

Rubella Virus Seroprevalence and Associated Factors in Pregnant Women with and without Previous Spontaneous Abortion

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Abstract

Background: Rubella virus infection is associated with various pregnancy outcomes. Usually, such infection is more prevalent among women with low positivity for protective immunoglobulin G (IgG). Several factors are known to influence the seroprevalence of this virus. **Objectives:** This study aimed to investigate the seroprevalence of anti-rubella IgG and immunoglobulin M (IgM) antibodies and associated factors among pregnant women with and without a history of abortion. **Materials and Methods:** A total of 91 pregnant women (79 women with a history of previous abortion and 12 women without such history) were enrolled in this cross-sectional study. Sera were collected from each woman, and the levels of rubella IgG and IgM were measured using enzyme-linked immunosorbent assay. Demographic and reproductive data for the women were also collected. Univariate logistic regression was used to find the association of factor with serostatus of the virus. **Results:** The overall seropositivity for IgG and IgM was 95.6%, (95% confidence interval [CI] = 91.3–99.9) 9.89%, (95% CI = 9.68–10.1), while six women (6.59%) were positive for both types of Igs. Two factors showed a significant association with rubella IgG seropositivity: A history of previous abortion (odds ratio [OR] = 0.68, 95% CI = 0.45–0.99, $P < 0.001$). Moreover, urban residence (OR = 1.09, 95% CI = 1.0–1.19, $P = 0.048$). On the other hand, younger age (≤ 28 years) (OR = 0.1, 95% CI = 0.01–0.82) and previous abortion (OR = 0.14, 95% CI = 0.03–0.61) were significantly associated with IgM positivity. **Conclusions:** Most women are protected from rubella virus infection through possessing a high level of IgG; however, there is a considerable proportion with evidence of acute infection which indicate that the virus is endemic in the study area.

Keywords: Abortion, pregnant women, rubella virus, seroprevalence

INTRODUCTION

In many developing countries, infection with rubella virus is considered a major public health concern.^[1] Although most infections with rubella cause mild, self-limiting measles-like disease, result in miscarriage, fetal death or congenital ophthalmic, auditory defect when occurs at early pregnancy. However, the actual threat arises when rubella virus infects the fetus – particularly during the first trimester – when infection can lead to congenital rubella syndrome (CRS).^[2] According to the World Health Organization global estimates, there were more than 110,000 infants who born with CRS exceeded worldwide, making rubella a leading cause of congenital anomalies. These estimates have pointed out that the highest CRS burden is occurring in the developing world, i.e., Southeast Asian region and African region.^[3]

While much progress has occurred after the introducing of rubella vaccine before about five centuries,^[4] rubella remains an important pathogen even in developed countries which implemented the vaccine in their national vaccination schedule. For example, a rubella epidemic had occurred in Japan, with more than 11,000 rubella infections during the first 6 months of 2013 with at least 13 CRS cases. These epidemic and alike highlight the fact that partial vaccination strategy can lead to major outbreaks.^[5] Although one dose of rubella vaccine can induce life-long protection in most

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countries using the measles and rubella (MR) or measles, mumps, and rubella vaccine vaccines, a second dose is preferred at 15–18 months or 4–6 years, as indicated for protection against measles and mumps.^[2]

Therefore, it is reasonable to assume that a considerable number of women at childbearing age are lacking the protective level of antibodies against rubella virus, which put them under the risk of infection. Accordingly, this study aimed to investigate the seropositivity of rubella immunoglobulin G (IgG) and immunoglobulin M (IgM) with different demographic and reproductive factors in a sample of pregnant Iraqi women with and without previous history of abortion.

MATERIALS AND METHODS

The study design and setting

This is a cross-sectional study including a total of 91 pregnant women (79 women with a history of previous abortion and 12 women without such a history). Those women were attending Abu-Graib General Hospital/Baghdad and nearby primary health centers from September 2017 to April 2019. These centers provide obstetrical care service for the majority of the city dwellers and many villages nearby.

