ORIGINAL ARTICLE

Eliminating congenital rubella: a seroepidemiological study on women of childbearing age and MMR vaccine coverage in newborns

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Key words

Congenital rubella • Seroepidemiology• MMR vaccination

Summary

Introduction. *Rubella can have particularly serious effects on the product of conception if contracted during pregnancy. Thus, the main aim of rubella vaccination programmes is to prevent infection during pregnancy.*
Materials and methods. *A seroepidemiological study was conducted from July 2006 to December 2007 on 1,000 women of childbearing age, 15 to 45 years old, using specific rubivirus antibody assays, IgG and IgM. A questionnaire administered at the same time allowed us to survey how much women knew about this disease. In addition, MMR vaccine coverage rates were analysed for cohorts born in the local health districts of Messina for the period 1993-2006.*
Results. *An analysis of the replies given to the questionnaire showed an estimated 42.8% of the women to have immunity from rubella, while the serological study showed an immunity coverage rate of 80.6%. Vaccination coverage in the local health districts regarding the first dose of MMR was 81% (cohorts 1993-2005), while the rate was only 24% for the second dose (cohorts 1993-2002).*
Conclusions. *Both immunity coverage in women of childbearing age and that for newborns (for the cohort considered) fall below the 95% target set by the National Elimination Plan for Measles and Congenital Rubella (PNEM). It is therefore necessary to provide women with adequate information about the risks of rubella during pregnancy and about the benefits of vaccination, as well as to recoup subjects at risk or those whose immune status is unknown. Public health authorities also need to make continued efforts to increase the number of MMR vaccinations throughout the region.*

Introduction

Rubella is an exanthematic disease which is generally mild but can have potentially dramatic consequences for the foetus if contracted during pregnancy. The rubella virus can transplacentally infect the product of conception. Indeed, 85% of infections contracted in the first trimester of pregnancy can cause spontaneous abortion, intrauterine death or extremely serious foetal malformations, such as deafness, mental retardation, cataracts and other eye diseases, heart defects, etc. (congenital rubella syndrome - CRS).
The main aim, therefore, of rubella vaccination programmes is to prevent pregnant women from becoming infected and, consequently, to prevent congenital rubella (CR).
In Italy, the rubella vaccine was introduced in 1972 and initially vaccination was recommended only for prepubertal girls. Currently, the national vaccination calendar provides for immunisation using the combined measles-mumps-rubella vaccine (MMR) for all newborn babies aged 12-15 months. In addition catch-up initiatives are organised under the National Elimination Plan for Measles and Congenital Rubella (PNEM) [1].
The medium-term targets set by the PNEM, regarding vaccination coverage for an MMR dose by the age of two years old, are to achieve and maintain, at both national and regional level, 85% coverage by 2004 and 90% by 2005. By 2006 the target is 95% coverage of at least one dose of MMR in children aged between 3 and 15 years. Routine statistics for the year 2005 show the national average to be 89% (range: 58-93%) [2]. Eight regions achieved the 90% target, while ten regions managed 85-89% coverage and three fell below 85%, including the region of Sicily with a vaccination coverage rate of 81%.
Although the national vaccine coverage rate achieved for newborns [3] has reduced the virus in circulation, it has not eradicated it. Thus, there still remains a significant risk of CR in Italy, where high levels of susceptibility to rubella exist in both the general population as well as in women of childbearing age. In the first half of the year 2008, point epidemics of rubella were recorded in the Italian regions of Friuli-Venezia Giulia, Piemonte and Calabria, with a parallel increase of cases occurring in pregnancy [4]. These outbreaks demonstrate the need to identify and recoup those women of childbearing age who are still at risk.

It has been estimated that to prevent CRS the percentage of susceptible women of fertile age must not exceed 5%, but the few studies of seroprevalence available show that the actual percentage still falls far short of national targets. In order to redress this shortfall, PNEM initiatives are designed to achieve and maintain over time a high rate of vaccination coverage in paediatric age and to assess the immunity of women of fertile age in order to vaccinate those susceptible prior to any pregnancy.
A seroepidemiological study was carried out in order to add to the current knowledge base regarding the available national statistics. The study was conducted on a female population of childbearing age and also assessed MMR vaccine coverage for cohorts born in the period 1993-2006 in the Italian city and province of Messina.
Moreover, given the unsatisfactory results so far obtained from the initiatives targeting women of childbearing age, a questionnaire was also given to the same sample of subjects. The aim was to study the level of knowledge and awareness of the potential dangers of rubella contracted during pregnancy.

