

Seroimmunity status to Measles-Mumps-Rubella-Varicella-Pertussis- Diphtheria -Tetanus among Students Accepted to Mazandaran University of Medical Science, Sari, North of Iran, 2018-2019: Planning for Prevetive Method.

Hana Saffar

IKHC. Teheran University of Medical Sciences

Sayed Jaber Mousavi

Mazandaran University of Medical Sciences

Hiva Saffar

Teheran University of Medical Sciences

Hanieh Shiraj

Mazandaran University of Medical Sciences

Saffar Mohammed-Jafar (✉ Saffar@softhome.net)

Mazandaran University of Medical Sciences

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Abstract

Background. Healthcare sciences students(HSS)are at the higher risk of exposure to several infections during training. The most important are measles, mumps, varicella, pertussis and influenza, that are transmitted easily via respiratory routes. These infections are vaccine preventable, and commonly are more complicated while develop during adulthood. Confirming immunity before training are recommended, however, adherence to the policy is not satisfactory universally. To evaluate immunity status, and to determine the most appropriate approach to provide full protection against these infections, this study was designed.

Methods. A cross-sectional study among newly accepted HSS was conducted. Their past vaccination status, and medical history of compatible clinical diseases were sought by personal interview and self-administered questionnaire. Sera specific IgG antibodies to these infections were measured using ELISA. The relative proportion of seroimmune students were calculated. The correlation between past clinical diseases and their immune status particularly among those who showed no history of earlier vaccination were determined. The most appropriate policy to provide full protection was determined. The collected data were analyzed using descriptive statistical methods as appropriate.

Results. Overall, 242 students with mean age 23.9 years, 59% female were participated. All HSS declared that they had been vaccinated according to the national immunization program. Among them 188 students with additional dose of measles- rubella (MR), and 54 by measles- mumps- rubella (MMR) vaccines were re-vaccinated.

Overall seropositivity rates were as: measles-80.1%, mumps-64%, rubella-93.4%, varicella-78.5%, pertussis-46.5%, diphtheria-87.3%, and tetanus-87.2%. There were not significant differences between two groups of HSS; MR vs MMR re-vaccinated students. The most cost-benefits strategy to provide immunity against MMR agents were universal vaccination.

Conclusion. Nearly 63%of HSS were susceptible to MMR viruses, and universal MMR vaccination of the students just before training was the most appropriate policy to provide immunity. Efforts should be made to incorporate adult-type acellular pertussis vaccine to diphtheria- tetanus toxoids to and varicella vaccine provide protection against these agents.

Background

Healthcare personnels (HCP) are at greater risk to expose to several infections during their work. This risk is much higher among healthcare sciences students (HSS) because of their lower skill and experiences at contact with patients and/or procedures on training. Among these infections, the most important are including: measles, mumps, rubella (MMR), varicella, pertussis, and influenza that are transmitted mainly and easily via respiratory routes. The natural courses some of these infections may be more severe and with higher complications in adults than in children(1-4). These infections represent a high occupational risk for HCP/HSS, and if they become infected may act as a source for infecting vulnerable staff and patients(5). Many reports account for hospital transmission and outbreaks of these infections with considerable consequences on the high-risk population, and a heavy financial burden on the health system(6-14). These infections are vaccine preventable, and immunization is an important intervention measure to protect these high-risk groups against these infections, mainly during their training, just before contact with patients. General recommendations regarding vaccination of these groups have been published(1-4). Occupational programs may vary between countries, but, always include those vaccine preventable diseases that might lead to nosocomial outbreaks and/or fatal outcomes for HCP or patient. Despite these recommendations, adherence to the guidelines are not satisfactory universally, and outbreaks of these infections in the healthcare settings from patient to HCP and vice-versa were reported(15-18).

In this study, the serological immunity status against these vaccine preventable infections among newly accepted HSS was evaluated. Also, the correlation between self-reported history of clinical diseases and/or vaccination with their immunity status were determined. Moreover, the most appropriate and cost-benefit policy to provide protection against these infections was estimated.

