

Research Article

Rubella Immune Status in Pregnant Women in Central Morocco

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Abstract

Rubella is a contagious viral infection that affects pregnant women during early pregnancy which leads to the infection of a developing fetus, causing congenital rubella syndrome (CRS). Although rare in many industrialized countries, because of the success of vaccination programs, rubella continued to occur in many developing countries with no vaccination program. Rubella immunization rates are not optimal; World Health Organization (WHO) recommends that countries without vaccination programs should assess the burden of rubella infection and CRS. In Morocco, Rubella containing vaccine (RCV) was introduced in routine immunization of children in 2003. In a retrospective cross-sectional study was conducted between January and December 2015, we sought to determine the sero-prevalence of anti-rubella IgG in 1399 pregnant women in our region. The mean age was 31.20 ± 5.90 years (range 17 - 45 years) using chemiluminescent microparticle immunoassay and we examined for anti-rubella IgM antibodies for sera considered negative (< 10 IU/mL) for rubella IgG. A questionnaire was used to obtain the socio-demographic and behavioral characteristics for 280 the pregnant women. A total of 1240 of the pregnant women examined were positive (≥ 10 IU/mL) for rubella IgG giving a prevalence of 88.6 %, and 159 (11.4%) were susceptible. There was no evidence of recent infection within the study period. Study period as shown by negative IgM result.

The quantitative analysis for rubella IgG showed a noticeable variability in the values of antibodies that ranged between 0-263 IU/ml. A clear majority of the sample had values of antibodies > 50 IU/ml. Although most women tested were seropositive for rubella IgG (81% - 94.6 %) according to the socio-demographic and obstetrics characteristics, suggesting a natural virus circulation within the community, screening for protective immunity followed by vaccination to those who were susceptible should be enforced to prevent possible rubella congenital syndrome. Most (11.4%) of the pregnant women who were sero-negative in their first pregnancy were not immunized against rubella.

INTRODUCTION

Rubella is an infectious disease caused by a virus belonging to the *Rubivirus* genus in the family *Togaviridae*. The virus is mainly transmitted from human to human by direct contact with infected bodily fluids or respiratory droplet secretions from infected people, usually characterized by a mild febrile rash illness [1]. It mainly affects children aged 2-12 years. However, various proportions of women reach childbearing age without being 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. 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 [2]. With the fact that there is no in-utero treatment available for these fetuses,

prevention remains the best strategy to eradicate all cases of CRS. The World Health Organization (WHO) has therefore encouraged all countries to assess their rubella population immunity status and introduce immunization and surveillance, if appropriate. Although rubella and CRS are not included in the surveillance system in Morocco, a retrospective assessment of the CRS burden in the country estimated its incidence at 8.1-12.7 cases per 100 000 live births [3]. As the clinical diagnosis of rubella is unreliable, serological tests are needed for a diagnosis, especially when a patient is pregnant. The role of the laboratory is crucial in the management of rubella infection during pregnancy and rubella serological results must be interpreted with caution. The sero-epidemiology of rubella virus infection in pregnant women in central of Morocco is largely unknown. Therefore, this study aimed at detecting the presence of both anti-rubella IgM and IgG antibodies in pregnant women attending Moulay Ismail Military Hospital (MIMH) in Meknes, thereby giving a complete picture of the occurrence of the disease among pregnant women

in central Morocco. Seroprevalence association with the socio-demographic characteristics, obstetric history, and knowledge of risks of congenital rubella syndrome and rubella immunity of the pregnant women was also investigated.

MATERIALS AND METHODS

A retrospective cross-sectional study was conducted. The study population comprised pregnant women in different trimesters of pregnancy who expressed interest in participating in the study and gave consent and had undergone rubella serology screening at the microbiology department of the MIMH, Meknes, Morocco, during a 12-month period between January 1, 2015, and December 31, 2015, were included in the study. Socio-demographic characteristics, the obstetric history, awareness and knowledge of rubella immunity were obtained from the pregnant women by structured questionnaire. Socio-demographic items included age, residence, educational level and socio-economic status. In addition, the obstetric history (month of pregnancy, number of pregnancies, and miscarriages) from each participant was recorded.

