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COVID-19 Vaccine Acceptance during Pregnancy: Lessons Learned and How to Design the Best Strategy to Increase Vaccination Acceptance in the Future

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Abstract

Objective: The present study aimed to study the vaccination acceptance of COVID-19 vaccine in the Hellenic pregnant population and make a high relative analysis of the factors that contribute to decision-making concerning the acceptance of the vaccine during pregnancy. Findings could be leveraged for improving the vaccination communication strategy to pregnant women to increase the vaccination acceptance rate.

Study design: The present study is a prospective cross-sectional study conducted from October 1, 2021 until March 2022 to 800 pregnant women receiving prenatal care at a tertiary University Hospital. Data was gathered through a face-to-face questionnaire and documented via the official vaccination certificate.

Results: The vaccination coverage rate was 53.9%. Employment, older age, and higher monthly income were significantly and positively associated with vaccination ($p<0.001$). Information provided by health professionals ($p=0.004$) and scientific sites ($p=0.028$); sufficient knowledge of vaccines were also positively related to vaccination ($p<0.001$); pediatric vaccination of their children in the family ($p=0.003$); vaccination against influenza during pregnancy (past: $p<0.001$ and present pregnancy: $p<0.001$); and vaccination against pertussis during pregnancy (present pregnancy: $p<0.001$) were also positively associated with vaccination. Intention to vaccinate their children in the future with all recommended vaccines; belief in the safety of the vaccines; and belief that vaccination protects children from serious diseases were positively related with vaccine acceptance. Reduced vaccination hesitancy due to the pandemic; and fear of severity of COVID-19 infection ($p<0.001$ in each case) associated also positively with COVID-19 vaccination.

Conclusion: In conclusion we need to improve the face-to-face communication with pregnant women, focusing more on safety and effectiveness data, sharing information about surveillance programs, using clinical experience from other maternal vaccination, and presenting the benefits from vaccination to the mother and the offspring.

Keywords: Vaccination rate, Pregnancy, Acceptance, Hesitancy, Communication strategy, Maternal immunization, Safety

Introduction

The COVID-19 pandemic caused unpredictable global health, humanitarian, and economic crises, which have had negative impacts on individual, social, political, and economic levels. The public health, work, communication, and commerce sectors have faced unprecedented and difficult challenges leading to the revision of the traditional definition of working, communicating, trading, and production [1-3].

Now, under the burden of 637 million cases and 6.5 million deaths, there is an extensive database to analyze the contribution of vaccination to the mitigation of the COVID-19 pandemic [4]. However, vaccination is a complex issue that

involves the design and manufacturing of vaccines, the demanding approval procedure of marketing authorization, the implementation of appropriate vaccination strategy and finally and possibly most important, the communication strategy that enhance vaccination acceptance and coverage rates. High vaccination coverage of the targeted population –beyond establishing official vaccination recommendations and reimbursement – is critical [5].

Vaccination of pregnant women against COVID-19 represents a scientific challenge of great importance for public health, withholding ethical and scientific issues as well. However, several studies demonstrated that pregnant and lactating women are at increased risk of developing serious illnesses, hospitalizations, admissions to ICUs, respiratory support, and premature birth compared to non-pregnant women [6,7]. WHO has categorized vaccine hesitancy as one of the top ten threats to global health, even before the COVID-19 pandemic [8,9].

International and Hellenic studies demonstrate that there is vaccination hesitancy among pregnant and lactating women, those who wish to conceive and among healthcare workers, indicating the need of improved strategies [10,11]. Understanding the factors that determine vaccination hesitancy is of utmost importance to ensure that appropriate patient information is provided to optimize acceptance rates. The present study aimed to study the vaccination acceptance of COVID-19 vaccine in the Hellenic pregnant population and make a high relative analysis of the factors that contribute to decision-making concerning the acceptance of the vaccine during pregnancy.