Materials and methods

The study was carried out from July 2006 to December 2007 on a total of 1,000 women aged between 15 and 45 years who were resident in the province of Messina.
Having obtained their informed consent, a blood sample was taken from each woman to assay the anti-rubella antibodies IgG and IgM. The samples were taken at the University hospital in Messina (AOU "G. Martino") at the outpatient clinic and at our facility. Commercial kits were used to assay the antibodies, i.e. AxSYM Rubella IgG and Rubella IgM (ABBOTT Diagnostics Division), using the Microparticle Enzyme Immunoassay (MEIA). On the basis of assay criteria, the results equal to or greater than 10 UI/ml were considered positive for IgG anti-rubella antibodies, while samples with an index equal to or greater than 0.800 were considered positive for IgM anti-rubella antibodies.
Each woman who took part in the study was given a questionnaire (Fig. 1) to collect their demographic data, including level of education. The questionnaire also in-

Fig. 1. Questionnaire used.

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Form No. □□□□ **Date** □□□□

Surname and first name_____ **Date of birth** _____ **Nationality** _____

Education and qualifications Primary school □ Lower secondary school □ Higher secondary school □ Degree □

Are you aware of the damage that rubella contracted during pregnancy can cause the foetus? YES □ NO □

If yes, how did you obtain this information? _____

Have you ever been pregnant ? YES □ NO □

Have you ever had rubella ? YES □ NO □ NOT KNOWN □ if YES, when □□□□

Have you been vaccinated against rubella? YES □ NO □ NOT KNOWN □ if YES, when □□□□

If YES :

Was information provided by your family? YES □ NO □

Were you vaccinated at lower secondary school? YES □ NO □

Were you vaccinated before a pregnancy? YES □ NO □ NOT KNOWN □

Were you vaccinated after a pregnancy? YES □ NO □ NOT KNOWN □

cluded a series of questions designed to obtain information about subjects' level of knowledge about the risks of rubella in pregnancy, about any prior history of the disease and vaccinations received.
The women recruited to take part in this study were divided into three age-groups as follows: 15-25, 26-35, 36-45 years.
The replies to the questionnaire were assessed using the software Epi Info 6.04d (Centers for Disease Control and Prevention – Atlanta - USA).
Administrative data held by the local health unit 5 (ASL) of Messina were used to assess MMR vaccine coverage in cohorts born between 1993-2006. Local health unit 5 comprises the following eight Health Districts that cover all of the 108 local council areas that make up the entire Province: Messina, Taormina, Milazzo, Lipari, Barcellona, Patti, Mistretta and S. Agata Militello.

Results

The analysis of the replies to the questionnaire showed that 646 of the women interviewed (65% of the sample) were aware of the harm that rubella may cause a foetus if the disease is contracted during pregnancy. As shown in Figure 2, the main source of this information (55%) came from subject's own studies, 19% came from a G.P. (General Practitioners) and only 4% from a gynaecologist.
The majority of the women interviewed had a medium-high level of education, 21% held a university degree, 55% a higher secondary school leaving diploma, 22% held a lower secondary school diploma and 2% a primary school leaving certificate (Fig. 3).
On the basis of the answers given to certain items in the questionnaire, the estimated number of women that declared being immune to rubella was 428 (42.8%); while 326 (32.6%) stated that they had already had the disease and 102 (10.2%) said they had been vaccinated in the past. As regards the latter, 17 women (16.7%) declared having been vaccinated at secondary school, 9

Fig. 2. Sources of information.

