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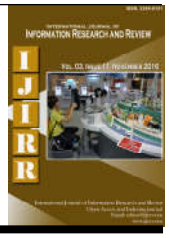

Research Article

SEROPREVALENCE OF RUBELLA IgG ANTIBODY IN PREGNANT WOMEN IN YAOUNDE, CAMEROON

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ABSTRACT

Background: Rubella is an acute infectious disease that normally has a mild clinical course. Rubella Virus infection among pregnant women vary widely troughout causes severe birth defects known as congenital rubella syndrome. In Cameroon, rubella vaccination is not included in the national immunization schedule and there is not therefore no antenatal screening for this viral disease. This study was undertaken to establish the sero-positivity rate of rubella among pregnant women attending antenal care hospital in Yaoundé, Cameroon.
Methods: From July 2013 to April 2014, a total of 400 pregnant women were enrolled and their serum samples collected and analyzed using the Architec anti-rubella virus IgG test. Data analysis was done using Statistical Analysis System (SAS version 9.1).
Result: An overall seropositivity rate of 91.75% (367/400) was found, with a higher percentage in the urban population and in the oldest age group. None of the possible risk factors studied were significantly associated with infection. None of the women ever had previous rubella vaccination.
Conclusion: The prevalence of rubella IgG antibody among pregnant (91.75%) was high in the absence of routine vaccination suggesting a continuous transmission of endemic rubella virus in Cameroon.

INTRODUCTION

Rubella is a mild exanthematic illness. However, if contracted during pregnancy, it may result in miscarriage, stillbirth or can cause severe birth defects known as Congenital Rubella Syndrome (CRS) (De Santis *et al*., 2006). Clinical signs of CRS include cataract(s), deafness, glaucoma, heart disease, loss of hearing, and pigmentary retinopathy. The global burden of CRS is estimated at 110,000 cases per year (Robertson *et al*, 2003). The sero-positivity for rubella among pregnant women varies widely in different countries. As a matter of fact, in many developing countries, rubella sero-positivity among pregnant women has been reported to range from 54.1% to 95.2% (Shah *et al*., 2010; WHO, 2011; Linguissi *et al*., 2012; Uyar *et al*., 2008). Clinical diagnosis of rubella during pregnancy proves difficult as only approximately 50% of the infected people present with typical exanthematous skin lesions (Shah *et al*., 2010; Usonis *et al*., 2011).

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Hence, serological screening of rubella, based on the detection of IgG and IgM antibodies, remains the mainstay for diagnosis (Binnicker *et al*., 2010). Many persons residing in African countries, including Cameroon, remain susceptible to rubella infection due to low levels of rubella vaccination. Since no specific treatment exists for rubella, vaccination before pregnancy is the only mean to prevent congenital infection. In developed countries, rubella infections are indeed prevented by active immunization given as part of a MMR vaccine (Usonis *et al*., 2011). The World Health Organization (WHO) has recommended that countries take the opportunity of the current goals of control and elimination of measles to introduce rubella vaccines in combination with other vaccines (WHO, 2012). However, in Cameroon, rubella vaccination is not included in the national immunization programme (WHO, 2011). In Cameroon and other neighbouring countries, there are no screening programs for rubella among pregnant women and the magnitude of the problem is therefore unknown. This study was carried out to determine the sero-positivity rates of rubella

infection among pregnant women attending antenatal clinics in Yaoundé, Cameroon.

METHODS

A Cross sectional descriptive study was carried out in pregnant, outpatient's women visiting the Yaoundé Catholic Hospital, Cameroon. This Hospital was chosen because of its high patient's attendance resulting the cheaper counts of consultation and administrative facilities. The sample size of 400 was calculated using a formula suitable for cross-sectional study (Fokunang *et al*., 2010). Collected blood specimens were analyzed at the Biology and Medical Analysis Laboratory (BMAL) of Pasteur Institute Dakar, Senegal. This study ran from July 2013 to December 2014. The serum samples were screened automatically for rubella- specific IgG antibodies using a chemiluminescent microparticle immunoassay for the quantitative determination and qualitative detection of IgG antibodies on the ARCHITECT *i system*. All equivocal samples were retested and if the result was confirmed, the sample was classified as equivocal, otherwise as positive or negative.