Data collection

A consent form explaining the dimensions of the study was obtained from each woman either as a written form or an oral form. Data including age, gravida, parity, number of previous abortion, gestational age, and residence were obtained through direct interview and reported in a well-prepared questionnaire.

Blood sample collection

Approximately 4 mL of venous blood were obtained from each participant in plain vacutainer tubes. Sera were separated after blood clotting and centrifugation and stored at -70°C until processing. A commercial enzyme-linked immune-sorbent kit (Immulite® 2000 XPI/Siemens Healthcare Diagnostics) was used to measure serum levels of rubella IgG and IgM. The system is fully automatic, with random access from the primary sample, and is based on solid-state immunometric dosage in amplified chemiluminescence. The manufacturer's instructions were followed precisely. The positive cutoff value for IgG and IgM were ≥ 10 IU/mL. The sensitivity and specificity of the test for both categories was $>97\%$.

Data analysis

Data were initially entered into the Excel sheet in Microsoft office and analyzed with statistical package for social sciences, version 25 (IBM Corp./Michigan/United State). Numerical variables were presented and mean $\pm$ standard deviation and analyzed with Student's *t*-test, while dichotomous variables were presented as number and frequency and analyzed with Chi-square test. Univariate logistic regression was used to predict the risk of each demographic and reproductive factor on the occurrence of abortion. $P \leq 0.05$ was considered statistically significant.

RESULTS

The mean age of the enrolled women was 28.74 ± 6.53 years (range 18–47 years). Almost half of the women were 28-year-old or younger [Table 1]. The history of previous abortion was reported in 12 (13.19%) women. At the time of sampling, about 60% of women were in their first trimester of gestational age, while only 12% of them were in their third gestational age. There was a wide variation in gravida which ranged from 1 to 10 (mean 4.6 ± 2.26). Around two-third of the women had 4 or more pregnancies compared to one-third who had 1–3 pregnancies. Keeping in mind that the most women experienced abortions, the parity has reduced to 0–7 (mean $\pm 2.5 \pm 1.76$) with 56% of women had ≤ 2 births. A positive family history of rubella infection was reported in 59 (31.16%). Included women were almost evenly distributed between rural and urban areas.

Overall seropositivity for rubella immunoglobulin G and immunoglobulin M

Out of investigated women, 87 (95.6%, 95% confidence interval [CI] = 91.3–99.9) were positive for rubella IgG, and 9 (9.89%, 95% CI = 9.68–10.1) were positive for rubella IgM [Figure 1], with six women (6.59%) were positive for both types of IGs.

The association of seropositivity with demographic and reproductive characteristic of women

Rubella immunoglobulin G

Out of seven included factors, only two showed significant association with rubella IgG seropositivity [Table 2]. All IgG-negative women had a history of previous abortion,

Table 1: Demographic and reproductive characteristics of the study population

Variable	Frequency (proportion)
Age (years)	
≤ 28	44 (48.35)
> 28	47 (51.65)
Previous abortion	
No	12 (13.19)
Yes	79 (86.81)
Gestational	
First trimester	54 (59.34)
Second trimester	26 (28.57)
Third trimester	11 (12.09)
Gravida	
1-3	32 (35.16)
≥ 4	59 (64.84)
Parity	
≤ 2	51 (56.04)
> 2	40 (43.96)
Family history	
No	59 (64.84)
Yes	32 (35.16)
Residence	
Urban	47 (51.65)
Rural	44 (48.35)

whereas, none of the IgG-positive women had such history (odds ratio [OR] = 0.68, 95% CI = 0.45-0.99, $P < 0.001$). Likewise, all IgG-negative women are residing in rural districts, while all women residing the urban districts were positive for rubella IgG (OR = 1.09, 95% CI = 1.0-1.19, $P = 0.048$).

Factors such as older age, early gestational age and the presence of family history were associated with increased IgG-negativity compared to their counterpart traits; however, the differences were not sufficient to reach the acceptable level of significance. On the other hand, gravida and parity appear to have no influence on the rubella IgG seropositivity.

