

# Seroprevalence of Measles Antibodies in Healthcare Professionals in a Central Hospital in Portugal



## Seroprevalência de Anticorpos Contra o Sarampo em Profissionais de Saúde de um Hospital Central em Portugal

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### ABSTRACT

**Introduction:** Immunity against measles may result from previous contact with the virus or vaccination. In this study we aimed to evaluate the prevalence of immunity to measles in healthcare professionals of a central hospital.

**Material and Methods:** Retrospective study, with description of the results of measles-specific IgG assay in healthcare professionals, between May 2010 and March 2018.

**Results:** The results of 1339 healthcare professionals were analyzed. The average age was  $39.3 \pm 10.11$  years, 71.1% female. The prevalence of positive IgG was 81.5%, higher among professionals in the age groups 40 - 49 and over 50 years (91.9% and 94.6% respectively). Healthcare professionals who presented negative or equivocal IgG were mostly under 40 years old (83.1%) ( $p < 0.05$ ).

**Discussion:** The prevalence of serological immunity to measles in healthcare professionals was found to be lower than in other studies. That may be due to differences between the characteristics of the studied samples. Susceptibility to measles was higher in lower age groups. These results may reflect low vaccination coverage in this age group, an incomplete vaccination schedule, or the possibility of older healthcare professionals having the disease, which may confer an immune response with higher IgG levels.

**Conclusion:** Knowing the prevalence of susceptibility to measles in healthcare professionals enabled the establishment of prevention strategies for outbreaks that may occur. Vaccination remains the best preventative measure, but a third dose of vaccine may be considered in certain epidemiological contexts, particularly in the youngest exposed healthcare professionals.

**Keywords:** Health Personnel; Measles/epidemiology; Portugal; Seroepidemiologic Studies

### RESUMO

**Introdução:** A imunidade contra o sarampo poderá resultar do contacto anterior com o vírus ou da vacinação. O objetivo deste estudo foi avaliar a prevalência de imunidade contra o sarampo em profissionais de saúde de um hospital central.

**Material e Métodos:** Estudo retrospectivo com caracterização dos resultados do doseamento de imunoglobulina G (IgG) específica contra o sarampo em profissionais de saúde, entre maio de 2010 e março de 2018.

**Resultados:** Analisaram-se os resultados de 1339 trabalhadores, média de idades  $39.3 \pm 10.11$  anos, 71,1% mulheres. A prevalência de IgG positiva foi de 81,5%, mais elevada entre os profissionais nas faixas etárias dos 40 aos 49 e mais de 50 anos (91,9% e 94,6% respetivamente). Por sua vez, 83,1% dos profissionais com IgG negativa ou equivoca tinham maioritariamente idades inferiores a 40 anos ( $p < 0,05$ ).

**Discussão:** Verificou-se que a prevalência de profissionais imunes ao sarampo foi mais baixa que noutros estudos, podendo, contudo, esse resultado dever-se a diferenças entre as características das amostras estudadas. Foi encontrada uma maior suscetibilidade ao sarampo em profissionais nas faixas etárias inferiores. Estes resultados podem refletir uma baixa cobertura vacinal nesta faixa etária, um esquema de vacinação incompleto, ou a possibilidade dos profissionais mais velhos terem tido a doença, o que contribuiu para uma resposta imunitária com níveis de IgG mais elevados.

**Conclusão:** Conhecer a prevalência de profissionais suscetíveis ao sarampo, permitiu definir estratégias de prevenção face aos surtos que possam vir a acontecer. A vacinação continua a ser a melhor medida preventiva, uma terceira dose de vacina poderá vir a ser equacionada em determinados contextos epidemiológicos, especialmente nos profissionais expostos mais jovens.

**Palavras-chave:** Estudos Soroepidemiológicos; Portugal; Profissionais de Saúde; Sarampo/epidemiologia

### INTRODUCTION

Healthcare workers (HCWs), mainly unvaccinated, seem to be at a higher risk of developing measles when compared to the general adult population,<sup>1-4</sup> due to higher-risk exposure.

