Rubella Immunity Across Generations: A Longitudinal Study of IgG Seroprevalence in Females (2000–2024) in Palestine

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Abstract

Background and Objectives: *Rubella remains a significant public health concern, particularly for women of reproductive age due to the risk of congenital rubella syndrome (CRS). Monitoring immunity through Rubella IgG seroprevalence is essential to ensure adequate protection, particularly in regions with variable access to vaccination. This study aims to assess Rubella IgG seroprevalence among females in Palestine over a 24-year period (2000–2024), with a focus on age-specific and geographical variations in immunity. Identifying immunity gaps will provide insights into the effectiveness of vaccination programs and inform potential public health interventions.*

Materials and Methods: *A total of 7,296 females, aged 0-59, were tested for Rubella IgG antibodies at Medicare Laboratories between 2000 and 2024. Seroprevalence was categorized into negative (<5 IU/ml), grey zone (5-10 IU/ml), and positive (>10 IU/ml). Participants were stratified by age and locality, and seroprevalence trends were analysed over time. Data were sourced from the Laboratory Information System (LIS), and statistical analyses were conducted to assess immunity levels across age groups and regions, as well as time-based trends.*

Results: *Overall, 89.2% of the study population tested positive for Rubella IgG, indicating strong immunity. However, 7.5% of individuals were in the grey zone, and 3.2% tested negative, highlighting potential susceptibility. The highest immunity levels were observed in women aged 20-39 years, with 89.7% testing positive. Children aged 0-9 years had the highest proportion of negative results (26.5%), indicating gaps in early childhood vaccination. Geographically, Ramallah and Hebron demonstrated the highest immunity levels, while Bethlehem, Jerusalem, and smaller regions exhibited greyer zone and negative cases, signalling regional disparities in immunity. Immunity levels increased consistently from 2001 to 2024, though grey zone cases also rose, indicating potential waning immunity.*

Conclusion: *Rubella immunity is robust in the female population of Palestine, particularly among women of reproductive age. However, the presence of grey zone and negative results in children and certain regions highlights gaps in vaccination coverage and potential waning immunity. Targeted booster vaccination campaigns and improved adherence to the Palestinian immunization schedule are recommended to close these gaps and sustain immunity, particularly in vulnerable populations.*

Keywords: Rubella, IgG seroprevalence, Palestine, Immunity, Vaccination, Congenital Rubella Syndrome, Public Health, Women of Reproductive Age

1. Introduction

Rubella, also known as German measles, is a viral infection primarily transmitted through respiratory droplets [1]. Though generally mild or asymptomatic in children and adults, Rubella poses a significant risk to pregnant women, particularly during the first trimester [2]. If contracted during pregnancy, Rubella can lead to congenital rubella syndrome (CRS), which can cause miscarriage, stillbirth, or severe birth defects, including deafness, heart malformations, and developmental delays. As a result, monitoring and maintaining population-level immunity to Rubella, especially among women of childbearing age, is of utmost importance [3].

The introduction of the Rubella vaccine in many countries has led to substantial reductions in both Rubella infections and CRS cases[4]. In Palestine, vaccination efforts have been integrated into national immunization programs [5]. The measles, mumps, and rubella (MMR) vaccine, which incorporates Rubella, has been routinely administered as part of routine childhood immunizations to prevent outbreaks and protect the population, particularly women who may become pregnant [1]. However, long-term immunity from the vaccine, as well as gaps in vaccine coverage or compliance, may result in variations in immunity levels across generations and regions [6].

Rubella IgG antibodies serve as markers of immunity, either from previous infection or vaccination [7]. Serological testing for Rubella IgG levels allows for the assessment of population immunity and the identification of at-risk groups who may lack sufficient protection. In women of reproductive age, ensuring adequate immunity is critical to prevent CRS and its associated complications [6].

1.1 Study Focus
This longitudinal study examines Rubella IgG seroprevalence among females in Palestine over a 24-year period (2000–2024). By analysing Rubella immunity trends in women, this research aims to provide valuable insights into the effectiveness of vaccination programs and the persistence of immunity across generations. Furthermore, the study seeks to identify potential gaps in immunity that may warrant targeted public health interventions, such as booster vaccination campaigns or enhanced surveillance in regions with lower immunity levels.

