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Immunity gap for measles in young adults: Seroprevalence study in blood donors in southern Italy

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ABSTRACT

Following the COVID-19 pandemic, measles has seen a resurgence across Europe, including Italy. Increased vulnerability among young adults has raised concerns about waning vaccine-derived immunity. This study evaluated measles immunity among adult blood donors in the Apulia region to identify sero-susceptibility patterns and inform targeted public health strategies. A retrospective seroprevalence study was conducted using sera from 1579 healthy blood donors, aged 18 to 65 y, who attended donation centers in Apulia region between November 2023 and February 2024. Anti-measles virus (MV) IgG antibodies were measured using the ELISA test. Statistical analyses to identify associations between sero-susceptibility and demographic factors were performed. Overall seroprevalence of anti-MV IgG was 85.3% (95% CI: 83.4–87.0). The prevalence of sero-susceptibility varied significantly by age ($p < .0001$), ranging from 39.8% among individuals aged 18–24 y to 4.0% among the 45–54 age group. No differences were observed based on sex or province of residence. Among sero-susceptible individuals with known vaccination status, 77.2% were under 35 y of age, and 69.6% had received two doses of the measles vaccine. Geometric Mean Concentration levels increased with age and were significantly higher in unvaccinated individuals, which suggests that natural infection provides more lasting immunity. However, measles immunity among adults in Apulia remains below the elimination threshold, with a substantial immunity gap concentrated among young adults, despite high vaccination coverage. These results suggest a decline in vaccine-induced immunity and underscore the importance of targeted surveillance and preventive strategies, such as evaluating booster vaccination policies, to prevent future epidemics.

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Measles; seroprevalence study; surveillance; vaccine-preventable infections; epidemiology

Introduction

Measles is an acute highly contagious viral disease caused by the measles virus (MV), an enveloped, single-stranded RNA virus of the *Morbillivirus* genus within the *Paramyxoviridae* family. Humans are the only known natural host, with no animal reservoirs.[1,2] Transmission occurs primarily through respiratory droplets or aerosols from infected nasopharyngeal secretions, which can remain suspended in the air for up to 2 hours.[1] The incubation period is 8–14 d followed by prodromal symptoms, including fever, cough, coryza, conjunctivitis and pathognomonic Koplik spots. A characteristic maculopapular rash typically spreads from the face craniocaudally.[2,3] Infectivity peaks three days prior to rash onset, with 75–90% secondary attack rates among susceptible household contacts.[3] Complications, most frequent in young children and immunocompromised individuals, include otitis, laryngotracheobronchitis, pneumonia, encephalitis and subacute sclerosing panencephalitis (SSPE) up to 7 y post-infection.[1]

The introduction of the measles vaccine dramatically reduced the global burden of disease. Measles-related deaths decreased by 87% from 2000 to 2023.[4] Despite substantial progress, measles remains a major cause of vaccine-preventable morbidity and mortality, particularly among children <5 y of age. In 2023, this

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age group accounted for over 40% of all reported cases across 53 countries in Europe and Central Asia, with more than half requiring hospitalization.[5]

Globally, annual measles cases declined by 44.3% from 2000 to 2024, with annual incidence falling from 144.6 to 62.6 per million population. Reported cases peaked in 2019 but sharply declined during the COVID-19 pandemic, largely due to the implementation of non-pharmacological interventions.[6] In Europe, reported cases increased with a rate of 77.4 per million population in 2024, with children <10 y of age being the most affected. In Italy, 1057 measles cases were reported in 2024, reaching the highest post-pandemic figure to date.[7] At the beginning of 2025, an estimated 9.2% of the Italian population remained susceptible to measles, with susceptibility reaching 11.8% among individuals <20 y of age.[8]

