Original article

Seroprevalence of measles antibodies among health professionals of Estonia

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Abstract

Objectives: Outbreaks of measles have been reported in Europe, including in countries that have previously eliminated endemic transmission. Seroprevalence data are needed to predict the outbreak cycles. No published measles seroprevalence data is available from Estonia and only few from Eastern Europe have been published. The objective of this study is to describe measles seropositivity in Estonia.

Methods: Between February and June 2019, all 1300 health care workers of an academic hospital were invited. From the 738 (56.7%) respondent (90% female, mean age (SD) of 47 (12) years), IgG measles titre were measured.

Results: Among the participants, 71% were seropositive. When data were further analysed according to vaccination birth cohorts, the oldest cohort (born before vaccination was introduced in 1964) had the highest seropositivity proportion (91%), vs. other birth cohorts with various types of vaccines (around 60%).

Conclusions: Measles seropositivity is lower than the threshold level to interrupt endemic virus transmission. No difference in seroprevalence among participants who received various types of measles vaccines.

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Seroprevalencia de anticuerpos frente a sarampión entre los profesionales sanitarios de Estonia

Resumen

Objetivos: Se han reportado brotes de sarampión en Europa, incluyendo en países en los que se había eliminado la transmisión endémica previamente. Son necesarios datos sobre seroprevalencia para predecir los ciclos de los brotes. No existen datos publicados sobre seroprevalencia del sarampión en Estonia, y se han publicado pocos datos procedentes de Europa del Este. El objetivo de estudio es describir la seropositividad del sarampión en Estonia.

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Métodos: Entre febrero y junio de 2019 se invitó a participar a los 1.300 profesionales sanitarios de un hospital académico. De los 738 (56,7%) respondedores (90% de mujeres, con edad media (DE) de 47 (12) años), se midieron los títulos séricos de IgG frente a sarampión.

Resultados: Entre los participantes, el 71% fue seropositivo. Al volver a analizarse los datos con arreglo a las cohortes de nacimiento con respecto a las vacunas, la cohorte de mayor edad (nacida antes de la introducción de la vacuna en 1964) tenía el mayor porcentaje de seropositividad (91%), vs. otras cohortes de nacimiento con diversos tipos de vacunas (cerca del 60%).

Conclusiones: La seropositividad frente al sarampión es inferior al nivel umbral para interrumpir la transmisión endémica del virus. No se encontró diferencia en cuanto a seroprevalencia entre los participantes que recibieron diversos tipos de vacunas frente al sarampión.

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Introduction

Measles is a highly contagious viral disease with basic reproduction rate (R0) estimated at 12 to 18.1 Prior to the introduction of a vaccine in 1963, it killed more than 2 million people every year in the world.1 Vaccine, together with economic development, improved nutritional status and improved supportive care such as antibiotic therapy to treat measles-associated bacterial pneumonia, has led to significant decrease of measles associated mortality.1

In Estonia, measles vaccination was started in 1964, and between 1964 and 1979 monovalent measles vaccine was given to baby of 9 months of age. However, due to the concern that this Soviet Union type of vaccine was unstable in the cold chain since only 54% of vaccinated children developed immunity,2 other vaccine from Western Europe was imported, leading to the use of, another type of monovalent vaccine between 1980 and 1994, and people vaccinated using previous vaccine could get revaccination if they wanted to. The combined measles, mumps and rubella (MMR) vaccine was introduced in Estonia in 1994, scheduled for children of 1-year-old and the second dose for children at age of 13-years-old. The vaccine coverage in Estonia in 2017 was above 90% but the trend was declining since 20123 and the coverage for the second dose was 89%.4

Outbreaks of measles have been reported in Europe, including in countries that have previously eliminated or interrupted endemic transmission and in 2019, countries such as Greece and the United Kingdom lost their measles elimination status.5 In 2019, there were 10 deaths due to measles (case fatality 0.09%) among countries that reported their data to the European Center for Disease Prevention and Control.5 While low vaccination coverage is the main reason for measles outbreaks, secondary vaccine failure may play a role in highly vaccinated populations.6