1.2 Rationale
Palestine, like many regions, has faced challenges in ensuring consistent vaccination coverage due to socio-political instability, resource limitations, and population displacement [8]. These factors may have contributed to uneven vaccination rates and immunity across different regions and age groups [8]. Therefore, an in-depth analysis of Rubella IgG seroprevalence over two decades provides critical information on the successes and challenges of Rubella control in Palestine.

The primary objectives of this study were:
1. To evaluate the overall trends in Rubella IgG seroprevalence in females in Palestine from 2000 to 2024.
2. To assess age-specific immunity levels, particularly among women of reproductive age.
3. To identify geographical variations in immunity across different regions of Palestine.
4. To explore the potential need for additional public health interventions, such as booster vaccinations, to maintain adequate immunity.

1.3 Public Health Significance
Maintaining high levels of immunity to Rubella is essential for preventing outbreaks and protecting pregnant women from infection [9]. This study's findings will help guide policymakers in Palestine on vaccination strategies, highlighting areas where immunity may be waning and where interventions are needed to sustain population-level protection. Additionally, this research contributes to the global understanding of Rubella immunity trends, particularly in regions with unique public health challenges.

2. Methods
2.1 Data Collection
The data for this study were obtained from Medicare Laboratories' Laboratory Information System (LIS) records, covering the period from 2000 to 2024. These records document Rubella IgG test results for females who either visited the lab voluntarily or were referred by healthcare professionals for testing. The LIS data includes detailed demographic information, such as age and geographic location, allowing for an in-depth analysis of immunity trends across different age groups and localities.

The dataset comprises 7,296 female individuals, each tested for Rubella IgG, with records categorized by age group and geographic region. This comprehensive data provides a valuable overview of Rubella immunity levels across the population.

2.2 Study Population
The study population includes females across all age groups who were tested for Rubella IgG at Medicare Laboratories during the 24-year period. The data are divided into six distinct age groups, ranging from children to older adults, with a focus on the reproductive age group of 20–39 years.

The study also categorizes participants by geographical location, covering several major cities and regions in Palestine, which provides the basis for assessing regional differences in immunity levels.

2.3 Statistical Methods
The statistical analysis will involve the use of descriptive statistics to summarize the study population, including the distribution of Rubella IgG seroprevalence by age groups and geographic locations. The study will examine immunity levels across various age cohorts, with a particular focus on women in their reproductive years, as well as assess regional differences in immunity within Palestine.

Additionally, a time-trend analysis will be conducted to track changes in Rubella IgG seroprevalence from 2000 to 2024, identifying any fluctuations that may be linked to vaccination campaigns or other public health initiatives. Where possible, the study will also explore the correlation between IgG positivity and vaccination rates, providing insights into the effectiveness of Rubella vaccination programs over the study period.
Results

2.4 Age Distribution
A total of 3,296 females underwent Rubella IgG testing between 2000 and 2024, with a strong skew toward younger adults, particularly those in the reproductive age range. The largest cohort

was the 20-29-year-old group, which comprised 4,793 individuals (65.7%). The 30-39 age group followed, with 1,810 individuals (24.8%), collectively representing over 90% of the study population. This focus on reproductive-age females is critical given the risk of congenital rubella syndrome (CRS) in pregnant women.

The younger age groups (0-9 years and 10-19 years) represented 1.4% and 6.1% of the population, respectively, while the older groups (40-49 and 50-59 years) made up 2.0% and 0.1%. The data underscores the emphasis on testing women of childbearing age, a demographic crucial for monitoring Rubella immunity.

2.5 Summary Statistics
The average age of the participants was 26.43 years (SD = 6.04), with a median of 26 years, reflecting a predominantly young adult population. The age range spanned from 1 to 56 years. Testing was conducted from 2000 to 2024, with the mean year of testing being 2015. This extended timeframe allows for a comprehensive longitudinal assessment of Rubella IgG seroprevalence in a key demographic.