In 2013, the National Integrated Measles and Rubella Surveillance System was implemented in Italy to monitor measles circulation.[8] In Italy, the live attenuated measles vaccine was introduced in 1976 and recommended as a single dose at 15 months starting in 1979.[9] During the 1990's, the combined MMR vaccine became the standard, although measles vaccination coverage remained low (around 40–50% in the early 1990's, rising to 70% in 2000) and geographically heterogeneous. A two-dose regimen (second dose at 5–6 y) was only systematically implemented nationwide with the National Plan for the Elimination of Measles and Rubella in 2003. Following a large outbreak in 2017, the trivalent measles-mumps-rubella (MMR) vaccine became mandatory for all children <16 y of age.[8,10] Nevertheless, sporadic outbreaks continue to occur. Between December 2019 and March 2020, a measles outbreak was reported in the Apulia region with 39 laboratory-confirmed cases identified in the Lecce province, and 35 cases were reported across the region in 2024.[11,12]

The World Health Organization (WHO) aims to achieve and sustain measles eradication by 2030,[13] through ≥95% two-dose vaccination coverage (based on R_0).[14] However, coverage remains suboptimal in several countries, including Italy.[13,15] In Apulia, the first-dose coverage averaged 90.4% between 2012 and 2023 and second-dose coverage averaged 85.1% between 2013 and 2023, both below the WHO-recommended threshold for elimination.[16]

Recent European and national surveillance data indicate a resurgence of measles following the COVID-19 pandemic, suggesting a potential increase in population susceptibility to measles infection and raising important public health concerns. Few studies are available on the seroprevalence of anti-MV antibodies as a correlate of protection in Italy. Seroprevalence data from southern regions remain particularly limited.

This study aimed to evaluate the prevalence of anti-MV IgG antibodies among healthy blood donors in the Apulia region of southern Italy. The primary objective was to assess sero-susceptibility to measles infection within the regional adult population. The secondary objective was to identify groups with increased sero-susceptibility by stratifying population by age, gender, vaccination status and province of residence, with the aim of informing targeted public health interventions and vaccination strategies.

Materials and methods

Study population

A retrospective cross-sectional study was conducted by analyzing sera from healthy blood donors aged 18–65 y who attended blood donation centers located in five of the six provinces of the Apulia region (including Bari, Barletta-Andria-Trani [BAT], Foggia, Lecce and Taranto) between November 2023 and February 2024. Ethics approval was obtained from the Ethics Committee of the IRCCS Istituto Oncologico Giovanni Paolo II, Bari, Italy (Prot. N. 594, 24/10/2023 – Studio 1408/CEL – WNV Pug.23). Written informed consent and a serum sample were collected from each blood donor. The samples were anonymized, centrifugated and sent for testing to the Laboratory of Molecular Epidemiology and Public Health at the Policlinico Hospital of Bari, the regional reference laboratory for diagnosis of measles infection. Data for each donor were collected, including date of birth, gender and, residence. Measles vaccination status and the number of vaccine doses were obtained from the regional computerized vaccination registry (GIAVA) at enrollment.

Laboratory testing

All sera were tested for anti-measles virus (anti-MV) IgG antibodies using a semi-quantitative commercial ELISA kit (anti-measles IgG ELISA, EI2610-9601 G, EUROIMMUN, Lübeck, Germany) according to the manufacturer's instructions. Results were expressed as the ratio of sample absorbance to calibrator. Ratios ≥1.1 were considered positive ratios <0.8 seronegative, and ratios ≥0.8 to <1.1 borderline. Absorbance values were converted into antibody concentrations expressed in international units per liter (IU/L) and used to calculate geometric mean concentrations (GMCs). According to the manufacturer-defined cutoffs, concentrations <200 IU/L were classified as negative, 200–274 IU/L as borderline and ≥275 IU/L as positive. For the purposes of this study, borderline and negative results were grouped together and classified as "sero-susceptible" to measles. According to the manufacturer's instructions, the sensitivity and specificity of the kit are both 100%.

