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How pregnant women perceive the risk related to Congenital Rubella Syndrome: a prospective study conducted at University "Federico II" of Naples.

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ABSTRACT

Objective: evaluate the knowledge of congenital rubella infection consequences and of immunoprophylaxis among pregnant women admitted at University Hospital "Federico II" of Naples, in order to make them conscious about the importance of active prophylaxis to prevent CRS.

Methods: we interviewed all the pregnant women admitted at the Emergency Room and/or at the Department of Obstetrics and Gynecology of University "Federico II" of Naples, from March to September 2016, using a multiple choice questionnaire.

Results: 131 pregnant women were enrolled. One hundred patients (76,3% of the total) declared not to be vaccinated against rubella: 65 patients (49,6%) stated to be not enough informed about the consequences of CRS. Moreover, 85 patients (64,8%) declared to be willing to vaccinate themselves once conscious about the risk related to CRS.

Conclusions: the study revealed a low grade of knowledge of the risks on the newborn due to rubella and an insufficient level of compliance to the vaccinal practice, but at the same time a reborn interest to this issue and a willingness to perform vaccination in the post-partum era came out. Future developments are necessary to train and form women in fertile age about consequences of CRS, punctuating on the importance of vaccination to prevent it.

Key words: rubella, pregnancy, CRS, vaccine, pneumococ, deafness, blindness, heart defects

SOMMARIO

Obiettivo: valutare la conoscenza delle conseguenze legate all'infezione da Rosolia Congenita e dell'immunoprofilassi tra le gravide afferenti al Policlinico Universitario "Federico II" di Napoli, allo scopo di renderle consapevoli in merito all'importanza della profilassi attiva (vaccinazione) per prevenire la Sindrome da Rosolia Congenita (SRC).

Metodi: abbiamo intervistato tutte le gravide afferenti al Pronto Soccorso Ostetrico o al Dipartimento di Ostetricia e Ginecologia dell'Università "Federico II" di Napoli, da Marzo a Settembre 2016, usando un questionario a scelta multipla.

Risultati: 131 gravide sono state arruolate. 100 pazienti (76,3% del totale) hanno dichiarato di non essere state vaccinate per rosolia: 65 pazienti (49,6%) hanno affermato di non essere state adeguatamente informate sulle conseguenze della SRC. Inoltre, 85 pazienti (64,8%) hanno dichiarato di volersi vaccinare una volta rese edotte sulle conseguenze della SRC.

Conclusioni: lo studio rivela un basso grado di conoscenza dei rischi a carico del neonato dovuti alla rosolia ed un insufficiente livello di aderenza alla pratica vaccinale ma allo stesso tempo un rinnovato interesse nei confronti di questa tematica e il desiderio di praticare la vaccinazione nel post-partum. Futuri sviluppi sono necessari per informare e formare le donne in età fertile sulle conseguenze della SRC, puntualizzando sull'importanza della vaccinazione per prevenirla.

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INTRODUCTION

Rubella⁽¹⁾, also known as “German Measles”, is a exanthematous contagious disease, with human transmission, due to an enveloped togavirus (Rubella virus)⁽¹⁾. It is usually a mild viral infection in childhood, but it can have serious consequences for offspring, causing also the Congenital Rubella Syndrome (CRS), if contracted during the pregnancy⁽²⁻⁵⁾: in fact, it is able to infect the embryo and the placenta when the infection is contracted during the course of pregnancy⁽²⁻⁵⁾. The risk of fetal death and malformations increases as more early is the onset of the maternal infection; in fact, in the first trimester of pregnancy this event is higher than 80%, thereafter it reduces up to 15% in later trimester⁽²⁻⁵⁾.

The risk of CRS is very high when the women had been infected by rubella during the first trimester of pregnancy; in this case the CRS often results in multiple birth defects including heart defects, deafness and blindness, with remarkable lifelong complications and disabilities⁽²⁻⁵⁾.

In Italy⁽⁸⁾, as most developed Countries, the epidemiological burden of the rubella has been changed respect to the past. After the outbreaks occurred in the years 2002-2003 and 2006, rubella has reached a minimum of historical reports (257 cases) in 2006. In the same period (2005-2013), 150 cases of Rubella in pregnancy were notified, of which 139 confirmed, 8 probable and 3 possible; additional 102 notifications had not been classified because of lacking information. In the setting of the pregnant women, a peak of reports had been observed in 2008 (77 cases) and in 2012 (41 cases). The mean age of infected pregnant women was 27 years and only a minority of them (15 %) were stranger. In the same period, 78 cases of congenital Rubella were reported, 64 of whom confirmed and 14 probable; additional 63 reports were unclassifiable for lacking of information or lacking of monitoring until the exclusion or confirmation of diagnosis. In the symptomatic neonates/babies with SRC, the symptoms most frequently reported are congenital heart disease, deafness/hypoacusia, meningoencephalitis and cataract (11 children). Regarding the distribution of congenital Rubella in the various regions of Italy, in 6 regions the annual average of incidence has been over 1 case on 100,000 live births, particularly in Campania⁽¹³⁾.

