A review of anti-measles and anti-rubella antibodies in 15- 25 year old women in Jahrom City in 2011

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Abstract

Introduction: Measles and rubella are acute viral diseases. Rubella often has mild clinical symptoms and cannot be diagnosed. Pregnant mother's infection with this disease causes serious complications, especially congenital rubella syndrome which is one of the causes of neonatal mortality, severe congenital defects and permanent disability in children. In contrast, measles often occurs with severe symptoms. This study aimed to determine the immunity level of Jahrom's young girls and women against measles and rubella 7 years after the public vaccination comparing to determine the percentage of infection with these two viruses, the effectiveness of the vaccine and an appropriate method to prevent the complications of these two diseases.

Methodology: This study was a cross-sectional descriptive study. According to the previous study conducted one year after the public vaccination in Jahrom City, 100% of the subjects were given immune anti-rubella antibody titer and 94% received immune anti-measles antibody titer. Now this study measured anti-measles and anti-rubella antibody titers (IgG) in 180 women and girls aged 15-25 in Jahrom City through ELISA assay.

Results: 165 subjects (91.7%) had positive rubella titer, 13 subjects (7.2%) had suspected rubella titer and 1 subject (0.6%) had negative rubella titer. Meanwhile, 170 subjects (94.4%) had positive, 6 subjects (13.3%) had suspected and 3 subjects (1.7%) had negative measles titer. Regarding suspected cases as positive for long-term maintenance of serums, a total of 98.5% of people were immunized measles and 97.5% were immunized rubella. With increase of age, antibody titer significantly increased (p<0.05). There was no significant relationship between taking or not taking steroids, immunity repressor and the subjects' immunity percentage (p<0.05).

Conclusion: The results showed that although the national vaccinationcomparing in 2003 has been effective in immunizing the women of gestational age to measles and rubella, it seems that due to the gradual reduction of this immunity, all women, before pregnancy, should undergo a test to determine their immunity to these two diseases and if necessary, booster vaccine should be inoculated.

Key words: Measles, Rubella, Congenital rubella, vaccination, IgG.

Introduction

Measles is a highly contagious disease the incidence of which declined due to widespread vaccination. However, there are still outbreaks of the disease worldwide, which can be due to the primary vaccine failure in a small percentage of children and the lack of vaccination in some percentage of preschool children and, finally, because of the reduction in the anti-measles antibody levels in children born to the mothers with no history of wild virus infection [1]. Measles vaccine failure was reported in 5% of those who received only one dose of vaccine at 12 months of age. However, weaning immunity can be observed in some people after each vaccine [2]. Rubella is a mild disease with cutaneous rash that is more severe in children and infants than in adults, and the worst problem with rubella is its trans-placental transmission, fetal infection and congenital malformation which causes eye symptoms (cataract, glaucoma, etc.), microspheres, PDA, nerve deafness, etc. in the infants. Before vaccination, rubella epidemics were observed every 6 to 9 years. Now after vaccination, the incidence of the disease has reduced by 99% [1]. Infection with rubella was asymptomatic in 25-50% of cases, and immunity after infection with virus and with vaccine was prolonged. However, at the same time, some rare cases of infections were reported [2]. After the injection of MMR vaccine, sero conversion rate was different in children. In a study conducted in Korea, after MMR injection to 121 children 1-2 years old, sero conversion rate was reported to be 97-97% for rubella and 100% for measles. Regarding the children aged 4-6, who were sero negative, all 39 children had 100% sero conversion rate for measles and rubella after MMR injection [3]. In the study conducted by Dr. Zamani and Dr. Daneshjoo in Tehran in 2004 on 1,665 schoolchildren aged 6 to 12, 68.5% had no anti-rubella antibody titer. A year after the mass MR vaccination in Iran in 2004 and during that time all women under the age of 25 were vaccinated with MR. In a research project conducted in the city of Jahrom, IgG rate against measles and rubella was reviewed in girls of 15-25 year old by ELISA method and the seropositivity rate of the vaccinated subjects was reported to be 100%. The pregnant mother's infection with measles virus, and especially rubella virus in the first three months, can have harmful irreparable effects on the fetus. The goal of measles and rubella vaccine preparation and all its immunization programs was to avoid these complications, especially congenital rubella syndrome. Selection of the appropriate measles and rubella vaccination requires obtaining information about these diseases and their complications and performing community-based epidemiological studies, especially in pregnant women and women of reproductive age, to determine their level of immunity.

