



Sero-prevalence of IgM antibody to Rubella Virus in pregnant women in Zaria, Nigeria

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ABSTRACT

Rubella is a contagious viral infection, which in pregnant women leads to infection of a developing fetus causing fetal death or Congenital Rubella Syndrome. A cross-sectional study involving 180 women was carried out between June and August 2012 to determine the seroprevalence of IgM antibody to rubella in their serum using ELISA. The women comprised 160 pregnant women attending the ante-natal clinic of Ahmadu Bello University Teaching Hospital, Zaria and 20 non-pregnant women of childbearing age studying at Ahmadu Bello University, Zaria. Prior to sample collection, structured questionnaires were administered to gather relevant medical information, obstetrical and socio-demographic characteristics from the women. IgM antibody was detected in 62 (38.8%) of the pregnant women and 8 (40%) of the non-pregnant women. The majority (33: 53.2%) of the pregnant women who were positive were in their second trimester while 11 (17.7%) were in their first trimester. Infection with Rubella virus was not significantly associated with age, clinical symptoms and the possible risk factors studied ($p > 0.05$). The level of awareness and knowledge of rubella and its transmission was extremely low for both population and uneducated pregnant women had the highest prevalence (54.5%: 6/11). The study showed seroprevalence higher than any previous reports in Nigeria with almost equal rate amongst the two populations. The high prevalence suggests that an outbreak might have occurred during the time of the study and emphasizes the need for the initiation of a national rubella vaccination program in Nigeria.

KEY WORDS: *Seroprevalence; IgM antibody; Rubella; Pregnant women; Zaria; Nigeria*

INTRODUCTION

Rubella also known as German measles is a contagious viral infection that is caused by Rubella virus, a member of the family *Togaviridae*¹. The virus causes a mild rash-like disease that is associated with low-grade fever, lymphadenopathy and a short-lived morbilliform rash². Rubella is predominantly a childhood disease which is endemic throughout the world^{1,3-5}. In contrast to the mild infections caused in early childhood or adult life, rubella in pregnant women causes Congenital Rubella Syndrome

(CRS), which is the infection of a developing foetus following transplacental transmission of rubella virus from the mother to the foetus². Complications can occur in an unborn baby if the mother becomes infected during pregnancy, resulting in a miscarriage, stillbirth or a child born with birth defects⁶.

In the first 3 or 4 months of pregnancy, rubella infection provides opportunities during the period of maternal viremia for invasion of the placenta and subsequent fetal infection⁷. The risk to a fetus is highest in the first few weeks of pregnancy and then declines in terms of both frequency and severity, although some risks still exist in the second trimester⁸. After placental infection is established, there can be subsequent dissemination of virus to the fetus². After entry, the virus is capable of spreading widely throughout the developing fetus, and almost any organ may be infected^{2,7}. A chronic and generally non-lytic infection is then established in the fetus². In the congenitally infected fetus and infant, virus persistence occurs in the presence of neutralizing antibodies; therefore immunological tolerance does not develop⁷. Although a comprehensive vaccination program in most industrialized regions such as North America, Europe, Japan and Australia has reduced the incidence of the disease in these areas to low levels, vaccination is not carried out in many developing countries² including Nigeria. Epidemics occur every 6-10 years, with strong pandemics occurring every 20-25 years⁵. Epidemics in tropical countries usually pass unrecognized due to the lack of significant clinical symptoms in infected children².

One of the antibodies associated with rubella is the Immunoglobulin M (IgM) antibody. The IgM antibody rises and peaks 7-10 days after infection and then declines after several weeks. Therefore, the presence of IgM antibody indicates a recent

infection, reinfection or false-positive IgM^{9,10}. This study is aimed at detecting the presence of IgM antibody to Rubella virus in pregnant women in Zaria and also to compare seroprevalence between pregnant and non-pregnant women. Together with the clinical symptoms, risk factors and level of awareness assessed in the study, this study will provide information necessary for health care administrators and providers in Nigeria to initiate a nationwide rubella vaccination program.