2.6 Geographical Distribution
Rubella IgG testing was distributed across several regions in Palestine, with the highest concentration of participants from Ramallah and Al-Bireh, which accounted for 54.3% of the total sample (3,926 individuals). Hebron followed with 970 individuals (13.4%), while Jerusalem and Bethlehem contributed 10.6% each. Smaller regions like Nablus (6.3%) and Jenin (1.4%) had lower representation, with even fewer participants from Jericho, Salfit,

and Tubas.

This geographical variation highlights differing levels of access to testing and healthcare services, particularly in smaller regions with fewer participants. These data provide important insights into regional differences in Rubella immunity and will aid in identifying areas that may require targeted public health interventions.

2.7 Rubella IgG Seroprevalence Over Time (2000–2024)
Between 2001 and 2024, 7,235 females were tested for Rubella IgG, with the results classified as negative (<5 IU/ml), grey zone (5-10 IU/ml), and positive (>10 IU/ml). A total of 6,459 individuals (89.3%) tested positive for Rubella IgG, indicating widespread immunity. However, 540 individuals (7.5%) were in the grey zone, suggesting borderline immunity, and 236 individuals (3.3%) tested negative, indicating susceptibility to Rubella infection.

The number of tests conducted annually increased steadily from 2001, peaking in 2019 with 539 tests. Positive results dominated throughout the study period, with over 90% of tests showing immunity after 2008. Negative results remained consistently low, with fewer than 23 cases per year. The grey zone cases peaked in 2019 (51 cases), potentially reflecting waning immunity or vaccine efficacy issues in certain cohorts.

In recent years (2020–2024), immunity levels remained high, despite a slight decrease in the number of tests, potentially due to healthcare disruptions caused by the COVID-19 pandemic. The most recent data from 2023 and 2024 reported 360 and 181 positive cases, respectively, as shown in Table 1.

Year	Negative	Positive	Total	Positive Percentage
2001	1	20	21	95.2%
2002	1	26	27	96.3%
2003	3	20	23	87.0%
2004	5	44	49	89.8%
2005	9	73	82	89.0%
2006	5	54	59	91.5%
2007	9	95	104	91.3%
2008	6	304	310	98.1%
2009	19	410	429	95.6%
2010	19	323	342	94.4%
2011	27	328	355	92.4%
2012	48	334	382	87.4%
2013	48	337	385	87.5%
2014	48	337	385	87.5%
2015	52	416	468	88.9%
2016	28	384	412	93.2%
2017	54	419	473	88.6%
2018	74	417	491	84.9%
2019	70	469	539	87.0%
2020	63	343	406	84.5%

2021	41	360	401	89.8%
2022	62	394	456	86.4%
2023	49	360	409	88.0%
2024	49	239	288	83.0%
Total	790	6506	7296	89.2%

Table 1: Rubella Seroprevalence by Sample Year

2.8 Geographical Distribution of Rubella IgG Seroprevalence
Across the various localities in Palestine, regional immunity levels were generally high, though some variations were observed. Ramallah and Hebron demonstrated the highest immunity rates, with over 89% of participants testing positive for Rubella IgG. Smaller regions, such as Jericho (84.1%) and Tubas (85.7%), had high immunity levels but limited sample sizes. However, regions such as Tulkarm and Jenin showed slightly lower immunity levels at 81.5% and 82.4%, respectively.

Jerusalem and Bethlehem exhibited robust immunity levels at 88.1% and 89.0%, but their higher proportions of grey zone cases highlight areas for targeted vaccination programs. As shown in **Table 2**, these findings point to the need for interventions in regions with lower overall immunity.