Rubella immunoglobulin M

Younger age (≤ 28 years) was significantly associated with IgM positivity (OR = 0.1, 95% CI = 0.01-0.82). Moreover, 4 women with previous abortion out of 12 were positive for IgM compared with only 5 women of 79 without a history of previous abortion who were positive for IgM (OR = 0.14,

95% CI = 0.03-0.61). Urban residents had a marked increase in IgM positivity compared with rural residents; however, the difference was not a significant [Table 3].

DISCUSSION

The current study aimed to investigate the prevalence of seropositivity to rubella antibodies among pregnant women in Abu-Graib city/Baghdad. The overall prevalence of IgG was 95.6%. Compared with other developing countries, this proportion is relatively high. For example, in Namibia 85%,^[6] in Sudan 65%,^[7] in Bangladesh 84.33%,^[8] in Italy, 85.3%,^[9] and slightly lower than that reported in Turkey (96.1%)^[10] and in Mexico 97.1%.^[11]

Similarly, the study revealed a high proportion of IgM positivity (9.89%) compared with that reported in Turkey (0.2%)^[10] and in Tanzania (3.7%),^[11] and lower than that reported in Iran.^[12]

These variations can be attributed to two main factors. The first one is the implementation of rubella vaccination program within the national schedule. Almost all countries that do not use rubella vaccine, like most African countries, have a relatively low rate of IgG positivity, while countries using rubella vaccination like Iraq usually have a high rate of IgG positivity. The second factor is concerning study methodology and includes the variation in sample size, laboratory technique, and the differences in the cutoff point of the assay.

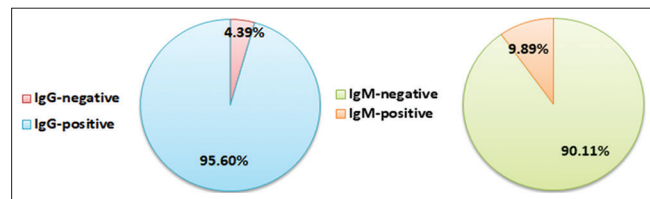


Figure 1: Seropositivity for rubella immunoglobulin G and immunoglobulin M

Table 2: Association of rubella IgG seropositivity with demographic and reproductive characteristic of women

Variable	Number of women tested	IgG-positive (n=87), n (%)	IgG-negative (n=4), n (%)	P	OR (95% CI)
Age (years)					
≤28	44	43 (49.43)	1 (25)	0.339	1.0
>28	47	44 (50.57)	3 (75)		2.93 (0.29-29.3)
Previous abortion					
No	12	8 (9.2)	4 (100)	<0.001	1.0
Yes	79	79 (90.8)	0 (0)		0.68 (0.45-0.99)
Gestational					
First trimester	54	51 (58.62)	3 (75)		1.0
Second trimester	26	25 (28.74)	1 (25)	0.742	0.68 (0.07-6.87)
Third trimester	11	11 (12.64)	0 (0)	0.423	0.94 (0.88-1.08)
Gravida					
1-3	32	30 (34.48)	2 (50)	0.525	1.0
≥4	59	57 (65.52)	2 (50)		0.53 (0.07-3.93)
Parity					
≤2	51	50 (57.47)	1 (25)	0.201	1.0
>2	40	37 (42.53)	3 (75)		4.05 (0.41-40.55)
Family history					
No	59	58 (66.67)	1 (25)	0.88	1.0
Yes	32	28 (32.18)	3 (75)		6.0 (0.6-60.2)
Residence					
Rural	47	43 (49.43)	4 (100)	0.048	1.0
Urban	44	44 (50.57)	0 (0)		1.09 (1.0-1.19)

OR: Odds ratio, CI: Confidence interval

Table 3: Association of rubella IgM seropositivity with demographic and reproductive characteristic of women

