A Relatively High Number of Pregnant Women in Kuwait Remain Susceptible to Rubella: A Need for an Alternative Vaccination Policy

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Key Words
Rubella · Hepatitis B · Pregnant women · Kuwait

Abstract
Objective: To measure the prevalence of anti-rubella IgG and hepatitis B surface antigen (HBsAg) among pregnant women in Kuwait in order to assess the effectiveness of the current vaccination programs.

Subjects and Methods: This retrospective study involved 4,062 pregnant women evaluated in health centers in the Hawalli Province of Kuwait. They were screened for anti-rubella IgG and HBsAg using commercially available assays. The data were obtained from medical laboratory records.

Results: The mean age of the pregnant women was 29.2 ± 5.26 years (range 17–49). The rubella IgG prevalence among the pregnant women was 88.4% (n = 3,589); 276 (6.8%) of the pregnant women had no antibody to rubella, and 197 (4.8%) had rubella antibody levels ≤10 IU/ml. Therefore, 473 (11.6%) of the pregnant women were susceptible to rubella. The proportion of susceptible women increased with increasing age from 3.4 to 10.3% and from 3.4 to 6.7% among women aged <20 years and those aged ≥40 years, respectively (p = 0.016). The prevalence of HBsAg was 0.3%, and it did not vary with age.

Conclusion: The prevalence of both anti-rubella IgG and HBsAg among pregnant women in Kuwait was relatively high. However, about 11.6% of pregnant women in Kuwait remain susceptible to rubella infection and hence congenital infection and fetal malformation.

Introduction
Rubella, also called German measles, is a disease of childhood that has markedly declined in incidence due to routine childhood rubella vaccination [1]. Primary infection with the rubella virus results in a mild, self-limiting disease in the majority of cases. However, infection during pregnancy results in severe manifestations to the fetus. Maternal rubella infection is associated with spontaneous abortion, intrauterine death, severe alterations in fetal growth and development, microcephaly, cataracts, hepatosplenomegaly, heart disease, deafness, meningitis, and other disorders [2–4]. In many countries, rubella seropositivity ranges between 54.1 and 95% among women of childbearing age [5, 6]. Absence or low levels (≤10 IU/ml) of rubella IgG before or during the first trimester of pregnancy identifies women who may be at risk of infection and hence congenital transmission of the virus [7].
Hepatitis B is one of the world’s major public health problems, affecting about 350 million people (about 5% of the human population) [8]. Whether the hepatitis B virus (HBV) infection becomes chronic mainly depends on the age of the individual at time of infection. The prevalence rate of chronicity among infants and young children born to women who are carriers varies between 30 and 90%, whereas among adults the rate of chronic infection varies between 5 and 10% [8–11]. Therefore, the best strategy to prevent chronic HBV infection is to immunize all newborns against hepatitis B, especially infants who are at risk of infection from their HBV-carrying mothers [9].

This retrospective study aims to determine the prevalence of rubella IgG antibody and hepatitis B surface antigen (HBsAg) among pregnant women attending health centers in the Hawalli Province of Kuwait.

**Subjects and Methods**

This retrospective study was conducted between December 2012 and February 2013 in a group of pregnant women aged <20, 20–29, 30–39, and ≥40 years. A total of 4,062 pregnant women were referred to different health clinics in the Hawalli Province for pregnancy-related health checks. The study population was divided into 4 groups based on age for analysis: <20, 20–29, 30–39, and ≥40 years. Screening for rubella IgG antibody and HBsAg was performed in the Virology Unit of the Faculty of Medicine of Kuwait University in Kuwait. These tests are done routinely as part of prenatal blood care in Kuwait.

A sample of 5 ml was collected from each pregnant woman and sera were stored at −20 °C until testing. Sera were analyzed for anti-rubella IgG and HBsAg using commercial microparticle enzyme immunoassays (ARCHITECT i1000SR and ARCHITECT i2000SR Systems; Abbott Laboratories, Abbott Park, Ill., USA). The assays were performed according to the manufacturer’s instructions. Levels ≥10 IU/ml were regarded as positive protective levels for anti-rubella IgG, whereas levels of rubella IgG <10 IU/ml were considered to be susceptible. Index values for the HBsAg level were determined according to the assay.

Statistical Package for Social Science (SPSS, version 17.0) software was used for statistical analysis. A χ² test was used to calculate statistical differences between proportions. p < 0.05 was considered statistically significant.

**Results**

A total of 4,062 pregnant women were enrolled into this study. The collected samples were convenience samples. The mean age was 29.2 ± 5.26 years (range 17–49). The highest percentage (2,120; 52.2%) of pregnant women who were tested for anti-rubella IgG and HBsAg were aged between 20 and 29 years, while only 58 (1.4%) of the pregnant women were aged <20 years. Of these pregnant women, 2,605 (64.1%) were non-Kuwaiti, whereas 1,457 (35.9%) were Kuwaiti. The non-Kuwaiti women were from different countries because many nationalities work in Kuwait.

