

# Prevalence of rubella IgG antibodies among Syrian females of childbearing age

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## ABSTRACT

**الأهداف:** التعرف على الانتشار الويائي المصلي الحالي للحصبة الألمانية الحميرة IgG لدى الفتيات السوريات اللواتي في سن الحمل ولم يتتسن لهن الحصول على اللقاح.

**الطريقة:** أجريت دراسة مقطعية على طالبات سليمات من جامعة القلمون – كلية الصيدلة – سوريا. تم جمع 90 عينة مصل خلال الفترة من مارس حتى مايو 2008م. خضعت جميعها للبحث عن الأضداد النوعية ضد الحصبة الألمانية الحميرة من نمط IgG مع تحديد عيار هذه الأضداد بواسطة تقنية المقايسة المناعية الأنزيمية الموفرة من قبل شركة Diamed Eurogen وتم الاختبار في مختبر الأحياء الدقيقة في كلية الصيدلة.

**النتائج:** أظهر التحليل الكمي للحصبة الألمانية الحميرة توزعاً ملحوظاً في القيم بين المجال 0-363 وحدة دولية في المل. تبين أن 77 عينة خضعت للاختبار كانت ايجابية معطياً انتشاراً مفصلياً للأضداد بنسبة 85.6% تاركة نسبة عالية نسبياً من المشاركات قدرها 14.4% غير محصنة ضمن مجموعة الاختبار.

**خاتمة:** على الرغم من أن معظم المشاركات في هذه الدراسة كان محصنات تجاه الإصابة بحمة الحميرة IgG، غالباً نتيجة للاشتراك الطبيعي للحصبة الألمانية ضمن المجتمع، فإن التحري عن مستوى المناعة ضد هذه الحصبة متواوباً بإعطاء اللقاح لم يتقدم للتلقيح ضمن البرنامج الوطني يعد من الضروريات للوقاية من حدوث متلازمة الحصبة الألمانية الحميرة. إضافة إلى ذلك، فإن إعطاء جرعة ثانية من اللقاح لن خضعن له مسبقاً يعد أيضاً من الضروريات وذلك لاحتمال انخفاض تركيز الأضداد دون المستوى اللازم للحماية من الإصابة.

**Objectives:** To examine the current sero-epidemiology of rubella IgG among Syrian females of childbearing age that missed rubella vaccination.

**Methods:** A cross-sectional study examined healthy female students of the Pharmacy College, Kalamoon University, Deratiah, Syria. Ninety sera were collected

between March and May 2008, and were subject to rubella specific IgG screening and titration using an enzyme-linked immunosorbent assay-based technique provided by Diamed Eurogen in the Microbiology Laboratory, Faculty of Pharmacy.

**Results:** The quantitative analysis for rubella IgG showed a noticeable variability in the values of antibodies that ranged between 0-363 IU/ml. A total of 77 participants were positive for rubella IgG giving a prevalence of 85.6%, and leaving a relatively high proportion of susceptibility (14.4%) among the tested group.

**Conclusion:** Although most women tested were seropositive for rubella IgG, suggesting a natural virus circulation within the community, screening for protective immunity followed by vaccination to those who missed the regular vaccine program should be enforced to prevent possible rubella congenital syndrome. In addition, adding a second shot of rubella vaccine to those who were subject to the national program of vaccination is a must since the concentration of antibodies may drop below the recommended levels necessary for protection.

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Rubella is a viral infection caused by the rubella virus, usually characterized by a mild febrile rash illness. It mainly affects children aged 2-12 years. However, various proportions of women reach childbearing age without having been infected during their childhood. The most serious consequences of rubella result from infection during the first trimester of pregnancy where rubella is transmitted from the blood of the infected mother

to the fetus.<sup>1,2</sup> With the lack of protective antibodies, rubella infection during the first trimester is associated with congenital defects, known as congenital rubella syndrome (CRS), affecting all organs in the developing fetus and causing miscarriage and fetal death.<sup>3</sup> With the fact that there is no in-uterus treatment available for these fetuses, prevention remains the best strategy to eradicate all cases of CRS. The live-attenuated rubella vaccine was available for use since 1969 and many developed countries were able to implicate it effectively reducing rubella cases and preventing the consequences of CRS.<sup>4</sup> However, the permanence of antibody after vaccination and the possibility that vaccinated women during infancy might lose protection has raised many concerns regarding vaccination strategies.<sup>5</sup> In addition, CRS continues to be a major public health problem in much of the developing world as the vaccination strategies vary among countries, and the percentage of non-immune women of childbearing age is largely unknown, but still significantly large.<sup>6</sup> In Syria, the nationwide rubella vaccination program was introduced by the Syrian Ministry of Health (MoH) in 1999 to provide protection against rubella as a single dose at the age of 15 months as part of the measles, mumps, and rubella (MMR) vaccine.<sup>7</sup> Before 1999, rubella was not a reported disease, and no data regarding its incidence among the Syrian population were available.<sup>7,8</sup> After 1999, the Syrian MoH added rubella and CRS to the immediate notification guidelines system to early detect and eradicate such cases.<sup>9,10</sup> Since most women of childbearing age are not included in the vaccination program, determining the ratio of susceptible women is highly important to evaluate the current vaccination strategies, and decide whether or not more procedures should be undertaken. The aim of our study was to determine the current rubella antibodies circulation among unvaccinated Syrian females of childbearing age.