Measles virus is a highly contagious RNA virus<sup>5,6</sup> of the genus Morbillivirus, family Paramyxoviridae. It is transmitted from person to person by airborne route via aerosols

containing very small droplets. Infected people are usually contagious from four days before to four days upon the onset of the rash.<sup>5</sup>

Humans are the only natural host of the virus, which makes global eradication of the disease theoretically achievable once an effective and safe vaccine is available.<sup>5</sup> Seroconversion rates of approximately 95% have been found

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with a single dose of the vaccine<sup>7</sup> and up to 99% with two doses.<sup>8</sup> Unvaccinated people are most frequently affected, even though vaccinated people can also be affected.<sup>9-14</sup>

Significant advances towards achieving measles elimination have been reached in many countries.<sup>2,11,13,15</sup> Recent outbreaks in Europe have led to particularly relevant challenges, mostly due to imported cases, associated with sub-optimal vaccination coverage among specific subpopulations (there are still significant variations between European countries in terms of vaccination policies and their implementation)<sup>3,14,15</sup> and the emerging anti-vaccination movement.<sup>7,11,16</sup>

"The monovalent measles vaccine (MV) was included in the Portuguese National Vaccination Programme (*Plano Nacional de Vacinação - PNV*) in 1974 and was replaced in 1987 by the MMR (combined measles, mumps and rubella) vaccine. A second dose of the MMR vaccine given at the age of 11-13 was introduced in the PNV in 1990, in order to overcome primary vaccine failures (about 5% of vaccinees). The second dose of the vaccine was brought forward to 5 - 6 years of age in 2000 (2000 PNV) and, in 2012, the age of administration of the first dose was brought forward to 12 months of age".<sup>17</sup>

According to the 2018 World Health Organization data, 78 people died due to measles and about 82,000 people contracted the disease within 47 of the 53 countries in the European region.<sup>18</sup> A total of 112 cases of measles were confirmed in 2018 in Portugal, 99% were adults, 13% unvaccinated, 9% with incomplete immunisation status and 79% of cases affecting HCWs.<sup>19</sup> Since most of the HCWs were vaccinated and presented mostly with mild clinical illness<sup>6,20</sup> and were potentially less contagious,<sup>3,13</sup> issues related to the interval between the last dose of the vaccine and exposure could have had an impact on maintaining the immune response (even though considering that it is a live attenuated vaccine and therefore associated with stronger and long-lasting immune response).

According to the 2016-2017 National Serological Survey carried out by the National Institute of Health *Doutor Ricardo Jorge*, a 94.2% and 5.8% measles seropositivity and seronegativity rates were found in the general population, respectively. A >95% seropositivity rate (positive IgG) was found in children aged 2-9 and in patients over 44. The distribution of seropositive cases ranged between 77.9% (20 - 29 years) and 91.0% (30 - 44 years) in the remaining age groups.<sup>21</sup>

Some studies on measles immunity in HCWs have found a susceptibility to the disease ranging from 3.3% to 16%.<sup>1,22-26</sup>

However, the susceptibility of HCWs depends on the epidemiology of the disease in the country where the study took place, the date of the study, the age of the HCWs and their vaccination coverage, among other factors.

To the authors' knowledge, no data have been ever published on the prevalence of measles seroconversion in Portuguese HCWs. Immunity to measles, shown by the presence of positive specific IgG, may result from previous contact with the virus (with or without previous history of disease) or from vaccination. This study was aimed at assessing the prevalence of immunity to measles, shown by positive specific IgG titres in a sample of HCWs from a Portuguese university hospital and some factors that may be associated with negative and equivocal IgG results.

## MATERIAL AND METHODS

This was an observational and cross-sectional study including a retrospective analysis of clinical records.

HCWs assessed at the occupational health department of a central university hospital were included as study population and those who underwent measles IgG testing between May 2010 and March 2018 were selected (no immunisation record or clinical history).

The participants' clinical records were analysed throughout the last semester of 2018, aimed at obtaining socio-demographic and occupational data and the results of measles serological tests. The immunisation status of the group of HCWs who had presented negative and equivocal IgG testing results was obtained.

Measles IgG antibody testing was carried out by the clinical pathology department of the hospital by use of the ELFA method (enzyme-linked fluorescent assay), a variant of the enzyme-linked immunosorbent assay (ELISA). A < 0.5 (negative), ≥ 0.5 - 0.7 (equivocal) and ≥ 0.7 (positive) RFV (Relative Fluorescence Value) cut-off was defined by the laboratory.

