

## Evaluation of Rubella IgG Antibodies Among Women at Marriage in Kermanshah City, Before and After Mass Vaccination

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### ABSTRACT

**Background:** Rubella is a mild viral infectious disease, usually occurs subclinically without a serious complication. But if occurs during pregnancy, specially the first trimester, it can transmit and invade to fetus causing congenital rubella syndrome or fetal death. In 2003, nearly all Iranians at the age of 5 to 25 years old were vaccinated against rubella and the vaccine was included in the compulsory immunization, MMR afterwards.

**Methods:** This study was carried out on girls attended at a marriage consultancy center in Kermanshah city (West of Iran) in 2006. Considering 95% of confidence, the sample size was estimated at 140. All samples were tested using ELISA serologic method and compared with similar study conducted on 240 unvaccinated girls at the same place in 1999.

**Results:** Antibody positivity was observed in 99.3%, compared to 79.58% of the previous study. A rise of 19.72% (95% CI 12.7%-26.7%) of seropositivity was observed in vaccinated girls versus unvaccinated ones ( $P < 0.001$ ).

**Conclusion:** In our previous study, we had recommended to screen for susceptibility to rubella before marriage, which is no longer required since more than 99% of vaccinated girls showed immunity at the time of marriage. However, as sustainability of immunity after rubella vaccination is usually less than immunity due to illness, we recommend screening for rubella protective antibody every few years.

**Keywords:** Congenital rubella, immunity, rubella, seroepidemiology, vaccination

### INTRODUCTION

According to the WHO experts, if rubella infection occurs during the early stages of pregnancy, the potential of passing the virus through the placenta and reaching the fetus is about 90%.<sup>[1]</sup> The most important complication of rubella is “congenital rubella syndrome (CRS),” which directly relates to lack of immunity during pregnancy. On the other hand, by vaccination of all the susceptible people or women in reproductive age, or the susceptible girls at the time of marriage and induce immunity

in them, it is possible to prevent the disease in mothers and its possible serious complications in their fetus.<sup>[2]</sup> So the primary purpose of rubella vaccination is to prevent congenital infection with rubella virus and CRS, which affects an estimated 110,000 infants each year in developing countries.<sup>[3]</sup>

The disease is spread globally, and before vaccination era at the Northern hemisphere the maximum of its attacks had been between February and April<sup>[4]</sup> in the countries without effective policy for childhood vaccination or those countries where the vaccination policies only targeted the females, still rubella is endemic and in winter and early spring it causes some outbreaks.<sup>[5]</sup> In the closed populations such as military camps or prisons, the attack rate may reach to 90%–100%. However, in those who had suffered from this disease or vaccinated before, the possibility of infection is minimized.

The disease is usually rare in infants born from IgG positive mothers due to antibody transfer and they will be immune for the first 4–6 months of their life.<sup>[6]</sup> In general, the spread of the disease among the children has been seriously decreased, by extensive vaccination.<sup>[4,6]</sup>

The most commonly used vaccine globally is derived from the RA27/3 virus strain, which makes more immunity in comparison with other vaccines and the immune response is more similar to the immunity after natural infection<sup>[4]</sup> and one dose induces seroconversion in  $\geq 95\%$  of vaccinated persons.<sup>[7]</sup>

A variety of seroepidemiological studies have been done globally to evaluate the situation of protective antibodies and need assessment to vaccinate against rubella virus.<sup>[8]</sup> For example in Australia, the rubella vaccination was established for the schoolgirls since 1971 and the CRS was significantly decreased thereafter.<sup>[9]</sup> In Denmark, the vaccination policy was optional for the schoolgirls from 1974, but in 1987 it was replaced by extensive vaccination with two doses of MMR. Nine years later, the anti-rubella antibody rose to 96.5% in vaccinated people. However, this was considerably lower in unvaccinated persons.<sup>[10]</sup>

