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Seroprevalence of Rubella Virus Antibodies and Antibody Titer Among Childbearing Aged Women

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Abstract

Introduction: Rubella is a viral infection that poses a significant public health threat, particularly to women of childbearing age. Maternal rubella infection, especially during the first trimester of pregnancy can lead to congenital rubella syndrome resulting in severe birth defects including deafness, cardiac disease, intellectual disability, and ocular conditions.

Despite the significant decline of cases globally, rubella remains a global health concern, especially in regions such as Africa, East Asia, and South Asia. The aim of this research is to provide new data for the seroprevalence of rubella antibodies and antibody titers among childbearing aged women studying or working at the Libyan International University, and to assess the need for a booster dose of MMR vaccine.

Methods and Materials: A cross-sectional, observational, descriptive study was conducted to assess the seroprevalence of rubella virus-specific antibodies and antibody titers in the serum of 166 women of childbearing age (16-45 years) using chemiluminescent immunoassay. The samples were collected using a convenience sampling approach. Statistical analyses were performed using a chi-square test and the Statistical Package for the Social Sciences (SPSS) software.

Results: The overall seroprevalence of rubella-specific IgG-positive antibodies was 86.7%, while 6% were IgG-negative and 7.2% were IgG-equivocal. Seroprevalence increased with age, reaching 100% in the 36-45 years age group. Only 0.6% were positive for rubella-specific IgM antibodies.

Conclusion: These findings suggest relatively high immunity against rubella in this population, though a significant proportion remain unprotected. This may guide decision makers regarding implementation of relevant public health strategies and vaccination programs.

Key Words:
Rubella virus, Seroprevalence, Congenital Rubella Syndrome, Gestation, TORCH, Infection, Vaccination, Measles-rubella vaccine, MMR vaccine Libya, Benghazi.

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Introduction

Rubella virus is the sole member of the Rubivirus genus in the Matonaviridae family, previously classified under the Togaviridae family, that causes German measles. Humans are the only natural hosts for this virus. The virus is transmitted via respiratory droplets, and starts replication in nasopharyngeal lymphoid tissue, and then spreads to regional lymph nodes.[1]

Manifestation of infection starts 16-20 days after exposure, with maculopapular rash first appears on the face then spreads to the trunk, and finally to the extremities. Other symptoms include low grade fever, sore throat, general malaise, and a characteristic posterior cervical and occipital lymphadenopathy that can persist even after the rash resolves.

Antenatally, the outcomes depend on the timing of infection during gestation. The risk of developing congenital defects is low after 17 weeks of gestation; however, maternal infection during early pregnancy can lead to congenital rubella syndrome. Clinical manifesta-

tions of congenital rubella syndrome (CRS) include deafness, cardiac disease, mental retardation, ocular conditions like glaucoma and cataracts, and insulin dependent diabetes mellitus as late sequela.

Complications are more prevalent and severe in women, including arthritis and arthralgia, thrombocytopenic purpura, and post-infectious encephalopathy. Additionally, progressive rubella panencephalitis can occur as a late complication of childhood rubella.[1]

Following rubella virus infection, IgM antibodies typically appear 3 to 7 days post-onset of symptoms and persist for a few weeks. Subsequently, IgG antibodies appear a few days after the initial IgM response and can persist for a lifetime. However, previous research has shown that rubella-specific IgG antibody levels may gradually decline after approximately 20 years, potentially leading to decreased long-term humoral immunity. [2]

While global prevalence of rubella virus infections have declined over time, the virus continues to circulate, especially in regions such as Africa, East Asia, and South Asia. According to data from the (CDC), in 2019 approximately 49,000 rubella cases were reported globally, with this number decreasing to around 10,000 cases in 2020. However, CRS remains a significant public health concern, with more than 100,000 infants born annually with CRS worldwide.[3]

MMR vaccine is a live attenuated combination vaccine that stimulates the immune system to provide protection by producing antibodies. The key difference between natural and vaccine-induced immunity is that natural rubella infection triggers a rapid, high-level IgM response that quickly diminishes, whereas rubella vaccination results in a lower, more prolonged IgM response that can persist for up to 6 months, but it generally produces lower IgG levels compared to natural infection.[4]

All licensed rubella vaccines induce a good IgG antibody response, although titers are usually 1/8 to 1/4 to the level of those following natural infection.[5] In accordance with the prescribed immunization protocol for the measles, mumps, and rubella (MMR) vaccine in Libya, a two-dose regimen is administered, with the first dose administered at 12 months of age, followed by the second dose at 18 months of age. According to the Centers for Disease Control and Prevention (CDC) adults who don't have presumptive evidence of immunity should get at least one dose of MMR vaccine. The WHO also recommends that adults such as post high school students, healthcare workers and international travelers who are at a high risk for infection of mumps, measles and rubella should get two doses of MMR vaccine.[6]

Research Question: What is the seroprevalence of Rubella Virus antibodies and antibody titers among women of childbearing age studying or working at the Libyan International University and is a booster dose of MMR vaccine needed for women of childbearing age?