Data collection and laboratory procedures

Data were collected using a standardized data collection tool. Information on socio-demographic characteristics and relevant medical and obstetric characteristics were gathered. Each patient was made to sit comfortably, then the arm region intended for the venupuncture was cleansed with an alcohol swab, the selected vein pricked with a sterile needle attached to a syringe (5 ml) and 3-4 ml of blood drawn. The needle was then with drawn under a dry cotton and brief haemostasis effected by digital pressure with the swab at the puncture site. The blood sample was put in a sterile dry tube. Centrifugation was done at 1500 rotations per minute (rpm) for 15 minutes. Serum was collected in cryotubes and stored in refrigerator at -20 degree Celsius. Cryotubes were put inside a cold box and kept at 80°C until transportation to the BMAL of Pasteur Institute of Dakar, Senegal for subsequent analysis of rubella-specific IgG antibodies using ARCHITEC System Ci4100. The obtained serum samples were numbered and Manufacturer reference values for positive results were anti-rubella IgG ≥ 10 IU/ml and anti-rubella IgG ≤4.9 IU/ml for negative results. An IgG value between 5.0 and 9.9 was considered as borderline.

Data analysis

The programme Microsoft Office Excel 2007 was used to enter the data according to codes given and data were analyzed using the SAS version 9.1 (Statistical Analyse system, USA). Categorical variables were summarized as proportions and were analyzed using the Pearson's Chi-square test to observe the differences among the various groups. Continuous variables were summarized as median with interquartile range.

Ethical approval: The study protocol was approved by the National Comitee Ethics. An informed written consent was sought from each pregnant woman prior to her enrolment.

RESULTS

Demography

A total of 400 pregnant women were randomlly reported in this study. Out of these, 59 (14.75%) were married and 341(85.25%) were unmarried (Table1). The mean age was 24.6±5.1 (range 13-42) years.

Table 1. Age distribution and marriage status of the study population

Indicator	Frequency	Percentage
Age range		
13-17	17	4.25
18-22	139	34.75
23-27	140	35.00
28-32	75	18.75
33-37	20	5.00
38-42	9	2.25
Total	400	100.0
Marriage status		
Single	341	85.25
Married	59	14.75
Total	400	100.0

The subjects were distributed in first, second and third trimesters as shown in figure 1. One hundred and twenty two (30.5%) and 269 (67.25%) of the women were in their first and second trimester of pregnancy respectively. The partition of subjects based on history of spontaneous abortion showed that (Figure 2) a low incidence of subjects 95 (23.75%), with any history of Spontaneous abortion. There was a high subject population 305 (76.25%) with no history of spontaneous abortion in the study. The two following clinical presentation was observed: fever (20.75%) and rash (31%). Of 400 women in the analysis, 337 were from urban areas, 59 from suburban areas and 4 from rural area. Concerning nkowledge about vaccination, 379 (94.75%) haven't nknowledge and only 5.25 have a nkowledge about it. None of the 400 patients were vaccinated.

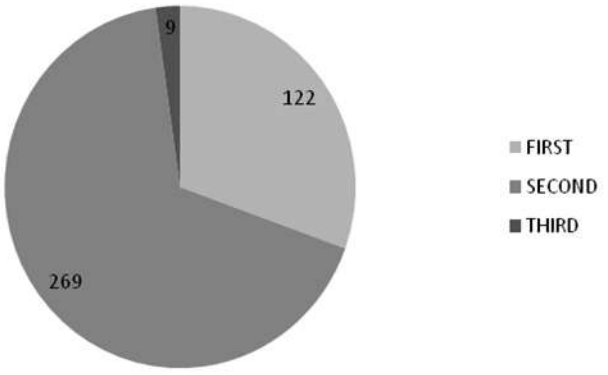

Figure 1. Distribution of subjects by pregnancy duration in trimester

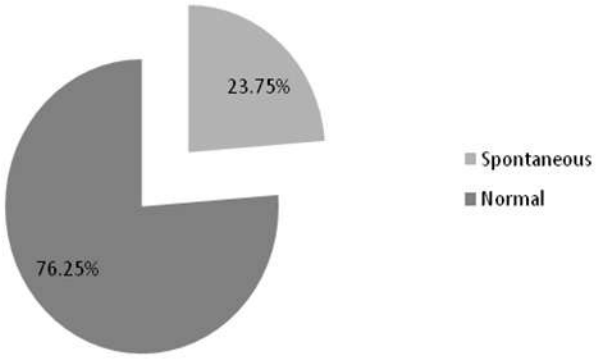

Figure 2. Distribution of subjects according spontaneous abortion

Rubella serology

Out of 400 sera from pregnant women tested for rubella IgG antibody, 367 (91.75%) were positive, 18 (4.5%) were negative and 15 (3.75%) were equivocal. The prevalence of rubella IgG antibody in relation with age of pregnant women is presented in table 2. The nine respondents in the age group of 38-42 tested positive giving prevalence of 100% while more than three quarters, 88.2%, had a positive result in the age group of 13-17 years. However, there was no statistically significant difference between age groups with respect to prevalence rates (P = 0.733).

