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RESEARCH PAPER

Seroprevalence for vaccine-preventable diseases among Italian healthcare workers

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ABSTRACT

Healthcare workers (HCWs) have an increased risk to be exposed to infectious diseases compared to the general population. For this reason, according to the National Immunization and Prevention Plan, all HCWs should have demonstrable evidence of immunity to measles, mumps, rubella, varicella and Hepatitis B. Earlier studies have already shown that a large percentage of Italian operators lacked immune protection for one or more of those pathogens.

The aim of this study was to evaluate the immunization status for vaccine-preventable diseases of HCWs in a large Italian teaching hospital. We retrospectively evaluated clinical records and serological data of HCWs who followed the occupational health surveillance program between January 1 and December 31 2019. We reviewed the clinical records of 1,017 HCWs: 393 males and 624 females with a median age of 35.69 y (range: 19–67). Protective IgG antibody values were documented in the 88.0%, 75.7%, 90.3%, 87.4% and 85.7% of the HCWs screened, respectively, against measles, mumps, rubella, varicella and Hepatitis B. Age was significantly related to serological protection against measles, mumps and varicella but was not significantly related to protective IgG levels for rubella and HBV.

Female gender was significantly related to a higher protection rate against Hepatitis B (87.8 vs 82.4%; $p < .01$) whereas males were significantly more protected against varicella (92–4 vs 84.1%; $p < .01$).

Our study shows suboptimal levels of protection among Italian HCWs and a consequent increased risk of infection for them and their patients. Public health policies should be focused on improving preventive strategies, including serological screening and workplace vaccination of nonimmune individuals.

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Introduction

Based on documented cases of nosocomial transmission, healthcare workers (HCWs) are considered to be at significant risk for acquiring or transmitting infectious diseases as hepatitis B, influenza, measles, mumps, rubella, pertussis and varicella.[1]

World Health Organization (WHO) declared that healthcare facilities around the world employ over 59 million workers who are potentially exposed every day to multiple occupational biological hazards while working with patients and contaminated body fluids and medical supplies.[2]

Due to their work, HCWs are at higher risk of contracting infectious diseases than the general population. Several clusters of vaccine-preventable diseases, especially of measles, have been described in Italian and European healthcare facilities, and in some of these settings, the index case was an HCW; so strict infection control and immunization plan are essential to prevent nosocomial outbreaks.[3–7] Vaccination of HCWs against hepatitis B, measles, mumps, rubella, diphtheria-tetanus-acellular pertussis (dTap), and flu is also strongly recommended by the Italian National Plan for Immunization and Prevention issued in 2017.[8,9] According to the Italian vaccination program, operators working in healthcare facilities should have presumptive evidence of immunity to those pathogens. Active vaccination must be promoted by the occupational medicine service in all those operators lacking demonstrable immunization history or serological evidence of vaccination coverage.

Three doses with Hepatitis B virus vaccine are about 95% effective in immunocompetent subjects[10] and provide long-lasting immunity; protective anti-HBs (Hepatitis B surface) antibody titer was found in 88% of vaccinated HCWs, 20 y after the primary vaccination schedule.[11,12] Two doses of measles, mumps, rubella vaccine (MMR) are considered highly effective and a presumptive evidence of immunity for those diseases.[13,14]

Since the immunogenicity of mumps vaccine has reported to be lower than Measles and Rubella ones, a significant rate of the HCWs could remain serologically unprotected for mumps despite a previous administration of two doses of MMR vaccination. For this reason, in October 2017 ACIP recommended a third dose of a mumps virus–containing vaccine for operators who are at increased risk for acquiring the disease because of an outbreak.[15,16]

Regarding prevention of Varicella, caused by the Varicella Zoster Virus (VZV), the administration of two doses of live-attenuated vaccine is considered highly effective in inducing seroconversion in up to 99% of vaccinated individuals, and the immunization of susceptible HCWs can lead to 80% reduction in the expected number of cases.[17–19]

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Despite the above issue, suboptimal immunization rates for some relevant vaccine-preventable diseases were reported among Italian HCWs, including those operators employed in high-risk settings.[15,20–23] Some seroprevalence studies, carried out in a group of large hospitals in central and northern Italy, have shown suboptimal immunization of healthcare workers against measles, mumps, rubella, varicella and hepatitis B.[24,25]

According to the European Center for Disease Prevention and Control (ECDC), HCWs are the most trusted source of information regarding their patients so their level of knowledge and confidence in vaccination practices can have a significant influence on the phenomenon of the so-called "vaccine hesitancy".