Subjects And Methods

A cross-sectional study between 1-November 2018 and 28-February 2019, was conducted. Target population were first year HSS being accepted in the Mazandaran University of Medical Sciences, Sari, North of Iran, before their hospital training on a voluntary basis. For every semester of the academic year, nearly 390 HSS are accepted. In every faculty an oral presentation about the scope of the study was made, and all students were invited to participate in the study. Those with acute or chronic diseases, malignancies, immunodeficiency's, and receipt of blood and blood products within last 12 months were excluded. Study have been performed in accordance with the Declarations of Helsinki and have been approved by the Ethic Committee of the Mazandran University of Medical Sciences; (IR,Sari.MAZUMS.Rec.96.3082), and informed written consent was obtained. Information was gathered via personal interview and self-administered questionnaire. In addition to the age, gender, the type of faculty, the history of vaccination during childhood and/or later years, and the past medical history of clinical diseases compatible with mumps and varicella (chickenpox) were sought. For history of vaccination, documentation was made if vaccination record was available, or was postulated based on the age, (date of birth) of the students and the national immunization programs. In Iran, since year 1984, routine universal vaccination of children against polio (OPV), diphtheria, tetanus, pertussis (DTP), tuberculosis (BCG), and measles with monovalent measles vaccine (mMv) administered at the age of 9 and 15 months was started. From the year 1986-1987, the coverage rate of vaccination was increased to more than 95%, in most parts of the country(19). Also, to cover the immunization gaps, on a compulsory basis, the vaccination status of all children just before entrance to the primary school were monitored. Therefore, we postulated that all Iranian children, who had born after the year 1988, were fully immunized with 4-5 doses of DTP, OPV, and 2-doses of mMv vaccines upon school entrance. At the December 2003, a nationwide campaign of measles-rubella (MR) immunization program to cover all 5-25 years-old population with more than 99% coverage rate was conducted. Based on the national supplementary immunization programs, all children that had born during years 1999-2003, and were not included in the national MR campaign, with one dose of MMR vaccine at the time of school entrance (6-year of age) were re-vaccinated. Therefore, all HSS included in this study with 4-5 doses of DTP, 3-doses of measles, one-dose of rubella and a minority, with one dose of mumps vaccines were vaccinated.

Blood samples were obtained from each HSS on a voluntary basis, and sera were stored at -20°C to testing. The serum concentrations of specific antibodies were measured using ELISA. According to the manufacturers instructions the concentrations of specific immunoglobulin G (IgG) antibodies against MMR agents and varicella were measured qualitatively, using ELISA kits. [Vircell Microbiologist measles-mumps-rubella- varicella ELISA kits (vircell,S,L. Parquet Technologico delasalud. Vecina8, 18016Granada, Spain)] and for DTP agents, using ELISA kits (Demeditec Diagnostic GmtH, Germany). Antibodies against MMRV agents were measured according to the manufacturer guidelines with positive and negative control of <0.5 , and >0.9 and cut-off control >0.55 - <1.5 , respectively. The results were interpreted as antibody index, and were calculated as: $\text{antibody index} = (\text{sample OD} / \text{cut-off serum mean OD}) \times 10$. Samples with antibody index >11 were considered as positive (having specific IgG antibodies per agent). Samples with index <9 were considered negative (not presence of specific antibody). Samples with index between 9-11 were rechecked, and if >11 were considered positive and <11 as negative. Mean concentrations of antibodies (MCAs) of seropositive samples for each MMR agents was calculated.

For diphtheria, titers: <0.01 , 0.01 - 0.1 , and >0.1 , and for tetanus, titers: <0.1 , 0.1 - 1 , and >1 IU/mL were considered as highly susceptible, susceptible, and protected, respectively. For pertussis, titer >11 U was considered positive (possibly developed

by natural pertussis infection), and <9 U as negative. Samples with titers 9-11 U were rechecked, and if >11 was considered positive, and <11 as negative.

Vaccination policy and cost-benefit estimation. The total costs of two-preventive strategies programs were calculated: Universal vaccination without any serological testing VS selective immunization; only vaccination of susceptible subjects determined following serological testing. Estimation was based on the current costs of an ELISA serological testing for each agent and the total respective vaccination costs of MMR (only one dose) and 2-doses of varicella vaccination for two programs.

Statistical analyses: Collected data were analyzed using SPSS version 16.0. For qualitative variable, percentage and mean with standard deviation (SD) were calculated. Chi-Square tests was used to compare categorical variable. A P value <0.05 was considered statistically significant.