Materials and Methods

This was a prospective cross-sectional study to evaluate COVID-19 vaccination acceptance of pregnant women receiving prenatal care at a tertiary University Hospital. The study started in November 2021, when the implementation of the vaccination for pregnant women in Greece launched according to official recommendation and ended in March 2022. The primary study endpoint was the acceptance of the COVID-19 vaccine. Data was gathered through a face-to-face questionnaire and documented via the relevant vaccination certification that was issued automatically from the Greek government platform. Secondary endpoints include the reasoning behind vaccination acceptance and defining the factors with positive impact. Findings could be leveraged to present proposal for improving the vaccination communication strategy to pregnant women to increase the acceptance of COVID-19 vaccination.

A standardized questionnaire with three groups of close-ended questions was used as the research tool, referring to a) sociodemographic features, b) perceptions of vaccination in pregnancy and childhood in general and history of vaccination in pregnancy with Flu vaccine and Tdap vaccine c) attitudes on COVID-19 infection, attitudes on COVID-19 vaccination and attitudes about the impact of the pandemic on their perception for vaccines. The sample size was determined after power analysis (a=0.05, 1-β 0.95, x^2 test, df=1, effect size=0.15). The inclusion criteria were: pregnant women regardless of trimester, attending the 1st Obstetrics and Gynecology clinic of the National and Kapodistrian University of Athens, writing and speaking Greek fluently and having no psychiatric disorder. Pregnant women who were already been vaccinated before last menstrual cycle and pregnant women that didn't provide vaccination certification were excluded.

All women were briefly informed about the risks of COVID-19 infection for both the pregnant woman and the fetus and about the need to be vaccinated against COVID-19 according to official Hellenic Recommendation that has included pregnant women in mandatory vaccination. They had also been given information about the purpose of the study and they gave their informed consent. Vaccination was evaluated through inspection of the certificate of vaccination.

The study was conducted according to the declaration of Helsinki – ethical principles for medical research involving human subjects. It was approved by the "Alexandra" hospital's ethics committee (no. of approval:92046 (04/11/2021).

Statistics

Quantitative variables were expressed as mean ± standard deviation or median ± interquartile range. Qualitative variables were expressed as relative frequencies. Independent samples, student's t-tests and Mann-Whitney tests were used to compare continuous variables between the two groups. For the comparison of discrete variables, the chi-square test was used. Logistic regression analysis was performed using the backward stepwise method and the assessment of all variables with a p-value<0.10 in the multinomial analysis to identify the impact of associated factors with vaccination during pregnancy. Adjusted odds ratios (OR) with 95% confidence intervals (95% CI) were computed from the logistic regression analysis results. All reported p-values are two-tailed. Statistical significance was set at $p<0.05$, and analyses were conducted using SPSS statistical software (version 22.0). G-Power 3.0 was used for power analysis. It was calculated that with the sample size of 800 participants, the study would have >95% power to ensure that the 95% confidence interval estimate of the proportion would be within 5% of the true proportion.

Results

During the study period, 980 pregnant women were approached for enrollment, of which 800 individuals were consecutively recruited since pregnant women who had already been vaccinated before last menstrual cycle and women that did not document the vaccination with the

respective certification of vaccination were excluded. Therefore, the study sample comprised 800 women [mean age 33.1 years (SD=5.1 years)]. The vaccination acceptance rate was 53.9%, meaning that over half of the sample (N=431) had been vaccinated with the COVID-19 vaccine during their pregnancy.

Concerning sociodemographic features, working women, older age, and higher monthly income were significantly and positively associated with vaccination acceptance (p<0.001). Chronic comorbidities, smoking, and miscarriages were not related to vaccination acceptance (**Table 1**).

With regards to information sources, factors positively associated with vaccination acceptance were information provided by health professionals (p=0.004) and by scientific sites (p=0.028). Sufficient knowledge of vaccines was also positively related to vaccination acceptance (p<0.001). Factors negatively associated with vaccination acceptance were information sources that included friends/family (p=0.005), media (p<0.0010) and the internet (p=0.028). With regards to vaccination history, factors positively related to vaccination were: a) vaccination of their children in the family (p=0.003); b) maternal vaccination against influenza during pregnancy (past: p<0.001 and present pregnancy: p<0.001); and c) maternal vaccination against pertussis during pregnancy (present pregnancy: p<0.001).