The aim of our study was to evaluate the serological immunity to some vaccine-preventable diseases (hepatitis B, measles, mumps, rubella and varicella) among the HCWs employed at a teaching hospital in Rome.

Methods

The Ethical Committee for Research in Human Subjects of the "Policlinico di Tor Vergata" (PTV) in Rome approved this retrospective observational study. In this study, we collected clinical and laboratory findings of HCWs, including some medical students, who underwent the annual medical screening of occupational health, from January 1 to December 31 2019.

For each subject, we collected the following data: age, gender, IgG-specific antibodies titer against Measles, Mumps, Rubella, Varicella and Hepatitis B Virus. Data were extracted from the "ModuLab" software adopted by the Chemical Analytical Laboratory of the hospital.

We considered protective serum specific IgG antibody values higher than 16.5 and 11.0AU/ml, respectively, for measles and mumps.[26]According to literature, the protective level was considered 10 IU/ml, 165 mIU/ml and 10 IU/L, respectively, against rubella, varicella and hepatitis B.[1,18] In our hospital, the evaluation of the immunization against measles, mumps, rubella, varicella and hepatitis B is performed by means of the LIAISON® IgG EIA assay and the LIAISON® Anti-HBs EIA assay.

HCWs with incomplete clinical and serological data were excluded from the study. Analyses were performed using IBM SPSS software (release 23). Results were considered statistically significant at a p-value threshold of <0.001.

Results

We reviewed the clinical records of 1,017 HCWs (393 males and 624 females). The main characteristics of the study population are reported in Table 1. Protective IgG antibody values against, respectively, measles, mumps, rubella, varicella and hepatitis B were documented in 88.0%, 75.7%, 90.3%, 87.4% and 85.7% of the HCWs screened.

Female gender showed higher vaccine coverage for measles (88.8 vs 86%; p = n.s.), mumps (77.9 vs 72.3%; p = n.s.), rubella (91.2 vs 88.8%; p = n.s.) and hepatitis B (87.8 vs 82.4%; $p < .01$) than male gender, whereas men were significantly more protected for varicella than women (92–4 vs 84.1%; $p < .01$).

Table 1. Demographic characteristics and vaccination coverage status of HCWs (n = 1017)

Characteristics	N (%)	Mean age (SD)
Total number	1017 (100)	35.69 ± 4.42
Gender		
Male	393 (60.4)	23.49 ± 2.65
Female	624 (39.6)	22.97 ± 2.41
Vaccination Coverage	N (%)	95% C.I.
Measles	895 (88.0)	85,8–89,9
Mumps	770 (75.7)	72,9–78,3
Rubella	918 (90.4)	88,3–92,0
Varicella	889 (87.4)	85,2–89,3
Hepatitis B	872 (85.7)	83,4–87,1

Table 2. Logistic regression analysis of vaccination coverage of HCWs for measles, mumps, rubella, varicella and hepatitis B by age (regression coefficients, *P*-values and 95% confidence interval C.I.)

	Coefficient	P-value	C.I.
Measles	0.067	<.01	0.042–0.092
Mumps	−0.019	<.01	−0.034 – −0.005
Rubella	0.015	n.s.	−0.007–0.037
Varicella	−0.024	<.01	−0.042 – −0.005
Hepatitis B	−0.009	n.s.	−0.027–0.008

Vaccination coverage by age is shown in Table 2. We found significant differences in the vaccination coverage only for measles (higher protection with increasing age), mumps and varicella (lower protection with increasing age) but not for Hepatitis B and rubella.

Discussion

We found a relatively high percentage of subjects lacking immunity for one or more vaccine-preventable diseases. Suboptimal rate of protected subjects was found for all pathogens and particularly for mumps, according to previous published data.[13,21,27] Recent studies show that mumps IgG titers decline over years[28] after either mumps vaccination and natural mumps infection, compared to the responses to other pathogens (measles and rubella). Although high levels of circulating mumps antibodies are recognized to be protective against mumps, no established cutoff level has been identified and, therefore, a subject exposed to mumps could be infected if the specific IgG titer is not high enough, regardless of the vaccine status.[29] According to those findings we observed a significant decline in the rate of immune subjects in the subjects.

The percentage of operators unprotected for measles, mostly among younger operators, is also worrisome. Measles infection in Europe is a major public health concern: in the period from January 1 to December 31 2019 in Italy 1627 measles cases were reported and 96 of them involved HCWs. Most of cases happened among not vaccinated or incompletely vaccinated subjects as a result of suboptimal vaccine coverage rate. Due to the risk of measles infection and transmission for HCWs, the promotion of an adequate vaccination program should be considered ad a priority for occupational medicine services.