Results

From 390 matriculated HSS, 242 (62%) students consented to participate and completed the study. The demographic characteristics and the relative contribution of the students related to each faculty are presented in table 1. All HSS declared that they had been vaccinated according to the national immunization programs until entrance to primary school. Based on their birth date and the national immunization program and supplementary immunization activities performed in the country, study subjects to two-groups were classified. Group a: consist of 188 out of 242 (77.7%) HSS who had born before the year 1999, were vaccinated against measles at the age of 9 and 15 months, and re-immunized, were with MR vaccine in the year 2003, and Group b: including 54 of 242 (22.3%) students, who had born within years 1999-to 2003, and were immunized with two-dose of mMV at the age of 9 and 15 months and were reimmunized with one-dose of MMR vaccine upon school entrance. The pattern of MMR vaccination of studied students are shown in Table 2. As are seen, all students with 3-doses of measles containing vaccine, one dose of rubella vaccine were vaccinated. Only a minority against mumps were immunized. After the primary series of DTP immunization to 6-years of age, no body received any additional dose of DTP containing vaccine during later years. The seroprevalence rates against MMR agents, varicella, and pertussis are presented in table 3. As are shown, of 242 HSS, 194 (80.1%) serologically were immune to measles, 155 (64%) to mumps, 226 (93.4%) to rubella, 190 (78.5%) to varicella, and 40 of 86 tested samples (46.5%) to pertussis. While seroprevalence rates and MCA levels, comparison was made between 2-groups of MR vs MMR re-vaccinated students regarding to MMR agents, there were no significant differences between two groups for seroprevalence rates: $p=0.4$, $p=0.806$ and $p=0.37$, respectively. Also, the estimated MCA levels for measles and mumps were not different, but for rubella was significant, $p=0.011$. Results are presented in Table 4. In this study, 86 samples for specific antibodies against DTP agents were tested. Of those, 40 (46.5%) were positive for pertussis, 2 (2.3%) and 3 (3.5%) of the students were highly susceptible; 9 (10.4%) and 8 (9.3%) susceptible to diphtheria and tetanus, respectively. Based on the study findings on their past medical history of clinical diseases of 242 HSS, 94 students responded, and all denied any compatible illness. Of those 68% to measles, 57.4% to mumps, 87.2% to rubella and 84% to varicella were immune.

According to the current costs of serological testing for each agent, and the costs of each dose of respective vaccine, our data showed that universal MMR vaccination of the newly accepted HSS without serological screening was the most appropriate and cost-benefit approach. However, due to varicella vaccine cost, selective vaccination after screening will be the cost-benefit.

Discussion

For this study all students declared that they had been vaccinated according to the national immunization programs. Results showed nearly 20% of our students to measles, 36% to mumps, 6.6% to rubella, 12.5% to either diphtheria or tetanus were serologically susceptible and 46.5% showed evidence of immunity to pertussis (most possibly acquired by national pertussis infection). Moreover, in the absence of any history of respective vaccination, 78% and 63.3% of HSS were protected to varicella and mumps infections, via natural infection. Study showed that relying on the past medical history of clinical disease to predict immunity status was not reliable.

In this study, nearly 63% of students were susceptible at least to one of the MMR agents. As these infections are transmitted via respiratory routes, they represent a high occupational risk for HCP/HSS, and for patients with whom they may come in contact(20-22).

Measles is a highly contagious viral infection which affects susceptible individuals of all age groups. Nosocomial transmission of measles is well documented, and may aid in the propagation of community outbreaks(6-8). Any community with less than 95% population immunity is at risk for an outbreak(20). Mumps and rubella are less contagious than measles, but outbreaks and nosocomial transmission of both infections may occur, and can result in a heavy financial burden on the healthcare facilities or have a considerable consequences(9,10,20-22). Therefore, all people who work in healthcare settings should be immune to measles, mumps, and rubella infections, documented by adequate immunization or laboratory evidence of immunity(1-4,20-22). MMR vaccination is the most effective preventive measure to protect HCP/HSS from acquiring these infections(1-4,20). The susceptibility rates to these infections are varied widely even within a country according to country's immunization practices, and time elapsed since the last dose of respective vaccine was administered(1-4,20). In This study, nearly 20%, 36%, and 6.6% of studied students were serologically susceptible to MMR agents respectively. There is no accurate information toward immunity status regarding to these infection among Iranian HSS. However, few studies in this regard were performed(23-27). The results were varied considerably: 52%(24)-to 88%(26) for measles, 64%(23)-to 76%(24) for mumps, and 96%(23)-to 100%(24) for rubella. Similar to these data and heterogeneity in seroprevalence rates were also, observed worldwide(28-34). As are presented in the Table 5, the reported rates for measles were: 57%(28)-to 98%(33), for mumps: 68%(30)-to 92% (31), and for rubella: 83%(31)-to 97%(34). These variations could be explained possibly by difference in the national immunization program including implementation of some regional supplementary immunization activities, and the time elapsed since the last dose of the respective vaccine that was administered. Based on our data, regarding susceptibility to MMR agents and in accord with other reports(28,30,31), to provide a full protection against these viruses among Iranian HSS, universal MMR immunization is the most appropriate and cost-benefit strategy.