METHODOLOGY

Study area and population

A cross-sectional study was carried out between the months of June and August 2012, in the antenatal clinic of Ahmadu Bello University Teaching Hospital (ABUTH), Shika, Zaria, Nigeria. The hospital is a referral hospital that receives patients from all over Kaduna State and some neighboring states like Zamfara, Katsina and Kano State. 160 pregnant women in different trimesters of their pregnancy and 20 non-pregnant of childbearing age took part in the study. The non-pregnant women were involved in the study in order to compare prevalence between pregnant and non-pregnant women within the same community and to determine if exposure to infection occurs more frequently before or during pregnancy and also to establish if awareness of the infection was higher in an academic environment.

Ethical approval for the study was obtained from the ethical committee of ABUTH and oral consent was obtained from both pregnant and non-pregnant women for their participation in the study. Blood samples were collected consecutively, once a week for a period of 7 weeks from the pregnant women and non-pregnant women were approached randomly within the university female hostels for a week. Prior to sample collection, structured questionnaires were administered to gather

relevant medical information, obstetrical and socio-demographic characteristics from the women.

Sample collection and processing

A total of 180 blood samples were collected from 160 pregnant women and 20 non-pregnant women of childbearing age. Three milliliters of venous blood was collected from the women using 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 2500 revolutions per minute for 5 minutes and sera separated. The sera were stored at -20°C until analyzed.

Analysis of samples

All the serum samples were analyzed for anti-rubella IgM antibody using Sandwich Enzyme Linked Immunosorbent Assay (ELISA) commercial diagnostic kit (Diagnostic Automation, Inc. Immunodiagnostics, USA). The assay was carried out according to the manufacturer's instructions. The results were read using a microplate ELISA reader (GF-M3000; B Bran Scientific & Instrument Co. England) and compared in a parallel manner with the calibrator and controls. Samples were interpreted as positive if their rubella IgM index was equal to or higher than the defined rubella IgM index, which was 1. All samples with an index of 0.90 or less were interpreted as negative and those with an index of 0.91-0.99 were equivocal.

Analysis of results

The data obtained from the questionnaires and the results of laboratory analysis were entered into Microsoft excel, analyzed using SPSS (statistical package for social sciences) version 16 and reduced to percentiles and figures. The Pearson Chi square test at 95% confidence interval and a significance level

of 0.05 (p value ≤ 0.05) was used to determine the relationships between the demographic data and prevalence rates.

RESULTS

Seroprevalence of IgM antibody

A total of 160 pregnant and 20 non-pregnant women took part in the study. Out of the 160 pregnant women, 62 (38.8%) were positive for rubella IgM antibody and 98 (61.2%) were negative. For the 20 non-pregnant women, 8 (40%) were positive for rubella IgM antibody and 12 (60%) were negative. 33 (53.2%) of the pregnant women who were positive were in their second trimester, 18 (29.0%) in their third trimester and 11 (17.7%) in their first trimester as shown in **Table 1**.

Table 1: Seroprevalence of IgM antibody to Rubella virus amongst pregnant women according to trimester of pregnancy

Trimester	Number analyzed	Number positive	Percentage Positive (%)
First	31	11	17.7
Second	82	33	53.2
Third	47	18	29.0

($\chi^2=0.220$, $df=2$, $p=0.896$)

Age distribution and reproductive characteristics

The age of the pregnant women ranged from 18 to 47 years (mean - 27.8 yrs) while that of the non-pregnant women was from 17 to 43 years (mean - 23.3 yrs) as shown in **Table 2**. More than half of the pregnant women (51.2%) were in their second trimester, with only 31 (19.4%) in their first trimester. Reproductive characteristics such as the number of term delivery, preterm delivery, life birth, still birth, spontaneous abortion, surviving children and malformed children were studied (**Table 3**). The mean of term delivery, pre-term delivery, life birth and surviving children are 2.8 (94/160, min. 1, max. 11), 1.1 (16/160, min. 1, max. 2), 2.7

(92/160, min. 1, max. 11) and 2.5 (89/160, min. 1, max. 8) respectively. 33 (20.6%), 14 (8.7%) and 4 (2.5%) of the pregnant women had history of spontaneous abortion, still birth and malformed children respectively. More than a quarter (28.1%) of the pregnant women had at least 5 children residing with them while even more (33.8%) had less than 5 children living with them. Most (103/160) of the pregnant women were educated up to the tertiary level and 78 of them were involved in occupation that involve children.