**Methods.** This cross-sectional study examined female students of the Pharmacy College, University of Kalamoon, Deratiah, Syria, aged between 18-30 years old. Students were informed of the study through announcements posted on billboards in the laboratories and the university campus. They comprised information of the aims and the importance of the study, the voluntary nature of the study and the procedures of the study (including the steps that the volunteers have to go through and the time they have to spend during the study). The contact of the researchers was provided in case students required further information.

Sera were collected between March 2008 and May 2008 and tests were conducted in the Microbiology Laboratory, Faculty of Pharmacy, University of

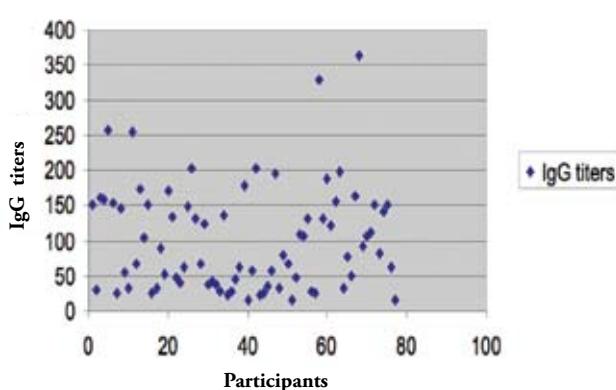
Kalamoon, Deratiah, Syria. Demographic information, such as name, age, marital status, and residency was obtained from the participants. Vaccination history was ruled out since rubella vaccine was only introduced in Syria in 1999. However, proof of previous vaccination was demanded to exclude any possible vaccinees from the study. Informed consent was obtained from all participants. A total of 104 sera were collected. Of those, 90 samples were tested for rubella specific IgG using the Diamed Eurogen rubella IgG, an enzyme linked immunoassay. Rubella IgG titers greater than 13 IU/ml were considered positive; those between 8-13 IU/ml were equivocal, and those of less than 8 IU/ml were considered negative. The project was ethically approved by the Pharmacy College Council of the Private University of Kalamoon, Syria.

Data were analyzed using the Statistical Package for Social Sciences (SPSS) Version 13. Descriptive statistics were used to describe the sample characteristics, rubella IgG antibody concentration (IU/ml), and the prevalence of seropositivity in the sample.

**Results.** By the time of data collection (March and May 2008), the Faculty of Pharmacy in the University of Kalamoon registered 376 female students. Of those, 104 students agreed to participate in the study. The response rate was 27.7%. The relatively low response rate was probably due to the dislike that many individuals have towards needles and blood collection. Also, rewards for participating in the study were not offered to volunteers. Ninety females were tested for rubella specific IgG using the ELISA method. The other 14 samples were excluded from analysis due to hemolysis of the blood and insufficient data from participants. Most participants were  $\leq 22$ -year-old (88%), single, and living in various areas of Syria. Table 1 shows the descriptive statistics for the age of participants and IgG titers. Results showed

**Table 1** - Descriptive statistics for age of participants and IgG titers distribution.

Variables	Total sample (n=90)
<i>Age (years)</i>	
Mean	21.09
SD	1.86
Median	21.00
Range	18 -30
<i>IgG titers (IU/ml)</i>	
Mean	86.96
SD	77.15
Median	62.05
Range	0 - 363.7



**Figure 1** - Distribution of positive IgG titers in the sample.

that 85.6% (77 samples) of the cohort was seropositive; while a relatively high proportion of participants were rubella susceptible subjects (14.4%; 13 samples). Figure 1 shows the distribution of positive IgG titers among participants. As it can be observed, there was variability in the positive values of antibodies that ranged between 13.6-363 IU/ml. Only 3 participants had antibodies values close to the cut-off of 13 IU/ml for positivity (13.6IU/ml, 14.3IU/ml, and 14.7IU/ml). A total of 23 participants (29.9%) had antibodies values between 20-50 IU/ml; while, a clear majority of the sample had values of antibodies >50 IU/ml.

