

# PREVALENCE OF MEASLES IGG ANTIBODIES AMONG HEALTHCARE WORKERS IN BULGARIA

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## ABSTRACT

**Background:** Healthcare workers are at a greater risk of acquiring measles than the general population. Transmission occurs from infected patients to staff and from infected staff to patients and colleagues. In inpatient and outpatient settings, susceptible patients especially those suffering from preconditions like the elderly and severely ill patients in intensive care units, are at a high risk of severe disease or death if additionally infected with measles. The most effective preventive measure against measles is vaccination with two doses of a measles-containing vaccine.

**Aim:** To perform a serological assessment of the presence of measles IgG antibodies among healthcare workers.

**Materials and Methods:** The present study involves serological testing performed on samples from persons working in hospitals and Regional Health Inspectorates in the country.

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Screening started in connection with a reported measles outbreak in Bulgaria in 2019, and continued into early 2020. An indirect ELISA assay for the detection of specific measles IgG antibodies in serum samples was used.

**Results:** The tested 152 healthcare workers were from 5 regions in the country, i. e. Sofia-capital (n=87), Burgas (n=6), Blagoevgrad (n=5), Dobrich (n=8) and Pazardzhik (n=46). Anti-measles IgG antibodies were detected in 85.5% of the participants (130/152). Negative results, indicating a possible lack of protective immunity against measles, were obtained primarily in samples from persons younger than 40 years of age.

**Conclusion:** Screening to identify healthcare workers who lack presumptive evidence of protective immunity against measles should be reinforced, especially among younger healthcare workers, in order to minimize the risk of measles both among healthcare workers and patients.

**Keywords:** *measles, healthcare workers, measles IgG immunity, elimination*

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## INTRODUCTION

Measles is transmitted from person to person by the airborne route. It is characterized by a high contagious index (over 95%), which determines the rapid spread of infection among unprotected population groups (1, 2, 3). Immunization with two doses of measles-containing vaccine (MCV) provides protection among over 95% of vaccinated individuals, and is the most effective prevention measure against measles. The currently available MCVs provide lifelong immunity and their widespread use has drastically reduced the incidence of severe measles requiring hospitalization.

In Bulgaria, the measles immunization program dates back to 1969. Since then, the immunization schedule has undergone a number of changes, including improved availability, measures to increase the uptake, and adoption of improved vaccine formulations as they became available. Since 1992 a three-component vaccine (MMR - measles, mumps and rubella) was introduced

for the first dose of the vaccine administration at 13th month of age instead monovalent measles vaccine but the second dose was performed with monovalent measles vaccine. Since 2002, measles immunization in the country has been carried out solely with a three-component vaccine (MMR - measles, mumps and rubella). Bulgaria like the most of the countries on the European continent, applies the first dose of the vaccine at 13th month of age and the second one (re-immunization) at 12 years of age. The adoption of measures for the specific prophylaxis of measles has, through time lead to significant changes in the epidemiology of the disease. Overall, measles incidence has decreased by 90-99%, inter-epidemic periods have lengthened to 6 - 10 or more years, and disease occurrence has shifted towards older age groups. Even under high immunization coverage, infection of individuals who are not subjects to vaccination, due to age or health reasons, remains a risk. Additionally, for various reasons, including vaccine hesitancy or lack of adequate access to health services, there are clusters of the population where MCV uptake may be lower than the optimal level for population protection. Such clusters have been associated with quickly evolving measles outbreaks over the last years (4, 5). In order to ensure adequate protection of the whole population, it is therefore important to monitor vaccine uptake and susceptibility. Monitoring is particularly important in populations which have been identified in surveillance and outbreak investigations as having a higher risk of contracting the disease and/or a higher risk of disease complications.

Healthcare workers (HCWs) are a population group known to be under a higher risk of contracting infectious diseases, including measles (6, 7, 8). Transmission can occur from infected patients to staff and from infected staff to patients and co-workers. In both inpatient and outpatient settings, susceptible patients suffering from other preconditions, especially the elderly and severely ill patients in intensive

care units, are at a high risk of severe disease or death (9, 10). The risk of healthcare-associated spread of measles is increased in the presence of unprotected hospital staff.

The present study has been carried out in 2019 and 2020, and **aims** to provide an assessment of anti-measles IgG seropositivity among HCWs in Bulgaria, who are employed in hospitals and regional health inspectorates (RHI), as an indicator for protective immunity against measles in this risk group. The study was initiated in the context of an outbreak of measles, which started in February 2019 and lasted until May 2020. During this period, nearly 2,000 cases of measles were reported in 16 out of each 28 regions in the country. 91% (1354) of the cases were reported from six regions, namely: Sofia district, Sofia capital, Montana, Pernik, Kyustendil and Blagoevgrad (11). The care required for the monitoring of patients, as well as the high contagious index of the measles virus necessitated testing of the infectious wards staff in hospitals in order to determine their immune status and the level of protection against measles. Additionally, RHI staff was involved in the outbreak investigation and in the implementation of disease control measures and was likely under a higher risk of contracting the disease. The study focused on two of the more affected regions – Sofia and Blagoevgrad, and three less affected regions – Pazardjik, Dobrich and Burgas. HCWs were informed about IgG results.