The IBM Statistical Package for the Social Sciences (SPSS®) software, version 25, was used for the statistical analysis. A descriptive analysis was aimed at defining the population characteristics according to the serological result of the specific IgG against measles. Chi-square test was used to analyse the associations between variables and a five per cent significance level was considered.

The procedures followed were in accordance with the regulations established by the Ethics Committee of the hospital and in accordance with the Helsinki Declaration of the World Medical Association.

**Table 1** – Seroprevalence of measles IgG antibodies according to socio-demographic and occupational characteristics of our group of participants

Measles IgG test		Positive n (%)	Equivocal n (%)	Negative n (%)	Total n (%)	p
Gender						
	Male	306 (79.1)	31 (8.0)	50 (12.9)	387 (100)	
	Female	785 (82.5)	59 (6.2)	108 (11.3)	952 (100)	0.315
	M + F	1,091 (81.5)	90 (6.7)	158 (11.8)	1,339 (100)	
Age group						
	< 30	158 (62.9)	31 (12.4)	62 (24.7)	251 (100)	
	30 - 39	367 (76.5)	39 (8.1)	74 (15.4)	480 (100)	0.000
	40 - 49	319 (91.9)	13 (3.7)	15 (4.3)	347 (100)	
	≥ 50	247 (94.6)	7 (2.7)	7 (2.7)	261 (100)	
Occupation						
	Nursing staff	362 (81.5)	28 (6.3)	54 (12.2)	444 (100)	
	Healthcare assistant	307 (83.9)	25 (6.8)	34 (9.3)	366 (100)	
	Physicians	208 (77.9)	24 (9.0)	35 (13.1)	267 (100)	0.442
	Pathology technician	96 (85.7)	4 (3.6)	12 (10.7)	112 (100)	
	Technical assistant	69 (81.2)	4 (4.7)	12 (14.1)	85 (100)	
	Others	49 (75.4)	5 (7.7)	11 (16.9)	65 (100)	

## RESULTS

A total of 1,339 HCWs were submitted to measles IgG testing during the study period [mean age  $39.3 \pm 10.11$  years (median 38; range 19 - 65; 71.1% female)], mainly including nursing staff and healthcare assistants.

A total of 6,281 employees worked at the hospital by December 2018, including administrative managers (48), physicians (1,442), nurses (1,940), senior health technicians and other senior technicians (255), pathology technicians (494), technical assistants (601), healthcare assistants (1,472) and non-clinical staff – essential to the hospital functioning (29), including lawyers or computer engineers.

No clinical evidence of any pathology usually associated with immunosuppression, autoimmune diseases or immunosuppressive medication was found in any clinical record regarding any of the study participants.

### Distribution of IgG results

Out of total 1,339 workers, 81.5% (n = 1,091) had a positive, 6.7% (n = 90) equivocal and 11.8% (n = 158) negative IgG result (Table 1).

No significant differences between genders were found as regards the serological results. Higher prevalence rates of immunity against measles (positive measles IgG test) were found in 40-49 and >50 age groups (91.9% and 94.6%, respectively), while the lowest prevalence rates (62.9%) were found in 19-29 age group. Negative or equivocal IgG tests were mostly found in <40 age groups (83.1%). Statisti-

cally significant differences were found between age groups ( $p = 0.000$ ).

The highest rates of negative or equivocal IgG result were found in 'other HCWs' and 'physicians' groups (24.6% and 22.1%, respectively), even though younger individuals were predominantly found in these groups (11/16 of 'other HCWs' were aged 30 - 39; 32/59 of 'physicians' were aged <30 and 23/59 were 30 - 39), with no statistically differences between occupational groups.

### Immunisation status of HCWs with equivocal IgG result

Out of total 90 participants with equivocal IgG result, 41.1% (n = 37) received two doses of the vaccine and 24.4% (n = 22) received a single dose (Table 2).

Almost half (42.4%; n = 25) of the 59 participants who had a vaccination record (MV/MMR) had received the vaccine 11 - 20 years earlier (median of 15 years) (Table 3). When analysing in terms of the participant's age, 84% of HCWs under 30 years of age with equivocal IgG result received a second dose 11 - 20 years earlier and 42.9% of those aged 30 - 39 years received it 21 - 30 years earlier (Table 4).