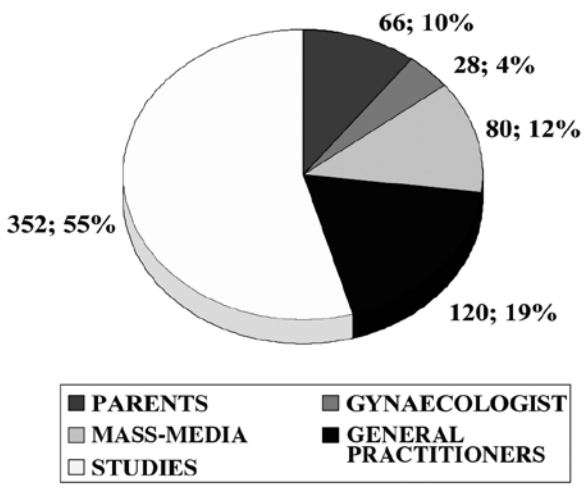
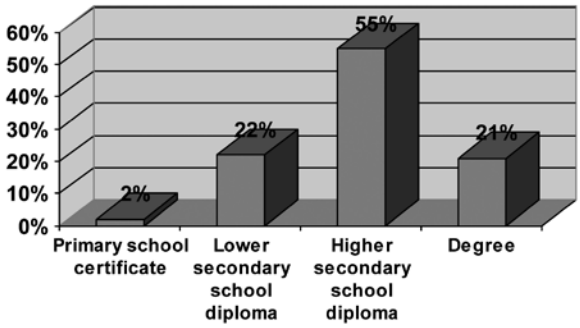
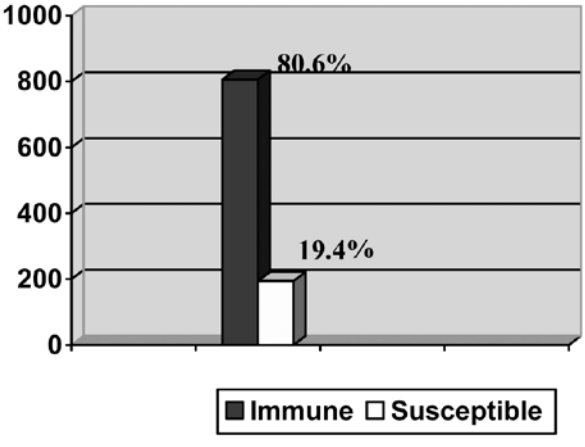


Fig. 3. Educational level of population sample studied.



(8.8%) prior to a pregnancy and 31 (30.4%) postpartum, while the remaining 45 women (44.1%) were unable to indicate when they had been vaccinated.
However, the serological tests showed the actual immune coverage of the population studied to be 80.6% (Fig. 4). Indeed, 806 of the 1000 sera samples examined, presented specific IgG anti-rubella antibodies while 194 were negative. No positive cases of IgM were found. Table I shows the results by age group. The highest immune coverage (41.2%) was found in the 15-25 year-old group followed by 33.5% in the group aged 26-35 years and, finally, 25.3% for the group aged 36-45 years.
As regards the IgG concentrations for the individual samples, the geometric mean of antibody titres was 128.23 UI/ml in 15-25 year-olds, 119 UI/ml in the 26-35 age group and 117.24 UI/ml in 36-45 year-olds.
The women that were found to be susceptible were encouraged to have an anti-rubella vaccination and were

Fig. 4. Immunity status of population sample studied.



Tab. I. Immunity status analysed by age-group.

Age	15-25	26-35	36-45	Total
Immune	332 (41.2%)	270 (33.5%)	204 (25.3%)	806
Susceptible	78 (40.2%)	52 (26.8%)	64 (33%)	194

Tab. II. MMR vaccine coverage for entire ASL 5 local health authority area.

Year of birth	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	Mean (%)
ASL 5 (%)	62	71	71	75	85	88	87	82	95	87	87	86	82	81

Tab. III. MMR vaccine coverage: first dose by year of birth and health district.

Year of birth	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	Mean (%)
Messina	54	62	66	70	82	87	84	82	99	93	87	81	77	79
Taormina	56	62	64	58	70	74	73	72	89	89	82	80	90	74
Milazzo	82	87	83	82	93	93	93	87	91	87	93	90	90	89
Lipari	10	40	47	49	43	47	79	68	97	83	79	45	48	57
Barcellona	69	78	72	83	87	81	83	81	91	83	92	77	79	81
Patti	63	84	83	93	97	99	99	77	84	70	78	68	72	82
Mistretta	61	82	67	82	90	91	89	56	97	93	89	90	98	83
S.Agata M.	73	73	71	74	83	88	90	86	89	81	86	81	47	79

N.B.: Data refer to cohorts aged 24 months

offered this free of charge. This enabled us to vaccinate 62 (32%) of the non immune women at our facility.
Administrative data regarding MMR vaccination coverage in the province of Messina, for all health districts in the province, was updated to 31 October 2008. The data were complete for cohorts born in the years 1993-2005 but only partially complete for cohorts born in 2006. Vaccination coverage for the ASL 5 Local Health Authority district regarding the first dose of MMR was 81% for 1993-2005 cohorts (Tab. II), while the second dose covered only 24% of 1993-2002 cohorts (Tab. V).
Table III shows the percentage of vaccination coverage achieved by MMR dose analysed by year of birth and for each individual health district. What strongly emerges is how widely coverage varies from district to district, from 10% for year of birth 1993 in the district of Lipari up to 99% for the years 1998 and 1999 in the district of Patti, a level also achieved in Messina but only for the year 2001. Furthermore, an increase can be seen in almost all districts up to 2001. However, in subsequent years a decrease in coverage was seen in more than half of these districts.
Table IV reports the partial data for the first dose of MMR for cohorts born in 2006, updated to 31 October 2008.