Clinical Symptoms and Awareness

Both pregnant and non-pregnant women were observed for symptoms such as fever, swollen and tender lymph nodes, rash, headache and aching joints (**Table 4**). Of the 160 pregnant women 26 (16.2%), 23 (14.4%), 5 (3.1%) and 9 (5.6%) had fever, aching joints, rash and headache at the time of the study respectively. None of them had

swollen lymph nodes at the back of their neck or behind their ears. Similarly, 1 (5%) of the non-pregnant women had rash, headache and swollen lymph nodes while 2 (10%) had fever and aching joints.

Only 20 (12.5%) and 5 (25%) of the pregnant and non-pregnant women respectively had knowledge of rubella and how it could be transmitted. 15 (9.4%) of the pregnant women claimed to have been vaccinated against rubella while none of the non-pregnant women had ever received vaccination against rubella (**Figure 1**).

Risk Factors

Because rubella is predominantly a childhood disease, situations that involve or result in having numerous children around were considered in this study as possible risk factors (**Table 5**). All the possible risk factors considered in this study were, however, not significantly associated with Rubella virus infection.

Table 2: Distribution of IgM antibody to Rubella virus amongst pregnant and non-pregnant women according to age group

Age group	Number Analyzed	Number Positive	Percentage (%)	p value
Pregnant Women				
18-22	23	10	43.5	0.113
23-27	52	21	40.4	
28-32	58	22	38	
33-37	21	4	19	
38-42	5	4	80	
43-47	1	1	100	
Non-pregnant Women				
17-19	2	2	100	0.151
20-22	7	2	28.6	
23-25	10	3	30	
Above 26	1	1	100	

*($\chi^2=8.891$, $df=5$, $p=0.113$); *pregnant women

**($\chi^2=4.549$, $df=3$, $p=0.151$); **non-pregnant women

Table 3: Seroprevalence of IgM antibody to Rubella virus amongst pregnant women according to reproductive characteristics

Reproductive characteristic	Number Analyzed	Number Positive	Percentage (%)	p value
Term delivery				
None	66	24	36.4	0.671
1-4	76	29	38.2	
5-8	15	8	53.3	
9-12	3	1	33.3	
Pre-term delivery				
None	144	56	38.9	0.914
1-4	16	6	37.5	
Spontaneous abortions				
None	127	48	37.8	0.627
1-4	33	14	42.4	
Life births				
None	68	26	38.2	0.984
1-4	73	28	38.4	
5-8	17	7	41.2	
9-12	2	1	50	
Still births				
None	146	55	37.7	0.377
1-4	13	7	53.8	
5-8	1	0	0	
Surviving children				
None	71	28	39.4	0.915
1-4	75	28	37.3	
5-8	14	6	42.9	
Malformed children				
None	157	62	39.5	0.164
1-4	3	0	0	

Table 4: Seroprevalence of IgM antibody to Rubella virus according to clinical symptoms associated with rubella

Clinical symptoms	Number Analyzed	Number positive	Percentage (%)	p value
Pregnant Women				
Mild fever				
Yes	26	10	38.5	0.974
No	134	52	38.8	
Lymphadenopathy				
Yes	0	0	0.0	
No	160	62	38.8	
Rash				
Yes	5	2	40.0	0.954
No	155	60	38.7	
Headache				
Yes	9	3	33.3	0.731
No	151	59	39.1	
Arthralgia				
Yes	23	7	30.4	0.376
No	137	55	40.1	
Non-pregnant Women				
Mild fever				
Yes	2	1	50	0.761
No	18	7	38.9	
Lymphadenopathy				
Yes	1	0	0	0.402
No	19	8	42.1	
Rash				
Yes	1	0	0	0.402
No	19	8	42.1	
Headache				
Yes	1	0	0	0.402
No	19	8	42.1	
Arthralgia				
Yes	2	1	50	0.761
No	18	7	38.9	