Statistical analysis

Demographic data, vaccination status, blood sampling date and IgG titers for all donors were collected in a Microsoft Excel database. The distribution of continuous variables was assessed using the Shapiro-Wilk test. Differences in IgG concentrations and susceptibility rates across age groups were evaluated using the non-parametric Kruskal-Wallis test. Post hoc pairwise comparisons were performed using Dunn's test to identify age groups with statistically significant differences. Differences in seroprevalence rates between vaccinated and non-vaccinated groups and between genders were assessed using the Wilcoxon-Mann-Whitney test. A multivariable linear regression model was fitted to investigate the association between antibody titers and gender, age group and vaccination status using natural log-transformed antibody levels. Regression coefficients with 95% confidence intervals (CIs) were reported. All analyses were performed using STATA MP16.1® (College Station, TX), and statistical significance was set at $p < .05$. Uncertainty surrounding seroprevalence and GMC estimates was reported as 95% CIs.

Results

A total of 1,579 subjects were tested for anti-MV IgG antibodies. The median age of participants was 47 y (interquartile range [IQR]: 37–53 y), and 75% were male. Seroprevalence analysis showed that 1347 subjects (85.3%, 95% CI: 83.4–87) tested positive for anti-MV IgG, while 232 (14.7%, 95% CI: 12.9–16.4) were classified as sero-susceptible. Among the sero-susceptible individuals, 224 (14.2%, 95% CI: 12.5–16) tested negative, and 8 (0.5%, 95% CI: 0.2–1) had borderline anti-MV IgG levels. Demographic characteristics (age group, gender and province of residence) and vaccination status of the total study population and the sero-susceptible subgroup are summarized in Table 1. No significant differences in sero-susceptibility were observed by gender ($p = .99$) or province of residence ($p = .764$). However, significant differences were found by age group ($p < .0001$) and vaccination status ($p < .0001$) (Table 1).

Sero-susceptibility rates decreased progressively with increasing age, from 39.8% (95% CI: 31–48.7) and 38.8% (95% CI: 32.4–45.3) in the 18–24 and 25–34 age groups to 4% (95% CI: 2.4–5.6) and 6.2% (95% CI: 3.6–8.7) in the 45–54 and >54 age groups, respectively (Figure 1). This difference in sero-susceptibility across age groups was statistically significant ($p < .0001$).

Among subjects with known vaccination status, 100% of the 18–24 age group were vaccinated and 38.4% of these resulted sero-susceptible to measles (Figure 2). Both the proportion of vaccinated and sero-susceptible individuals declined with increasing age. The 45–54 age group showed the lowest susceptibility rate (3.4%) with 2.6% of this group vaccinated. In contrast, no subjects older than 54 y were vaccinated and 7.8% of these were susceptible.

Among the sero-susceptible group with known vaccination status (n = 92), 77.2% were aged <35 y of age. Among those >44 y none had received the measles vaccine. In contrast, among those <35 y, 97.2% had received at least one dose of the vaccine (Figure 3).

The distribution analysis of anti-MV IgG titers by age group revealed that subjects aged >35 y had higher median antibody titers compared to those aged <34 y (Figure 4). A significant difference in the distribution of IgG concentrations across the five age groups was observed ($p < .0001$). Post

Table 1. Demographic characteristics and vaccination status of measles-seropositive and measles-sero-susceptible groups.

		Seropositive group			Sero-susceptible group			
		N	%	CI 95%	N	%	CI 95%	*p*-value
Total		1,347	85.3	83.6–87.1	232	14.7	12.9–16.4	
Gender	Female	337	25	81.8–88.8	58	25	19.4–30.6	.99
	Male	1,010	75	83.3–87.3	174	75	69.4–80.6	
Province of residence	Bari	754	56	82.5–87.2	135	58.2	51.8–64.5	.764
	BAT	58	4.3	83.5–97.8	6	2.6	0.5–4.6	
	Foggia	269	20	81.2–89	47	20.3	15.1–25.4	
	Lecce	173	12.8	80.3–90.1	30	12.9	8.6–17.2	
	Taranto	93	6.9	80.5–93.3	14	6	3.0–9.1	
Age groups (years)	18–24	71	5.3	51.3–69	47	20.3	15.1–25.4	<.0001
	25–34	134	9.9	54.7–67.6	85	36.6	30.4–42.8	
	35–44	288	21.4	79.6–87.4	57	24.6	19–30.1	
	45–54	529	39.3	94.4–97.6	22	9.5	5.7–13.3	
	>54	319	23.7	91.3–96.4	21	9.1	5.4–12.7	
	unknown	6	100.0		–			
Vaccination status	No	262	19.5	90.7–96.4	18	7.8	4.3–11.2	<.0001
	Yes	118	8.8	54.6–68.3	74	31.9	4.3–11.2	
	1 dose	23	19.5	54–85.4	10	13.5	5.7–21.3	
	2 doses	95	80.5	52.1–67.4	64	86.5	78.7–94.3	
	unknown	967	71.8	85.4–89.3	140	60.3	54.1–66.6	