Five milliliters of venous blood sample was collected from each of the women using a standard aseptic technique into properly labeled plain bottles. The blood samples were allowed to stand at room temperature to allow for blood clotting, after which samples were transported to the laboratory, centrifuged at 2,500 rpm for 10 minutes, and sera separated. Sera were stored at -20°C until analysis.

Sera were examined for anti-rubella IgG antibodies by a commercially available chemiluminescent micro particles immunoassay (Architect i1000/Abott Diagnostics). The assay is quantitative determination and qualitative detection intended to aid in the determination Rubella immune status, specific IgG antibody concentrations, expressed as International Units/millimeter (IU/ml). It was considered negative (susceptible) if lower or equal to 10 IU/mL, were considered as a cut-off for seropositivity, and positive (immune) if higher than 10 IU/mL, this titer suggests protection against rubella. Sera of the participants considered negative were kept frozen until examined for anti-rubella IgM antibodies by the same a commercially available chemiluminescent immunoassay (Architect i1000/Abott Diagnostics). All tests were performed according to the manufacturer's instructions. The recommended control requirement assay is that a single sample of each control be tested once every 24 hours each day of use kit control. The Control values must be within the acceptable ranges specified in the control package insert. If a control is out of its specified range, the associated test results are invalid and samples must be retested. Recalibration may be indicated.

If laboratory quality control procedures require more controls to verify test results or in case of lack of kit control, we use the control samples in the home.

Rubella IgM assay is a qualitative method for the detection of Rubella specific IgM antibodies in human serum. A value of a sample equal to or greater than 1.60 Index (1.00 S/CO) is considered reactive for IgM antibodies to Rubella. Any sample with a value less than 1.20 Index (0.75 S/CO) is considered nonreactive. Reactivity for IgM antibodies to Rubella may

indicate current infection, reactivation or recent vaccination. The generated data was analyzed using SPSS 21.0 (Armonk, NY: IBM Corp.) to give descriptive statistics which included frequencies, percentiles, and ratios.

RESULTS AND DISCUSSION

A number of 1399 serum samples from pregnant women, during the studied period, and 1240 (88.6%) of the pregnant women examined were positive for rubella IgG antibodies (≥ 10 IU/mL) and 159 (11.3%) were susceptible. After completion of informed consent, 280 women were interviewed using a questionnaire. Their mean age was 31.20 ± 5.90 years (range 17 - 45 years), 75.5% of occurred among women aged 25-44 years (Table 1). There was no evidence of recent infection within the study period, none of the 159 pregnant women were positive for anti-rubella IgM antibodies. As it can be observed, there was variability in the positive values of antibodies that ranged between 11.6-263 IU/ml. A total of 623 serum samples (44.5%) had antibodies values between 15-50 IU/ml; while, a clear majority of the sample had values of antibodies >50 IU/ml.

Very little is known about the serological status against rubella virus in pregnant women in central Morocco. Results indicate that 88.6% of the pregnant women studied had protective antibodies against rubella virus infection, this immunity may have been acquired from previous infection with the rubella virus during childhood or adolescence. In the public sector, national vaccination program against rubella started in 2003. The data collected between 1970 and 1999 among women of childbearing age showed that 66.5%-85.5% seropositivity for anti-rubella virus IgG [4]. The incidence of rubella was comparable with the results from recent national study found a 90.2% in Rabat 2012, and was high compared with previous Moroccan studies. This may be explained by an increase in the rubella vaccination coverage for the primary school in the country [5]. In Morocco, several barriers remain to achieving rubella vaccination coverage in persons of childbearing age. A major barrier is limited access to preventive health care by rubella-susceptible populations. Because rubella vaccination is not mandated and universally provided for adults, more complex, targeted strategies are needed to ensure that adults of childbearing age are rubella immune.