### Immunisation status of seronegative HCWs

Out of total 158 seronegative HCWs, 51.9% (n = 82) were fully vaccinated and 22.2% (n = 35) had only received one single dose of the vaccine (incomplete immunisation status) (Table 2).

**Table 2 – Immunisation status of HCWs with equivocal and negative test result**

IgG test		Immunisation status			
		Incomplete	Complete	Unknown	Total
Equivocal	n	22	37	31	90
	%	24.40%	41.10%	34.40%	100%
Negative	n	35	82	41	158
	%	22.20%	51.90%	25.90%	100%
Total	n	57	119	72	248
	%	23.00%	48.00%	29.00%	100%

Out of 117 seronegative participants who have received at least one dose of the vaccine, more than half (55.6%; n = 55) had received the last dose 11 - 20 years earlier (median 15 years) (Table 3). When the participants' age was considered, it was found that 84.2% of seronegative participants aged < 30 years had received their last dose 11 - 20 years earlier, while the greatest variation regarding the time interval from the last dose of the vaccine was found in seronegative participants aged 30 - 39 years (between 11 and 39 years before the test) (Table 4).

## DISCUSSION

An 81.5% prevalence rate of immunity against measles has been found in our group of HCWs, showing a lower prevalence rate of IgG positive results in the <30 age group, when compared to the results of the most recent 2016-2017 national serological survey (62.9% vs 77.9%). In Portugal, it has been almost 45 years since a coordinated measles vaccination program was started. "MMR vaccination coverage (one or two doses), at national level, has been above 95% at least since 2006. No uniform value has been found, with regional and local asymmetries increasing the presence of pockets of susceptible population, even in geographi-

cal areas with high overall vaccination coverage".<sup>17</sup> Testing in different laboratories<sup>27</sup> and at different times may have contributed to the differences found, as well as for different vaccination rates or even the rate of participants with equivocal IgG result. In fact, if those showing equivocal IgG result were included as having immunity against measles, the prevalence rate would increase up to 88.2%. In fact, the meaning of this serological result is uncertain, but it makes us assume that the antigen is not at all unknown to the organism and may possibly indicate that serum antibodies may have decreased over time after the initial immune response, maintaining some immunological memory. Therefore, in a new contact with the antigen, a secondary response would be potentially triggered.

In our study, a higher susceptibility to measles in HCWs has been found when compared to literature (with similar methodology).<sup>22-25,28-30</sup> A 6% susceptibility to measles has been found in a study from Catalonia,<sup>25</sup> while a 3.3% rate was found in another study in the United Kingdom,<sup>23</sup> 16% in a study from Italy,<sup>26</sup> 4% in a US study<sup>1</sup> and 8.2% in Japan.<sup>24</sup>

However, our results may reflect the use of a convenience sample, which is a limitation of this study. Only HCWs whose vaccination record was unknown at the time

**Table 3 – Time between immunisation and IgG testing in HCWs with equivocal and negative result**

IgG test result		Time between immunisation and IgG test (years)				Total
		1 - 10	11 - 20	21 - 30	31 - 43	
Equivocal	Incomplete	n	1	3	7	22
		%	4.50%	13.60%	31.80%	50.00%
	Complete	n	6	22	8	37
		%	16.20%	59.50%	21.60%	2.70%
	Total	n	7	25	15	59
		%	11.90%	42.40%	25.40%	20.30%
Negative	Incomplete	n	1	4	11	35
		%	2.90%	11.40%	31.40%	54.30%
	Complete	n	1	61	16	82
		%	1.20%	74.40%	19.50%	4.90%
	Total	n	2	65	27	117
		%	1.70%	55.60%	23.10%	19.70%

**Table 4** – Time between immunisation and IgG testing, according to age groups in HCWs with equivocal and negative test