**Discussion.** Rubella is a contagious disease characterized by generalized rash and apparently only minor complications. However, exposure to the virus for the first time in the first trimester of pregnancy results in congenital defects that can be prevented with the presence of sufficient maternal immunity.<sup>11</sup> Our study aimed to clarify the trend of rubella prevalence in Syria by screening for rubella IgG among female students attending a Syrian University. In Syria, the nationwide vaccination program started in 1999,<sup>7</sup> therefore, at the present time, most women of childbearing age over 16 years old did not have the chance to be vaccinated against the rubella virus. According to the United Nations 2007 report, the population of Syria is 19,929,000; of those, 26.9% are females aged between 15-49 years old (5,361,000).<sup>12</sup> This means the youngest women were born in 1992 or before. As a result, those females most probably have missed the shot of MMR vaccine. Our findings showed that 85.6% of the subjects tested had IgG against the rubella virus. This immunity may have been acquired from previous infection with the rubella virus during childhood or adolescence. Since the national vaccination program against rubella was initiated in 1999,<sup>7</sup> we could almost rule out the possibility that our subjects acquired those antibodies

through vaccination. Of the participants, a relatively high percentage (14.4%) needed vaccination as they did not have sufficient immunity for the rubella virus. Our results agree with the universal trend for rubella virus infection ratio, where 80-90% of the populations showed immunity in the pre-vaccine era.<sup>13</sup> A study conducted in Thailand addressing rubella seroprevalence in the age group 19-33, showed 85% antibody positivity.<sup>14</sup> Another study revealed that 15% of Turkish women between 20-29 years of age lack antibodies to rubella.<sup>15</sup> A previous study carried out in Syria, showed that females of childbearing age from Damascus city aged between 20-45 years old had seropositivity of 96%.<sup>16</sup> The higher seropositivity rates found by Monem et al<sup>16</sup> compared to the ones reported by our study may be due to the fact that in their study they included individuals with different demographic characteristics, such as age, and residency.

The major limitation of our study was the low number of samples tested. Also, we tested a specific population of participants, single females, and university students. Although, the generalization of our findings may be precluded to all female Syrian population, our study draws attention to the fact that the unvaccinated population in Syria is still high. Therefore, precautionary actions should be taken, especially, if one considers that these females may get married and decide to get pregnant. Our study constitutes essential preliminary data on rubella antibody circulation among unvaccinated Syrian females of childbearing age, since very little is known about this topic in Syria. We strongly recommend that larger studies are performed in the future, targeting different demographic groups, namely, a broader age range. This would allow a more detailed statistical analysis, which could provide important insights on rubella antibody circulation among unvaccinated Syrian females of childbearing age. Also, findings would allow the design of interventions to be targeted at high-risk individuals. The Syrian MoH has undertaken, in addition to the routine vaccination program initiated in 1999, several campaigns to vaccinate those who had missed the regular shot of MMR and targeted students in the sixth to ninth grades. The third stage was implemented in September 2008 and lasted 3 months. Although the main objective of these campaigns was to halt the local transmission of measles virus in the community, and to reduce the number of children at risk of contracting measles,<sup>17</sup> those campaigns achieved more by increasing the numbers of the protected population against rubella virus among those who were not immune. However, these campaigns left the older female students unvaccinated and susceptible to infection during pregnancy. It is crucial to keep in mind that widespread pediatric vaccination coverage with

incomplete catch-up immunization among adolescents and young adults would lead to an increase in CRS cases. This theoretical concern was demonstrated to be significant in Greece, where 2 rubella outbreaks occurred after the introduction of the rubella vaccine into the national vaccination program.<sup>18</sup> For older years, we believe that a mass campaign for rubella vaccination for adolescents in Universities is the best precautionary method for CRS as it does not only cover women of childbearing age for the prevention of rubella, but also decreases the overall rubella transmission. However, cost effectiveness studies should be performed whether routine serological tests before rubella vaccination are required.

In conclusion, our study shows a relatively high percentage of unprotected women of childbearing age against rubella. Although most women tested were seropositive for rubella IgG, suggesting a natural virus circulation within the community, screening for protective immunity followed by vaccination of those who missed the regular vaccine program should be enforced to prevent possible rubella congenital syndrome. We could also assume that, adding a second shot of rubella vaccine to those who were subject to the national program of vaccination is a must since the concentration of antibodies may drop below the recommended levels necessary for protection.

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## Related topics

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