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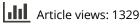
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Attitude for vaccination prophylaxis among pregnant women: a cross-sectional study

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ABSTRACT

Pregnant women and newborns are considered a subgroup of population at increased risk for several infectious diseases, some of which are vaccine-preventable. Anti-diphtheria-tetanus-pertussis vaccine (dTpa) and influenza vaccine are recommended for pregnant women. We carried out a study to evaluate the knowledge of new mothers toward the main vaccine-preventable diseases and to assess their compliance with recommended vaccinations. Using the Hospital Discharge Forms (SDO), the list of women who gave birth in 2018 was generated. Women were interviewed by a questionnaire administered by telephone. The study sample consisted of 145 subjects, with an average age of 35.0 ± 5.9 years (range = 18.0-47.0). 5/145 (3.4%; 95% CI = 1.1-7.9%) subjects were advised during pregnancy to have the flu shot; only 1/145 (0.7%; 95% CI = 0.5-71.6%) reported the flu vaccine during the last pregnancy. 94/145 (64.8%; 95% CI = 57.2-73.2%) respondents declared that they had carried out the TORCH panel exams before pregnancy; of these 18/94 (19.2%; 95% C = 11.8-28.6%) were susceptible for rubella. Of these subjects, for 7/18 (38.9%; 95% CI = 17.3-64.3%) rubella vaccination was offered and 5/7 (71.4%; 95% CI = 29.0-96.3%) decided to carry out the vaccination. Greater efforts must be made by public health institutions to raise awareness and improve vaccination compliance in this population.

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Influenza vaccine; dTaP vaccine; MMR vaccine; rubella; torch complex; pregnancy; prevention

Introduction

Pregnancy is a physiological process, and as such, it should not be considered a disease; nevertheless, pregnant women and newborns are considered a subgroup of vulnerable people with an increased risk of several infectious diseases, some of which are vaccine-preventable.^{1,2} In the pregnant woman, the increased susceptibility to infections seems to be due to a modulation of the maternal immune system by hormones, cytokines, and immunity cells and by structural changes in the endometrium.^{3,4} In the newborn, the inability to generate an efficient and effective immune response seems to be linked to the functional immaturity of the immune system. However, infants in the first months of life can take advantage of the passive immunity acquired during gestation thanks to the transfer of maternal antibodies through the placenta.⁵ Therefore, immunization during pregnancy offers direct protection to the pregnant woman, reduces the probability of maternal-fetal transmission of any infections and provides passive immunity to the newborn first through the transplacental passage of antibodies and then through breast milk.⁵

In the first months of life, following contact with pathogens, the adaptive immune system of newborns is unable to generate a completely protective response. Fetal and neonatal T lymphocytes predominantly provide Th2-type responses, which are ineffective against intracellular pathogens, as well as antibody responses are inefficient against bacterial polysaccharides. At this stage, newborns can count on the protection acquired during gestation, thanks to maternal antibodies passively transferred across the placenta. However, the titer of maternal specific antibodies is often sub-optimal and may therefore not be sufficient to confer complete immunity to infants, or may only protect them for a limited period of time, as serum levels of maternal antibodies tend to decrease in the 6 months after birth. The purpose of maternal immunization is therefore to increase the concentration of circulating antibodies in the mother, to increase their passive transfer to the fetus, thus reducing the vulnerability window of the newborn until the appropriate time for its vaccination or after the period of greatest susceptibility.⁶

Maternal immunization has been an effective strategy for over 30 years, as demonstrated by the drastic reduction in cases of neonatal tetanus due to the administration of the tetanus vaccine during pregnancy. A 2013 study conducted by De Micheli showed that tetanus vaccination in women of childbearing age and pregnancy reduces of almost 94% neonatal tetanus mortality.⁷ Several studies demonstrated the absolute safety and efficacy of maternal immunization in preventing diseases such as pertussis, which in newborns can complicate with bronchopneumonia, encephalitis and death, and influenza, which in pregnant women and newborns generally has a more severe course and can lead to death; those are diseases for which acellular and inactivated vaccines are available, respectively.⁸ Particular attention should be paid to live and attenuated virus vaccines such as the measles-mumps-rubella (MMR) vaccine, which are currently contraindicated in

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pregnancy, although accidental vaccination in women who did not know their pregnancy status did not show an increase in the number of abortions or malformations.⁹