## MATERIALS AND METHODS

### Materials

Serum samples, collected from HCWs were tested for the detection of specific anti-measles IgG antibodies. The study employed a convenience sample was taken among hospital and RHI staff in five regions in the country after receiving their informed consent. Samples were collected in period of measles outbreak in Bulgaria (February 2019 - May 2020). The laboratory assays were performed at the National Reference Laboratory

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## Methods

### • Serological analysis

All serum specimens were tested for the presence of anti-Measles IgG with a commercial indirect enzyme-linked immunosorbent assay (Anti-Measles IgG ELISA, Euroimmun, Germany). The absorbance values of tested samples were divided by the mean absorbance values of the cut off (calibrator) and the results were interpreted qualitatively as positive, negative or equivocal. The tests and results interpretation were performed in accordance with the manufacturer's instructions (a test was considered positive for measles if the calculated ratio was above 1.1).

### • Statistical Analysis

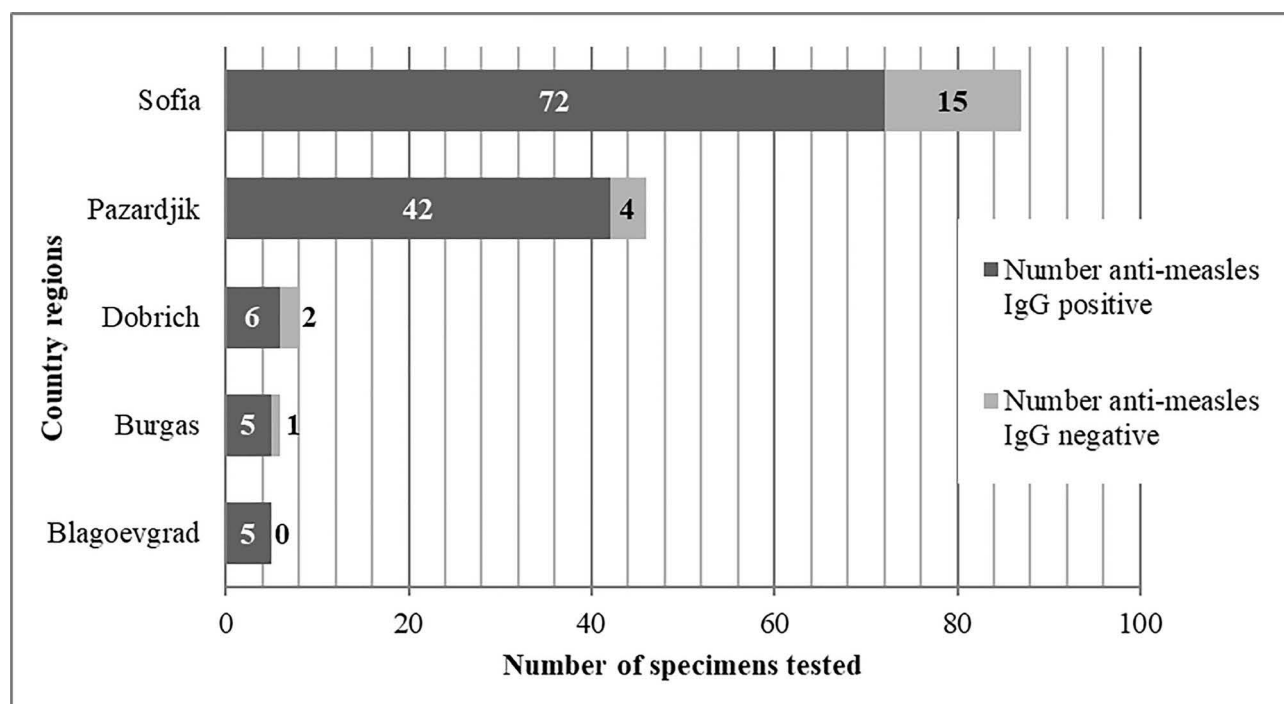
We calculated overall and group-specific percent seropositivity. In order to compare seropositivity

among the different groups under investigation, we used the Fisher's exact test and considered results as significant if the p-value was  $\leq 0.05$ .

## Results

Samples from a total of 152 HCWs were tested, and 86% (130/152) had IgG antibodies against measles (positive anti-measles IgG marker), whether as a result of vaccination and/or illness. Most samples came from Sofia-capital and Pazardjik (Figure 1). No statistically significant differences in positivity were identified through the Fisher's exact test.