As far as perceptions of vaccination in pregnancy and childhood in general, factors positively associated with vaccination acceptance were a) intention to vaccinate their children in the future with all recommended vaccines; b) belief in the safety of the vaccines; c) belief that vaccination boosts the immune system and d) belief that vaccination

Table 1. Participants' characteristics and their association with vaccination acceptance.

		Total sample (N= 800; 100%)	Vaccinated against COVID-19		
			No (N = 369; 46.1%)	Yes (N = 431; 53.9%)	**P**
		N (%)	N (%)	N (%)	
Age, mean (SD)		33.1 (5.1)	31.8 (5.1)	34.2 (4.8)	**<0.001‡**
Married/ Living with partner	No	104 (13.0)	46 (44.2)	58 (55.8)	0.699+
	Yes	694 (87.0)	321 (46.3)	373 (53.7)	
Nationality	Greek	724 (90.7)	328 (45.3)	396 (54.7)	0.224+
	Other	74 (9.3)	39 (52.7)	35 (47.3)	
Children	No	353 (44.1)	167 (47.3)	186 (52.7)	0.551+
	Yes	447 (55.9)	202 (45.2)	245 (54.8)	
Number of children, median (IQR)		1 (1 — 2)	1 (1 — 2)	1 (1 — 2)	0.321‡‡
Employed	No	262 (32.9)	153 (58.4)	109 (41.6)	**<0.001+**
	Yes	535 (67.1)	213 (39.8)	322 (60.2)	
Sufficient monthly income [1], median (IQR)		3 (2 — 3)	3 (2 — 3)	3 (3 — 3)	**<0.001‡‡**
Suffer from chronic disease	No	700 (87.7)	329 (47)	371 (53)	0.126+
	Yes	98 (12.3)	38 (38.8)	60 (61.2)	
Smoking	No	622 (77.8)	290 (46.6)	332 (53.4)	0.597+
	Yes	178 (22.3)	79 (44.4)	99 (55.6)	
Gestational age (weeks), mean (SD)		24.3 (9.6)	24.7 (10)	24 (9.3)	0.328‡
Miscarriages	No	591 (73.9)	270 (45.7)	321 (54.3)	0.675+
	Yes	209 (26.1)	99 (47.4)	110 (52.6)	
Number of miscarriages, median (IQR)		1 (1 — 2)	1 (1 — 2)	1 (1 — 2)	0.991‡‡
Conception	Automatic	722 (91.6)	323 (44.7)	399 (55.3)	0.077+
	IVF	66 (8.4)	37 (56.1)	29 (43.9)	

[1]scale from 1 (not at all) to 5 (very much); +Pearson's chi-square test; ‡Student's t-test; ‡‡Mann-Whitney test

protects children from serious diseases. All these factors were significant at p<0.001 level. Perceptions negatively associated with vaccination acceptance were a) negative attitude towards value of vaccination in general and b) concerns about the side effects of vaccination. All these were significant at p<0.001 level (**Table 2**).

Table 2. Information on participants' attitudes towards vaccination and its association with vaccination acceptance.

