

Correlation of Herd Immunity to Measles Vaccination Rate and Disease Incidence

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Abstract

Background: Measles is one of the most contagious diseases faced by humans. Despite considerable progress, measles remains one of the leading global causes of death among children.

Methods and Results: The seroprevalence of antibodies against measles in Kosovo was determined with a serological survey of measles. In total, 768 participants aged between 3 days and 45 years of both sexes were included. Enzyme-linked immunosorbent assay results revealed total seropositivity of 74.5% (95% CI: 0.70–0.88) among participants. Those in the unvaccinated 0–1.9-year age group had the lowest seropositivity (33.2%). The 2–6-year age group, which received one dose of the vaccine, had higher seropositivity (78.6%) than the youngest group. The 8–17-year age group, which received two doses of the measles vaccine, had significantly higher seropositivity (91.3%) than the 2–6-year age group. The highest level of seropositivity (93.4%) was observed in the 18–45-year age group. An analysis of sex-specific IgG antigen levels indicated that female participants had significantly higher seropositivity than male participants ($P < 0.01$).

Conclusion: The seroprevalence of measles antibodies in Kosovo has not yet reached the required 95% threshold, and the threat of a possible measles epidemic exists. An immunization strategy that targets vulnerable groups and the entire population is required. (International Journal of Biomedicine. 2023;13(1):151-155.)

Keywords: measles • seroprevalence • vaccination

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Abbreviations

MMR, measles–mumps–rubella; MCV, measles-containing vaccine; NTU, NovaTec Units.

Introduction

Measles is one of the most contagious diseases faced by humans.⁽¹⁾ Despite considerable progress in reducing the incidence of measles, it remains one of the leading global causes of death among children.⁽²⁾ To control measles and prevent outbreaks and deaths, vaccination coverage rates with

the required MCV1 and MCV2 vaccines must reach and be maintained at 95% at the national and sub-national levels.⁽¹⁾ Global MCV1 coverage has stagnated at 84%–85% for over a decade. Although a safe and cost-effective vaccine is available, global measles deaths have continued to climb and surged worldwide in 2019, when the highest number of reported cases in the previous 23 years were reported.⁽¹⁾

Measles outbreaks continue to occur in countries in which the population is unvaccinated or under-vaccinated, as well as in countries with highly vaccinated populations.⁽³⁾ Despite the universal use of the two-dose trivalent measles–mumps–rubella (MMR) vaccine in the past two decades,

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outbreaks of these diseases still occur in countries with high vaccine uptake, giving rise to concerns about the primary and secondary failure of MMR vaccine components.⁽⁴⁾

In addition to the factors presented above, the COVID-19 pandemic has considerably disrupted health services worldwide because of associated healthcare staff shortages and the requirement for social distancing.⁽⁵⁾ The suspension of measles campaigns because of the COVID-19 pandemic in some countries will inevitably lead to an increase in measles cases in these countries.⁽⁶⁾ The WHO has targeted measles for elimination by 2020, an ostensibly challenging goal.⁽⁷⁾ The organization assumes that the recommended measles vaccination coverage rates will generate and maintain the herd immunity required to prevent the transmission of measles in the community.⁽⁸⁾

During the 2000–2020 period, measles vaccination prevented an estimated 31.7 million deaths globally, making the measles vaccine one of the most cost-effective programs in public health.⁽³⁾ Several countries that have achieved sustained measles control now demonstrate that the level of measles-specific IgG antibodies declines with time from vaccination. Given the strong epidemiologic evidence for population-level protection, the implications of declining measles-specific IgG antibody levels to the maintenance of measles eradication remain unclear.⁽⁹⁾