As reported in the National Vaccine Prevention Plan 2017–2019¹⁰ and as confirmed by the Ministry of Health on 7 August 2018,¹¹ the vaccinations strongly recommended in pregnancy in Italy are the diphtheria-tetanus-pertussis vaccine (dTpa) (from the 27th to the 36th week of gestation, ideally around the 28th week) and the influenza vaccine (in any trimester of pregnancy). A different speech deserves the measles-mumps-rubella (MMR) vaccination, which, although contraindicated in pregnancy, is strongly recommended in women of childbearing age to avoid the risks of congenital rubella, especially if they plan to become pregnant and are still susceptible to rubella.¹²

Based on these considerations, we carried out a study with the aim of evaluating the knowledge of new mothers toward the main vaccine-preventable diseases and to assess their compliance with their respective vaccinations. The study was carried out on a sample of women who gave birth in 2018 at the three main hospitals in the city of Bari (Italy, Puglia Region, around 4,000,000 inhabitants): the Bari Policlinico University-Hospital, the "Di Venere" Hospital and the "S. Paolo" Hospital.

Material and methods

This is a cross-sectional retrospective study.

The study population is made up of all women who gave birth in 2018 at the three public hospitals in the city of Bari (Bari Policlinico University-Hospital, the "Di Venere" Hospital, and the "S. Paolo" Hospital).

Using the Hospital Discharge Forms (SDO),¹² the list of women who gave birth in 2018 was generated. We considered all records referred to pregnancy using the ICD 9 codes 630-679.xxx (Complications Of Pregnancy, Childbirth, And The Puerperium) in primary diagnosis. The calculation of the sample size was performed using the appropriate function of the software STATA MP17. To establish the sample size, we compared the flu vaccine coverage reported by Napolitano F et al. (9.7%)¹³ with a hypothesized flu vaccine coverage in our sample of 3.5% (researchers' hypothesis). To analyze the results, the chi-square test was used; a significance level (alpha) of 0.05 was set and the power of the test was 80%. Therefore, a sample size of 250 subjects was estimated, chosen by simple causal randomization; the final sample consisted of 145 women (response rate: 58%). The data was collected through a telephone interview during which an ad hoc questionnaire was administered, developed by the graduate student after a careful analysis of the literature in the sector and preliminarily tested in a small subgroup of women.

The questionnaire investigated demographics data and knowledge about medical recommendations during pregnancy. It consisted of the following items:

- (1) Anagraphical data
- (2) Marital status
- (3) Educational qualification

- (4) Occupation
- (5) Attendance of a prenatal course during pregnancy
- (6) Structure that organized the course
- (7) Whether the woman received advice on flu vaccination during pregnancy and from whom
- (8) Influenza vaccination during pregnancy (YES/NO)
- (9) Execution and outcome of the TORCH panel in the last pregnancy
- (10) Advice on carrying out the rubella vaccination before pregnancy in the case of a susceptible person
- (11) Carrying out the rubella vaccination before pregnancy in the case of a susceptible person (YES/NO)
- (12) Reasons for failure to vaccinate against rubella before pregnancy in case of susceptible person
- (13) Knowledge of the risks associated with rubella infection in pregnancy
- (14) Carrying out diphtheria-tetanus-pertussis (dTap) vaccination during pregnancy (YES/NO)
- (15) If not performed, reasons for not having diphtheriatetanus-pertussis (dTap) vaccination
- (16) Knowledge of the risks associated with pertussis in children if contracted in the very first months of life

The questionnaire was administered in the period January– June 2019. The collected data were imputed in an Office Excel spreadsheet and analyzed with Stata MP16 software.

Continuous variables were expressed as mean \pm standard deviation and range; categorical variables such as proportions, with an indication of the 95% confidence interval (95% CI).

To evaluate the association between each of the following outcomes:

- having had rubeo test and/or TORCH complex before pregnancy (YES/NO)
- receiving the anti-flu vaccine during pregnancy (YES/ NO)
- execution of the rubella vaccine before pregnancy (YES/ NO)
- execution of the dTaP vaccine during pregnancy (YES/ NO)
- knowledge of the risks related to influenza (YES/NO)
- knowledge of the risks related to rubella (YES/NO)
- knowledge of the risks related to pertussis (YES/NO)

and specific determinants (age, years of study, marital status, work situation) the univariate logistic regression was used; the Odds Ratio was calculated, indicating 95% CI.

Subsequently, a multivariate logistic regression model was constructed for each outcome, using as determinants those variables that proved to be associated with the single outcome in the univariate logistic regression; the aOR (adjusted Odds Ratio) was calculated, with an estimation of 95% CI.

For all tests, a p-value <0.05 was considered statistically significant.

The research conducted for this study was carried out in accordance with the Helsinki Declaration. The protocol of the survey was approved by the Apulian Regional Observatory for Epidemiology.