N: number; NA: CI: confidence interval.

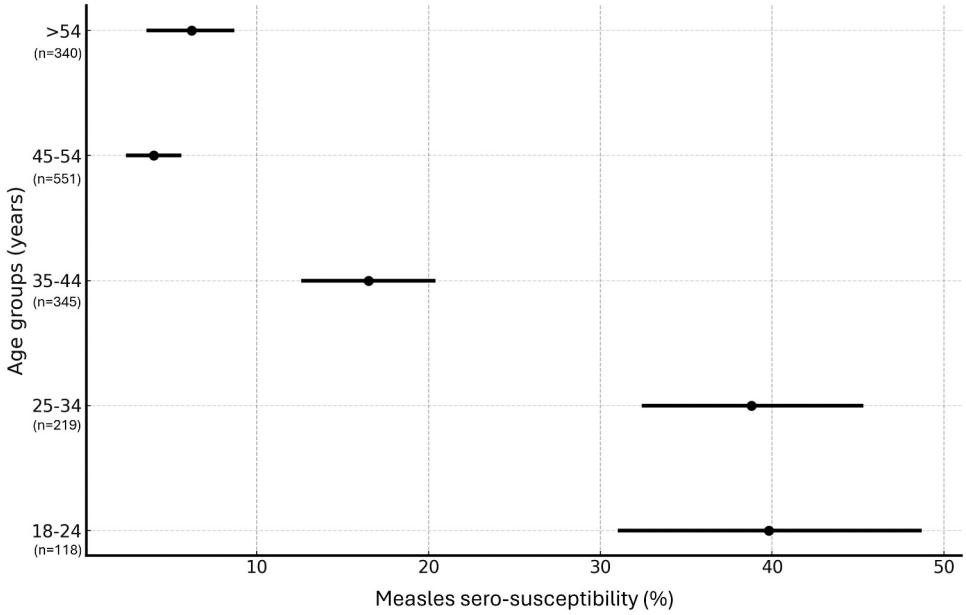

Figure 1. Forest plot of susceptibility rates to measles by age group (n = 1,573).

hoc pairwise comparisons using Dunn's test showed significant differences in most age groups. However, the 18–24 and 25–34 groups ($p = .176$) and the 45–54 and >54 groups ($p = .912$) were not statistically significant.

Multivariable linear regression analysis identified a strong association between IgG antibody titers, vaccination status and age group ($p < .001$) (Table 2). Specifically, antibody titers were negatively associated with vaccination status, with non-vaccinated individuals exhibiting higher titers than vaccinated ones. Moreover, antibody titers increased significantly with age. No significant association was found between IgG antibody titers and gender.

The GMC of anti-MV antibody titers was 2,687.9 IU/L. Analysis of GMCs by gender, age group, and vaccination status demonstrated significant differences by age group ($p < .001$) and vaccination status ($p < .001$) (Table 3).