Variable	Number of women tested	IgM-positive (n=9), n (%)	IgM-negative (n=82), n (%)	P	OR (95% CI)
Age (years)					
≤28	44	8 (22.22)	36 (51.22)	0.01	1.0
>28	47	1 (77.78)	46 (48.78)		0.1 (0.01-0.82)
Previous abortion					
No	12	4 (44.44)	8 (9.76)	0.004	1.0
Yes	79	5 (55.56)	74 (90.24)		0.14 (0.03-0.61)
Gestational					
First trimester	54	6 (66.67)	48 (58.54)		1.0
Second trimester	26	2 (22.22)	24 (29.26)	0.633	0.68 (0.13-3.55)
Third trimester	11	1 (11.11)	10 (12.2)	0.844	0.8 (0.09-7.4)
Gravida					
1-3	32	3 (33.33)	29 (35.37)	0.904	1.0
≥4	59	6 (66.67)	53 (64.63)		1.09 (0.26-4.7)
Parity					
≤2	51	4 (44.44)	47 (57.32)	0.46	1.0
>2	40	5 (55.56)	35 (42.68)		1.68 (0.42-6.71)
Family history					
No	59	5 (55.56)	53 (64.63)	0.539	1.0
Yes	32	4 (44.44)	28 (34.15)		1.54 (0.38-6.21)
Residence					
Rural	47	3 (33.33)	44 (53.66)	0.247	1.0
Urban	44	6 (66.67)	38 (46.34)		2.32 (0.54-9.9)

OR: Odds ratio, CI: Confidence interval

Six women (6.59%) in the current study were found to be positive for both types of immunoglobulins. In a similar study, Tamirat *et al.*^[13] found that 1.9% of the pregnant women were positive for rubella IgM and IgG, while Wondimeneh *et al.*^[14] found a higher rate reached 8.2%. This group of women may have a primary rubella infection.

The present study revealed a significant inverse association between previous abortion and IgG positivity (OR = 0.68, 95% CI = 0.45-0.99, $P < 0.001$). This implies that IgG-positive women are about 1.5-time protected against rubella virus infection compared with IgG-negative women. Similar results were frequently reported by many previous studies, all of which emphasized the protective role of IgG seropositivity against rubella virus infection.^[13,14] However, Jubaida *et al.*^[8] reported a higher incidence of IgG positivity (86.84%) in women with adverse pregnancy outcomes than those with normal pregnancies (80.65%).

According to the result of the current study, the inverse association between IgG positivity and abortion can be explained by the fact that rubella virus infection is an important cause of abortion. The presence of specific anti-rubella IgG antibodies in a high titer can protect a woman from infection with a consequence reduction in the incidence of abortion.

Urban residence was associated with a high rate of IgG positivity (OR = 1.09, 95% CI = 1.0-1.19, $P = 0.048$), which means that women residing and rural district has 1.09-time greater opportunity to have a protective IgG than women

residing in urban district. This finding was also supported by reports from local previous study.^[15] In addition, in line with this result is the study Alvarado-Esquivel *et al.*^[11] in Mexico who found 97.3% versus 90% prevalence of IgG in urban and rural area, respectively.

This relatively high rate of IgG positivity in urban population may be because they are more likely to live in crowded situations and become susceptible to a rapid spread of the infection.

In the present study, the age was found to inversely associate with IgM seropositivity; as age increase, IgM declines. Such a result has also been reported by many previous studies.^[2,13] As rubella IgM mostly declines after 2-3 months' postinfection, this result suggests that women positive for IgM may have an active infection with the virus.

An interesting result in the present study is the significant association of IgM positivity with the previous history of abortion. In accordance with this result are local studies in as well as some global studies.^[12,14,16] An explanation for this result is that these group of women are more vulnerable to rubella infection although the mechanism is not clear.^[17] Thus, there is a recurrent infection accompanied with abortion in many cases.

The main limitation of this study was that advanced techniques such as conventional and real-time polymerase chain reaction were not use for viral detection because of the shortage in facilities. Furthermore, the sample was relatively small, and

the results cannot be generalized to all pregnant women in the study area.