		Total sample (N= 800; 100%)	Vaccinated against COVID-19		P
			No (N=369; 46.1%)	Yes (N=431; 53.9%)	
		N (%)	N (%)	N (%)	
Have you vaccinated your children [1]	No	24 (5.4)	18 (75)	6 (25)	**0.003+**
	Yes	423 (94.6)	186 (44)	237 (56)	
Sufficient knowledge on vaccines[2], median (IQR)		3 (3 — 4)	3 (3 — 3)	3 (3 — 4)	**<0.001‡‡**
Information sources on vaccination					
Health professionals	No	122 (15.3)	71 (58.2)	51 (41.8)	**0.004+**
	Yes	678 (84.8)	298 (44)	380 (56)	
Friends/ Family	No	731 (91.4)	326 (44.6)	405 (55.4)	**0.005+**
	Yes	69 (8.6)	43 (62.3)	26 (37.7)	
Newspapers, magazines or television	No	696 (87)	300 (43.1)	396 (56.9)	**<0.001+**
	Yes	104 (13)	69 (66.3)	35 (33.7)	
Internet	No	496 (62)	215 (43.3)	281 (56.7)	**0.044+**
	Yes	304 (38)	154 (50.7)	150 (49.3)	
Sites of Scientific constitutions	No	641 (80.1)	308 (48)	333 (52)	**0.028+**
	Yes	159 (19.9)	61 (38.4)	98 (61.6)	
Do you believe that vaccination protects children from serious diseases?	No/ Partially	230 (28.8)	164 (71.3)	66 (28.7)	**<0.001+**
	Yes	569 (71.2)	204 (35.9)	365 (64.1)	
Attitude towards vaccination in general[3], median (IQR)		2 (2 — 3)	2 (2 — 3)	2 (1 — 2)	**<0.001‡‡**
Are you going to vaccinate your children in the future?	Only with obligatory vaccines	280 (35)	174 (62.1)	106 (37.9)	**<0.001+**
	With some vaccines	205 (25.7)	120 (58.5)	85 (41.5)	
	With all vaccines	293 (36.7)	56 (19.1)	237 (80.9)	
	No	21 (2.6)	19 (90.5)	2 (9.5)	
Worried about the dangers in vaccination[1], median (IQR)		3 (2 — 3)	3 (2 — 4)	2 (2 — 3)	**<0.001‡‡**
Do you believe that vaccination boosts the immune system?[1], median (IQR)		3 (3 — 4)	3 (3 — 4)	4 (3 — 4)	**<0.001‡‡**
Do you believe that vaccines are safe?[1], median (IQR)		3 (3 — 4)	3 (3 — 4)	4 (3 — 4)	**<0.001‡‡**
Have you been vaccinated for influenza in the past?	No	490 (61.5)	288 (58.8)	202 (41.2)	**<0.001+**
	Yes	307 (38.5)	80 (26.1)	227 (73.9)	
Have you been vaccinated for pertussis in the present pregnancy?	No	507 (65.8)	278 (54.8)	229 (45.2)	**<0.001+**
	Yes	263 (34.2)	81 (30.8)	182 (69.2)	
Have you been vaccinated for influenza in the present pregnancy?	No	422 (53.3)	286 (67.8)	136 (32.2)	**<0.001+**
	Yes	370 (46.7)	76 (20.5)	294 (79.5)	

[1]referred only in women with children; [2]scale from 1 (not at all) to 5 (very much); [3]scale from 1 (very positive) to 5 (very negative); +Pearson's chi-square test; ‡‡Mann-Whitney test.

In addition, we investigated the relation of attitudes on COVID-19 infection, attitudes on COVID-19 vaccination and attitudes about the impact of the pandemic with the vaccination acceptance. We found out that pregnant women who accepted COVID-19 vaccination, stated that they a) believed that vaccination against COVID-19 is beneficial for their life and for their offspring; b) that the pandemic changed positively their previous intention to vaccinate their children in the future; c) that the pandemic reduced their previous vaccination hesitancy; d) pregnant women who accepted the vaccine stated that COVID-19 vaccination should be mandatory for all population and not only for health professionals and vulnerable groups; and stated e) that they had significant fear of severity of COVID-19 infection (p<0.001 in each case). Absence of COVID-19 infection in both pregnant women and their family members before pregnancy were not positively related to vaccination acceptance (p<0.001 and p=0.005, respectively) (**Table 3**).

Table 3. Information on participants' attitudes towards COVID-19 vaccination and its association with vaccination acceptance.