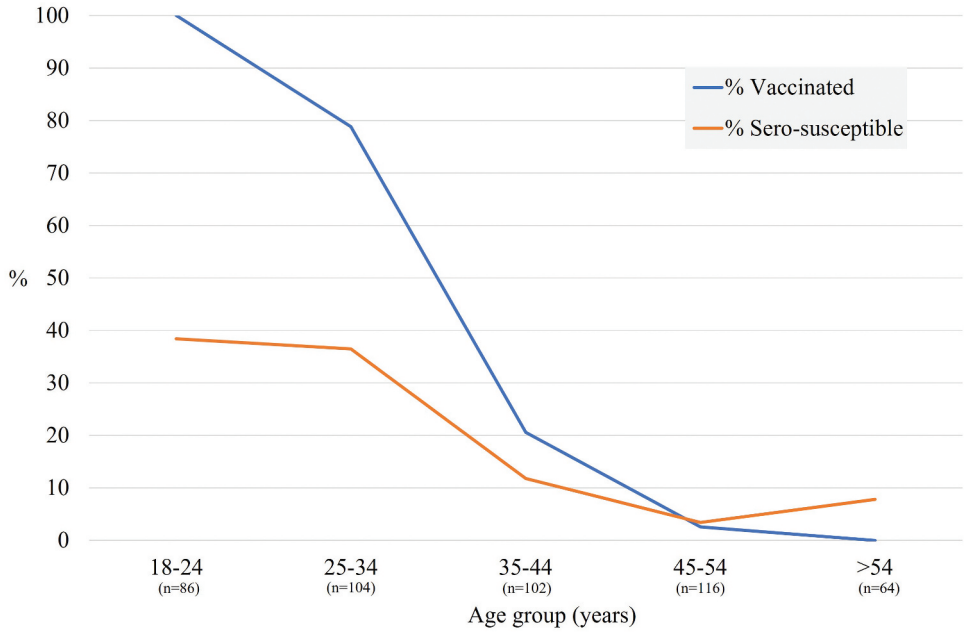

Figure 2. Proportion of vaccinated and sero-susceptible individuals by age group (n = 472).