Healthcare workers (HCWs) are at risk of encountering an infection and may spread infections to patients, colleagues, and communities through family members and relatives. Therefore, they are an important target group for vaccination. Seroprevalence data are needed to assess vaccination effectiveness, and these data among HCWs are needed to inform vaccination policy, for example whether re-vaccination is needed. Moreover, the data can also be used for modelling to estimate (nosocomial) outbreak. To the best of our knowledge, no published seroprevalence data is available from Estonia. The objective of this study is to describe measles seroprevalence among HCWs in Estonia and to explore factors that may play a role in this seroprevalence.

Methods

Population and study design

This is a retrospective cross-sectional study using data that were already collected at East-Viru Central Hospital, the largest hospital and employer in the East-Viru County (population of 136,240 in 2019). Between February and June 2019, all 1300 employees of the hospital were invited for measles serological testing. Employee who agreed to participate was requested to report their vaccination status during serological testing visit.

Serological test

IgG measles titre was measured using a commercial ELISA-based, automated, in-vitro test system for the quantitative determination of IgG antibodies (Orgentec, Mainz, Germany). Measuring and interpretation were performed as per manufacturer’s instruction. An IgG level ≥250 IU/L was interpreted as seropositive, as recommended by the manufacturer.7

Statistical analysis

Continuous variables were presented based on their distribution, either mean (with standard deviation, SD) or median (with inter-quartile range, IQR). We compared the IgG measles titres between male and female, and between vaccinated and non-vaccinated using unpaired t-test. Furthermore, we compared the seropositivity of these groups using chi-square test.

Throughout its history, three types of vaccine have been used in Estonia, two of them were monovalent vaccine when Estonia was still part of Soviet Union: one type that was used between 1964 and 1979, and another that was used between 1980 and 1994. Since 1994, combined measles
vaccine (MMR) was used. We compared the IgG measles titres among these cohorts and the cohort that did not receive vaccine (those who were born before 1963) using ANOVA, and the seropositivity using chi-squared test. p < 0.05 was considered as significant. Data were analysed using SPSS Statistics 26 (SPSS Inc., Chicago, Ill, USA).

Results

Characteristics of the participants

Among the 1300 invited employees, 738 (56.7%) responded (90% female, mean age (SD) 47 (12) years (Table 1). Reasons for not participating were not obtained from non-participants.

Among the participants, 521 (71%) were seropositive. The median (IQR) of the IgG among the participant was 478 (217–1848) mIU/ml.

Gender and vaccination status on IgG measles titres and seropositivity

There was a significant higher median IgG measles titre in male in comparison to female (664 mIU/ml vs. 455 mIU/ml), and when the seropositivity was compared, a higher significant proportion was also shown in male than female (81.9% vs. 69.4%) (Table 1).

Vaccination status was available from 295 out of 524 (56.3%) of the participants who were eligible for vaccines (i.e. birth cohort after the introduction of vaccine). There was no statistical significant difference in median IgG measles titre between vaccinated and not-vaccinated subjects. Seropositivity was noted in 59.2% vaccinated and 72.2% not-vaccinated participants, but the difference was not statistical significant.

Birth cohort and IgG measles titres and seropositivity

The birth cohort before 1963, i.e. those who were not vaccinated had significant higher median IgG measles titres than other birth cohorts who received various vaccines (Table 2). The seroprevalence of this birth cohort (91.1%) was also significantly higher than that of other vaccination cohorts, where the prevalence was around 60%.