	IgG test result	Time between immunisation and IgG testing (years)				Total	
		1 - 10	11 - 20	21 - 30	31 - 43		
Equivocal	< 30	n	1	21	3	0	25
		%	4.00%	84.00%	12.00%	0.00%	100%
	30 - 39	n	5	4	12	7	28
		%	17.90%	14.30%	42.90%	25.00%	100%
	40 - 49	n	0	0	0	5	5
		%	0.00%	0.00%	0.00%	100.00%	100%
	> 50	n	1	0	0	0	1
		%	100.00%	0.00%	0.00%	0.00%	100%
	Total	n	7	25	15	12	59
		%	11.90%	42.40%	25.40%	20.30%	100%
Negative	< 30	n	1	48	8	0	57
		%	1.80%	84.20%	14.00%	0.00%	100%
	30 - 39	n	0	16	19	20	55
		%	0.00%	29.10%	34.50%	36.40%	100%
	40 - 49	n	1	1	0	3	5
		%	20.00%	20.00%	0.00%	60.00%	100%
	Total	n	2	65	27	23	117
		%	1.70%	55.60%	23.10%	19.70%	100%

of the medical examination were submitted to the serological testing, which was not requested for HCWs who had a record of having been fully vaccinated (MV/MMR vaccine) (an acceptable presumptive immunity evidence was assumed)<sup>6</sup> or a single dose of MV/MMR vaccine (these have received a second dose in order to complete their immunisation schedule). Therefore, a higher prevalence rate of seropositive HCWs would probably have been obtained, as all HCWs would have been included regardless of the presence of a immunisation record at the time of health assessment. On the other hand, the fact that a young group or participants has been included in our study (median age of 38) may also have contributed to a lower prevalence of seropositivity.<sup>30</sup>

A percentage of 79% of the 112 confirmed cases in the 2018 Portuguese measles outbreak were HCWs. Out of total cases, only 13% were unvaccinated and 9% had an incomplete immunisation status.<sup>19</sup> A high percentage of seronegative HCWs had received one or two doses of vaccination. Almost half (48%) of the HCWs with negative or equivocal IgG result ( $n = 248$ ) were fully vaccinated and 23% received one single dose. When only seronegative HCWs were considered, 51.9% were fully vaccinated and only 25.9% (41 HCWs) had no record of any measles vaccination. These results made us consider a third dose of the vaccine in outbreaks for exposed HCWs.

In our study, measles susceptibility, as assessed by measles-specific IgG, was found to be higher in younger HCWs (under 30 years of age), in line with other studies.<sup>22-26</sup> These results may reflect low vaccination coverage in this age group or an incomplete immunisation status,<sup>4,15</sup> in addition to the fact that older HCWs had had contact with the disease, allowing a more robust immune response.

Our results prevented us from suggesting an association between the time interval between the last dose of vaccine and the presence of negative or equivocal IgG seroprevalence. In fact, we have confirmed that seronegative HCWs having received at least one dose of the vaccine did it mostly 11-20 years earlier, most frequently in people aged < 30 years. The type and characteristics of our sample and the study design may have been at least partially responsible for the results found. Therefore, further longitudinal randomised studies are required to conclude on the influence of this variable on serological test results.<sup>7,30</sup>

## CONCLUSION

An 81.5% measles seropositivity rate was found, mostly among HCWs aged 40-49 and over 50 (91.9% and 94.6% respectively). In turn, 83.1% of the HCWs showing negative or equivocal IgG results were under 40 ( $p < 0.05$ ). Prevention strategies regarding future outbreaks in our hospital will certainly be more accurately shaped by knowing the

prevalence of susceptibility to measles,<sup>3,20,26,30,31</sup> namely with systematic testing to assess the immunisation/immunity status included in pre-appointment health check, vaccination of HCW when required, training and information on the individual risks and development of internal guidelines regarding unprotected exposure to patients with measles. Vaccination remains the best preventive measure,<sup>2,3,7,16,20,26,31</sup> not only in preventing nosocomial transmission of the disease, but also in contributing to the eradication of measles. However, a third dose<sup>15</sup> of vaccine could be considered in specific epidemiological contexts, in the presence of outbreaks in younger healthcare professionals.

## HUMAN AND ANIMAL PROTECTION

The authors declare that this project complied with the

regulations that were established by the Ethics and Clinical Research Committee, according to the 2013 update of the Helsinki Declaration of the World Medical Association.

## DATA CONFIDENTIALITY

The authors declare that they have followed the protocols of their work centre on the publication of patient data.

## CONFLICTS OF INTEREST

The authors declare that there were no conflicts of interest in writing this manuscript.

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