The prevalence of rubella antibody among pregnant women in Kuwait was 88.4% (n = 3,589), while 6.8% (n = 276) were seronegative for rubella. Furthermore, 4.8% (n = 197) had levels of rubella IgG <10 IU/ml. Therefore, 473 (11.6%) of the pregnant women were susceptible to rubella. Of the 473 susceptible women, 163 (4%) were

**Table 1. Frequency of seropositive and seronegative tests for anti-rubella IgG and HBsAg among Kuwaiti and non-Kuwaiti pregnant women and among different age groups**

|                    | Rubella IgG | HBsAg |                  |                  |
|--------------------|------------|-------|------------------|------------------|
|                    | ND <10 IU/ml ≥10 IU/ml total |                  | ND detected total |
| Nationality        |            |       |                  |                  |
| Kuwaiti            | 66 (4.5) 97 (6.7) 1,294 (88.8) 1,457 | 1,452 (99.7) 5 (0.3) 1,457 |
| Non-Kuwaiti        | 210 (8.1) 100 (3.8) 2,295 (88.1) 2,605 | 2,597 (99.8) 6 (0.2) 2,603 |
| Total              | 276 (6.8) 197 (4.8) 3,589 (88.4) 4,062 | 4,049 (99.7) 11 (0.3) 4,060 |
| Age group          |            |       |                  |                  |
| <20 years          | 2 (3.4) 2 (3.4) 54 (93.1) 58 | 58 (100) 0 58 |
| 20–29 years        | 118 (5.6) 104 (4.9) 1,898 (89.5) 2,120 | 2,111 (99.6) 8 (0.4) 2,119 |
| 30–39 years        | 139 (8.1) 80 (4.7) 1,719 (87.3) 1,719 | 1,716 (99.9) 2 (0.1) 1,718 |
| ≥40 years          | 17 (10.3) 11 (6.7) 137 (83.0) 165 | 164 (99.4) 1 (0.6) 165 |
| Total              | 276 (6.8) 197 (4.8) 3,589 (88.4) 4,062 | 4,049 (99.7) 11 (0.3) 4,060 |

Values are given as numbers (%). ND = Not detected (seronegative).
Kuwaiti and 310 (7.6%) were non-Kuwaiti. Among the 1,457 Kuwaiti pregnant women, 1,294 (88.8%) had high levels (≥10 IU/ml) of anti-rubella IgG. Ninety-seven (6.7%) had antibody levels <10 IU/ml and 66 (4.5%) were seronegative. The prevalence of HBsAg among pregnant women in Kuwait was only 0.3% (table 1) and it was similar among both Kuwaiti and non-Kuwaiti women.

The proportion of pregnant women who were seronegative for anti-rubella IgG or had levels ≤10 IU/ml increased with increasing age from 3.4 to 10.3% and from 3.4 to 6.7% among women aged <20 years and those aged ≥40 years age, respectively (p = 0.016) (table 1). On the other hand, there was no significant association between the different ages and the proportion of pregnant women who were HBsAg positive or negative (p = 0.325) (table 1).

**Discussion**

The frequency of Kuwaiti and non-Kuwaiti pregnant women who were positive for HBsAg (0.3%) was low, probably due to the effective HBV vaccination policy which was introduced in Kuwait in 1990. In infancy, the first dose of viral hepatitis B vaccine is given on the first day of childbirth. The current prevalence of HBsAg carriers in pregnant women in Kuwait is similar to that in Spain (0.1%) [12] and Northern and Central European counties [13, 14].

The prevalence of anti-rubella IgG in this study was comparable to the 85–90% in European women [15], in Turkey [16], and in Australia [17]. However, other studies revealed lower prevalences of anti-rubella IgG. In Nigerian pregnant women, 54.1% were positive for rubella IgG antibody [18], while the seroprevalence of rubella in pregnant women from Sri Lanka was 76% [19], and in Russian pregnant women it was 77.5% [20].

The age range of 20–39 years in this study is similar to those of other studies [16, 17], thereby indicating a normal childbearing age in Kuwait. The high percentage of non-Kuwaiti pregnant women in this study is consistent with the population demographic in the country and probably indicates that non-Kuwaiti women use government clinics more frequently than do Kuwaiti women who tend to use private clinics.

That 473 (11.6%) pregnant women were susceptible to rubella could indicate that, despite naturally acquired rubella and vaccination which was started 30 years ago, a high number of pregnant women in Kuwait remain susceptible to and hence at risk for congenital infections. It should be noticed that rubella vaccination is part of the measles, mumps, and rubella vaccination which is given to 1-year-old children.

Also, the finding that 11.6% of women in Kuwait were seronegative confirmed the findings of previous studies [21–23] in which 5.6, 7.7, and 4.2%, respectively, were seronegative. The findings of this study further confirmed the prediction made by Hathout et al. [21] that in order to eliminate the 5–7% rate of females who remain susceptible because they are uninfected and therefore at risk, an alternative vaccination policy should be followed. That is, since premarital sex in Kuwait is assumed to be generally negligible and provided that they take contraceptives for 3 months, all women should be screened for rubella antibody at marriage and those found to be seronegative should be given the vaccine. It was hypothesized at that time that since naturally acquired infection could not eliminate the 5–7% rate of women who remain susceptible, vaccination, with a potential vaccine failure rate of 5%, was unlikely to eliminate the rate of those who are susceptible. Indeed, in 1983 a rubella outbreak among pregnant women in Kuwait resulted in a high percentage of congenital infection and malformation [23]. Therefore, there is a need to include rubella antibody testing in the current routine premarital testing (which includes screening for HBsAg) that was introduced in Kuwait in 2009, to define the rubella immune status of women at marriage, and to select those who are susceptible and hence offer vaccination. This would most likely prevent rubella infection in pregnancy in Kuwait.

**Conclusion**

Our results showed that the prevalence of both anti-rubella IgG and HBsAg among pregnant women in Kuwait is relatively high. However, about 11.6% of pregnant women in Kuwait remain susceptible to rubella infection. This percentage can be reduced by screening all women for rubella antibody as a part of routine premarital testing and vaccinating women who are seronegative.
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