Discussion

The present study is perhaps the first study of seroprevalence of measles in HCWs in East Europe. In this study, we found seroprevalence of around 70% in HCW’s. This number is clearly lower than the number of vaccine coverage in Estonia that is above 90% according to the literature. A possible explanation for this mismatch is that the vaccine coverage data comes from a more recent statistic and it is not known whether the vaccine coverage in the past was also so high, and vaccine coverage data might not always reliable in the past. Yet, among the participants in this study, >90% reported of being vaccinated. Another possible explanations for low seroprevalence as observed in this study are the inefficiency of the type of vaccine used, and the cut-off used to determine the seropositivity.

Yet, if we lowered the threshold of seropositivity to >200 mIU/L, there would be additional 5% positive HCW’s (i.e. 556 (75.3%), vs 521 (70.6%) when manufacturer’s threshold was used), but this number is still low.

In this study, we observed that the oldest cohort group, despite that they did not receive measles vaccination, had the highest seropositivity proportion (91% vs. around 60% other birth cohorts who received various types of vaccines). This observation seems to be consistent in the literature. The cause is perhaps the accumulation of measles exposure. IgG measles titre in not an ideal method to assess vaccine effectiveness since it cannot differentiate between immunity due to vaccine from immunity due to exposure to measles virus.

Comparison of serosurveillance studies results is difficult because of variation in the countries policies regarding vaccines, study population, sample size, age groups, genders, and tests used. There is also scarcity of data from East Europe. A study on medical students, who could be considered as HCW’s in Slovenia showed measles seroprevalence of 96.4% (measured using Serion ELISA Classic, Measles Virus IgG, Virion-Serion, Würzburg, Germany) among 256 medical students in Ljubljana.

HCWs themselves are normally not considered to be representative of the general population since depending on their workplace, the risk of exposure may be higher and often special vaccination policies are in place. The policy consequence of the finding from this study is that the HCWs were offered to receive a re-vaccination because low (71%) seroprevalence

Table 1 – Measles IgG titres and seroprevalence of the health care workers included in this study stratified among gender and vaccination status.a

<table>
<thead>
<tr>
<th></th>
<th>Male vs. female</th>
<th>Vaccinated vs. not vaccinated</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median titres, mIU/ml (IQR)</strong></td>
<td>Total (n = 738)</td>
<td>Male (n = 72, 9.8%)</td>
<td>Female (n = 666, 90.2%)</td>
</tr>
<tr>
<td>Seropositive, n (%)</td>
<td>521(70.6)</td>
<td>455 (204-1752)</td>
<td>462/666 (69.4)</td>
</tr>
<tr>
<td></td>
<td>478 (217-1848)</td>
<td>664 (286-3584)</td>
<td>59/72 (81.9)</td>
</tr>
</tbody>
</table>

(a) Participants with birth cohort eligible for measles vaccines of with available vaccine status.

(b) Statistical significant at p < 0.05. Abbreviation: IQR, interquartile range.
among HCWs can lead to outbreaks, as they may spread infections to patients, colleagues and relatives.

The strength of this study is that it accumulated relatively large amount of data from relatively homogenous population; Estonia is a small country with relatively homogenous population. There are several limitations of this study. First, the response percentage was not so high, which might introduce bias, but it there is no reason to assume that this bias will underestimate the results (i.e. vaccinated health care workers tend not to participate in this study). Second, there was limited data available on vaccination status since no documented vaccination data were available, and the available vaccination data might be not reliable due to recall bias. We cannot therefore draw any conclusion on vaccine effectiveness is from this study.

In conclusion, we found lower measles seroprevalence than the threshold needed to interrupt endemic virus transmission. Re-vaccination has been offered to the HCWs to prevent measles outbreaks.

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Next to routine salaries, no additional funding was received for this study.

Conflicts of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Statements of ethical approval

This study is a retrospective study that used data that had been collected for a project on vaccination and re-vaccination of HCW’s at the East-Viru Hospital. Laboratory data could not be linked to any specific HCW since the HCW’s were anonymised in the database. Moreover, regarding the data protection, the study was approved by head of the hospital and the department of data protection.

References