A Nationwide Study on the Seroprevalence of Measles, Mumps, and Rubella in Iranian Children and Adolescents

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Abstract

Background: Assessing the prevalence of infections, which are preventable by vaccination, is crucial to monitor the vaccination program efficacy, and it can demonstrate the gaps in population immunity. The current study attempted to assess the specific Immunoglobulin (IgG) antibody against measles, mumps, and rubella (MMR) in Iranian children and adolescents, years after their vaccination.

Methods: This cross-sectional study was conducted in Iran. Serum samples of 2100 students, aged 7-18 years, included in a national health survey, were tested for MMR antibodies by ELISA assay. Multistage random cluster sampling was used to select subjects from 30 provinces in Iran.

Results: Overall, 1871, 1718, and 1678 serums were tested for measles, mumps, and rubella antibodies, respectively. The prevalence of positive test was 1231 (65.8%) for measles, 1327 (77.2%) for mumps and 1344 (80.1%) for rubella.

Conclusion: Despite high vaccination coverage in Iran, IgG antibody against measles, mumps, and rubella was not detected in a considerable proportion of children and adolescents aged 7-18 years. In case of contacts with residents of other countries, where measles or rubella have not yet been eliminated, it may create problems for Iranian children.

Keywords: Measles; Mumps; Rubella; Children; Adolescents; Iran

Available at: http://ijph.tums.ac.ir

Introduction

Measles, mumps, and rubella (MMR) are three contagious diseases with a viral cause, which sometimes lead to serious illness, disability, and even death in developing countries (1). Before the measles vaccination, 2.6 million deaths from measles occurred in the world each year. In 2016, almost 89780 cases died from measles, which most of them were children under five years of age (2). Mumps, similar measles, still occur in worldwide. Over the past decade, the largest mumps outbreak reported in the USA in 2006 with 6,584 cases (3). Rubella is endemic in most countries. The WHO reported that rubella infection in the African and the South-East Asian has increased during 2000 and 2009 (4).

Measles and mumps belong to the Paramyxoviridae family, and rubella belongs to the Togaviridae family, all of them are RNA viruses, and humans are the only usual host of these viruses (4). In temperate counties, MMR incidence has a peak in late winter and spring (4-6).

MMR, are prevented by vaccination (7). In Iran, MMR Posed a considerable public health challenge for years. In December 2003, the Expanded Program of Immunization (EPI) started to eliminate measles and rubella during the campaign using the measles and rubella vaccine for all Iranian 5–25 years of age (8). In 2004, mumps vaccine was included into the National Infant Immunization Program. According to the immunization schedules, all Iranian children were vaccinated with MMR vaccine at 12 months for the first time and then at 4 – 6 years of age. This policy was changed in 2007, and children are vaccinated in 18 months for a second dose (9). MMR vaccine is sensitive to light and heat. In Iran, these vaccines have been kept in the recommended conditions for handling and storing vaccines.

The norm vaccination coverage in Iran is more than 95% (9). Epidemiologic studies have indicated that vaccine coverage probably does not represent the real immunity level of the community. Combining information on vaccination coverage and antibody prevalence data could be a more effective tool (10, 11). Most of researches in Iran were limited to detect the situation of immunity before and after vaccination (12-13). There are limited investigations about the presence of antibody against MMR in adolescents who received the vaccine several years ago. The majority of recently mentioned studies have been conducted with small sample size, and most of them are out of date (14-19). Therefore, the immunity situation vaccinated adolescents are not clear, and existing reports are not sufficient to inform policymaking.

The purpose of our work was to assess the presence of MMR's specific Immunoglobulin in a large population of Iranian pediatrics and to investigate infection risk factors among them.

Methods

To detect antibodies against MMR in Iranian adolescent, we used serum samples, which were previously collected in a multicenter cross-sectional study (CASPIAN-V study) on 7–18-year-old students in 2015 (20). A multistage stratified cluster sampling method was used to select the participants. Rural and urban regions of thirty provinces of Iran included in this survey. The criteria used for school selection consisted of the area of residence (rural/urban), school grade (elementary/ intermediate) and with equal sex ratio. Clusters were determined at school levels. The size of each cluster was ten students, which means that 10 statistical units (including ten student and their parents) would be considered in each cluster. The students in each school were randomly selected. The sample size was 480 students in each province (48 clusters of 10 students). A total of 14,400 students were entered in the project. Two questionnaires were used in CASPIAN-V study: a student's questionnaire and parents' questionnaires. The questions were about health status and health-related behaviors students and their family. Blood samples were

randomly collected from 3843 students, and after centrifugation, serum samples were aliquot and stored at −70 °C. The parents agreed and assigned written informed consent and permitted to use the samples in the others' epidemiological studies. Verbal consent was also obtained from the student.