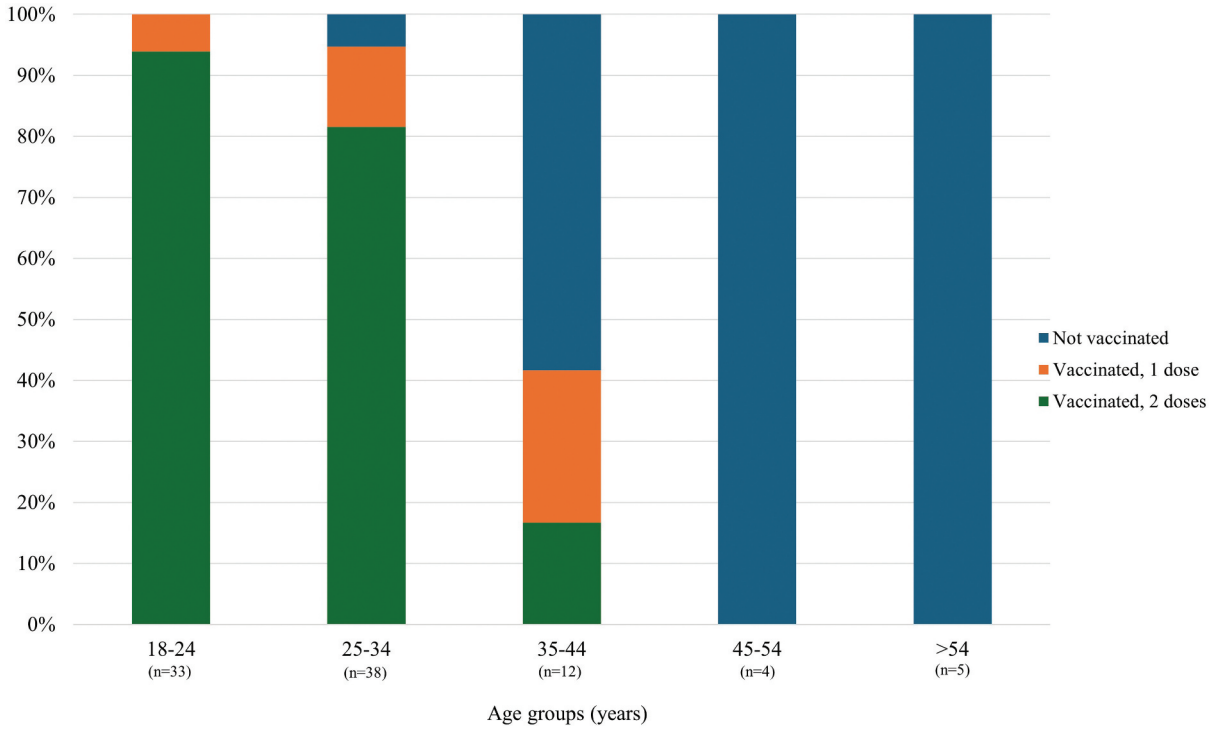

Figure 3. Vaccination status and number of vaccine doses received by age group (n = 92).

Discussion

This study assessed the seroprevalence of anti-MV antibodies among healthy blood donors in Apulia to evaluate immunity levels and susceptibility gaps within the adult population.

Overall, seroprevalence was 85.3%, indicating that immunity remains below 95%, threshold required for measles elimination.

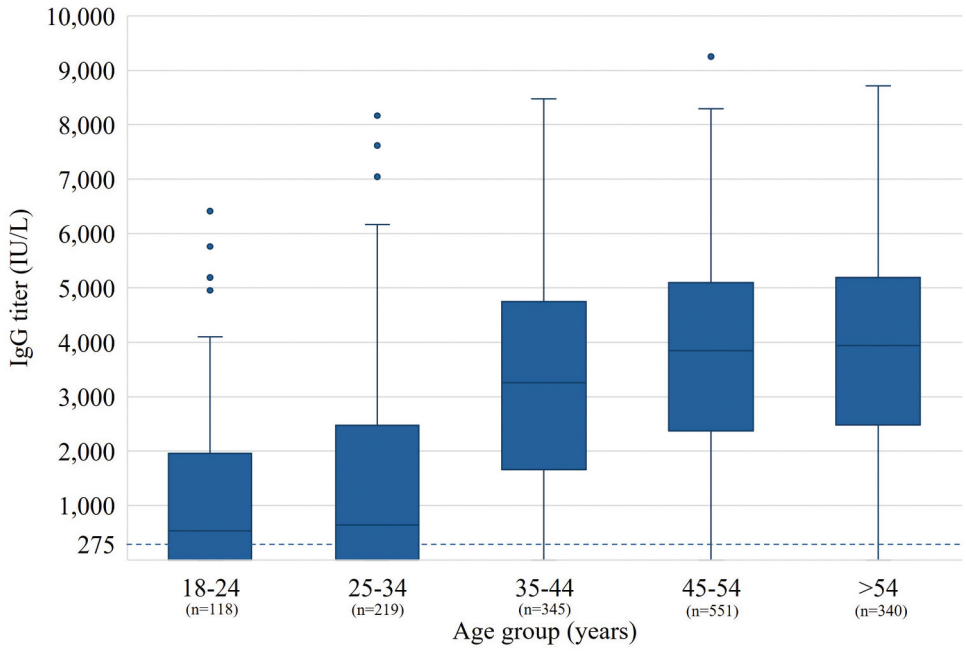

Figure 4. Box plots of the distribution of anti-MV IgG titers by age group (n = 1,573).

Table 2. Multivariate linear regression model of anti-measles IgG antibody titers and their association with gender, vaccination status and age group.

		Factor	95% CI	*p*-value
(Intercept)		6.590	[5.675; 7.505]	<.001
Vaccination	Yes (vs. No)	−1.552	[−2.301; −0.804]	<.001
Gender	Female (vs. Male)	−0.080	[−0.543; 0.383]	.734
Age group (vs. 18–24)	25–34	−0.076	[−0.763; 0.610]	.828
	35–44	0.994	[0.101; 1.887]	<.05
	45–54	1.357	[0.379; 2.335]	<.05
	>54	1.082	[0.019; 2.145]	<.05
Adjusted R-squared			0.242	

Notes: Regression coefficient were obtained by fitting a linear regression model for the natural log of the antibody titer.
Abbreviation: CI, confidence interval.