		Total sample (N= 800; 100%)	Vaccinated against COVID-19		P
			No (N=369; 46.1%)	Yes (N=431; 53.9%)	
		N (%)	N (%)	N (%)	
Infected by COVID-19 before pregnancy?	No	612 (77.2)	256 (41.8)	356 (58.2)	**<0.001+**
	Yes	112 (14.1)	68 (60.7)	44 (39.3)	
	During pregnancy	69 (8.7)	42 (60.9)	27 (39.1)	
Family member infected by COVID-19	No	474 (59.5)	199 (42.0)	275 (58.0)	**0.005+**
	Yes	323 (40.5)	168 (52.0)	155 (48.0)	
Family member with chronic disease	No	562 (70.6)	270 (48.0)	292 (52.0)	0.070+
	Yes	234 (29.4)	96 (41.0)	138 (59.0.)	
Fear of COVID-19[1], median (IQR)		3 (3 — 4)	3 (3 — 4)	3 (3 — 4)	**<0.001‡‡**
Changed mind for vaccines after the pandemic	The hesitation for the vaccines had been reduced	161 (21.0)	35 (21.7)	126 (78.3)	**<0.001+**
	The hesitation for the vaccines had been increased	180 (23.5)	124 (68.9)	56 (31.1)	
	The hesitation for the vaccines had remained the same	424 (55.4)	203 (47.9)	221 (52.1)	
Has the pandemic affected your intention to get vaccinated in the future[1], median (IQR)		2 (1 — 3)	3 (1 — 3)	2 (1 — 3)	**<0.001‡‡**
Do you think that vaccination against COVID-19 should be obligatory	No	291 (36.8)	189 (64.9)	102 (35.1)	**<0.001+**
	Yes, for everyone	169 (21.4)	19 (11.2)	150 (88.8)	
	Yes, for health professionals	193 (24.4)	112 (58.0)	81 (42.0)	
	Yes, for health professionals and vulnerable groups	137 (17.3)	41 (29.9)	96 (70,1)	
Has the pandemic affected your intention to vaccinate your children?	Yes, positively	146 (18.6)	19 (13.0)	127 (87.0)	**<0.001+**
	Yes, negatively	178 (22.7)	130 (73.0)	48 (27.0)	
	No	461 (58.7)	208 (45.1)	253 (54.9)	
Has the pandemic changed your position toward obligatory vaccination?	Yes, I believe more that vaccination should be obligatory (reference)	155 (19.6)	16 (10.3)	139 (89.7)	**<0.001+**
	Yes, I believe more that vaccination should not be obligatory	250 (31.7)	164 (65.6)	86 (34.4)	
	No	384 (48.7)	181 (47.1)	203 (52.9)	

[1]scale from 1 (not at all) to 5 (very much); +Pearson's chi-square test; ‡‡Mann-Whitney test

Higher statistical significance was observed among participants vaccinated for influenza during pregnancy having an almost 6-times greater probability of accepting the COVID-19 vaccine as well. Participants who believed that vaccination should be mandatory for everyone had a 3.47 times greater probability to accept COVID-19 vaccination. Participants who believed that COVID-19 vaccination should be mandatory only for health professionals, had 2.17-times greater probability to be vaccinated. Participants who believed that in addition with health care professionals, vaccination should be mandatory for vulnerable groups had 2.54-times greater probability to be vaccinated. We have to notice that COVID vaccination was mandatory for all population including pregnant women. Furthermore, women who stated that pandemic increased their trust in pediatric vaccination had a 3 times greater probability of accepting the COVID -19 vaccine (**Table 4**).

Among pregnant individuals who reported vaccine hesitancy, the most common reasons were concerns about side effects for the mother and the offspring (53%), lack of data (44%) and the fear of long-term side effects (26.6%). Among the pregnant individuals who accepted the vaccination, the most common reasons were the need to protect themselves (81.5%) and the baby (66.0%) and the recommendation by the attending Obstetrician (36.1%).

Discussion

The present study analyzed the acceptance of vaccination against COVID-19 in a population of pregnant Hellenic women, thoroughly analyzing the factors contributing to the decision for vaccination acceptance. Being vaccinated against Influenza and Pertussis in present or previous pregnancy and having trust in pediatric vaccination were factors who

Table 4. Multiple logistic regression results having as dependent variable participants' being vaccinated during pregnancy, in a stepwise method.