These data clearly show that in Italy, as well as other western countries, the rubella virus still circulates and can affect pregnant women. Therefore, the most effective preventive measure of CRS is represented by the vaccination of childbearing women^(6,7). The Rubella vaccine is

available since 1969; it contains live attenuated virus, and in Italy is available conjugated with measles (bivalent MR) or measles and mumps (trivalent MPR). In Italy the vaccination anti-rubella, together with vaccines for mumps, measles and pertussis, is free of charge and strongly recommended, although not mandatory, for all newborns; in addition the National PNEMoRC planned to improve the spreading of free of charge vaccination among fertile women. It has been estimated that the percentage of childbearing women susceptible for rubella must not be exceed 5%. Unfortunately, Italy seems to be far from that goal. In fact, a survey of serum prevalence of antibodies against rubella carried out in 2004 showed that the rate of childbearing women susceptible to rubella ranged from 11% in 15-19 years aged women to 8 % in 20-39 years aged ones. Another survey (PASSI project: progress in health care organizations in Italy) carried out in 2007 showed that on 9.442 women aged 18-49 years, 55% was immune to rubella because of the vaccination (32%) or for natural coverage detected by positive rubeotest (23%), but the remaining 42% did not know their immune status about Rubella and 3% of women was certainly susceptible⁽⁹⁾.

Since many years, a safe, effective and inexpensive vaccine^(6,7) against Rubella entered the market; in Italy, as well as many other developed countries, the vaccine, available combined with measles vaccine (MR) or with measles and mumps vaccines (MMR), is strongly recommended but not mandatory.

Unfortunately, also in countries where the vaccine is available, often the incomplete coverage of childhood, due to the parents refusal for different reasons such as lack of confidence in vaccines, social poverty, and lacking information about the disease), encourages the persistent circulation of the virus and recurrent outbreaks every three-four years^(8,9).

In order to achieve the global eradication of Rubella and CRS, the World Health Organization implemented the Global Measles and Rubella Strategic Plan as a result of the Global Vaccine Action Plan, endorsed by the World Health Assembly^(10,11). This plan has targeted the elimination of these vaccine-preventable diseases in at least five of the six WHO Regions by 2020.

On this path, the Italian Ministry of Health has proposed a National Plan for the Eradication of Measles and Congenital Rubella Syndrome (PNEMoRC), aimed to achieve these objectives more even the at least 95% coverage of adults

during supplementary immunization activities in setting as paramedics, teachers, soldiers and nomadic groups, and lastly improve the spreading of the Plan among fertile women, paramedics and civil population⁽¹²⁾.

For these reasons, we have believed important to verify in the largest urban area of Southern Italy (Naples town) how a sample of pregnant women perceive the risk of congenital rubella infection, mainly testing their knowledge about both the potential consequences of rubella on offspring and the importance of vaccination for rubella.

MATERIAL AND METHODS

We have planned along with fellow gynecologists and obstetrics of the Department of Obstetrics and Gynecology of University "Federico II" of Naples a prospective study aimed to evaluate the level of knowledge about both the potential consequences of rubella infection during pregnancy on offspring and the importance of vaccination for rubella in childbearing women. So, the study had been designed to only evaluate the level of knowledge of this disease among our patients, and not to verify their rubella serologic status.

The study population consists of a sample of patients admitted at the Emergency Room or at the Department of Obstetrics and Gynecology of University "Federico II" of Naples, in the period from March to September 2016.

All the women aged over 18 years had been asked to give written informed consent to be interviewed administering a multiple choice questionnaire, available in anonymous form (*Annex 1*).

All the patients had been encouraged to ask medical doctors and obstetrics any question for their concerns about rubella and CRS congenital rubella syndrome or receive any further clarifications in case of difficulty in understanding the questions.

In addition, beside the questionnaire, we provided a concise fact sheet about the risks related to CRS to all the patients enrolled in the study (*Annex 2*); this sheet has been developed according to WHO's Rubella and Measles Eradication Campaign aims.

The study had been approved by the Ethical Committee of University of Naples Federico II. The authors agree to provide copies of the appropriate documentation if requested.