Methods

A descriptive, cross-sectional, observational, study was conducted to assess the seroprevalence of rubella virus-specific antibodies and antibody titers among women aged 16-45 years, at the Libyan International Medical University. The study was carried out between May 4th, 2024 and July 24th, 2024.

Ethical approval was granted by the ethical committee of the Libyan International University. Sample size of 160 participants was calculated by Cochran's formula ($n_0 = (Z^2 \times p \times q) / e^2$) considering 95% confidence level, 5% margin of error and 85.9% seroprevalence rate of rubella antibodies. Before collecting samples, written consent was obtained from the participants, and verbal details of the research were provided.

A total of 166 blood samples were collected using a convenient sampling approach from female participants within the target age range. The blood samples collected were analyzed for the presence and concentration of rubella-specific IgG and IgM antibodies. These antibody markers serve as indicators of past exposure (IgG) and current infection (IgM) with the rubella virus.

Quantitative assessment of rubella-specific antibodies was performed using a chemiluminescence immunoassay (CLIA) technique. Specifically, the Mindray CL-series Chemiluminescence Immunoassay Analyzers were the instruments used for serological testing.[7]

The presence or absence of the rubella virus IgG/IgM antibodies is determined by comparing the RLU measurement to an established cutoff value from the calibration. A cutoff index (COI) is calculated by Sample RLU/Cutoff RLU. Antibody concentration results were interpreted as follows:[7]

Table 1: IgG/IgM Levels Interpretation in IU/mL

	IgG	IgM
Negative	<10	<0.8
Equivocal	10 to < 15	≥ 0.8 to <1.2
Positive	≥ 15	≥ 1.2

The data collected in this study was analyzed using SPSS statistical software. Descriptive statistics were calculated, including the mean and standard deviation for the rubella-specific IgG and IgM antibody titers. The seroprevalence of rubella IgG and IgM antibodies was calculated as the proportion or percentage of women in the negative, equivocal, and positive categories for each antibody. To assess the statistical significance of differences in rubella IgG and IgM seroprevalence across the different age groups, chi-square (χ^2) tests were performed. The level of statistical significance was set at $p<0.05$ for all analyses.

Results

The study included 166 females with ages ranged from 16 to 45 years, with a mean and standard deviation of 22.7 ± 5.4 years. Out of the total number of participants, 135 were in the 16-25 year age group, 24 were in the 26-35 year age group, and 7 were in the 36-45 year age group (Table 2).

The mean and standard deviation of rubella-specific IgG antibody level among the females at LIMU was 64.8 ± 71.5 (range: 1.4 to 350). The overall proportion of IgG-negative women, defined as 'unimmunized', was 6%, the overall proportion of IgG-equivocal women was 7.2%, and the overall proportion of IgG-positive women was 86.7% (Table 3).

The protective rates of women in the 16-25, 26-35, and 36-45 years age groups were 84.8%, 95.8%, and 100%, respectively. The mean titer of anti-rubella IgG was higher among women aged 16-25 years, at 51.7 (35.2-288.4) IU/mL, but the titers were not significantly different from the other age groups (Table 4).

The mean and standard deviation of rubella-specific IgM antibody level among the females at LIMU was 0.39 ± 0.49 (range: 0.20 to 6.5). Of the 166 women, 1 (0.6%) was positive for rubella IgM antibody, 161 (97%) were negative, and 4 (2.4%) were equivocal (Table 5).

The rubella IgM seroprevalence among women in the 16-25, 26-35, and 36-45 years age groups were 97.8%, 91.7%, and 100%, respectively. The mean titer of anti-rubella IgM was higher among women aged 16-25 years, at 0.404 (0.312–0.496) IU/mL (Table 6).

There were no statistically significant differences associated with rubella seropositivity (IgG and IgM) and age group (p>0.05) (Table 7).

Table 2: Age of Participants

Age Group in Years	Frequency	%
16-25	135	81.3
26-35	24	14.5
36- 45	7	4.2

Table 3: Seroprevalence of rubella IgG antibodies among females at LIMU

	Frequency	%
Positive (>15 IU/mL)	144	86.7
Equivocal (10 to <15 IU/mL)	12	7.2
Negative (<10 IU/mL)	10	6.0

Table 4: Percentage of rubella IgG levels within each age group.