Varicella-Zoster (chickenpox) infection is endemic in the country, and the majority of Iranian children became infected to adulthood(35-37). Seroprevalence studies among Iranian general population indicated that seroprevalence rates were increased steeply from childhood: 22%(35)-to more than 86% and 98%(36) after the age of 30 years. Varicella is a highly contagious infection, and is transmitted via respiratory droplets, air-borne, and direct contacts. Infection is preventable by active immunization. Because the high cost of the vaccine, and the usual benign course of the chickenpox during childhood, vaccination against varicella is not a public health priority in Iran, so, was not introduced in the national immunization programs. However, infection during adulthood is more severe and with the higher rates of complications, even death(38). Varicella nosocomial transmission and outbreaks has been reported(11). The number of studies that investigated the seroimmunity status among Iranian HCP/HSS are limited. However, as was observed in the general population, the seropositivity rates detected among HCP/HSS were varied greatly. While a 15% seropositivity rate was reported in one study from Shiraz(24), in other similar study this rate was 74.5%(39). As are presented in Table 5, similar to these variation, also were reported worldwide(28,20-34). Our data in this study are in parallel to that reported in Iranian population and nearly 78% of students as a results of natural infection were seropositive. Based on the data, if vaccine supplying was feasible, selective vaccination of susceptible students was the most appropriate and cost-benefit

approach. Also, result showed that the past medical history of chickenpox was not a reliable tool to predict immunity status.

Diphtheria-Tetanus-Pertussis are vaccine preventable infections. Full immunization series along with high vaccination coverage rates during childhood associated with periodic booster injection is necessary to preserve vaccine-induced immunity on long-time against these agents. Diphtheria is a contagious and life-threatening disease. Recent diphtheria outbreaks in several countries indicated inadequate vaccine coverage. Also, outbreaks showed that the majority of the cases were adolescents and young adults(40,41). Tetanus remains an important public health problem in many parts of the world. It was estimated that every year nearly 58000 neonates, and unknown numbers of mothers dies from tetanus(42). In the year 2015, about 34000 newborns died from neonatal tetanus, a 96% reduction since 1988(43). Although, during recent years, the incidence of diphtheria, tetanus, and neonatal tetanus were very rare in Iran(44,45), seroprevalence studies results among general population indicated that nearly one-fourth of young adults were serologically susceptible to either infection(46,47). Our data in this study provide additional evidence to earlier findings(40-47), and indicated that more efforts should be made to achieve timely booster injection to preserve long-term immunity to both agents.

Pertussis is a highly contagious respiratory infection that is endemic in all countries. The disease is most serious in infants, and a significant cause of illness and death in this age group. Adolescents and young adults plays an important role in transmitting infection to unvaccinated/partially vaccinated infants. After reduction of pertussis following universal vaccination, the incidence of pertussis cases increased among adolescents and adults because waning of vaccinal immunity over time(48). Nosocomial outbreaks with substantial disruption and cost to hospital and HCP, and also morbidity, and even mortality in patients were reported. In most of these cases HCPs were the source(12,13,49-51). Similar to data that were reported in the world, during recent years in the Iran, also, the incidence of pertussis cases increased among infants and adolescents and young adults who had been vaccinated at childhood(52-55). Also, seroprevalence studies results showed that the rates of pertussis specific antibodies increased after the age of 9-10 years, an evidence of subclinical/atypical cases of pertussis among these age groups(53). For this study, nearly 46% of studied HSS were seropositive to pertussis infection, most possibly, due to pertussis infection during recent years. Similar to our finding also were reported from other parts of the country(47,54,55). For example; in a similar multi-center study among 1617 university students with the mean age 19.6 ± 2.1 years, this rates were 31.6%(55).