A seroepidemiological study in Chahar Mahal-va-Bakhtiari province (Western Iran), on 1347 urban and rural females using the hemoagglutination inhibition (HI) method, indicated 90.5% immunity against rubella. In

another study in Tabriz (North-western Iran), the rubella level of immunity was 85.83%. In a study made on 400 high school girls in Ghaem Shahr (Northern Iran) in 1997, and using the ELISA method, 90.75% had immunity to rubella and 9.25% were susceptible. During the study in 1999 on 200 female university students in Kordestan (Western Iran), only 14.9% of them did not have anti-rubella IgG.<sup>[11]</sup> During a study made in 1999 in Kermanshahi girls at marriage, 41 out of 240 studied cases did not have protective antibody and so about 20% of the referred population were susceptible, and it was then prescribed that screening for them shall be done before marriage and in susceptible cases; they shall be vaccinated against rubella.<sup>[12]</sup>

It should be mentioned that due to these studies, finally the health plans policy makers and authorities concluded to add the rubella and mumps vaccines to the Iranian National Vaccination Plan and remove the worry resulted from the maternal rubella. So that this plan was implemented in 2003, and almost all of the 5 to 25 age group of Iranian (98%) have been vaccinated, and thereafter, the MMR vaccine was contained in the country vaccination program instead of measles vaccine alone and since then the trend associated with the studies on rubella seroepidemiology was changed to compare the situation of rubella protective antibody before and after vaccination.

The national immunity of measles–rubella program was commenced at December 2003, with the target of vaccination of 33,579,082 people of 5 to 25 years old Iranians and 98% of the target population were vaccinated. Such successful proceeding resulted in a decrease in the appearance of measles and rubella for less than one case per million.<sup>[13]</sup> The main goal of this survey was to evaluate and compare the susceptibility and resistance of Kermanshahi girls at marriage, before and after mass rubella vaccination.

## METHODS

This cross-sectional study was carried out on 140 premarriage girls in 2006. The samples were randomly selected from population referred to the main marriage consultancy center in Kermanshah city, West of Iran. About 10,000 girls in Kermanshah refer to Rafatieh health centre for their premarriage medical tests, annually. Since it was expected that

the immunity rate after rubella vaccination to be increased from 80% in 1999 to more than 90% in 2006, the sample size of 140 was calculated using the EpiInfo software and 95% confidence. All blood samples were taken and tested under similar conditions and by the same person at the reference laboratory. For quality assurance, about 10% of the samples were chosen, randomly, and rechecked at Red Crescent laboratory of Kermanshah. The titration was done by quantified ELISA method.

The data were analyzed and interpreted using percentages and confidence intervals (CI). The results of this study were compared to those of the previous similar study conducted by the main researcher in 1999 with similar design at the same place but unvaccinated girls.<sup>[11]</sup> Comparison of proportions formula was used for this mean.

## RESULTS

Age distribution indicated that the majority of the study population (35%) was 20–24 years old. Their average age was 21.95 (SD = 3.64), and the youngest and oldest were 15 and 30 years old, respectively. With respect to educational level, 20.14% of the samples were illiterate, 19.29% were in primary school, 20% in guidance school, 32.14% in secondary school, 5% have college degree, 11.43% were bachelor, and 2.86% were not identified. A sum of 19.29% of cases was living in rural and the rest (80.71%) in urban areas.

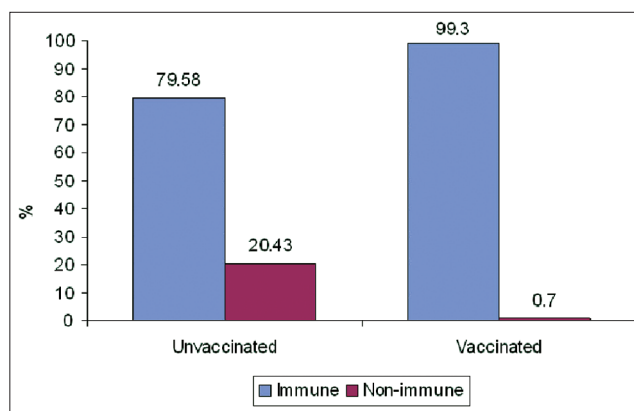
Positive antibody, immunity against rubella, was seen in 99.3% (139 out of 140 vaccinated girls, compared to 79.6% (191 out of 240 unvaccinated girls) [Figure 1] of the previous study. Therefore, we are faced to a significant rise of 19.7% (95% CI 12.7%–26.7%) of seropositivity and immunity against rubella in vaccinated versus unvaccinated girls ( $Z = 5.481$ ,  $P < 0.001$ ).