Before the introduction of the mandatory measles vaccine in Kosovo in 1971, large outbreaks of measles were recorded every 1–3 years. No cases of measles were registered between 2000 and 2017. During the 2017–2018 measles outbreak, 749 confirmed cases and two deaths were recorded. At the beginning of the outbreak, most confirmed cases were among hard-to-reach children from vulnerable groups; the outbreak then spread to the entire population.⁽¹⁰⁾ During the same period, a total of 41,000 confirmed measles cases, including 37 deaths that occurred in the first six months of 2018, were reported in seven European countries.⁽¹¹⁾

In Kosovo, the vaccination of individuals aged 0–18 years is in accordance with the Health Law, the Public Health Law, and the Law on Prevention and Control of Communicable Diseases.⁽¹²⁾ The vaccination calendar is dynamic and varies according to the epidemiological situation in the country and abroad. Children who receive one dose of BCG (Bacille Calmette-Guerin), three doses of IPV (Inactivated polio vaccine), DPT (diphtheria, pertussis, tetanus), HepB, (Hepatitis B), HiB (Haemophilus influenza type B), and one dose of MMR by the age of 12 months are considered; however, unregistered children and those who are hard to reach remain high-risk groups. The decrease in the vaccination coverage rate during the past 3 years has been driven by several factors: the COVID-19 pandemic, the difficulty reaching unregistered hard-to-reach children, the false association of the MMR vaccine with autism, and religious beliefs. The national level of vaccination coverage is satisfactory for registered children.

The purpose of the study was to assess the seroprevalence of measles-specific antibodies in 768 participants aged 0–45 years in Kosovo, where measles vaccination rates have been high (>95%), and cases have been very low for decades. We further aimed to identify possible demographic factors

associated with the seroprevalence of measles antibodies, MMR vaccination coverage, and the incidence of measles in Kosovo during the 2012–2021 period. Our main objective was to provide scientific evidence for ways to eliminate measles and guide relevant strategies to achieve eradication, protect public health, offer safe vaccines, and identify the additional vaccination coverage required to establish herd immunity against measles.

Material and Methods

The study was approved by the Ethical Committee of the Medical Faculty of the University of Pristina in Kosovo and was based on the committee's methodology. Written informed consent was obtained from each research participant (or the participant's parent/guardian).

The seroprevalence of antibodies against measles was determined using a serological survey of measles in Kosovo. Sera collection was conducted from 2017 to 2021. In total, 768 participants aged 3 days to 45 years of both sexes (48.7% male and 51.3% female) were included in the study. Using the Kish method,⁽¹³⁾ a representative sample was obtained from seven Kosovo regions (29 municipalities). Participants included in the research were healthy and active. Individuals who were infected during the 2017–2018 measles outbreak were excluded from antibody seroprevalence analysis. The numbers of sera by age group varied from 150 to 241. All participants were divided into four age groups: 0–1.9 years (n=190), 2–6 years (n=187), 8–17 years (n=150), and 18–45 years (n=241). Personal information, including sex, age or date of birth, measles vaccination, and sampling date, was collected. We assessed the correlation between MMR vaccination coverage and disease incidence in 2012–2021. Vaccination history was collected from the Immunization Program Management Database. Measles incidence data were obtained from the National Institute of Public Health annual reports for Communicable Diseases in Kosovo.

Serological tests were performed in the laboratory of the microbiology department of the Institute of Public Health. All samples were tested using the NovaTec (222 Thomas Ave, Baltimore, MD 21225, USA) enzyme-linked immunosorbent assay. A commercial kit was used for the qualitative determination of IgG antibodies against the measles virus in human serum or plasma. Samples were kept at 2–8°C if the assay was performed within 5 days of sample collection; otherwise, samples were aliquoted and were deep-frozen at –20°C. Samples were processed according to the First In, First Out principle. Washing was performed using automatic Tecan (Seestrasse 103, 8708 Mannedorf, Switzerland) equipment. Negative and positive controls were included in each enzyme-linked immunosorbent assay kit calibrator. A house control was included in each round of testing. Sensitivity diagnostic performance was 97%, and specificity was 100%. Results were calculated based on the protocol and were evaluated qualitatively as positive (>11NTU), negative (<9NTU), and intermediary (9–11NTU). Sera with intermediary values were subjected to repeated testing; in cases of repeated results, a new sample was requested.