City	Negative	Positive	Total	Positive Percentage
Jerich	10	53	63	84.1%
Hebron	86	888	974	91.2%
Jerusalem	93	687	780	88.1%
Bethlehem	85	690	775	89.0%
Jenin	18	84	102	82.4%
Ramallah	426	3528	3954	89.2%
Salfit	4	33	37	89.2%
Tubas	1	6	7	85.7%
Tulkarem	25	110	135	81.5%
Qalqilya	1	14	15	93.3%
Nablus	41	413	454	91.0%
Total	790	6506	7296	89.2%

Table 2: Locality Distribution of Participants

2.9 Age-Specific Distribution of Rubella IgG Seroprevalence
Rubella IgG seroprevalence varied across age groups, with the 20-29 and 30-39-year-old cohorts showing the highest immunity levels at 89.1% and 90.3%, respectively. These critical reproductive-age groups highlight the success of vaccination efforts. However, children aged 0-9 years had the highest proportion of negative results, with only 73.5% testing positive, indicating potential gaps in early childhood vaccination coverage.

The 10-19 age group showed a seroprevalence of 88.8% for Rubella IgG, but grey zone cases constituted 8.4%, raising concerns about waning immunity among adolescents. These findings underscore the need for sustained vaccination efforts to maintain high immunity across all age groups.

Age Group	Negative	Positive	Total	Positive Percentage
0-9	26	72	98	73.5%
10-19	50	395	445	88.8%
20-29	524	4269	4793	89.1%
30-39	176	1634	1810	90.3%
40-49	14	131	145	90.3%
50-59		5	5	100.0%
Total	790	6506	7296	89.2%
Total	790	6506	7296	89.2%

Table 3: Age Group Distribution of Participants

2.9.1 Cumulative Seroprevalence

Overall, Rubella immunity was strong across all age groups, with 89.3% of females testing positive. However, the 3.3% of females who tested negative represent a potentially vulnerable group, particularly in the reproductive age range. The grey zone category, comprising 7.5% of the population, signals the need for continued vigilance and possible booster vaccinations to sustain immunity.

2.9.2 Implications for Public Health

The results indicate high overall Rubella immunity across Palestine, particularly in women of reproductive age, which is crucial for preventing congenital rubella syndrome (CRS). However, the presence of susceptible individuals, especially in the younger and reproductive-age groups, underscores the need for ongoing vaccination efforts. Regions with higher proportions of grey zone or negative results, such as Jerusalem, Bethlehem, and smaller areas like Tulkarm, may require targeted public health interventions. Additionally, the relatively high proportion of non-immune children in the 0-9 age group suggests that efforts should be made to close vaccination gaps in early childhood.

3. Discussion

This study provides a comprehensive analysis of Rubella IgG seroprevalence in a population of 7,235 females in Palestine from 2000 to 2024, highlighting critical insights into immunity levels across different age groups and geographical regions. The findings underscore the overall success of Rubella vaccination programs in Palestine but also reveal key areas that may require public health attention to ensure sustained immunity, particularly among reproductive-age women and younger children.

3.1 Rubella Immunity in Reproductive-Age Women

The high seroprevalence observed in reproductive-age women (20-39 years) aligns with findings from similar studies in the region, confirming the effectiveness of national vaccination programs. With over 89% of women in these critical age groups testing positive for Rubella IgG, the risk of congenital rubella syndrome (CRS) appears to be well controlled. This is comparable to studies conducted in neighbouring countries such as Jordan and Lebanon, where Rubella IgG seroprevalence rates among reproductive-age women were similarly high, ranging from 85% to 95% [10,11]. These results emphasize the importance of sustained vaccination efforts to maintain high immunity levels and prevent CRS, a leading cause of congenital anomalies in developing countries.

In Cameroon, a study found that 94.4% of pregnant women were positive for rubella IgG, reflecting prior exposure to the virus and highlighting the success of vaccination initiatives [12]. Similarly, research from Sudan reported a seroprevalence of 91.1% among pregnant women, further supporting the notion that effective vaccination campaigns can lead to high immunity levels in reproductive-age populations [13]. In Iran, a nationwide vaccination campaign led to an impressive 98.9% seropositivity for rubella among women of childbearing age, demonstrating the potential for mass immunization strategies to control rubella and prevent CRS [14].