Table 5: Seroprevalence of IgM antibody to Rubella virus according possible risk factors

Risk Factors	Number Analyzed	Number positive	Percentage (%)	p value
Marriage type				
Polygamous	34	15	44.1	0.469
Monogamous	126	47	37.3	
Marriage order				
First	145	57	39.3	0.651
Second or more	15	5	33.3	
Occupation type				
Involving children	78	30	38.5	0.931
Not involving children	25	9	36	
Unemployed	57	23	40.4	
Husband's occupation				
Involving children	17	6	35.3	0.816
Not involving children	137	53	38.7	
Unemployed	6	3	50	
Type of housing				
Self contain	129	50	38.8	0.996
Compound house	31	12	38.7	

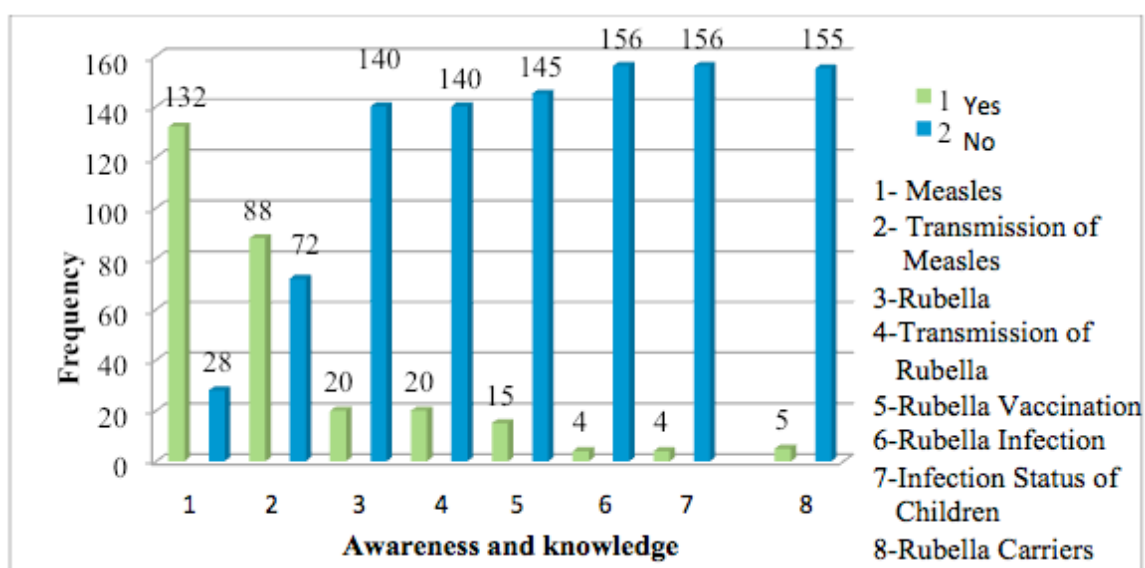


Figure 1: Level of awareness and knowledge of rubella amongst pregnant women

Analysis of the result showed that the difference observed in terms of age (pregnant women, $\chi^2=8.891$, $df=5$, $p=0.113$; non pregnant women, $\chi^2=4.549$, $df=3$, $p=0.208$) and the trimester of pregnancy ($\chi^2=0.220$, $df=2$, $p=0.896$) were not statistically significant. Similarly, the reproductive characteristics studied, socio-demographic data gathered and clinical characteristics observed were also not statistically significant for both pregnant and non-pregnant women (Tables 2 to 5).

DISCUSSION

Rubella IgM antibody was detected in 38.8% of the pregnant women and 40% of the non-pregnant women, indicating most probably that these women were infected recently. Nevertheless, the presence of anti-rubella IgM may also indicate reinfection or false positive results due to the presence of rheumatoid factors, cross-reacting IgM and infection with other viruses. Re-infection with rubella has been shown to be more frequent with vaccinated individuals than those infected naturally¹⁰ and this is less likely in this case. The use of sandwich ELISA with a specificity and sensitivity of 99.20% and 100% respectively for antibody detection in this study might also limit the possibility of false positive results.