Our results agree with the universal trend for rubella seroprevalence reported in previous international studies. Seroprevalence of rubella antibodies in many countries have shown a comparable among women of childbearing age; for example, 89.4 % in Nigeria [6], 88.1 % in Cameroon [7] and 84 % in the Democratic Republic of the Congo [8]. However, the rubella seroprevalence found in other studies is high with the 93.3% seroprevalence in pregnant women in Portugal [9], the 94.4% seroprevalence in pregnant women in Norway [10], and 95.3% seroprevalence in women of childbearing age in South Africa [11].

The level of natural immunity in these studies is lower than the immunity currently reported in Europe; this might be due to on-going vaccination programmes in developed countries [12]. Worldwide, over 100 000 babies are born with CRS each year [2,13]. The sero-positivity for rubella among pregnant women varies widely in different countries. As a matter of fact, in many

Table 1: Socio-demographic characteristics, obstetrical and descriptive data for rubella immunity of the pregnant women.

Characteristic	Pregnant women tested No. (%)	Rubella immunity (IgG+) No. (%)	Rubella susceptibility(IgG-) No. (%)
Total	1399	1240 (88.6)	159 (11.4)
Age groups (years), (mean: 31±5.6)			
15-24	52 (18.6)	44 (84.6)	8 (15.4)
25-34	153 (54.6)	137 (89.5)	16 (10.5)
35-44	64 (22.1)	56 (87.5)	8 (15.5)
≥45	11 (3.9)	10 (90.9)	1 (9.1)
Residence area			
Urban	251 (89.6)	223 (88.8)	28 (11.2)
Rural	29 (10.4)	24 (82.8)	5 (17.2)
Education level			
Illiterate	58 (20.7)	47 (81.0)	11 (19.0)
Primary	82 (29.3)	71 (86.6)	11 (12.4)
Secondary	102(36.4)	89 (87.3)	13 (13.7)
University	38 (13.5)	36 (94.7)	2 (5.3)
Occupation			
House wife	144 (51.4)	128 (88.9)	16 (11.1)
Employee	130 (46.4)	114 (87.7)	16 (14.0)
own initiative	6 (2.2)	5 (83.3)	1 (20.0)
Obstetric history			
Multiparous	198 (70.7)	179 (90.4)	19 (9.6)
Primiparous	82 (29.3)	68 (82.9)	14 (17.1)
Month of pregnancy			
1 -3	108 (38.6)	98 (90.7)	10 (9.3)
4-6	133 (47.5)	117 (88.0)	16 (12.0)
7-9	39 (2.1)	32 (82.1)	7 (17.9)
History of Miscarriages			
Yes	41 (14.6)	36 (87.8)	5 (12.2)
No	239 (85.3)	211 (88.3)	28 (11.7)
Rubella immunity			
known	154 (55.0)	133 (86.4)	21 (13.6)
Unknown	126 (45.0)	114 (90.5)	12 (9.5)
Rubella vaccine			
Yes	21 (7.5)	20 (95.2)	1 (4.8)
No	188 (67.1)	162 (86.2)	26 (13.8)
Unknown	71 (25.4)	65 (91.6)	6 (8.4)
Rubella risks of CRS			
known	65 (23.2)	58 (89.2)	7 (10.8)
Unknown	188 (76.8)	162 (86.2)	26 (13.8)

developing countries, rubella sero-positivity among pregnant women has been reported to range from 54.1% to 95.2% [2,14]. A systematic search of original literatures from different African countries, the natural immunity of rubella was found to range from 52.9 to 97.9 % between 2002 and 2014 [15]. Comparison of seroprevalence levels between studies is difficult owing to the different designs, sampling, timing of studies in relation to previous outbreaks, variability of laboratory procedures, and titer cut-off points used to define positivity of anti-rubella IgG.

Interpretation of our findings was based on the evaluations of results obtained from a previous study [16]. Immunity to rubella virus infection was thought to be represented when IgG values were greater than 25 IU/ml, usually between 50 - 200 IU/ml and negative sera reveal less than 10 IU/ml. Sera with titers between 10-25 IU/ml are rated as intermediate reactive. It could be assumed that this antibody concentration may fall below the

recommended levels necessary for protection. We can add one dose of rubella vaccine after delivery to this group of women to have a higher rate [17,18].