These findings emphasize the need for continuous public health efforts to sustain high vaccination coverage. The WHO recommends that countries maintain at least 95% vaccination coverage to achieve herd immunity and protect vulnerable populations, including pregnant women [14]. Data from various regions indicate that while significant progress has been made, ongoing vigilance is necessary to address potential gaps in immunity, particularly in areas where vaccination rates may fluctuate due to socio-economic factors or misinformation about vaccines [15].

In conclusion, the high seroprevalence of Rubella IgG among reproductive-age women is a positive reflection of the effectiveness of vaccination programs in preventing CRS. However, to ensure continued protection, it is essential to maintain high vaccination coverage and address any barriers to immunization. This approach will not only protect individual health but also contribute to the broader public health goal of eliminating Rubella and its associated complications.

However, the presence of gray zone results, particularly in the 20-29 and 30-39 age groups, suggests that a subset of women may have borderline immunity, potentially due to waning vaccine-induced protection. Studies from other regions, such as Turkey, have also reported similar findings of borderline immunity in younger adult populations, leading to recommendations for booster vaccinations. In our study, 8.2% and 5.5% of women in the 20-29 and 30-39 age groups, respectively, fell into the gray zone, highlighting the need for ongoing surveillance and possible booster vaccinations to sustain immunity in this vulnerable group.

3.2 Immunity Gaps in Children and Adolescents

The concerning finding of a relatively high proportion of Rubella-negative individuals (19.4%) in the 0-9 age group highlights potential gaps in early childhood vaccination coverage. According to the Palestinian territories' immunization plan, infants are recommended to receive two doses of the measles, mumps, and rubella (MMR) vaccine—the first dose at 12 months and the second at 18 months of age. However, delays or incomplete vaccinations may contribute to the lower immunity observed in young children. This trend is particularly alarming when compared to developed countries, where vaccination rates have consistently led to immunity levels exceeding 95% [12-14].

In the 10-19 age group, a seroprevalence of 88.7% for Rubella IgG was observed, which aligns with findings from other regional studies. However, the presence of grey zone cases (8.4%) indicates a need for ongoing monitoring of immunity, as borderline immunity in adolescents may suggest waning vaccine-induced protection [15, 16]. This observation supports the recommendations from the World Health Organization (WHO) for continued vaccination efforts, particularly in regions where vaccine coverage may be inconsistent [17,18].

The implications of these findings are significant. The high proportion of Rubella-negative children suggests that public health initiatives must prioritize adherence to the vaccination

schedule, particularly through catch-up vaccination campaigns for those who miss early doses. Such strategies are essential to close immunity gaps and provide adequate protection against Rubella at an early age [19,20]. Furthermore, the monitoring of immunity levels over time is crucial to ensure that the population remains protected, especially as adolescents transition into adulthood and may become mothers themselves [21,22].

In conclusion, addressing the gaps in vaccination coverage among young children and monitoring immunity in adolescents are critical steps in preventing Rubella and its associated complications, including congenital rubella syndrome (CRS). Public health efforts must be intensified to ensure that all children receive their vaccinations on schedule and that any missed doses are promptly administered.

3.3 Geographical Variation in Immunity

The geographical analysis revealed generally high immunity levels across most regions, with some regional disparities. Ramallah and Hebron demonstrated the highest immunity rates, with over 89% of participants testing positive for Rubella IgG. This could reflect better access to healthcare and vaccination services in these areas, as well as higher awareness of the importance of Rubella immunity among women of reproductive age.

Conversely, regions such as Bethlehem, Jerusalem, and smaller areas like Tulkarm and Jenin showed slightly lower immunity levels, with a higher proportion of individuals in the grey zone. These findings mirror similar trends observed in studies from countries with varied access to healthcare and vaccination coverage across regions. The presence of susceptible individuals in these regions highlights the need for targeted public health interventions, including booster vaccination campaigns and increased access to healthcare services to ensure comprehensive coverage.

Smaller regions such as Jericho and Sal fit, while demonstrating high immunity rates, had limited sample sizes, which may indicate lower overall testing rates and potentially reduced access to healthcare services. These regions should be prioritized for further research and public health outreach to ensure that immunity levels remain high.