The prevalence in both groups is similar, indicating that both pregnant and non-pregnant women are similarly at risk of Rubella virus infection. This is a cause for alarm because the fetuses of the pregnant women infected might be predisposed to Congenital Rubella Syndrome. In addition, if any of the non-pregnant women become pregnant during the time of infection, the fetuses might also be at a higher risk because the risk of congenital infection is majorly limited to the first 16 weeks of pregnancy¹¹.

The prevalence is alarmingly higher than the report of previous studies such as 0.2% in the Western region of Turkey¹², 1.1% in

Ilorin¹³, 4.2% in Makurdi, Benue State¹⁴, 6.8% in Umudike, Abia State¹⁵ and 10% in Benin City¹⁶. The high prevalence observed between two different groups of women in different areas but within the same community suggests the occurrence of an outbreak during the time of the study. This is because outbreaks have been shown to occur and go unnoticed in developing countries like Nigeria¹⁷ and rubella-induced rashes when present are often misdiagnosed. The result goes further to confirm the increased incidence of rubella in Nigeria between 2010 and 2011 where a 8-fold increase from 450 to 3691 cases was reported¹⁸. This is alarming as infected infants can serve as an important means of viral circulation as virus from congenital infections persist after birth and those with congenital infections can infect others after birth for a year or more⁸.

Pregnant women in their second trimester had the highest prevalence which contrast the results of the work carried out by Agbede *et al*¹³ and Ogbonnaya *et al*¹⁶ both of which had the highest prevalence in the first trimester. This may be due to the fact that majority of the pregnant women started seeking ante-natal care in their second trimester; as such the infection could not have been detected earlier.

Although not statistically significant, older pregnant women had the highest prevalence for the study population. For the control population, however, the highest prevalence was seen in younger women. This contrast between the age group of infection may be as a result of increased exposure of these women to the predisposing factors to the virus. A study carried out in Abia¹⁶ supports this assertion. Seroprevalence of Rubella virus insignificantly increased with parity. This may be due to the fact that increase in parity predisposes to Rubella virus infection as a result of a longer interaction with more children and an infectious environment. We

found little or no published work in Nigeria that reported the association between all the reproductive characteristics and risk factors considered in this study. However, Agbede *et al*¹³ reported that multigravidity was not a predisposing factor to rubella virus infection with primigravid women showing higher prevalence.

Generally, the socio-demographic data of the pregnant women did not vary significantly with the presence of IgM antibody. Ogonnaya *et al*¹⁶ was able to establish a higher prevalence in farmers in comparison to housewives, civil servants and traders. The highest prevalence in students may be attributed to the fact that Zaria is a town with many educational institutions. As such, many of the pregnant women are students in these educational institutions, which are mostly crowded thereby increasing their chances of being infected. The level of awareness and knowledge of rubella was low as previously reported by Mohammed *et al*¹⁹.

None of the risk factors that were studied had any association with the risk of infection. However pregnant women in polygamous homes and those whose husbands were unemployed had the highest seroprevalence. Although, pregnant women who had rashes had a higher prevalence, none of the clinical symptoms presented by the women were associated with the risk of infection. Agbede *et al*¹³ in a similar study also found none of the clinical symptoms presented by the women in their study associated with Rubella virus infection.

CONCLUSION

The high seroprevalence of IgM antibody to rubella found amongst the pregnant and non-pregnant women who were asymptomatic indicates that rubella is endemic in Zaria and that minor epidemics are occurring and going unnoticed. Many pregnant and non-pregnant women in Zaria are susceptible to the virus and if they

happen to come down with the infection during pregnancy, their fetuses might be predisposed to Congenital Rubella Syndrome. Rubella endemicity made the possible risk factors and clinical symptoms studied irrelevant. The level of awareness of Rubella virus and the infection it causes is very low and the antibodies were detected with higher frequency among pregnant women who knew about rubella. This indicates that awareness does not reduce the rate of infection, further emphasizes that vaccination remains the only means of prevention.

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