Age Group	Negative (<10 IU/mL)	Equivocal (10 to <15 IU/mL)	Positive (>15 IU/mL)
16-25	10 (7.4%)	11 (8.1%)	114 (84.4%)
26-35	0 (0)	1 (4.2%)	23 (95.8%)
36-45	0 (0)	0 (0)	7 (100%)

χ^2= 3.724, p-value= 0.445

Table 5: Seroprevalence of rubella IgM antibodies among females at LIMU

	Frequency	%
Positive (≥1.2)	1	0.6
Equivocal (0.8 to <1.2)	4	2.4
Negative (<0.8)	161	97.0

Table 6: Percentage of IgM levels within each age group

Age Group	Negative (<0.8)	Equivocal (0.8 to <1.2)	Positive (≥ 1.2)
16-25	132 (97.8%)	2 (1.5%)	1 (0.7%)
26-35	22 (91.7%)	2 (8.3%)	0 (0%)
36-45	7 (100%)	0 (0%)	0 (0%)

χ^2= 4.461, p-value= 0.347

Table 7: Rubella IgG and IgM seroprevalence among women according to age group

Age Group	IgG Positive	IgM Negative
16-25	114 (84.4%)	132 (97.8%)
26-35	23 (95.8%)	22 (91.7%)
36-45	7 (100%)	7 (100%)

IgG p-value: 0.181, IgM p-value: 0.243

Discussion

The results of this cross-sectional study provide updated but limited epidemiological data on rubella virus seroprevalence in a specific community in Benghazi, Libya. The findings should be interpreted in the context of the study's limitations. The population was restricted to women aged 16-45 years within the Libyan International University. The non-random sampling technique limits the representativeness of the sample to the broader Libyan population.

Despite these limitations, the study's findings contribute to the understanding of progress towards the World Health Organization's (WHO) goal of eliminating rubella virus worldwide by 2030.[7] The seroprevalence of rubella IgG antibodies in the studied population was 86.7%, significantly higher than the 44.2% reported in a previous study involving 95 cases of women with abortions in El Beida, Libya.[8] This high seroprevalence may be attributed to the effective implementation of routine childhood vaccination programs, as evidenced by a recent nationwide vaccination campaign in 2017 that achieved coverage rates of 93% for the MMR vaccine.[9]

The percentage of women with positive anti-rubella IgG antibodies were highest among women aged 36 to 45 years compared to other age groups, however, that did not achieve statistical significance due to the small number of patients in this age group. This is consistent with a cross-sectional study conducted in Kerala, India, from June 2016 to June 2017 included 604 women aged 18–48 years. The participants were grouped into three

age categories (18–28, 29–38, and 39–48 years), with the highest IgG seropositivity observed in the oldest age group.[10]

A concerning finding is that approximately 13.2% of the sample population exhibited a gap in immunity to rubella. This group, comprising of both seronegative and equivocal individuals, is at increased risk of contracting rubella infection and potentially transmitting the virus to others, particularly pregnant women.

This highlights the need to strengthen vaccination efforts, particularly among women of childbearing age, to ensure their immunity and prevent the potential transmission of rubella to their unborn children. Strategies involve implementing catch-up vaccination campaigns, conducting routine screening for rubella immunity, and promoting public health education initiatives to emphasize the importance of vaccination.

Six percent of the population were seronegative for rubella IgG, indicating susceptibility to rubella infection. This is lower than the 14.1% susceptibility rate reported in a study on 502 pregnant women from Rabat, Morocco.[11] This translates to an estimated 100 or more women within the study population who are unimmunized against rubella and at risk of contracting the disease, especially during pregnancy. Additionally, 7.2% of the population had equivocal results for rubella IgG.

The low percentage (0.6%) of actively infected individuals observed in this study reflects the overall decline in reported rubella incidence in the Eastern Mediterranean region, likely due to the implementation of widespread vaccination programs. However, the WHO has identified Libya as a priority country for rubella elimination due to reported active outbreaks in the past two years.[10] Establishing robust rubella surveillance systems and periodic seroprevalence surveys will be crucial for continuous monitoring of progress towards elimination goals and guiding future public health interventions.

Strategies to improve rubella vaccination coverage could include implementing routine screening of women's rubella immunity status during preconception or prenatal care visits, offering catch-up vaccination for unimmunized women, and promoting public awareness campaigns to emphasize the importance of rubella vaccination, particularly for women planning pregnancy. Additionally, healthcare workers, who are at increased risk of exposure to rubella, should be prioritized for vaccination to protect both themselves and their patients.

Further research involving a larger and more diverse sample of the Libyan population would enhance our understanding of the epidemiology of rubella virus, including potential regional variations and the long-term dynamics of antibody waning.

In conclusion, this study suggests a relatively high seroprevalence of IgG anti-rubella antibodies, and suggests that the current two-dose MMR vaccination schedule for children may be effective in providing long-term protection against rubella. However, a small portion of the population remains unprotected and susceptible to infection, highlighting the need for targeted interventions to ensure that all women of childbearing age, including those who may have missed childhood vaccination, have adequate immunity against rubella. Continuous monitoring of rubella seroprevalence and the implementation of evidence-based public health strategies are crucial in achieving the goal of eliminating rubella and its devastating consequences in Libya and the surrounding region.

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Disclosure Statement

The authors declare no conflicts of interest.

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