All the data collected has been elaborated via SPSS 18.0 for Mac, using the chi square test.

RESULTS

A total of 131 pregnant women admitted at the Emergency Room and/or at the Department of Obstetrics and Gynecology of University "Federico II" of Naples were enrolled from March and September 2016. A multiple choice questionnaire was administered to those patients, in order to investigate their perceived risk related to CRS.

One hundred patients (76.3% of the total) declared not to be vaccinated against rubella: 24.4% of women among them said to have been affected by rubella, 1.5% of those patients assumed that vaccine is dangerous, 13.7% of them didn't think that vaccination is important and 40.4% declared not to be informed about. At the same time, 19 patients (14.5% of the total) declared to be vaccinated against Rubella and 12 patients (9.16% of the total) declared to do not know their vaccination status.

65 patients (49.6% of the total) admitted to be not enough informed about the consequences of CRS: 37.4% of them stated to have not been informed about, while 14.5% of them told us to have been trained from the gynecologist but didn't care about. 66 patients (50.3% of the total) were informed yet about the consequences of CRS at the moment of the enrollment.

Moreover, 85 patients (64.8% of the total) stated to be willing to undergo vaccination once conscious about the risk related to CRS, while 13.7% of them declare not to be in favor of vaccination anyway: 5.3% of them said to be scared about vaccination, 6.8% admitted not to be informed about risks related to vaccination side effects, 2.2% considered dangerous the vaccination. One patient (0.4% of the total) still doesn't know if access to vaccination after receiving clarification about the risks related to CRS. For 19.08% of the total patients the data are missing.

57 (43.5%) of pregnant women ignored those information about rubella and CRS at the moment of the enrollment, as well as the importance of vaccination before or after the pregnancy, while 74 patients (56.4% of the total) were informed yet. 12.9% of them have been informed by their general practitioner, 22.9% by the gynecologist, 13.7% by their family members, 5.3% by TV programs, 11.4% by web sites, 1.5% by friends and 2.2% by other way. For 41.2% patients the data are missing.

The total amount of participants in the study found interesting those information.

Briefly analyzing those data (summarized in Table I), we figured out that the majority of our patients (76.3% of the total) were not vaccinated at the moment of enrollment justifying themselves to be not enough informed about or to have been still affected by rubella in the youth. Moreover, we got useful data on misinformation about congenital rubella syndrome (CRS) but at the same time, we are able to assume that, once informed, mostly of our patients (64.8% of the total) are willing to undergo vaccination against rubella: this data results to be statistically significant ($p=0.002$, chi square test) at our statistical analysis conducted using SPSS 18.0 for Mac OS. Among the patients who still prefer not to access to vaccination, despite this informative campaign, most of them can't explain the motivation of this choice (85.4% of the total) or stated to be not informed enough to take such an important decision (6.8% of the total): this means that is necessary to improve the capillary diffusion of those information. Focusing on pregnant women enrolled in the study who were yet informed about CRS consequences, we conducted a linear regression analysis to explain the relationship among the source of those information and the trust placed in from our patients in terms of access to vaccination and we figured out a strong statistically significant correlation with the figure of gynecologist or the family physician in carrying those information. The weakest correlation is the word-of-mouth, this is why we decided to produce and distribute a vademecum (fact sheet) in order to improve this gap (*Annex 2*).

The total amount of interviewed patients assumed that this initiative is useful.

The results of our study seems to be disappointing; our data indicated the lacking information about the risk potential risk of congenital rubella in pregnant women of the Naples'area and the vaccination practice. In fact more than two-thirds of the interviewed women declared that they had not been vaccinated or did not remember. About half of the sample declared that they did not know the potential consequences of CRS; in addition, some women, despite having received a correct information from the gynecologist, did not to have kept any account.

Lastly, in the women who already did know the risk of rubella, only about 46% had received information from a medical source (gynecologists or general practitioner), whereas the remaining ones had received information from family

members/ friends or by TV programs or web sites.

At the same time, encouraging data of our study could be the high level of adherence to the study by the pregnant women and the statement by more than half of the sample that they willing to be vaccinated since they had understood the risk related to CRS. Although it could be very interesting to figure out how many of those women willing to undergo vaccination against rubella in the post partum have really been vaccinated in postpartum, we don't have this information because, after discharge, those women recruited in our study have been committed to their primary care physicians.

CONCLUSION

In conclusion, our study confirmed that most pregnant women had a not sufficient level of knowledge about both the potential consequences on offspring and about the importance of vaccination in a region as Campania where the incidence of SRC is still higher respect to other Italian regions. Although the data collected give information only on the cluster of patients recruited in Campania Region, limiting the possibility to generalize the results, those data are comparable to ones collected in other Italian Regions that, unlike the Campania ones, are available on ISS website.