		OR (95% CI)+	P
Age		1.07 (1.03 — 1.12)	**0.001**
Employed	No (reference)		
	Yes	1.59 (1.04 — 2.44)	**0.034**
Informed for vaccination from newspapers, magazines or television	No (reference)		
	Yes	0.41 (0.22 — 0.77)	**0.005**
Attitude towards vaccination in general[1]		0.58 (0.40 — 0.82)	**0.002**
Worried about the dangers in vaccination[2]		0.76 (0.60 — 0.98)	**0.031**
Have you been vaccinated for influenza in the present pregnancy?	No (reference)		
	Yes	5.67 (3.76 — 8.54)	**<0.001**
Fear of COVID-19[2]		1.39 (1.10 — 1.76)	**0.005**
Do you think that vaccination against COVID-19 should be obligatory	No (reference)		
	Yes, for everyone	3.47 (1.51 — 7.96)	**0.003**
	Yes, for health professionals	2.17 (1.23 — 3.82)	**0.007**
	Yes, for health professionals and vulnerable groups	2.54 (1.43 — 4.50)	**0.001**
Has the pandemic affected your intention to vaccinate your children?	Yes, negatively (reference)		
	Yes, positively	3.05 (1.30 — 7.16)	**0.010**
	No	1.76 (0.99 — 3.13)	0.056
Has the pandemic changed your position toward obligatory vaccination?	Yes, I believe more that vaccination should be obligatory (reference)		
	Yes, I believe more that vaccination should not be obligatory	0.26 (0.09 — 0.72)	**0.01**
	No	0.28 (0.10 — 0.74)	**0.011**

[1]scale from 1 (very positive) to 5 (very negative); [2]scale from 1 (not at all) to 5 (very much); +Odds Ratio (95% Confidence Interval)

positively related to vaccination acceptance with the higher statistical significance. In addition, women who accepted the COVID-19 vaccination believed that vaccination should be mandatory for all population. Older age, positive attitudes towards vaccination, limited concerns about vaccination safety and bigger fear of COVID-19 infection were significantly associated with a greater probability of accepting the COVID-19 vaccine. Working women had also greater probability of being vaccinated during their pregnancy. Factors that are negatively related to vaccination acceptance were: information intake about COVID-19 vaccination from newspapers, magazines, and television instead of Health Care Professionals and official scientific websites; negative attitude towards other established vaccinations; the perception of non-mandatory of COVID-19 vaccination. Participants who believed that pandemic didn't change their attitudes towards vaccination or might lead to an even more negative attitude for vaccines in general were also negatively related with COVID-19 vaccination acceptance.

The most common reasons for the non-acceptance of the COVID-19 vaccine were concerns about side effects for the mother and the offspring (53% of non-vaccinated pregnant women), lack of clinical data (44%) supporting safety and effectiveness of COVID-19 vaccine and the fear of long-term side effects (26.6%). Similar findings have also been shown in other studies reinforcing the conclusion that the main reason for hesitancy was the fear of possible side effects, especially the long-term side effects, that could affect the pregnant woman and the offspring [12,13].

Studies about the acceptance rate of vaccination suggest different medical interventions, including strategies improving access to vaccination, incentive strategies, recall strategies, and information campaigns to the public [14]. In addition to COVID-19 vaccine accessibility that was in Greece at very good level, the implementation of recall strategy and public campaign, the present study provides important findings that could improve the communication between pregnant women and Health Care Professionals.

Established vaccination programs in pregnancy for other vaccines demonstrate that pregnant women are more vaccine hesitant than the general population [15]. Thus, although the seasonal influenza vaccine has been recommended with high priority for pregnant women since 2009, due to the severity of the H1N1 pandemic, the coverage rate remains suboptimal in many countries compared with the WHO target rate of 75% [28,29]. A Hellenic study on the effectiveness of maternal vaccination with quadrivalent inactivated influenza vaccine in pregnant women and their infants demonstrated a coverage rate with Flu vaccine in pregnancy of 61.4% [16]. In addition, although pertussis vaccination during pregnancy is recommended by national or supranational health authorities in more than 55 countries globally, many countries consistently fail to achieve a coverage rate as high as in childhood vaccination programs among pregnant women. According to a recent Hellenic study, maternal pertussis vaccination coverage is also estimated to be very low at 2% [17].