Table 3. Geometric mean concentration of anti-measles IgG antibodies in blood donors by gender, age groups and vaccination status.

	GMCs of IgG Antibodies	
	IU/L	*p*-value
Gender		
Male	2,703.08	.75
Female	2,643.08	
Age groups (years)		
18–24	986.63	<.001
25–34	1,263.78	
35–44	2,893.46	
45–54	3,286.19	
>54	3,319.55	
Vaccination status		
Yes	1,024.47	<.001
No	3,208.46	

GMC: geometric mean concentration.

The seroprevalence detected in our study is approximately 85%. Although the 95% threshold is the standard benchmark for vaccination coverage, a seroprevalence below this level does not necessarily imply the absence of protective immunity at the population level. Nevertheless, approximately 15% of subjects were sero-susceptible to infection, a concerning finding given the high transmissibility of measles and the

potential for severe, debilitating and sometimes fatal complications. These findings are consistent with studies conducted on the Italian population, which report anti-MV seroprevalence rates ranging from 77.2% to 91.2%.[17–19] However, the prevalence observed in the present survey (85.3%) represents a notable decline from the 95.1% reported in the Apulian adult population in 2012.[20] This comparison suggests that population immunity to measles has declined substantially over the past decade, with approximately 10% more adults now potentially susceptible to infection. Notably, the study by Tafuri et al., surveyed healthcare workers, a category subject to occupational health surveillance. Therefore, these estimates may not accurately reflect susceptibility rates in the general population. Factors contributing to the seroimmunity gap may include persistently suboptimal vaccination coverage in the region and reduced opportunities for natural immune boosting.

Estimates of vaccination coverage calculated in 2018, one year after the introduction of mandatory MMR vaccination in Italy, are available at a provincial level. In the cohort of 16-y-olds (born in 2001), the coverage for two doses of MMR varied across provinces, with the lowest (76.5%) in the Bari province and the highest (91.3%) in the Taranto province.[21] These data seem to reflect our findings showing a higher immunity gap in the province of Bari, although no statistically significant differences emerged across the provinces.

Age-stratified analysis showed a pronounced contrast between extremes of age, with young adults having the highest sero-susceptibility rates despite high vaccine coverage and adults aged >40 y exhibiting the lowest sero-susceptibility rates. These findings align with studies showing consistently higher antibody concentrations among adults aged ≥40 y (92.2%–100%) compared to younger groups.[17–19,22]

Surveillance data from the Regional Reference Laboratory for measles diagnosis in Apulia also corroborates this trend, with approximately 75% of measles cases reported in Apulia between 2012 and 2024 affecting individuals aged 18–34 y [moronetlab.it]. Collectively, these observations indicate that older adults have higher levels of protection for MV, which may result from natural immunity acquired from MV infection throughout their lifespan.

Among participants with known vaccination status, the majority were unvaccinated, with vaccination rates decreasing progressively with age, from 100% in individuals aged 18–24 y to 0% in those aged >54 y. This observation was predictable since routine MMR vaccination in childhood was introduced in Italy only in the 1990's.

When both age and vaccination status were considered, an inverse correlation emerged. Measles immunity was lower among younger vaccinated subjects aged <35 y and higher among unvaccinated individuals aged >45 y. In addition, GMCs analysis of anti-MV IgG antibodies demonstrated a positive association with age and a negative association with vaccination status, as antibody titers were lower in vaccinated and younger subjects (<35 y) and higher in unvaccinated and older subjects (≥35 y). These findings likely reflect differences in the source and duration of immunity. Although anti-MV antibodies levels are known to decline over the lifespan, antibodies acquired through natural infection tend to persist longer than those derived from vaccination.[23,24] Consequently, older adults who may have been naturally infected may retain durable immunity, whereas younger adults immunized during childhood may experience waning vaccine-induced immunity in the absence of natural boosting.[8] Moreover, evidence indicates that age of first measles immunization is a significant factor associated with measles immunity later in life, suggesting that early immunization might lead to less durable immunity in young adults.[25]