## DISCUSSION

This study revealed that mass vaccination of rubella caused a highly significant decrease in the rate of negative antibody from 20.42% to 0.7%. The finding is in line with reliable sources<sup>[7]</sup> and extensive country study, which has compared immunity rate before and after Iranian 2003 mass vaccination.<sup>[14]</sup> The result also agrees with the research conducted in Mashhad (East of Iran).<sup>[15]</sup> In addition, our study showed higher

immunity improvement than those reported from Shahre-Kord<sup>[16]</sup> and Hamadan<sup>[17]</sup> cities in the West of Iran.

During an extensive study made by Immunology Department researchers on 1217 serum samples before vaccination (on 324 susceptible and 893 immune persons), and 2007 serum samples after vaccination (24 susceptible and 1983 immune) in 5 to 15 years age group fulfilled in ten provinces, it was identified that the immunity rate of the prevaccination was raised from 73.4% to 98.8% of the postvaccination.<sup>[14]</sup> In another study in Mashhad, the level of immunity before and after vaccination has been 70.38% and 98.5%, respectively.<sup>[15]</sup> During a study made on 150 Shahr-e-Kord Medical University students, it was identified that 129 (86%) of them were immune before vaccination, while it increased to 96% after vaccination.<sup>[16]</sup> During a study at Hamadan Health Center, the level of anti-rubella antibody in Hamadani girls at marriage had been 83.5%, while two years after such program it has increased to 98.4%<sup>[17]</sup> [Table 1]. The effectiveness



**Figure 1:** Situation of anti-rubella antibody and immunity in unvaccinated (left) and vaccinated (right) Kermanshahi girls at marriage, 2006

**Table 1:** Rubella seropositivity before and after vaccination in Iran

Location	Vaccination		P Value
	Before	After	
Country <sup>[14]</sup>	73.40%	98.00%	$P < 0.001$
Mashhad <sup>[15]</sup>	70.38%	89.50%	$P < 0.001$
Shahr-e-Kord <sup>[16]</sup>	86.00%	96.90%	$P < 0.001$
Hamadan <sup>[17]</sup>	83.50%	98.40%	$P < 0.001$
Current study	79.58%	99.30%	$P < 0.001$

of the RA 27/3 vaccine has been demonstrated by the elimination of rubella and CRS from the western hemisphere and by the several European countries that have achieved and maintained high vaccination coverage with vaccines containing RA 27/3.<sup>[18]</sup>

## CONCLUSION

Mass rubella vaccination in 5 to 25 years old Iranian population during 2003,<sup>[13]</sup> and continued thereafter as MMR in national vaccination program,<sup>[19]</sup> has significantly resulted in increase in anti-rubella antibodies and immunity in high-risk people, as premarriage Kermanshahi girls, and in comparison to many of the results specified in local and international sources,<sup>[7,20]</sup> and due to the susceptibility of less than 1% of the Kermanshahi girls at marriage, there is no more need to screen the vaccinated girls at marriage, which was emphasized in 1999;<sup>[8]</sup> however, the screening studies is recommended every few years.

## RECOMMENDATION

As the dispersed studies associated with the rubella seroepidemiology in different locations of the country resulted in awareness of lack of immunity of about 20% of the most vulnerable society members, i.e., the pregnant women, and after that the policy makers decided to announce the rubella vaccine as the compulsory state vaccines, it is proposed such studies to be made for the immunity status against tetanus, diphtheria, etc. Additionally, due to the fact that neither rubella infection nor vaccination result in life-long immunity, it is proposed that once each couple of years the studies associated with the rubella seroepidemiology to be performed in different regions of the country and if necessary, the vaccination of vulnerable society members be made, like in 2003.

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