Statistical analysis was performed using the SPSS Version 26.0 (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp) statistical software package. Participants' demographic characteristics were analyzed using the descriptive method. The association between MMR vaccination coverage and the measles incidence rate was analyzed using Pearson's correlation. The Mann–Whitney test was used to determine the difference between male and female participants in measles-specific IgG levels. The association between age and measles-specific IgG levels was assessed using the Kruskal–Wallis test. A *p*-value less than 0.05 was considered statistically significant.

Results

Participants in the unvaccinated 0–1.9-year age group had the lowest seropositivity (33.2%). The 2–6-year age group, which received one dose of the vaccine (93.3% MCV1), had higher seropositivity (78.6%) than the youngest group. Higher seropositivity (91.3%) was observed in the 8–17-year age group, which received two doses of the MMR vaccine (96% MCV1, MCV2), than in the 2–6-year age group. The highest level of seropositivity (93.4%) was observed in the 18–45-year age group. The total seropositivity of participants was 74.5% (95% CI: 0.70–0.88; Table 1).

Table 1.

Participant characteristics and measles seroprevalence results of study participants

Age group (years)	Male (n)	Female (n)	IgG positive (n)	IgG negative (n)	Median IgG (IU/mL)	Seroprevalence (%)	95 % CI
0–1	102	88	63	127	0.14	33.2	0.12–0.16
2–6	88	99	147	40	0.79	78.6	0.71–0.91
8–17	76	74	137	13	0.97	91.3	0.85–1.07
18–45	108	133	225	16	1.23	93.4	1.11–1.39

A comparison by sex of IgG levels indicated that female participants had a significantly higher seropositivity rate than male participants ($P < 0.01$, Figure 1).

Figure 2 illustrates that the 0–1.9-year age group, which was not vaccinated with MMR, had significantly lower quantities of IgG than age groups that were vaccinated with one or two doses of MMR. The differences increase with age and there are significant statistical differences ($P < 0.01$).

Figure 3 shows a correlation between national MMR vaccine coverage and the incidence of measles per 100,000 inhabitants (0.89) from 2012 to 2021. The average vaccination

coverage from 2012 to 2019 was 95.2%, and it decreased by 5% during the COVID-19 pandemic. Vaccination coverage was higher at the beginning of the measles outbreak 2017–2018 than in 2012–2016 because of the vaccination campaigns undertaken during that period.

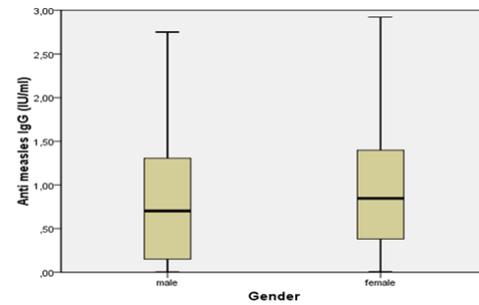


Fig. 1. Measles-specific IgG levels by sex.

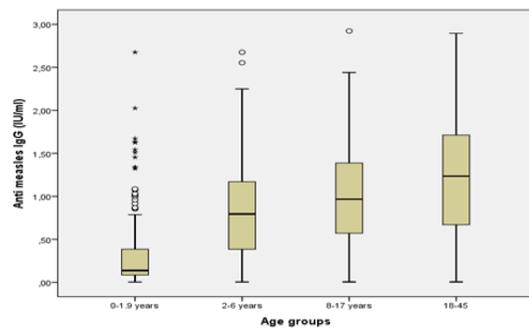


Fig. 2. Ig G levels by age groups.