In general, the presence of specific antibodies correlates with protection, there are differences between commercial kits exist, which reflect different antigen preparations and test parameters used. It is known that reinfection can occur in individuals with pre-existing antibody levels above the accepted cut-off level and is more common after immunization than after natural infection. Antibody levels greater than 15 IU/ mL are usually considered to be protective against reinfection [18].

The role of the laboratory is crucial in the management of rubella infection during pregnancy, Rubella serological results must be interpreted with caution, especially after asymptomatic reinfection or with specimen grossly hemolyzed or with heterophilic antibodies in human serum can react with reagent

immunoglobulins, interfering with in vitro immunoassays [19]. Diagnosis is usually made by detection of rubella specific IgM, none of the 159 pregnant women were positive for anti-rubella IgM antibodies. Although commercial assays are available, they vary in format, sensitivity, and specificity. Furthermore, rubella specific IgM may be present between 4 to 8 weeks or more after natural infection or vaccination and after asymptomatic reinfection. False positive results may also be due to cross reacting IgM antibodies or rheumatoid factor [20]. Consequently, in countries with limited laboratory facilities and expertise, diagnosis of rubella in pregnancy is problematic. It is essential that laboratory results be interpreted in the context of full clinical details, to avoid misinterpretation of results and to minimise anxiety for the patient, especially if termination of pregnancy is considered. To manage these cases close collaboration between obstetricians and virologists is essential at all stages, to avoid errors and unnecessary terminations and to decide whether prenatal diagnosis is indicated [20,21].

In the present study, seroprevalence no significant differences with age were reported as in other studies. However, in data from some countries, rubella seropositivity seems to increase with age [22]. This fact might reflect the higher coverage of rubella vaccination in young women in these countries.

The present study also revealed that 6.7 % (19/280) of pregnant women who were seronegative must be immunizing against rubella. The WHO recommends that such women must be vaccinated before discharge from hospital in order to achieve 100% seroprevalence [2]. This deficiency in the rubella prevention procedure is difficult to explain, but lack of knowledge among both health providers and majority of pregnant women (76.8%) unknown about the risks of CRS may be a part of the of the problem. Seroprevalence of rubella disease did not differ according to the maternal status of the women; no statistical difference in seroprevalence was seen between women in rural and urban areas (81.5% and 85.0% respectively).

Some women may be considered immune or susceptible to rubella infection. Specially, if anti-rubella IgG antibody levels of were near the cut-off for seropositivity. Under these conditions, it is imperative that sero-negative samples are analyzed in the same laboratory using the same technique, in order to avoid erroneous conclusions.

The objective of next study will to examine status for rubella specific IgM and IgG antibodies among infants suspected of having CRS aged less than 12 months compared with their clinical. In Morocco there is high level of consanguinity, and it has been shown to be associated with an increased risk of birth defects, some of which resemble CRS.

CONCLUSION

Rate of rubella immunity for pregnant women in central Morocco is relatively high (88.6 %), suggesting a sustained infection in the community and indicating endemicity. Outbreaks and possibly reinfections and are going unnoticed due to the absence of clinical symptoms. The majority had an IgG level of above 50 IU/ml, which is as indicated earlier a predictor for protective immunity. However, nearly 11.4% of pregnant women are susceptible to rubella and the risk of CRS in our setting and

76.8% of pregnant women ignored the disastrous consequences for her foetus. Therefore, to facilitate effective rubella control in Morocco we recommend institution of health policy that promotes awareness and screening for protective immunity for women of childbearing age followed by vaccination to those who were seronegative should be enforced to prevent possible rubella congenital syndrome.

Rubella serological results must be interpreted with caution, the Rubella seroprevalence did not differ according to the maternal status of the women and no association was recorded between anti-rubella IgG antibodies detection and age of the women.

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