We used all the serum samples that had the proper testing conditions like the color and clarity of the serums (hemolytic and lipemic samples were not used) and the volume of serums. The samples were transported to the laboratory of Infectious Diseases and Tropical Medicine Research Center, Isfahan under refrigerated conditions. Frozen samples were defreeze in room temperature and tested for IgG antibodies against measles, mumps, and rubella using commercial enzyme-linked immunosorbent assay (ELISA; EUROIMMUN, Germany) according to the manufacturer's instructions. The sensitivity of the tests was 100%, 99.3%, and 99.6% for measles, mumps, and rubella, respectively. The specificity was 100% for all of the tests. Demographic data [including age, sex, area of residence (rural/urban), an education level (elementary/ intermediate), Body mass index (BMI) and province] of the selected samples were extracted from CASPIAN-V database. Iran was divided into four main regions; north-northeast, central, west, and southeast based on geographical and socioeconomic state of the provinces, according to a previous study (22). BMI z-score was calculated based on the World Health Organization (WHO) growth references for each sex and age (23). A student was considered thinness if Z-score < -2, normal if -2 ≤ Z-score < 1, overweight if 1≤ Z-score < 2 and obese if Z-score ≥ 2.

The study protocol was confirmed to the principals of the Declaration of Helsinki and approved by the Research Ethics Committee of Isfahan University of Medical Sciences, Isfahan, Iran (project number: 295149).

Statistical methods

The categorical variables were expressed as frequencies and percentages, and were compared using the chi-square test. The continuous variables were presented as a mean (standard deviation) and were compared using ANOVA for parametric variables and Kruskal-Wallis test for nonparametric variables, after assessing normality assumptions.

The analyses were carried for samples that had complete information. The software SPSS 20.0 (IBM, Chicago, IL, USA) was used, and $P < 0.05$ was considered significant.

Results

Overall, 1871, 1718 and 1678 serum samples from 12 age groups were tested for measles, mumps and rubella antibodies respectively, of the 1231 (65.8%), 1327 (77.2%) and 1344 (80.1%) had positive results. All of the students had a history of twice vaccination against MMR according to the control of vaccination card by schools

Measles

The mean age of the participants was 12.46 ± 3.07 years. It was significantly lower in positive samples than in negative ones (12.19 ± 3.05 vs. 13.06±3.04 years, respectively, $P<0.001$). As shown in Table 1, the central region of Iran had the lowest prevalence (64.9%), whereas the north-northeast area had the highest prevalence (67.8%).

Mumps

Samples of 1718 students with mean age12.38 ± 3.06 years were studied. The mean age of the positive and negative samples was 12.25 ± 3.04 and 12.88 ±3.10 years, respectively ($P=0.001$). 48.6% of the children were female. The lowest (75.8%) and highest (80.4%) prevalence rates were observed in the west and central regions, respectively (Table 1).

Table 1: Descriptive based on population characteristics in 7 to 18-year-old adolescents in 30 Provinces of Iran: the CASPIAN-V Study

Variable		Measles			Mumps			Rubella		
		Samples tested (percentage)	Seropositive Samples (percentage)	P-value	Samples tested (percentage)	Seropositive Samples (percentage)	P-value	Samples tested (percentage)	Seropositive Samples (percentage)	P-value
Gender	Male	934 (52)	616 (66)	0.80	851 (51.4)	651 (76.5)	0.23	838 (52)	656 (78.3)	0.094
	Female	863 (48)	574 (66.5)		804 (48.6)	635 (79)		773 (48)	631 (81.6)	
	Missing Data		74 (3.96)			63 (3.67)			67 (3.99)	
Area of residence	Urban	1250 (72.6)	841 (67.3)	0.23	1156 (73)	895 (77.4)	0.97	1115 (72.3)	882 (79.1)	0.39
	Rural	472 (27.4)	303 (64.2)		427 (27)	331 (77.5)		428 (27.7)	347 (81.1)	
	Missing Data		149 (7.96)			135 (7.86)			135 (8.05)	
Education level	Elementary	916 (59.3)	645 (70.4)	0.001	847 (59.9)	687 (81.1)	0.002	838 (60.5)	677 (80.8)	0.62
	intermediate	628 (40.7)	389 (61.9)		566 (40.1)	420 (74.2)		547 (39.5)	436 (79.7)	
	Missing Data		327 (17.48)			305 (17.75)			293 (17.46)	

Rubella

Samples of 1678 children with a mean age of 12.46 ±3.12 years were examined. The mean age of positive subjects was 12.49±3.21, and the mean age negative subjects were 12.36±2.73 years (*P*=0.53). The proportion of participants with positive antibody was 82.4% for north-northeast, 80.5% for the west, 79.1% for central and 78.4% for southeast regions (Table 1).