Tab. IV. MMR vaccine coverage: first dose partilal data.

Year of birth	2006
Messina	71
Taormina	59
Milazzo	91
Lipari	50
Barcellona	74
Patti	89
Mistretta	99
S. Agata M.	73
Media (%)	76

N.B.: Data refer to cohorts aged 24 months

Table V reports the percentage of vaccination coverage achieved for the entire ASL 5 area for cohorts born between 1993-2002, with the first dose of MMR vaccine. It also shows the percentage vaccinated with the 2nd dose but this is updated to 31 December 2007. It can be seen from the Table that a coverage rate of over 85% for the first dose of MMR was achieved in the province of Messina only for the years 1998-99 and 2001-02 with a sharp increase in 2001 up to 95%, while the average percentage for the second dose was 24% with peak levels of 32% and 38% being achieved in the years 1998-99 respectively.

Discussion and conclusions

An analysis of the results prompts the following considerations.
35% of the women who took part in the study did not know of the damage that the rubella virus can cause to the foetus during pregnancy and of those who were aware of the risks only 4% reported that this information had come from a gynaecologist, 19% from a G.P. while the majority 55% had learned through their own studies. The latter is correlated with the high educational level of the subjects in our study (Pearson correlation coefficient = 0.657).
Interestingly, education influences only awareness of the risks but not the decision to be vaccinated. Indeed, there was no significant statistical difference between women who had been vaccinated and those who reported not having done so ($p > 0.05$), in relation to both educational level as well as the source of information about risks.
The results reported in Table I highlight how the percentage of immune women falls as age increases. When considering the overall immunity status (immune/non immune) by age-group there is a statistically significant difference only between the 26-35 age-group and 36-45 year-olds ($p < 0.05$).

Tab. V. MMR Vaccine coverage first and second dose.

Year of birth	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	Total
N. born for year	7202	6725	6396	6212	5888	5702	5597	5736	5515	5391	60364
N. vaccinated 1st dose	4453	4751	4568	4669	5024	5016	4905	4739	5288	4702	48115
% 1st dose	62	71	71	75	85	88	87	82	95	87	80
N. vaccinated 2nd dose	1558	1752	1583	1479	1474	1841	2137	1601	841	111	14377
% 2nd dose	22	26	25	24	25	32	38	28	15	2	24

N.B.: The number born for year are shown based on information collected by individual councils.

17.5% of the women who reported knowing the risks of rubella in pregnancy were not protected from those same risks and from checks on the vaccination status it emerged that 9.8% of the women who reported having been vaccinated did not have protective antibodies. This is probably due to the inadequacy of information given to the target population which led to confusion regarding the vaccinations given.

Only 42.8% of the population examined knew that they were immune to rubella while a high percentage (30%) of women were unaware of their own immune status.

The offer of a free anti-rubella vaccine allowed us to claw back only 32% of the women at risk. Indeed, resistance to the proposed vaccination was encountered in people who had not been immunised which is attributable more to unresolved doubts rather than to any concrete reasons.

The immunity coverage of the population examined of 80.6% falls far short of the 95% target set by the National Elimination Plan for Measles and Congenital Rubella. Based on administrative data, even the vaccination coverage rates achieved for newborns are lower than the PNEM targets set for the year 2005. The high vaccination coverage rates that were achieved in some districts up until 2002 can be traced to initiatives organised by the Sicilian Regional Authority which in 1998 strengthened the supply of MMR vaccinations [5]. Moreover, in the year 2000 it launched a regional project to prevent measles, mumps and rubella [6] which aimed to recoup people born between 1993 and 1999 who had not been vaccinated, and in 2004 it set up a catch-up MMR vaccination programme [7] which implemented a more effective MMR recruitment strategy for newborns and for the supply of a second dose of MMR at the age of 5 years old.

However, as normally happens once a special campaign comes to an end, the numbers accessing the vaccination programme subsequently diminished. This highlights that MMR vaccination requires a continued and constant effort by the public health system to cover the entire region.

A further point based on the above considerations is that women clearly need to be informed adequately and continuously about the risks of rubella in pregnancy as well as about the benefits of being vaccinated and that steps need to be taken to recoup susceptible women or women whose immune status is unknown.

It is vitally important, therefore, that all healthcare workers (G.Ps, gynaecologists, paediatricians, obstetricians) are involved and collaborate in this process. It is also important to provide informative material and use various means of communication to promote such an initiative. The final goal is to reduce the number of susceptible women of childbearing age to below 5%, the threshold set by the National Programme which is indispensable for congenital rubella to be eradicated.

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