Our data and other mentioned evidences of infection(52-55), indicated that pertussis is active in the Iran. This resurgence of the infection is most probably due to waning of immunity induced by childhood immunization program(48). With the licensure of adult-typed acellular pertussis vaccine combined with diphtheria-tetanus toxoids (dTaP) for use in adolescents/young adults, now it is possible to preserve vaccine-induced immunity against DTP agents among older children/ young adults, particularly HCP/HSS by dTaP vaccination. The Advisory Committee on the Immunization Practices(56), and other authorities(1-4,48) recommended that all HCP/HSS regardless of their age should receive this vaccine booster dose as soon as possible. Although, there is no accurate information toward burden of pertussis disease/infection in Iran, our findings along with mentioned data indicated that pertussis infection act as an important pathogen among Iranian infants and adolescents, that may result to a major public health problem associated with a significant consequences. While considering the results of study conducted worldwide to evaluate the impact of adolescents dTaP immunization in reducing the burden of pertussis infection and its consequences(1-4,15,56,57), vaccination of our HSS with dTaP instead of dT seems most appropriate policy to provide protection against the DTP agents.

For this study some limitation did exist. The main limitation was its reliance to recall about history of vaccination and clinical compatible diseases. Also the relative small size was the other limitation.

Conclusion

Study showed nearly two-third of HSS were susceptible to MMR viruses. Varicella and mumps were highly endemic in the country, and three-fourth of children to young adulthood got immunity by natural infection. Also, our data indicated without periodic booster injection against DTP agents seroprotection rates to diphtheria and tetanus declined and pertussis seropositivity rate increased over time. To provide appropriate protection against MMRDTP, universal MMR and dTaP vaccines immunization are recommended. Otherwise if Varicella vaccine was feasible, selective vaccination is most cost-benefit approach.

Abbreviations

MMR: Measles Mumps Rubella, ELISA: enzyme immune assay, HSS: Healthcare Sciences Student, IgG: Immunoglobulin G, MR: measles-rubella, HCP: Health Care Personnel, DTP: diphtheria-tetanus-Pertussis, MMRV: measles-mumps-rubella-varicella, OPV: oral polio vaccine, BCG: Bacillus Calmete-Guerine, MAZUMS: Mazandaran University of Medical Sciences, IU: international unit, MCA: mean Concentration Antibody.

Declarations

Ethic approval and Consent to Participate: The study have been performed in accordance with the Declarations of Helsinki and have been approved by the Ethic Committee of the Mazandran University of Medical Sciences; IR.MAZUM.REC.96.3082. The study obtained the consent of all participants and signed and informed consent form prior to investigation. They were assured about confidentially and that their contribution would be on a voluntary basis as well as that they had full rights to withdraw from the study at any time.

Consent for Publication: Not Applicable.

Availability of data and materials: obtained for this study will be available from the corresponding author at a reasonable request.

Competing interests: The authors declare that they have no competing interest

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Authors Contribution and Details: Hn.S, and Hv.S. Involved in study design, literature search, laboratory testing and writing the paper. J.M. data collection and statistical analysis and interpretation. H.Sh. recruiting, selection, and interview. M.S. all phases of the study.

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Tables

Table 1: Demographic characteristics of healthcare sciences students accepted to Mazandaran university of Medical Sciences, Sari North of Iran, 2018-2019.

| Faculties | Female (%) | Male (%) | Mean age years | Age range years |
|-----------------|------------|-----------|----------------|-----------------|
| Nurses n=138 | (50.7%) | (49.3%) | 22.3 | 19-28 |
| Midwives n=35 | (100%) | 0 | 27.8 | 20-47 |
| Paramedics n=42 | (61.9%) | (38.1%) | 22.6 | 18-31 |
| Medical n=27 | (44.49%) | 1 (55.5%) | 23.2 | 19-27 |
| Total n=242 | (59.1%) | (40.9%) | 23.9 | 18-47 |

Table 2. Measles-Mumps-Rubella vaccination status of Healthcare sciences students according to their date of birth and the national supplementary immunization activities programs.

| | number of vaccine doses | | |
|--|-------------------------|----------|----------|
| | Measles ^a | Mumps | Rubella |
| A*) Birth date: since 1981-1998 ^b | 3-doses | No | One dose |
| B) Birth date: 1999-2000 ^c | 3-doses | One dose | One dose |

a: both groups with two-doses of monovalent measles vaccine at the ages of 9 and 15 months were vaccinated.

b: This group with one-dose of MR vaccine at year 2003 were reimmunized

c: In addition to receiving two-doses of mMV at the ages of 9 and 15 months, they were MMR revaccinated at the age of 6 years.