Given that in 2003, public vaccination against these two diseases was carried out for the age group of 25.5 years, and after that several similar studies in Iran and a similar study in Jahrom City were conducted, and the immunity level of the subjects after the vaccination was investigated. This study aimed to determine the immunity level against measles and rubella 9 years after the public vaccination of 15 to 25 year-old women in Jahrom City to determine the sensitivity of individuals, the efficacy of the vaccine and an appropriate immunization method to prevent these two diseases.

Methodology

It was a cross-sectional descriptive-analytic study conducted to determine the immunity level of 15-25 year-old girls and women in Jahrom City against measles and rubella virus a few years after the public vaccination. Through convenience sampling method, a blood sample was taken from 180 women aged 15-25 years who referred to the laboratory of Peymaniyeh Hospital in Jahrom City. Then, that was centrifuged and frozen at 4°C. Then, anti-measles and anti-rubella IgE titer were measured using ELISA method and Spectrophotometer. After taking blood samples from 180 volunteers aged 15 to 25, who referred to the laboratory of Peymanieh Hospital in Jahrom, and serum centrifugation and isolation, serums were stored at 4°C for several months. The research methodology was based on the use of ELISA method, which showed 97% sensitivity and 94% specificity for anti-measles IgG and 95.5% sensitivity and 97.1% specificity for anti-rubella IgG. The samples were first placed at room temperature for one hour and shaken at form 8. 100 diluted serum was added to 5 serum. Meanwhile, 5 positive controls were added to one sample and 5 negative controls and 5 cut off controls were added to one sample. Then, the samples were shaken with sugar for 2 minutes and left in a 37°C incubator for 45 minutes. Then, the samples were washed with 0.3 volumes of solution 5 times. Immediately after that, 100 volumes of IgG solution were added to all samples and they were placed in a 37°C incubator for 30 minutes. For the second time, the samples were washed with rinsing solution 5 times and immediately after that 100 substrate solution was added to all samples. After the samples were kept away from the sunlight at room temperature for 20 minutes, 50 of stop solution was added to all of them, and finally, the samples were read using spectrophotometer with a wavelength of 450/620 nm one hour after stopping the test. Samples with a specific anti-measles IgG and specific anti-rubella IgG of less than 9 IU/ml were considered negative, those with 9-11 were considered suspected and those above 11 were considered positive according to the Kite manufacturer's instruction (Vircell Spanish Company). In this method, the antigen-antibody complex was determined by ELISA method and was read by spectrophotometer. Data were analyzed by SPSS V11 software at the descriptive statistics level and the required charts were also designed by Excel XP software.

Results

In this study, serum samples of 180 girls and women of 15- to 25 years in Jahrom City who had a history of public vaccination inoculation were evaluated in terms of measles and rubella IgG. IgG levels were measured by ELISA method based on the international unit of (IU/ml). ELISA method showed sensitivity of 97% and specificity of 94% for anti-measles antibody and 95.5% sensitivity

and 97.1% specificity for anti-rubella antibody. The kits used belonged to Vircell Spanish company. Samples with an antibody level below 9 IU/ml were negative, those with a level of 9-11 were suspected and those with a level of more than 11 were considered positive (according to the kit manufacturer's instructions). The results showed that 165 out of 180 subjects (91.7%) were positive for anti-measles antibody, 1 subject (5.6%) was negative and 13 subjects (17.2%) were suspected. Moreover, 170 subjects (94.4%) had positive anti-rubella antibody, 3 subjects (1.7%) had negative and 6 subjects (3.3%) were suspected. Since suspected cases were considered positive, eventually 98.5% of subjects are still immune against measles and approximately 97.5% are still immune against rubella. Meanwhile, this study reviewed the relationship between the individuals' immunity, steroid use, the incidence of autoimmune diseases, the use of specific drugs and vaccination, and no significant relationship was observed between the individuals' immunity or non-immunity and the use of steroids and self-immune drugs (p<0.05). In this study, 174 (96.7%) patients did not take steroids and 6 (13.3%) patients used steroids. Moreover, 97% of those who had positive anti-measles antibody and 96.5% of those with anti-rubella antibody had used no steroids. Meanwhile, 92% of those who did not take steroids had anti-measles antibody and 94.3% of those who did not take steroids had anti-rubella antibody (Table 1).