Discussion

Apparently, this research is one of the most extensive seroprevalence studies on MMR performed in a region in the Middle East and North Africa (MENA). The prevalence of IgG antibodies was 65.8%, 77.2%, and 80.1% for measles, mumps, and rubella, respectively. In Iran, several studies have assessed the presence of antibodies against MMR in adolescents, and different results have been reported. The antibody against measles was checked in 6-12 year's old students in Tehran and showed 72% seropositivity (14). In Mashhad City, north of Iran, measles IgG antibody was detected in 70% of students (17). In Shiraz, south of Iran, measles antibody were positive in 60.8%, 45% and 96.8% at 6, 10, and 15 years of age, respectively(18).

In a cross-sectional study in Gorgan, north of Iran, rubella antibody was assessed in 484 girls that 81.8% were seropositive (19). In a study conducted in Tehran on 541 vaccinated children and 1124 unvaccinated teenager, the prevalence of rubella-antibody was 38% and 29%, respectively. This study was carried out in 2003 before the national MR campaign in Iran (21). One thousand two hundred seventeen samples before the nationwide immunization campaign and 2007 after running the program were collected from 10 provinces of Iran and were tested for IgG antibody rubella. The antibodies increased from

73.4% before the operation to 98.8% after the vaccination (22-23).

The current study found that IgG antibody against measles, mumps, and rubella were not detected in 34.2%, 22.8%, and 19.9 of vaccinated children, respectively. Despite this result, epidemiological studies showed that measles had been eliminated in Iran (24-25). This could be a useful feature of the community immunity situation. However, it is necessary to monitor the MMR status during the elimination phase. During 2006 and 2007, few cases had been reported from measles in France. French health policymakers assumed to experience an elimination period. During 2008 to 2011, a massive measles outbreak occurred in this country, and almost 20000 measles cases were reported (26).

In Pakistan, measles IgG antibodies were detected in 86.27% and 91.67% of vaccinated children at age group 6-10 and 11-15 years, respectively (27). In Egypt, 88.9%, 77.8%, and 86.7% of the studied children were seropositive for MMR, respectively. Their ages were from 6 to 12 years, and all of the groups had received the vaccine (28). In Saudi Arabia, 75% children at six years, 96% at l3 years, and 98% at 17 years had protective measles antibody. Rubella antibody also was positive in 98% and 100% children at six years and l3 years respectively. The positivity rates in mumps were 64% at six years and 75% at l3 years (29). The IgG antibody against MMR in Germany was 80.2%, 75.1% and 75.2% among children and adolescents at age groups 7-10, 11-13, and 14-17 years, respectively. MMR vaccination rate were 92.5% at age group 7-10, 89.4% at age group 11-13 and 85.8% at age group 14-17 year (30). Different results in various studies are likely to be linked to different climatic conditions, vaccination coverage, and several doses of the vaccine.

Our study results showed an association between age and education level with IgG antibody against measles and mumps in univariate analyses.

We used the samples of CASPIAN study that had suitable conditions, so clusters lost their origin and logical instructions. On the other hand, the analysis was performed on the samples that have complete information. Therefore, we have missing data. Our results would be more accurate if we would not have lost this information. However, the study was conducted in 30 provinces of Iran on the 7-18-year-old student. Therefore, our result can be considered representative of Iranian children and adolescents.

Conclusion

Despite high levels of vaccination coverage with 2-dose of MMR, IgG antibody was not detected in a considerable proportion of children and adolescents. Given that Iran is in the elimination phase of measles, monitoring of MMR during this period is of crucial importance. In the case of contacts with residents of other countries, where measles or rubella have not yet been eliminated, it may pose problems in keeping the achieved elimination in Iran.

Ethical considerations

Ethical issues (including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Acknowledgements

Conflict of interest

None of the authors has any financial that could influence or bias the content of the paper.

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