3.4 Longitudinal Trends and Implications for Vaccination Strategies

Rubella IgG seroprevalence demonstrated consistent improvements from 2001 to 2024, with positive results dominating throughout the period. The highest number of tests was conducted in 2019, with a total of 539, and positive immunity levels remained above 90% in recent years. However, the rise in grey zone cases in the later years suggests a potential decline in immunity in certain subgroups. This pattern aligns with findings from other long-term studies, such as those conducted in Turkey and Egypt, where booster vaccination programs were introduced to sustain high immunity levels over time.

The data also reveal a significant increase in Rubella IgG testing after 2007, reflecting expanded public health efforts and greater awareness of the importance of Rubella immunity in preventing congenital rubella syndrome (CRS). The peak testing year of 2019, with 539 tests conducted, highlights the critical role that public health campaigns and access to healthcare play in ensuring comprehensive vaccination coverage.

Globally, the timeline of Rubella epidemiology underscores key milestones in the effort to control the disease and prevent CRS. The introduction of the Rubella vaccine in the 1960s and 1970s marked the beginning of global vaccination initiatives, which expanded further in the 1980s. However, the 1990s saw the emergence of epidemic cycles, revealing ongoing challenges in maintaining consistent immunity levels. The 2000s highlighted regional disparities, with countries like Bangladesh continuing to report CRS incidence despite vaccination programs. The introduction of the Measles-Rubella (MR) vaccine in 2008 aimed to enhance coverage but also resulted in shifts in disease incidence, particularly affecting older populations with lower immunity [22,23].

Enhanced surveillance during the 2010s, as seen in countries like Ghana, helped identify seasonal rubella transmission patterns[24]. Significant outbreaks, such as the one in Japan in 2013, emphasized the need for sustained vaccination efforts among adults, particularly women of childbearing age [25]. Fluctuations in rubella incidence persisted from 2015 to 2019, and the COVID-19 pandemic further disrupted vaccination programs in 2020, raising concerns about potential increases in rubella incidence due to decreased vaccination coverage [26].

The global epidemiological trends reinforce the need for ongoing public health initiatives, robust surveillance systems, and targeted vaccination campaigns. These efforts are essential to maintaining high immunity levels, preventing rubella outbreaks, and ultimately eliminating CRS.

3.5 Public Health Implications

The findings of this study have important implications for public health policy in Palestine. While overall immunity levels are high, the presence of grey zone and negative results, particularly in reproductive-age women and children, suggests that additional efforts are needed to close immunity gaps. Booster vaccination programs, particularly for women of reproductive age and children who may have missed early vaccinations, should be considered. Furthermore, targeted interventions in regions with lower immunity levels, such as Bethlehem, Jerusalem, and Tulkarm, are essential to ensure that all populations are protected against Rubella.

In addition, ongoing surveillance of Rubella IgG seroprevalence should be implemented to monitor trends over time, particularly in light of potential vaccine waning. The experience of other countries in the region, where booster vaccinations have been successfully implemented, could serve as a model for maintaining high immunity levels in Palestine.

4. Conclusion

This study highlights the overall success of Rubella vaccination programs in Palestine, with high immunity levels in most regions and among reproductive-age women. However, gaps remain, particularly among children aged 0-9 years and in regions like Jerusalem, Bethlehem, and Tulkarm. Public health efforts should focus on targeted booster vaccination programs and ongoing surveillance to sustain high immunity and reduce the risk of congenital rubella syndrome. Strengthening vaccination strategies and improving healthcare access will be key to ensuring Rubella control and improved public health outcomes.

Declarations

Conflict of Interest: The authors declare that there is no conflict of interest regarding the publication of this paper.

Human Ethics and Consent to Participate Declarations: This study utilized blind data, which were obtained from Medicare Labs without any identifying information about the patients. The research was conducted following ethical guidelines, and approval was granted by the Medicare Institutional Review Board (IRB) committee (Approval Number: 2024-IRB-13).

Consent for Publication: Not Applicable.

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