In our sample, we found the highest rate of protective antibodies for rubella. The vaccination rate among women

could be explained by the national vaccination programs for rubella prevention carried out in the last decades (among females at scholar age) in order to eliminate congenital rubella syndrome. Additional doses of vaccine and re-test should be considered for serologically unprotected female operators at childbearing age regardless the previous vaccination, whereas male individuals can be considered protected when one or two-doses MMR vaccination is documented even when anti-rubella IgG titer is below the cutoff value.

Regarding VZV, we found that the rate of serological protection was inversely related to age, with the highest percentage of immunity occurring in the younger subjects: those results could be explained by the effect of natural immunization after the repeated contacts with infected children that could induce exogenous boosting of VZV immunity. In fact, in the last decades, the incidence of the infection among the Italian population was higher than the actual.[30] Two-doses VZV vaccination should be offered to all unprotected operators who cannot exhibit a written documentation of previous infection or vaccination.

Moreover, our study shows suboptimal levels of protection for HBV among HCWs, despite vaccination became compulsory for newborn in 1990. According to the Italian vaccination program, the administration of two doses of MMR is strongly recommended for HCWs having nonprotective IgG titer. Previous studies showed that workplace vaccination strategy should be preferred since it is highly cost-effective and to result in adequate level of protection.[31–33]

The debate on the duration of protection following the administration of HBV vaccine is still open and the questions on the need and effectiveness of booster doses remain unanswered. In a previous study performed on a large group of medical students, we found that most of the unprotected operators became protected after the administration of a booster dose of HBV vaccine confirming the persistence of long-term immunological memory also in subjects with low levels of anti-HBs.[11]

Based on the results of our study, the actual Italian vaccination policy seems inadequate to reach the objective of 95% protection rate among HCWs assessed by the OMS.

One of the possible causes for decreasing vaccine coverage and increasing risk of vaccine-preventable disease outbreaks among HCWs is "vaccine hesitancy", that is a complex and growing phenomenon[34] attributable to the result of broader influences. Recent social science studies, in fact, have demonstrated that individual decision-making about vaccination should be framed in a larger socio-cultural context.[35]

A cross-sectional study conducted in the major hospitals of 10 Italian cities, which evaluated the vaccination coverage among healthcare workers, revealed inadequate rates in terms of preventing disease transmission for MMR.[36]

In a recent meta-analysis developed on Italian, the prevalence of HCWs susceptible to measles was found to be 11.5% (95%CI = 8.1–15.4);[37] vaccination of susceptible subjects and exclusion of those operators from work in high-risk setting were proposed by the authors as possible preventive strategies.

A study conducted among children who received the second measles vaccine dose, whose serum samples were collected periodically, demonstrated that measles antibodies persisted in all vaccines available for follow-up 10 y after the second dose of vaccine, with no seronegative results detected.[38]

A Finnish study evaluated the persistence of antibodies against measles, mumps and rubella induced by the measles-mumps-rubella (MMR) vaccine and the kinetics of antibody decline after 20 y. High rate of seropositivity was found 20 y after the first MMR dose, particularly for rubella and measles: the rate of seropositivity in initially seronegative vaccines was 95%, 74% and 100% for measles, mumps and rubella, respectively.[15]

Recent Italian studies evaluated the long-term immunogenicity of vaccination for HBV, measles, mumps and rubella; the administration of booster dose in operators lacking serological protection was found to be effective in increasing the rate of protection and evidencing the immunological memory of those individuals.[39–42]

Health professionals' knowledge and attitudes about vaccines are a recognized determinant of their intention to recommend the vaccine to their patients and of their own vaccine acceptance:[43,44] although HCWs should generally be strong supporters of vaccination, some of them could be categorized as vaccine-hesitant.[45] Serological screening for antibody titer assessment is recommended for susceptible HCWs exposed to the risk of vaccine-preventable diseases. Nonimmune subjects should receive the vaccine or a booster dose according to the Italian vaccination program.[8]

The study had some limitations. We did not evaluate records of past vaccination, but relied on self-reporting, and did not stratify the risk of measles exposure according to the specific tasks of HCWs in different hospital departments.

In conclusion, our study shows suboptimal levels of protection among Italian HCWs and an increased risk of infection for them and their patients. Occupational medicine services should improve preventive strategies, including serological screening and workplace vaccination of nonimmune individuals regardless of age.

Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

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