Results

The study sample consisted of 145 female subjects, with an average age of 35.0 ± 5.9 years (range = 18.0-47.0); 118/145 (81.4%; 95% CI = 74.1-87.4%) respondents report being married, 26/145 (17.9%; 95% CI = 12.1-25.2%) single and 1/145 (0.7%; 95% CI = 0.0-3.8%) separated/divorced.

On average, subjects studied for 13.9 ± 4.0 years (range = -6.0-23.0), 76/145 (52.4%; 95% CI = 44.0-60.8%) report having an occupation, with 46/76 (60.5%; 95% CI = 48.6-71.6%) employed and 30/76 (39.5%; 95% CI = 28.4-51.4%) self-employed workers.

41/145 (28.3%; 95% CI = 21.1-36.3%) respondents report having attended a pre-birth course, of which 21/41 (51.2%; 95% CI = 35.1-67.1%) at a counseling center, 9/41 (21.9%; 95% CI = 10.5-37.6%) at a hospital obstetrics unit and 11/41 (26, 8%; 95% CI = 14.2-42.9%) at another facility.

5/145 (3.4%; 95% CI = 1.1-7.9%) subjects were advised during pregnancy to have the flu shot, of which 3/5 (60.0%; 95% CI = 14.7-94.7%) by the gynecologist, 1/5 (20.0%; 95% CI = 0.5-71.6%) by the General Practitioner and 1/5 (20.0%; 95% CI = 0.5-71.6%) by a physician from Public Health Service; only 1/145 (0.7%; 95% CI = 0.5-71.6%) claimed to have had the flu vaccine during the last pregnancy. 55/145 (37.9%; 95% CI = 30.0-46.4%) women interviewed reported that they know the risks associated with the flu during pregnancy.

94/145 (64.8%; 95% CI = 57.2–73.2%) respondents declared that they had carried out the TORCH panel exams before pregnancy; of these 72/94 (76.6%; 95% CI = 66.7–84.7%) were immune to rubella, 18/94 (19.2%; 95% C = 11.8–28.6%) were susceptible and 4/94 (4.2%; 95% CI = 1.2–10.5%) did not remember the test results. Of the subjects found to be susceptible, 7/18 (38.9%; 95% CI = 17.3–64.3%) were offered rubella vaccination: 4/7 (57.1%; 95% CI = 18.4–90.1%) received this recommendation from the General Practitioner and 3/7 (42.9%; 95% CI = 10.0–81.6%) from the Gynecologist; 5/7 (71.4%; 95% CI = 29.0–96.3%) decided to carry out the vaccination. Of the two women interviewed seronegative for rubella who refused vaccination, 1/2 (50.0%) justified the choice for fear of side effects and 1/2 (50.0%) for timing incompatible with the pregnancy.

87/145 (60.0%; 95% CI = 51.5–68.0%) subjects declared that they knew the risks to the fetus related to rubella and one of the most frequently reported risks was spontaneous abortion (55.2%; graph 4.1).

Only 1/145 (0.7%; 95% CI = 0.0–3.8%) of the interviewed women underwent anti-dTap vaccination, recommended by the gynecologist; the remaining 144 interviewees did not carry out the vaccine because in most cases (87.5%) it has not been recommended.

Only 26/145 (17.9%; 95% CI = 12.1-25.2%) subjects declared that they know the risks associated with pertussis in newborns/infants; the most frequently reported risk is breathing difficulty (69.2%).

The main results of our survey are summed in Table 1.

From the univariate logistic analysis, a statistically significant association between

Table 1.	Characteristics	of the	sample	and	main	results.
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Variable	Value
Age (years)	5.0 ± 5.9 (range = 18.0–47.0)
Flu vaccine during pregnancy	1/145 (0.7%; 95% CI = 0.0-3.8%)
dTaP vaccine during pregnancy	1/145 (0.7%; 95% CI = 0.0-3.8%)
TORCH panel before pregnancy	94/145 (64.8%; 95% CI = 57.2–73.2%)

- the rubeo test and/or TORCH complex performed before pregnancy and
 - o age (OR = 1.08; 95% CI = 1.02–1.15; p = .009)
 - years of study (OR = 1.13; 95% CI = 1.02-1.23; p = .010)
- knowledge of the influenza-related risks (YES/NO) and having participated in a pre-birth course (OR = 0.4; 95% CI = 0.2-0.9; p = .038)
- knowledge of the rubella-related risks (YES/NO) and years of study (OR = 1.2; 95% CI = 1.1–1.3; p < .0001)
- knowledge of the pertussis-related risks (YES/NO) and having participated in a pre-birth course (OR = 0.3; 95% CI = 0.1-0.9; p = .047).

No further associations were observed between outcomes and determinants under analysis (p > .05).