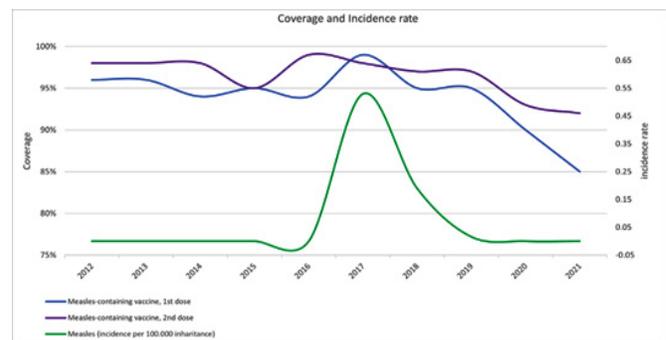


Fig. 3. National MMR vaccine coverage and measles incidence (2012–2021).

Figure 4 illustrates MMR vaccine coverage by Kosovo municipality. Findings indicate that most municipalities are within the national coverage level. The highest coverage was achieved in the municipalities of Hani i Elezit, Istog, Mamusha, Theranda, and Dragash—which are above the threshold of the national coverage level—whereas the municipalities of Gjilan, Prishtina, Lipjan, Peja, and Fushë Kosova were below the national threshold and had the highest incidence of measles during the 2017–2019 outbreak.

Discussion

Our results showed that 74.5% (95% CI: 0.70%–0.88%) of participants enrolled in the study had positive titers of measles-specific IgG antibodies. We assessed the seroprevalence of measles-specific antibodies, the influence of demographic factors, including age and sex, on measles-specific IgG levels, MMR coverage, and the incidence of measles. Compared with the results of other studies,^(14,15) the seropositivity results in our study were lower and were within an 80–96% range, similar to rates observed in Poland.⁽¹⁶⁾ The lower ratio of seropositivity in our study was found in the 0–1.9-year age group, which was unvaccinated.

Sex is a well-known biological variable that influences vaccine-induced immune responses.⁽¹⁷⁾ Consistent with the findings of previous reports, female participants in this study cohort had higher levels of measles-specific IgG than male participants (Figure 1). Higher measles-specific IgG levels in females could be explained by a stronger initial humoral immune response to measles vaccines⁽¹⁸⁾ or a slower waning of measles immunity in females than in males.⁽¹⁹⁾ In contrast to the results of Shoho et al.,⁽²⁰⁾ in our study, we observed a higher titer of antibodies in the group vaccinated with two vaccines than in the group that received one dose of the MMR vaccine. The titer among participants in the 18–45-year age group was higher than reported in other studies⁽²¹⁾ and was similar to values reported in studies conducted in Italy⁽²²⁾ and the Czech Republic.⁽²³⁾ Vaccination coverage with MMR in Kosovo from 2012 to 2019 was 95.2% and declined by 5% during the COVID-19 pandemic. The incidence of measles was 0.89 per 100,000 inhabitants during the 2017–2019 outbreak. Measles outbreaks mainly occur in unvaccinated or under-vaccinated populations. Vaccine failure and waning immunity may be contributing factors to measles outbreaks in the immunized population.⁽²⁴⁾ A threshold of 93–95% is needed to stop measles transmission.⁽²⁵⁻²⁶⁾

Conclusion

The population immunity level in Kosovo may still be below the criteria required for achieving eradication, and further population immunity is required. To keep measles under control, we must establish a high level of herd immunity, prevent and control the transmission of measles, and reduce infectious sources. An important measure is to encourage vaccination among family members of children to protect vulnerable infants from infection. Our study impacts public health by providing evidence of the low seroprevalence of measles in the population. Therefore, results could have implications for achieving the goal of measles elimination. Furthermore, low measles seroprevalence indicates the need to monitor routine immunization practices, especially vaccine storage and cold chain maintenance—processes that may lead to low serologic responses. Our findings highlight a low level of measles seroprevalence and suggest a high risk of measles outbreaks. Results further indicate the likely need to reevaluate the MMR vaccination program in Kosovo to increase herd immunity.

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Competing Interests

The author declares that there is no conflict of interest in this work.

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