Many pregnant women still believe that the vaccine against rubella is useless or can be dangerous for their health. Thus, we feel that informing and forming pregnant women about the risks of rubella and the benefit of vaccination is a key point to implement the National Plan for Measles and Rubeola Eradication in Campania, since the University of Naples Federico II is the gynecological and obstetrician reference regional center for infectious disease and AIDS and have a large basin of patients.

We have found that, by filling the questionnaires and reading the facta sheet, the pregnant women had shown a reborn interest about this issue and likely more compliance to perform vaccination in the post-partum era. The statistically significant difference, between pregnant women and those who accepted to practice vaccination, once informed about risks due to congenital infection, reinforced our hope.

According to the Ethic Code's articles, we feel that gynecologists and obstetricians have to play an important role in the women and the couple training and have to inform the woman about the

risks of rubella in pregnancy, without delegating this role to family or information networks. The obstetricians can play a key role during both the pre-marriage courses or birth preparation classes.

In this way, the National Plan for Measles and Rubella Eradication could have a better chance of being applied on the territory.

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None

Author contribution:

Anna Maria Spera: study design, planning and conduct of the study, data analysis, literature research, and manuscript writing;

Davide Simeone: study design, data analysis, literature research, and manuscript writing;

Vincenzo Bianco: study design, planning and conduct of the study, data analysis, literature research, and manuscript writing;

Barbara Donnarumma: collecting data, manuscript writing; *Grazia Tosone*: study design, planning and conduct of the study;

Rosanna Zapparella: planning and conduct of the study, trained our Obstetrician to collect data;

Orsola Tambaro: planning and conduct of the study;

Achille Tolino: manuscript supervision;

Raffaele Orlando: manuscript supervision.

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ANNEX I Questionnaire

1. Did you ever been vaccinated against Rubella?

- a. No
- b. Yes
- c. I don't know

2. If you answered "no", why?

- a. I contracted Rubella
- b. I think that the vaccination is dangerous
- c. I don't think that vaccination is important
- d. I've never seek information about rubella

3. Do you know that Rubella is dangerous for the product of conception if contracted during pregnancy?

- a. Yes
- b. No

4. If you answered "no", why?

- a. Nobody told me anything about complications of rubella in pregnancy
- b. My obstetrician informed me but I didn't care about

5. Now that you're conscious of Rubella's complications on foetus, are you willing to vaccine yourself before your next pregnancy?

- a. Yes
- b. No

6. If you answered "no", why?

- a. I think that vaccination is dangerous
- b. I'm not enough informed about any possible collateral risks
- c. Other: specify _____

7. Did you know those information?

- a. Yes
- b. No

8. If you answered "yes", how did you reach those information?

- a. Family doctor
- b. Obstetrician
- c. Family
- d. Tv
- e. Web
- f. Friends
- g. Other: specify _____

9. Did you found those information useful?

- a. Yes
- b. No

ANNEX II Rubella fact sheet for pregnant women

Do you know that Rubella is an infectious disease that can be transmitted from mother to the baby if contracted during pregnancy?

- » If the contagion happens during the first trimester rubella may cause abortion, intrauterine death or severe fetal malformations
- » The most severe consequences at the birth are ocular and earing defects, mental retardation, cardiac malformations, hepatic and bone marrow dysfunctions.
Why put your baby's life at risk?

Do you know that is possible to be vaccinated, before pregnancy, in order to prevent this infection?

- » Vaccine against rubella is effective and safe and has to be proposed, if necessary, to all the pregnant women who have not been affected by rubella yet.
- » Pregnant women cannot underdo vaccination, but they can postpone it after the delivery
- » The woman who has been vaccinated has to wait at least one month before to become pregnant again.

It is possible to refer to her own local health district in order to perform both laboratory test and vaccination against rubella free-of charge!

Table I. Results of questionnaire

	Yes	No	I don't know
Did you have been vaccinated against rubella?	19 (14,5%)	100 (76,3%)	12 (9,16%)
Do you know that rubella may have consequences on your baby during pregnancy?	66 (50,3%)	65 (49,6%)	66 (50,3%)
Now that you're conscious about consequences related with rubella in pregnancy, do you think to vaccine yourself for in the near future, after pregnancy?	85 (64,8%)	18 (13,7%)	1 (0,7%) 25 (19,08%) missing
Did you already know those information?	74 (56,4%)	57 (43,5%)	/
Did you find useful those information?	131 (100%)	/	/