It was not possible to evaluate the determinants of the variables "execution of the anti-influenza, anti-rubella, and anti-dTaP vaccine in pregnancy," due to their low variability.

The multivariate logistic analysis confirms what was highlighted in the univariate, i.e. that the execution of the rubeo test and/or TORCH complex before pregnancy is associated with age (aOR = 1.07; 95% CI = 1.00-1.14; p = .044) and years of study (aOR = 1.10; 95% CI = 1.00-1.21; p = .049).

Discussion

The study carried out had the purpose of evaluating the knowledge of new mothers toward the main vaccine-preventable diseases that represent a risk to themselves or to the unborn child and to assess their compliance with the respective vaccinations.

Only 28.3% of the women interviewed reported having attended a pre-birth course; this is an extremely low percentage if we consider that the Childbirth Preparation course represents the occasion in which specialized personnel can provide future parents with correct information in the context of health education interventions.

Only five women said they had been instructed to carry out the flu vaccination during pregnancy and only one of these opted to follow the physician's advice. This data shows the lack of attention shown by the health professionals involved (gynecologists, general practitioners, etc.) in adequately informing future mothers about the potential risks associated with the infection acquired during pregnancy, i.e. premature birth, low birth weight, fetal suffering. However, this data is consistent with what is reported in the literature; a 2013 Australian study reported that a quarter of the pregnant female population is absolutely unaware of the strong recommendation to get a flu shot and 34% think it is even contraindicated.¹⁴ As for the diphtheria-tetanus-pertussis vaccination, only one woman reported having carried out the vaccination; 87.5% of enrolled women reported they had not done it because it was not recommended. Furthermore, only 18% of the women interviewed knew the risks associated with pertussis in children. Also in this case, therefore, the absolute lack of communication by health professionals plays a fundamental role.

On the other hand, women seem to be more informed about rubella issues; 71.4% of women who were susceptible to rubella decided to carry out the vaccination on the advice of their gynecologist or general practitioner; 60% knew the risks associated with infection during pregnancy. Indeed, as reported in the literature, MMR vaccination is an efficient¹⁵ and safe^{16,17} tool to deal with people susceptible to rubella.

The univariate analysis showed that the attendance of a prebirth course is associated with less knowledge of the risks associated with influenza, if contracted during pregnancy, and pertussis, if contracted in the very first months of life. This data could be linked to the fact that the operators of the birth preparation courses themselves are not adequately informed and trained on the recommendations to be provided to pregnant women and must necessarily be deepened by further research. The multivariate analysis, on the other hand, showed that older women with a higher educational qualification were more inclined to perform the rubeo test and/or TORCH complex before pregnancy. This data could be linked to a greater attention of these women in following the pregnancy.

Our study confirms what has already been reported in the literature: a recent study, published in 2018 by a group of researchers from the University of Naples, highlights how low vaccination coverage in pregnant women is linked to a low perception of risk and to a lack of information on the subject by health professionals who should communicate with future parents.¹⁸

Among the strengths of the study, there is the adherence of women who responded with keen interest to the questions, emphasizing the relevance of the issue; this is also one of the few studies carried out in Italy after official recommendations about the vaccination of pregnant women.^{9,10} However, the study was conducted in a limited geographical area, and this is certainly limited. Furthermore, the response rate of 58% has potentially impaired the representativeness of the sample. So, it would be interesting in the future to extend the survey to other Italian regions to highlight any differences on the national territory.

It is therefore of fundamental importance that health-care personnel are adequately trained in order to disseminate correct information on such a relevant public health topic. In fact, pregnancy represents a particular moment in the life of every woman in which the sense of responsibility toward the unborn child increases. It would therefore be advisable to organize training events dedicated to vaccinations recommended in pregnancy aimed at all health professionals in the sector (gynecologists, pediatricians, general practitioners, obstetricians, nursing homes) in order to reassure future parents on the safety of vaccinations and improve compliance. Another proposal would be to be able to standardize the contents of childbirth assistance courses and integrate vaccinologists as teachers. In summary, greater efforts must be made by public health institutions to raise awareness and improve vaccination compliance in this population.

Finally, the ongoing COVID 19 pandemic proved to be a good opportunity to take charge of the pregnant women; indeed, this is a high-risk category that requires particular physical and mental care, as evidenced by many studies in literature.^{19–22} The Apulian experience proved that the privileged paths for this category of population at risk organized by public health institutions seem to be a good possibility to propose other vaccines in addition to the anti-COVID one.

Abbreviations

MMR	Measles, mumps, rubella
dTaP	Diphtheria-tetanus-acellular pertussis
SDO	Hospital Discharge Forms

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