Out of those who had positive anti-measles antibody, 98.2% and 97.6% of those with positive anti-rubella antibodies did not use the autoimmune disease drugs. Moreover, 92% of those who did not take the autoimmune disease drugs had anti-measles antibody and 94.3% of those who did not use steroids had positive anti-rubella antibody (Table 2).

There was a significant relationship between age and anti-measles and anti-rubella antibody titer (P<0/05). That is, the antibody titer increases with age increase, so that, regarding the suspected cases as immune, in the age group of 20-25 years, 99.2% are immune against measles and 97.8% are immune against rubella. However, in the age group of 15-19 years, 15-19, these figures are 92.6% and 97.5%, respectively. You can observe this comparison in Tables 3 and 4, respectively.

In general, the results showed that public vaccination was quite effective and an acceptable result was achieved after 9 years.

Discussion

To be able to judge the efficacy of public measles-rubella vaccination system, we needed to collect data about the immunity of people in society, especially young women of reproductive age before and after vaccination. For this purpose, various studies were conducted in Iran. In a study in Shahrekord, 150 students were examined 4 weeks before and 8 weeks after the public vaccination, 86% of whom were immunized against rubella before vaccination and 14% who were sensitive to virus. After vaccination, these figures changed to 96.9% of immune cases and only 3.1% of non-immune cases. In this study, the effectiveness of vaccination was reported to be 80.95% (5). This information was consistent with the findings from the previous study in which 100% of the subjects were immunized against rubella after a national vaccination (6). In Mashhad, the vaccination responsiveness in women aged 15 to 23 was studied. At first, 1698 subjects were examined before vaccination out of which 67.19% were immune against measles and 70.38% were immune against rubella. After vaccination, these figures reached 77.37% and 89.5%, respectively (7). In comparison with our findings from the previous study in which these figures were 94% and 100% respectively (6 - 8), the responsiveness rate was less in Mashhad due to the exclusion of some subjects from the study and the difference between the type of kit used. In Tehran, 390 women were investigated whose immunity against rubella virus was 80.59% before vaccination, and reached 96.8% during vaccination and 100% at the end of the program (9). The results of this study were quite similar to our previous research findings. In 2011 in Shiraz, Professor Alborzi examined 909 women aged 6 to 26 years in the Research Center for Microbiology and divided them into five groups to detect antibody. Measles was reported to be 80.6% for the age group of 10 to 6 years, 72.7% for the age group of 11-15 year, 84.9% for the 16-20 year old group and 87.5% for the 20-29 year old group before vaccination. After vaccination, these figures reached 91%, 99.6%, 99.6% and 97%. The immunity against rubella was reported to be 98.9%, and generalized to immunity against congenital rubella syndrome (10). In our recent study, the immunity rate against measles was reported as 97.5% for 9-15 year old subjects and 93.4% for 20-25 year old subjects, and the immunity rate against rubella was reported 97.5% and 93.4%, respectively. Therefore, our present study as well as the study conducted in Shiraz showed that women's immunity decreases a little with increased age. In Kerman, 4 weeks before and after the public vaccination, the antibody titer was studied in 1089 women. Before the program, 46% of the subjects aged between 5 and 14, 41.7% of the age group of 15-19 years, and 34.1% of the subjects aged 20-25 were immune against the measles virus. After vaccination, 100% of the vaccinated subjects were immunized against measles (11). The study results were consistent with our previous research and the immunity percentage of the individuals was 6% higher than our results, which contributed to the success of vaccination in Kerman, the lack of sampling error and follow ups of the subjects. Our previous study was conducted in Jahrom City on 15-25-year-old urban and rural women. Before the national vaccination, 84.35% of subjects were immune and 14.95% were non-immune against rubella. One year after the public vaccination, the subjects were re-examined and 100% of them were immune against rubella. Moreover, 84.3% of the subjects were immune against measles and 15.7% were sensitive before the vaccination. One year after the vaccination, 94.1% of vaccinated subjects were immunized against measles. In this study, there was no significant relationship between the antibody titers and the subjects' geographic status. However, the subjects' positivity percentage increased with increasing age (6 - 8). However, according