Among sero-susceptible individuals with known vaccination status, approximately 80% had been vaccinated, with about 70% receiving two doses. More than half of subjects were aged <35 y old, with approximately 87% receiving two doses. Currently, the MMR vaccination schedule in Italy consists of a first dose at 12–13 months and a second booster dose at 5–6 y.[26] In consideration of the serological evidence from this study highlighting a potential immunity gap in young adults, a revaluation of the national measles vaccination schedule might be considered in the future to optimize long-term protection, consistent with suggestions from previous research.[25]

This study has some limitations. Firstly, measles-specific binding IgG antibodies were measured as a correlate of immunity for MV however, lower susceptibility rates have been reported by measuring neutralizing antibodies, suggesting that measuring binding IgG antibodies may overestimate the degree of true protective immunity to measles in the population.[25] Secondly, while not formally evaluated in this study, additional research has considered the possibility that individuals exposed to wild-type or vaccine-derived MV may develop anti-MV IgG despite testing IgG-negative and may exhibit measles-specific $CD4^+$

and $CD8^+$ T cell responses in seronegative vaccinees, thus indicating a potential role for cell-mediated immunity in providing a degree of protection against MV.[27,28]

Thirdly, given the retrospective nature of the study, vaccination status was unavailable for a large portion of blood donors, which may have biased the seroprevalence estimates within the vaccinated and unvaccinated groups, and was assessed in a non-representative, nonrandomly selected population. Furthermore, as individuals under 18 y were not eligible for blood donation, additional sero-epidemiological studies in children and adolescents are warranted to provide a more comprehensive picture of population immunity.

Our study suggests that despite existing public health efforts to achieve measles elimination, immunity levels remain inadequate in the adult population, particularly in individuals aged 18–44 y, who show highest sero-susceptibility to infection. This finding has significant implications given the severe debilitating complications, high mortality rates, and healthcare costs associated with measles infection. Strengthening the National Integrated Measles and Rubella Surveillance System and implementing targeted preventive strategies specifically focused on vulnerable age groups are essential measures to close existing immunity gaps and prevent outbreaks. Furthermore, our findings underscore the need to conduct a national seroprevalence study on a representative sample of the population to provide more accurate estimates of immunity levels and help identify at-risk groups that should be targeted for catch-up vaccination. These actions would strengthen measles control efforts and contribute to the achievement of elimination goals.

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Author contributions

CRediT: **Francesca Centrone:** Conceptualization, Formal analysis, Methodology, Writing – original draft, Writing – review & editing; **Raffaella Melilli:** Data curation, Writing – original draft; **Vito Colella:** Investigation, Methodology; **Antonio Latela:** Formal analysis, Investigation, Software; **Alfredo Marziani:** Formal analysis, Validation; **Simone Lattarulo:** Data curation, Writing – original draft; **Angelo Ostuni:** Resources, Supervision; **Anna Sallustio:** Data curation, Investigation, Validation; **Maria Chironna:** Conceptualization, Funding acquisition, Writing – review & editing.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Notes on contributor

Maria Chironna, PhD in Infectious Diseases, is currently Professor of Hygiene and Public Health at the University of Bari and Head of the Public Health Laboratory at the Tertiary Care Policlinico Hospital in Bari. Her work focuses on molecular epidemiology and surveillance of infectious diseases of public health interest. She is particularly involved in respiratory infections and vaccine-preventable diseases. She is the author of over 250 peer-reviewed publications.

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Data availability statement

The data that support the findings of this study are available from the corresponding author, MC, upon reasonable request.

Ethics approval and consent to participate

Ethics approval was obtained from the Ethics Committee of the IRCCS Istituto Oncologico Giovanni Paolo II, Bari, Italy (Prot. N. 594, 24/10/2023 – Studio 1408/CEL – WNV Pug.23). Written informed consent was obtained from the participants.

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