Table 2. Seroprevalence of rubella IgG antibodies by age group and area of residence

No tested	No IgG positive	% IgG positive (95% Cl)
Age group (years)		
13-17	15	88.24
18-22	124	89.21
23-27	131	93.57
28-32	69	92.0
33-37	19	95.0
38-42	9	100.0
Area of residence		
Urban	310	91.99
Suburban	54	91.53
Semi-rural	3	75.0
total	367	91.75

In considering education, the highest prevalence of (95.5 %) was obtained in pregnant women who had primary level of education and the lowest prevalence of 90.9 % in those who had secondary education. Prevalence rates of rubella IgG antibody is presented in table 3. A higher prevalence of 91.9% was obtained in multigravid while primigravid showed a prevalence of 91.4%. There was no significant difference between the seroposotivity rates with respect to education (p=0.742) and gravidity (p=0.144). A higher number of pregnant women in the first and second trimester tested positive (91.8 % and 92.1%) while three-quaters of those in third trimester (77.8%) also had a positive result. However this difference was not statistically (p=0.628). In the case of profession, the highest prevalence of 92.1 % was obtained among housewives, 91.8 % among another employed women and student, while the lowest prevalence of 75.0 % was obtained among health-care worker women (table 3). There was not significant difference between the seropositivy rates with respect to gestational age (p=0.628) and profession (p=0.267). The sero-positivity rate was slightly higher among pregnant women residing in urban than in rural areas (92.0% vs. 75.0%) but this difference was not statistically significant (p = 0.265). The result also showed prevalence rate of 91.75 % in all non-vaccinated pregnant women. There was not vaccinated- women in our study.

DISCUSSION

To the best of our knowledge, this is the first study in Cameroon to provide rubella sero-prevalence IgG data among pregnant women attending prenatal care clinics in Yaounde. About 91.75% of the pregnant women had IgG antibodies to rubella virus. This value is similar to the 93.1% prevalence reported in Nigeria (Okikiola *et al*., 2015), 95.0% prevalence reported in Burkina Faso (Tahita *et al*., 2013) and 92.6% prevalence reported in Tanzania (Mwambe *et al*., 2014). The high overall immunity rate suggests a well-supported and continuous transmission of endemic rubella virus in the country. As a result most pregnant women had previously been exposed to the virus. The reported sero-prevalence in this study is higher than 85.8%, 77% and 53% reported from Southern Italy (Calimeri *et al*., 2012), Ouagadougou-Burkina Faso (Linguissi *et al*., 2012), Benin-Niger (Onakewhor *et al*., 2011). In addition, none of these women had previous history of vaccination of rubella virus. This high prevalence might suggest the presence of the wild type virus (WHO, 2000). The serosurvey showed that 91.75% of pregnant women in Yaounde had been exposed to rubella infection and 3.75 % had been equivocal. Based on these results only 4.5% of pregnant women in Yaounde remain susceptible to rubella. These findings are similar to those reported some 08 years earlier in a pregnant women in Public hospital in Yaounde where 187/211 (88.6%) had rubella IgG antibody, 19 (9%) were seronegative and 5 (2.4%) were found to be equivocal (Fokunang *et al*., 2010). The latter may be due to re-infection cases, the IgG is highly elevated whilst IgM may be demonstrable, giving equivocal results (Pak, 1992). For such cases, it is recommended to collect fresh samples taken within 7 to 14 days and repeat the assay in parallel (Dwyer, 2011), to confirm these equivocal cases. However, it was not possible to repeat the tests for these samples due to the time allocated for this study and also difficulties involved in scheduling another meeting with the subjects.

Prevalence based on age group showed 100% in 38-42 year old, followed by 93.6% in 23-27 year old, 89.2% in 18-22 year old and 88.2% in 13-17 year old age groups respectively (table 2). This correlates with the deduction that the percentage of immune women increase with increased maternal age (Bukbuk *et al*., 2002, Kolawole *et al*., 2014). There was no significant difference between age groups thus establishing the facts that rubella affects all age groups. This was probably due to the high endemicity of the virus in Yaounde, as it is in constant circulation. A woman's risk of acquiring the infection should expectedly increase with increasing age and parity due to the longer duration of interaction with an infectious environment, which activate the development of immunity to the virus.