Table 1: A description of the relationship between the absolute and relative frequency of the volunteers' immunity against measles and rubella and taking or not taking steroids

Suspected		Non-immune to rubella		Immune against rubella		Suspected		Non-immune against measles		Immune against measles		
%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	
100	6	100	3	96.5	164	92.3	12	100	1	97	160	Not taking steroids
0	0	0	0	3.5	6	7.7	1	0	0	3	5	Taking steroids
100	6	100	3	100	170	100	13	100	1	100	165	Total

Table 2: A description of the relationship between the absolute and relative frequency of the volunteers' immunity against measles and rubella and taking or not taking autoimmune disease drugs

Suspected		Non-immune to rubella		Immune against rubella		Suspected		Non-immune against measles		Immune against measles		
%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	
100	6	100	3	97.6	166	92.3	12	100	1	98.2	162	Not taking autoimmune disease drugs
0	0	0	0	2.4	4	7.7	1	0	0	1.8	3	Taking autoimmune disease drugs
100	6	100	3	100	170	100	13	100	1	100	165	Total

Table 3: Absolute and relative frequency distribution of volunteers by age and anti-measles antibody titer

Total		Suspected		Positive		Negative		Anti-measles antibody titer / Age
%	Number	%	Number	%	Number	%	Number	
100	41	4.8	2	92.6	38	2.4	1	Age group of 15-19 years
100	137	8.8	12	90.5	124	0.7	1	Age group of 20-25 years

Table 4: Absolute and relative frequency distribution of volunteers by age and anti-rubella antibody titer

Total		Suspected		Positive		Negative		Anti-rubella antibody titer / Age
%	Number	%	Number	%	Number	%	Number	
100	41	2.5	1	97.5	40	0	0	Age group of 15-19 years
100	137	3.6	5	93.4	128	3	3	Age group of 20-25 years

to the present study results, the subjects' positivity percentage of antibody titers gradually decreases after several years. According to the data obtained in these studies, this public vaccination program had a significant role in creating immunity against these two viruses and a successful implementation and the results were close to the determined goals. Finally, according to the article released by Esteghamati, stating that cluster sampling results in Iran suggested a high immunity level of 97% of Iranian women aged 25-40 against rubella. After the national vaccination program in Iran, seven thousand blood samples were collected with the help of UNICEF and over 97.4% of samples were immune to rubella virus. It has also been suggested that the immunity of the children under 5 increased by 53% against rubella and by 93% against measles. Meanwhile, with an immunity of 97% to 99%, the National Vaccination Program for measles and rubella has been successfully evaluated and because of high immunity, women will no longer be vaccinated against rubella (12-13). In our previous study, all subjects were also immune to rubella one year after the vaccination (6). However, this study was designed to determine whether

or not the subjects' antibody titer remains immune after several years of vaccination and whether there is a need to repeat public vaccination. The study results showed the immunity level of 15-25-year-old women to be 98.5% against measles and 97.5% against rubella 9 years after the public vaccination. In the study, 91.7% of the subjects were immune to measles, 0.6% was negative and 7.2% were suspected. Meanwhile, 94.4% of the subjects were immune to rubella, 1.7% was non-immune and 3.3% of cases were suspected. Due to the fact that the samples were stored at 4°C for several months before the test kits arrived and the probability that suspected samples were positive; suspected samples were considered positive. This statistic was consistent with the above mentioned point.