A total of 84% (127) of the samples were from people employed in regional hospitals, and an additional 16% (25) of the samples were from RHI employees. The small number of samples received from RHI led to the impossibility to make a statistically meaningful comparison of seropositivity between hospital and RHI workers.



**Figure 1.** Distribution of the tested HCWs by detection of anti-measles IgG marker and regions of the country (n=152)

The analysis with Fisher's exact test identified statistically significant differences between age-specific positivity and overall positivity for two age groups - 31-40 and 51-60 (Table

1). The positivity among the 31-40 age group was particularly low (48%, compared to the overall 86% and this differences was statistically significant ( $p < 0.0001$ ). Additionally, the positivity

**Table 1.** *Distribution of the tested HCWs by age groups and the presence of anti-Measles IgG marker*

Age groups	No tested	No (%) anti-Measles IgG positive	No (%) anti-Measles IgG negative
<b>20-30</b>	23	19 (83%)	4 (17%)
<b>31-40</b>	21	10 (48%)	11 (52%)
<b>41-50</b>	27	24 (89%)	3 (11%)
<b>51-60</b>	48	46 (96%)	2 (4%)
<b>&gt;60</b>	33	31 (94%)	2 (6%)
<b>Total</b>	<b>152</b>	<b>130 (86%)</b>	<b>22 (14%)</b>

among 51-60 (96%) year olds was significantly higher than the overall positivity ( $p=0.0132$ ).

## DISCUSSION

In recent years, a drop in measles vaccination coverage, which is likely responsible for multiple epidemic peaks, has been registered in Europe (5, 12, 13). In this context, growing attention has been paid to HCWs: compared to the general population, HCWs are estimated to be at a greater risk of acquiring vaccine preventable diseases such as measles, exposing both their colleagues and patients to contagion (14, 15). Measles can easily spread across nosocomial settings where a large number of contacts are possible. Nosocomial infections may be associated with a high risk of poor outcomes for hospitalized patients (5, 16, 17, 18, 19). Baccolini et al (10) analyzed in detail the importance for the health system of measles immunity of HCWs and described outbreaks in Italy. Other authors reported that approximately 7% of measles cases occurring in working-age people still involve HCWs, who have also been identified as index cases in outbreaks. Most of them are unvaccinated persons aged between 18 and 39 (5, 15, 20).

Our seroprevalence study revealed that 14% of HCWs participating in the study, were likely susceptible to measles. These results are similar to findings from studies done among HCWs

in other European countries (15, 21, 22). One limitation of the study is that it can't differentiate immunity acquired by vaccination from immunity acquired through natural infection. One of the main reasons was that even though participants were asked about their immunization status, more than 50% of them could not provide an answer as to whether they had been vaccinated against this disease as children. It must be noted that, particularly for older age groups, a lot of the individual vaccination information was paper-based and may not be directly available to people. This is not an issue unique to Bulgaria – similar situations with incomplete recall data on immunization have been encountered in France and Italy (4, 15). Other limitation is the use of a convenience sample. The HCWs included in the study were tested in connection with their official duties and contacts with confirmed measles cases during the measles outbreak in Bulgaria.

Our results indicate particularly low anti-measles IgG positivity among 31-40 year old participant HCWs and thus adds to evidence from other studies, indicating the need to place a special attention on this age group in general, and among HCWs in particular. The exact reasons for the effect need to be identified in further studies. One possible explanation is that this is the age group which grew up in a period of changing vaccination policies, whereby the country shifted

from a single-component measles containing vaccine to an MMR vaccine. This means that, for example, the vaccines received by people within these age groups may be a combination of single component vaccine first dose and MMR second dose. In order to test whether individual level variations in vaccine doses received may affect seropositivity, a study collecting individual level data both on the number of doses and type of vaccine received needs to be undertaken with this particular group in focus. Note, however, that the lower seropositivity within this group is not necessarily a direct indicator of high susceptibility. Seropositivity is only a proxy indicator for protective immunity.

## CONCLUSION

The immunity against measles virus is largely lifelong, and the MMR vaccine has been demonstrated to be the most effective preventive measure against measles in numerous studies. However, monitoring and periodic testing of HCWs for measles immunity, as is the practice against hepatitis B, is important. The detection of non-immune individuals and the administration of booster doses of vaccine are crucial for controlling the elimination process. Our study indicates a likely lower protection among 31-40 year old HCWs and points to the need to investigate susceptibility in this group, both in terms of seropositivity and actual protection. As an immediate measure, the study has allowed us to identify participants with a negative IgG result. These participants were informed and were recommended placing vaccine.

## Competing Interest

The authors do not have any competing interest.

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