Table 3. Prevalence of rubella IgG antibody by socio-demographic variables

Socio-demographic Variables	No examined	Rubella IgG positive	Rubella IgG Negative	Rubella IgG equivocal	P Value
Level of education					
Primary	24	23 (95.8)	1(4.2)	0 (0.0)	0.742
Secondary	333	303 (91.0)	16 (4.8)	14 (4.2)	
Tertiary	43	41 (95.4)	1 (2.3)	1 (2.3)	
Total	400	367 (91.75)	18 (4.5)	15 (3.75)	
Profession					
Employed women and student	257	236 (91.8)	12 (4.7)	9 (3.5)	0.267
Housewives	139	128 (92.1)	6 (4.3)	5 (3.6)	
Health-care worker	4	3 (75.00)	0 (0.0)	1 (25.0)	
Total	400	367 (91.75)	18 (4.5)	15 (3.75)	

The non-significant difference associated with the ages in this study, could also suggest that most infections were probably acquired before that age (Onakewhor *et al*., 2011). Antibodies were found in all the trimesters of pregnancy, with the highest prevalence being in the second trimester. This agrees with the work of Okikiola *et al* (2015) but contrasts with the reports of Bamgboye *et al* (2004) and Fokunang *et al* (2010), which showed the highest prevalence in pregnant women in their first trimester. The highest prevalence observed in the second trimester may have been because most of the pregnant women presented at the antenatal clinic in their fourth and fifth months of pregnancy. Prevalence recorded in multigravid was higher than this obtained in primigravid (Table 3). This is in agreement with the findings that there is an increase in the number of rubella immune women with each pregnancy outcome (Bukbuk *et al*., 2002). Then, primigravid were more susceptible to rubella and this suggests that their babies are at risk of CRS, thus agrees with the earlier study that the incidence of congenital rubella is higher in first born babies (Marsla, 1976).

There was little deviation in prevalence with regard to educational status. Despite the fact that the majority of the pregnant women were educated up to the secondary and the tertiary level, the level of awareness and knowledge of rubella and its transmission was very low among the study and control population. This low level of awareness was also seen in the study carried out by Okikiola *et al.* (2015) in Nigeria. This poses a serious problem, as knowledge of a disease and its mode of transmission is important in its prevention and control. The prevalence of 92.1% obtained in housewives in this study was congruent with another finding, which reported 95.7% prevalence in house wives and suggested this could result from living in crowded families with lower socio-economic conditions (Granjooie, 2003). A high prevalence of 75.0% obtained in this study among health care workers agrees with the findings that adduced this to chance of acquiring immunity as a result of work condition.

Although most of the pregnant women that participated in this study had living children, 91 (22.7%) reported pregnancy losses that could have occurred during organogenesis. Out of the 91 who had lost previous pregnancies, 86 (94.5%) had positive IgG antibody. This result shows that the pregnancy losses could have been a result of Rubella infections in these women. The mean antibody titre was also higher (91.9%) in women living in urban areas than in women living in rural areas (75.0%). This may relate to higher density of population leading to more widespread circulation of virus. None of the Pregnant women, had ever had prophylactic vaccination. Antenatal health-talks in Cameroon routinely do not incorporate information on Rubella infection. Vaccination against rubella is also not part of the Cameroon national or local immunization programs. Preconception counseling of women of Childbearing age about rubella is also not routine in Cameroon. General Nkowledge about rubella may thus be poor. In developed countries of North and Latin America and Europe, the goal taken in 2003, to eliminate rubella and CRS by 2010, is being pursued with vigor, after having met the goal that eliminated polio by 1991, and eradicated measles in 2000, with the introduction of the combined MMR (Measles, Mumps, Rubella) vaccination in pediatric vaccination schedules. MMR was recently introduced in Cameroon and is not free like other vaccination in pediatric vaccination schedules. In an attempt to eliminate rubella infection and prevent new cases of CRS, Brazil in September 2008, targeted adolescents and adults and vaccinated 70 million men and women across the country; one of the greatest rubella vaccination campaign in history. Unfortunately many developing countries including Cameroon is yet to learn from these experiences. None of the characteristics considered to be risk factors was a statistically signifcant predisposing factor to rubella infection. Some of the common clinical symptoms associated with rubella virus infection were observed in the pregnant women. They included mild fever and rash. This is similar to the report by Okikiola *et al* (2015). The pregnant women made complaints mostly of fever and rash. Very few of these women were, however, positive for rubella infection, suggesting that the fever and rash were due to other factors. This result shows that most of the infected patients were asymptomatic, and none of the clinical symptoms was signifcantly associated with the risk of infection.

Conclusion

In conclusion, this study presents for the first time rubella seroprevalence data for an urban and a rural setting in the central part of Cameroon. The prevalence of rubella IgG antibody among pregnant (91.75%) was high in the absence of routine vaccination suggesting a continuous transmission of endemic rubella virus in Cameroon. Based on these results, 4.5% of pregnant women in Yaounde remain susceptible to rubella; susceptible pregnant women should be thoroughly evaluated for possible rubella infection. A future study including children and adolescents of various ages would allow the identification of the most susceptible time frame of infection in Cameroon. We also strongly recommend a large follow up study of pregnant women to determine the outcome of the pregnancy and the magnitude of CRS in our settings.

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