [37], with women often valuing the recommendations and convictions of midwives over that of other health professionals [38]. However, a Canadian survey found that recommendations for influenza vaccination during pregnancy vary among healthcare members, with midwives (38%) being less likely than physicians (80%) to recommend the influenza vaccine to their patients [39]. Since the information often given to patients on maternal vaccination is often affected by personal perceptions, it is essential to educate all healthcare professionals on current guidelines, especially midwives, who have reported little undergraduate training on maternal vaccination [40]. Maternal age, parity, ethnicity and deprivation level have also been associated with vaccine coverage in other studies [41–43], but were not identified in our study.

Antenatal care providers must do an additional effort to keep in line with current guidelines. Although pertussis acceptance was high, almost two-thirds of women received the vaccine during the third trimester, even though current recommendations favour administration between 13 and 26 GW [22] for optimum antibody transfer [17] and protection of premature neonates [44]. In addition, 10% of women said they had not been proposed the influenza vaccine. As previously mentioned, this may be due to personal perceptions of healthcare providers, but it may also result from the seasonal nature of this vaccine, with caregivers being more likely to forget it, underlining the importance of integrating it into the standard of antenatal care.

The strengths of this study are that it is the first study in Switzerland regarding antenatal vaccine coverage, that it is multicentric and includes a large number of participants. Weaknesses are that data was obtained only in Geneva, and vaccination coverage probably varies greatly within the country. Also, factors that are known to affect vaccine uptake such as history of previous vaccination, number of prenatal care visits, perceived risk of disease, or previous chronic conditions [45,46] were not investigated further and are not incorporated into our analysis.

We did not record data on the type of prenatal care provider (midwife, private doctor, university hospital), thus omitting practice specific recommendations that may influence vaccine uptake, and which are therefore not accounted for in our multivariate analysis. However, the reason why this was omitted is because in Geneva, 80% of the women delivering in the university hospital receive prenatal care in private practices anyways, making the follow-up quite similar. We decided to focus on comparing type of delivery unit, as delivering in the university hospital versus delivering in private hospital/midwife-run unit, added the possibility of further proposing the vaccines at the end of pregnancy (women receiving prenatal care in private practice who plan to deliver in the university hospital are referred to the latter at 36 gestational weeks), as the university hospital has the policy to inform and propose both vaccines among un-vaccinated women regardless if they have been proposed by the treating obstetrician.

Further studies should focus on identifying more precisely the reasons behind the lack of interest in vaccines leading to refusal and the association between type of care provider and vaccine uptake in order to help direct efforts to improve immunization coverage.

5. Conclusion

In Geneva, most women receive pertussis vaccination during antenatal care. More efforts have to be done to increase rates of influenza immunization with strategies directed to better informing both patients and healthcare professionals. Ethnicity and deprivation level have no impact in vaccination uptake in Geneva.

6. Disclosure statement

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BMT has participated in advisory boards of GSK, Effik, Pierre-Favre and Norgine Pharma.

Author contributions

All authors attest they meet the ICMJE criteria for authorship. Conceptualization, MLA, BMT; methodology and data collection, MLA, BMT, AC, AV, MAM, JWG, SJ, AD, SQ; data analysis, CJ, MLA, JRVR; writing - original draft, MLA, BMT; writing - review and editing, AC, CJ, JRVR. All authors have read and agreed to the published version of the manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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