CONCLUSION

It can conclude that most women are protected from rubella virus infection through possessing a high level of IgG; however, there is a considerable proportion of women with evidence of acute infection which indicate that the virus is endemic in the study area, and the efficiency of vaccination program should be reviewed.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Lulandala L, Mirambo MM, Matovelo D, Gumodoka B, Mshana SE. Acute rubella virus infection among women with spontaneous abortion in Mwanza city, Tanzania. *J Clin Diagn Res* 2017;11:QC25-7.
2. Lambert N, Strebel P, Orenstein W, Icenogle J, Poland GA. Rubella. *Lancet* 2015;385:2297-307.
3. Centers for Disease Control and Prevention (CDC). Rubella and congenital rubella syndrome control and elimination – Global progress, 2000-2012. *MMWR Morb Mortal Wkly Rep* 2013;62:983-6.
4. Wang C, Zhu Z, Xu Q, Fang X, Liu X, Xiong P, *et al.* Progress towards rubella elimination after implementation of rubella immunization for over 20 years in Shandong province, China. *Sci Rep* 2017;7:17982.
5. Minakami H, Kubo T, Unno N. Causes of a nationwide rubella outbreak in Japan, 2012-2013. *J Infect* 2014;68:99-101.
6. Jonas A, Cardemil CV, Beukes A, Anderson R, Rota PA, Bankamp B, *et al.* Rubella immunity among pregnant women aged 15-44 years, Namibia, 2010. *Int J Infect Dis* 2016;49:196-201.
7. Hamdan HZ, Abdelbagi IE, Nasser NM, Adam I. Seroprevalence of cytomegalovirus and rubella among pregnant women in Western Sudan. *Viol J* 2011;8:217.
8. Jubaida N, Mondal ME, Kawsar NM. Seroprevalence of rubella antibodies in pregnant women. *J Armed Forces Med Coll Bangladesh* 2011;7:20-4.
9. Calimeri S, Capua A, La Fauci V, Squeri R, Grillo OC, Lo Giudice D. Prevalence of serum anti-rubella antibodies among pregnant women in Southern Italy. *Int J Gynecol Obstet* 2012;116:211-3.
10. Tamer GS, Dundar D, Caliskan E. Seroprevalence of *Toxoplasma gondii*, rubella and cytomegalovirus among pregnant women in Western region of Turkey. *Clin Invest Med* 2009;32:E43-7.
11. Alvarado-Esquivel C, Hernandez-Tinoco J, Sanchez-Anguiano LF, Ramos-Nevarez A, Cerrillo-Soto SM, Salas-Pacheco JM, *et al.* Rubella immune status in pregnant women in a Northern Mexican city. *J Clin Med Res* 2016;8:656-61.
12. Jahromi AS, Kazemi A, Manshoori G, Madani A, Moosavy SH, Seddigh B. Seroprevalence of rubella virus in women with spontaneous abortion. *Am J Infect Dis* 2011;7:16.
13. Tamirat B, Hussen S, Shimelis T. Rubella virus infection and associated factors among pregnant women attending the antenatal care clinics of public hospitals in Hawassa city, Southern Ethiopia: A cross-sectional study. *BMJ Open* 2017;7:e016824.
14. Wondimeneh Y, Tiruneh M, Ferede G, Abera B, Workineh M, Birhanie M, *et al.* Rubella virus infections and immune status among pregnant women before the introduction of rubella vaccine in Amhara regional state, Ethiopia. *Int J Infect Dis* 2018;76:14-22.
15. Hasan AR. Seroprevalence of anti-rubella IgG antibody among pregnant and childbearing women in Diyala province-Iraq. *Diyala J Med* 2011;6:16.
16. Mohammed LM. Prevalence of rubella virus in pregnant women in Kirkuk city-Iraq. *Kirkut Uni J Sci Stud* 2015;10:47-57.
17. Priyanka D, Ganesh V, Anupriya A, Uma A, Kalamani SM. Seroprevalence of rubella among asymptomatic pregnant women in a rural teaching hospital. *Int J Med Microbiol Res* 2017;1:7-12.