Association between COVID-19 vaccination with flu and pertussis vaccination in past or present pregnancy is shown in other studies as well. Women who had not been vaccinated against pertussis in pregnancy were four times more likely to also reject the COVID-19 vaccine during pregnancy [18]. Declining seasonal influenza vaccine has also been associated with non-acceptance of the COVID-19 vaccine in pregnancy [19]. These findings shows that clinical experience, based on safety and effectiveness data from other vaccination programs in pregnancy that are implemented for longer time, should be shared in medical communication with pregnant women to improve vaccination acceptance of COVID-19 vaccine.

The exclusion of pregnant women from initial vaccine clinical trials is a critical point since it led to limited data to guide clinical decision-making in this population, contributing certainly to vaccine hesitancy [20]. The encouraging data about the safety and efficacy of vaccination in pregnancy against COVID-19 that are currently exist, were not available at the beginning of the study [21-24]. Therefore, the inclusion of pregnant women in the clinical trial of COVID-19 vaccine, could provide the necessary clinical data and therefore must be carefully evaluated for the near future. Population-level data that have demonstrated the effectiveness of COVID-19 vaccines in pregnant women from severe COVID-19 infection and maternal mortality should be introduced to communication with pregnant women [24].

It is important to note that up to now, there are limited data concerning COVID-19 vaccination acceptance in pregnancy. Only a few studies have documented the vaccination acceptance rate in pregnancy based on vaccination records, databases, or vaccination certification. In these studies, vaccination uptake is reported as 32% (range, 4–46%) [12,13]. It is important to note that other studies present a higher coverage rate against COVID-19 in pregnancy, up to 68%, but are based on online surveys depending on the self-reported declaration [25]. Moreover, characteristics and perceptions associated with COVID-19 vaccination hesitancy among pregnant and postpartum individuals show a significant gap between willingness to be vaccinated and vaccination [26]. Blakeway et al. reported a lower uptake among younger women, non-White ethnicity, and lower socio-economic background [12]. Stock et al. reported that vaccine uptake was consistently lowest in younger (≤ 20 years) pregnant women and those living in the most deprived areas of Scotland [13]. Similar findings are demonstrated in the study of Kiefer et al. [26], showing that sociodemographic characteristics, such as younger age and lower education, were associated with lower acceptance of the COVID-19 vaccine but not clinical risk conditions. In combination with our findings younger

and lower education profile pregnant women might need more detailed communication to improve their vaccination acceptance rate.

However, vaccination acceptance of pregnant women is also related with corresponding behavior of HCPs and vaccination advisors. According to Daskalakis et al. [11] a study that conducted in the same period through an online questionnaire with 1226 HCPs, 75% of respondents favored immunization during pregnancy against COVID-19. However, approximately 40% of women in the specific study decline to receive the vaccination [11]. In the present study even though there was a personal communication between an HCP and pregnant women the vaccination acceptance was lower in comparison with other studies that demonstrate the significant increase of maternal vaccination uptake of Influenza and Pertussis vaccine, when vaccination was actively recommended by HCPs. The novelty of COVID-19 vaccine as well as the limited clinical experience in vaccination during pregnancy at the time of the study could have a negative impact on clear and strong advice of healthcare professionals [17].

The present study shows that an educational campaign must be provided to Health Care Professionals, to reverse any physicians' hesitancy [10]. In our study HCPs informed firstly the patients that they should be vaccinated according to National Recommendation and briefly about the benefit of protection. They did not focus to convince patient to be vaccinated based on safety and effectiveness data since clinical experience was limited. The results underline the importance of providing mainly safety data since pregnant women constantly emphasize the fear of side effects as the main reason for non-acceptance. Training should consider mainly clinical scientific data about the safety and effectiveness of the vaccine as well as data concerning the severity of the disease, and the benefits of vaccination. Health Care professionals need to spend sufficient time to explain question and provide scientific explanation about the official mandatory recommendation. Additionally, taking into consideration the high impact of misinformation that was present in the Pandemic, HCPs need also to educate pregnant women's ability to detect misinformation that substantially influence the vaccination hesitancy [27].