Table 3. Seroimmunity prevalence rates to measles-mumps-rubella-varicella and pertussis infections among newly accepted healthcare sciences students in relation to their faculty, Mazandaran University of Medical Sciences Sari-Iran: 2018-2019.

| Agent | Measles n= (%) | Mumps n= (%) | Rubella n= (%) | Varicella n= (%) | Pertussis ^a n= (%) |
|-------------------|-------------------|-----------------|-------------------|---------------------|----------------------------------|
| Nurses (n=138) | 109(78.9%) | 85 (61.6%) | 127 (92.0%) | 112 (81.1%) | 13 (15.1%) |
| Midwives (n=35) | 29 (82.8%) | 24 (68.5%) | 34 (97.1%) | 30 (85.7%) | 10 (11.6%) |
| Paramedics (n=42) | 34 (80.9%) | 28 (66.6%) | 40 (95.2%) | 28 (66.6%) | 9 (10.4%) |
| Medical (n=27) | 22 (81.4%) | 18 (66.6%) | 25 (92.6%) | 20 (74.0%) | 8 (9.3%) |
| Total (n=242) | 194 80.1% | 155 (64.0%) | 226 (93.4%) | 190 (78.5%) | 40 (46.5%) |

a: for pertussis 86 sera were tested

Table 4. measles-mumps-rubella immunity status among healthcare science students according to their respective immunization status: *MR VS MMR*, accepted to the Mazandaran University of Medical Sciences, Sari-Iran, 2018-2019.

| vaccination status MR VS MMR | Immunity status | | | | | |
|------------------------------------|------------------------------|------------|----------------------------|------------------|------------------------------|-------------|
| | Measles prevalence rates (%) | MCA* | Mumps prevalence rates (%) | MCA ^c | Rubella prevalence rates (%) | MCA* |
| MR ^a revaccinated n=188 | (80.3%) | 15.88±7.03 | (63.3%) | 20.885±7.207 | (94.7%) | 21.07±6.11 |
| MMR ^b revaccinated n=54 | (79.7%) | 14.7±7.42 | (66.6%) | 20.417±6.405 | (88.9%) | 18.49±11.63 |
| P Value | P=0.44 | P=0.291 | P=0.342 | P=0.806 | P=0.307 | P=0.011 |

a: MR: measles-rubella

b: MMR: measles-mumps-rubella

c: MCA: Mean Concentration of Antibodies

Table 5. Seroimmunity prevalence rates to Measles-Mumps-Rubella-Varicella among HCP/HCS reported from Iran and other countries.

Worldwide

| Authors country | journal (year) | number of HCP/HSS ^a | Measles (%) | Mumps (%) | Rubella (%) | Varicella (%) |
|---------------------------|---|--------------------------------|-------------|-----------|-------------|---------------|
| Karadeniz A, Turkey 28 | J infect public Health 2020 | 1053 HCP+HSS | 57.1 | 74 | 96.3 | 93.7 |
| Basu S, UK 29 | Epidemiol Infect 2013 | 392 new HCP | 88.2 | 68.8 | 93.9 | - |
| Arunkumar G, India 30 | Am J Ind Med 2013 | 790 HSS | 90.5 | 68 | 83.4 | 74.2 |
| Chamat Lebanon 31 | J Inf Pub Health 2011 | 502 HSS | 86 | 75 | 88 | 93 |
| Kumakura S, Japan 32 | Infec Chemo Ther 2014 | 1181 (<29 yr) HCP | 91.8 | 92.1 | 89.5 | 96.3 |
| Pavlopoulou ID, Greece 33 | Infect Control Hosp Epidemiol Infect 2009 | 187 HSS | 98.4 | 89.6 | 96.7 | 92.4 |
| Kafi Saudi Arabia 34 | J Famil Med Primary care 2020 | 1534 HCP | 79.3 | 75.5 | 95.8 | 67 |

Iran

| Authors Iran | journal (year) | number of HCP/HSS | Measles (%) | Mumps (%) | Rubella (%) | Varicella (%) |
|-----------------|-----------------------------------|--------------------------|-------------|-----------|-------------|---------------|
| Keshavarz 23 | Ir J Allergy Asthema Immunol 2016 | 53 Med stud ^b | 79.2 | 64 | 96 | - |
| Moattari 24 | Novel in Biomed 2014 | 180 HSS | 52 | 76 | 100 | 15 |
| Abdollahpour 25 | J Babol UMS | 236 HSS | 52 | - | 98.7 | - |
| Rahmani 26 | Zahedan J Res Med 2019 | 85 Med stud | 88 | - | 97.3 | - |
| Sadeghi 27 | Ir J Virol 2015 | 191 Med Stud | 68.9 | - | 99.5 | - |

a: HSS: healthcare science students, HCP: healthcare personnel

b: Med Stud: medical students