In this study, there was no significant relationship between the use of immunosuppressive drugs. These factors were not investigated in other similar studies conducted inside or outside Iran. According to the results obtained from other studies, as the age increases, the antibody titer increases (14-18). Most likely there will be a risk of exposure to these viruses or infection with them with an increase in age. However, our study showed a slight decrease in antibody titers with age increase. Moreover, the immunity of women of reproductive age before public vaccination was 87% (19) in Kyrgyzstan, (76.3%) in Turkey, (70%) in Brazil (16), (65%) in China and Taiwan (17 and 21), 55% in India (22), (84.6%) in Hong Kong (23) to rubella and (74.1%) in South Korea to measles (24, (84.6%) in Italy against rubella (15), (46%) in Costa Rica against rubella (25), 90.8% in Nepal (26), 50% in Egypt against measles (27), 92.9% in Romania (28), 46% in the UK against rubella (29), and 79% in Madrid against measles and rubella (30) and in Jeddah 71% were reported immune to measles and 90% immune to rubella (31). Only in a few of the reported countries, the percentage of responsiveness to public vaccination was examined. For example, the figures reached 90% in Italy (15), 98% in Costa Rica (25), (97.3%) in China (17), 90% in Egypt (27), 93% in Taiwan (21), 94.4% in Romania (28), 88% in the UK (32), and 73.7% in Jeddah for measles and 91.7% for rubella (31). The point to be noted here is that in this study the antibody titers below 9 units per ml were considered negative, which was used in accordance with the kit manufacturer's instructions. The kit used in this study belonged to the Spanish company Vircell. The values of 11-9 units per ml were considered suspected and the values more than 11 units per ml were considered positive. However, due to the cases mentioned, suspected cases were contractually considered positive. The kit used in one case was not similar to the kits used in the other domestic and international studies. Therefore, if the samples were measured using other kits standards, the number of positive cases would be possibly reduced. Thus, a greater percentage of women in the society can be considered sensitive to these two diseases. In our study, the relationship between the socioeconomic level (urbanism and ruralism) and the antibody titer was not measured. That is because the similar study of Namjoo in 2004 showed no significant relationship between these two cases due to the wide association of urban and rural areas

in Jahrom City (6 - 8). Whereas, the study of Majdzadeh in Tehran in 1997 showed a significant difference between the women living in the north of Tehran in terms of high socioeconomic status and the women living in the south of Tehran in terms of rubella antibody titers, so that Southern women had higher antibody titers (9). In a similar study in India in 1995, the same difference was observed between urban and rural residents. Rural women had higher antibody titers and immunity. That is because the risk of developing rubella in their childhood increases due to low hygiene (22). Moreover, in a study conducted in Italy in 2004, there was no significant relationship between the geographic region and the positive percentage of rubella antibody titers until the age of 14 years. However, during 15-19 years of age, it was more positive in the northern Italian population than those living in southern Italy. Meanwhile, between the ages of 20 and 39, it was lowest in the southern Italian population (a region with higher socioeconomic status) (15). The after vaccination results showed that most people have found an acceptable level of antibody, which indicates the ability of these vaccines and their immunogenicity to produce antibodies. The similar results observed in other countries were mentioned in the previous pages. Actually, the study on the vaccine effect survival over time was conducted only in a few countries, and the other countries have examined the positive rate of antibody titer in vaccine recipients. However, in those few countries mentioned, the research showed the subjects' acceptable immunity after several years (7 years in Iran). Therefore, the public vaccination program was satisfactory and there was no need to inject a booster dose, except for those who underwent serology test before marriage and if not immunized, booster dose should be inoculated. It is worth noting that during the implementation of the public vaccination plan, a large number of pregnant women were not aware of being vaccinated by this live attenuated vaccine (LAV) during their pregnancy. Thus, several studies were conducted in Tehran (33-34) and a study was conducted in Mazandaran (35) in order to investigate the probable infection of these mothers' infants with congenital rubella syndrome. Thankfully, the results of all studies showed that although the injection of a live virus vaccine is not recommended during pregnancy, its accidental injection in pregnant women did not have complications and even one case of congenital rubella syndrome after vaccination has not been reported.

Conclusion

According to what we obtained in this study, it appears that the public vaccination program was sometimes successful in starting a program for the elimination of measles, rubella and congenital rubella syndrome in the society. Meanwhile, the inclusion of a MMR vaccine in children's immunization program was also another effective step towards achieving this goal. However, as mentioned before, this program did not address the screening of women and women of reproductive age for the presence or absence of anti-measles and anti-rubella antibodies.

Research Limitations

Due to the randomized sampling method used in this study, it was not possible to compare the subjects' immunity level in different parts of the city in terms of different socioeconomic levels. However, the major problem was to provide kits, which was postponed several times due to the increased price. In addition, due to the limited availability of kits, we had to use 180 kits instead of 200 kits, because there were 89 kits in each package. Moreover, there was an interval of several months between the sampling time and the analysis of the data obtained from the test. Meanwhile, due to long-term maintenance of serums, a number of samples were reported suspected, which were considered to be positive in accordance with the instructions of the used kit and the recommendations of the lab specialists and the previous information.

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