A very interesting analysis is also the comparison of maternal acceptance coverage rate with the coverage rate of non-pregnant young women at similar age. This study shows that coverage in pregnancy (54%) is significantly inferior compared to vaccination coverage of non-pregnant Greek women of the comparable age range of 18-45 years old (70%) as well as compared to the older Greek female population 65+ (79%), even though the morbidity and mortality of pregnant women is significantly higher than the young population of the non-pregnant women of the same age [28]. Stock et al. [13], demonstrated similar findings, since vaccine coverage of 32.3% was substantially lower in pregnant women than in the young general female population of 18–44 years, which was shown to be 77.4%. In addition, according to Townsel et al. [29], pregnant participants were 6-times more likely to delay COVID-19 vaccination and twice as likely to decline compared to other women of reproductive age between 18–44 years old. Furthermore, Nery et al. reported that sex could influence vaccine acceptance showing that acceptance in women was lower (79.7%; 95% CI 77.7–81.6%) compared to men (84.9%; 95% CI 82.1–87.0%) [26]. These findings suggest that pregnant women's special attitude towards vaccination during pregnancy did not change dramatically despite the burden of the pandemic. Key driver of COVID-19 vaccine acceptance is the impact of vaccination to the fetus, underlining the need of COVID -19 vaccination safety data generation of the offspring.

The need for the participation of pregnant women in initial clinical programs is critical to provide efficient safety data. But could be not enough; ongoing surveillance for potential adverse effects is also essential to support public trust, using well-developed pharmacovigilance systems to track problems or adverse reactions not detected in clinical trials. Longitudinal/prospective studies are also required to monitor the outcome of the pregnancy and the effect on the newborn of a vaccinated mother. Furthermore, studies to demonstrate a possible benefit to the newborn of the vaccinated mother compared to unvaccinated mother could be an essential criterion for mitigating vaccination hesitancy in pregnancy.

Present study shows that another factor that could be leveraged to increase the acceptance is the level of trust in pediatric vaccines. High coverage rate, long term safety data and effectiveness data from pediatric vaccines could be used by HCPs to support the value of vaccination and increase the acceptance of this novel COVID-19 vaccine.

Finally, our findings show a strong correlation between acceptance and the perception that COVID-19 should be mandatory. These findings have limited value since vaccination was mandatory. The unvaccinated pregnant women faced the same restrictive measures as the rest of the population. Thus, we cannot extract valuable information for the time being.

Strengths and Limitations

This study is based on extensive and analytical research that was carried out on a large sample of women and was based on a questionnaire of 40 factors. Moreover, it refers to vaccination adoption rather than an intention to be vaccinated, indicating an actual and not notional acceptance of the COVID-19 vaccine. Therefore, these findings can be considered as a definitive approach to the current understanding of the population about the vaccination acceptance or hesitancy during pregnancy. It is important also to mention the timeframe of the study that went on the beginning of the vaccination program in pregnant women in Greece, representing the real situation that was in place at that time.

Among the limitations of the study, we should mention that the study was carried out in a specific population that may not be representative of the entire country. Also, the fact that it was carried out in a university clinic with well-educated staff, with extended experience from similar studies about vaccination in pregnancy could be not representative of all the country. Lastly, it was carried out in population living in the capital of Greece, that may be more positive to vaccination, in comparison with the rest of the country.

Conclusion

In conclusion, several parameters can be taken into consideration for the lower vaccination coverage of pregnant women against COVID compared to the WHO and ECDC target of 75% for Seasonal Influenza vaccination [28,29]. The findings of this study, along with the conclusions of other related studies, may help to design a more effective communication strategy, which will enhance trust in the COVID-19 vaccination in pregnancy but also provide some important findings for Maternal vaccination in general. Due to the urgency of the pandemic, it was impossible to proactively organize awareness and information for pregnant women. However, COVID-19 is still here; so pregnant women will continue to be vaccinated. Therefore, finding of this study could be leveraged to improve the existing communication strategy about COVID-19 vaccination to pregnant women.

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