

Research Article



Seroprevalence of Rubella IgG and IgM in Pregnant Woman Attending Antenatal Clinic of State Specialist Hospital Osogbo

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Abstract | Rubella virus continues to be a threat to the health of pregnant women who can be infected within the first 20 weeks of pregnancy. It has been estimated that-, up to 85% of neonates are born with a pattern of growth restriction and major birth defects known as congenital rubella syndrome (CRS) characterized by cerebral, ophthalmic and auditory manifestations. Determination of the susceptibility levels among pregnant women as well as factors influencing their susceptibility is an important first line approach. Hence, this study aimed to determine the seroprevalence of Rubella IgG and IgM and associated likely factors influencing susceptibility levels among pregnant women accessing antenatal care at the hospital. A cross-sectional study was carried out at the State Specialist Hospital, Osogbo. Structured questionnaires were administered to one hundred and seventy-one (171) pregnant women to obtain their socio-demographic information and five (5) mL venous blood samples were collected. The sera were separated in cryovials and stored at -20°C. They were screened for rubella IgG and IgM antibodies using Enzyme Linked Immunosorbent Assay (ELISA). The statistical analysis was carried out using the SPSS version 20, the Chi square test was performed at a p-value of 0.05 significance level. Of the 171 samples evaluated, 90 (52.6%) were positive for rubella Immunoglobulin G antibody (IgG) while 12 (7%) were positive for rubella Immunoglobulin M antibody (IgM). Ten (10) (5.9%) had both rubella IgG and IgM. Pregnant women within 26–30 years had the highest IgG level (38.9%), while those < 20 years had no detectable IgG (0.0%). However, for IgM, pregnant women within 20–25 years had the highest prevalence (58.3%), while those aged 26–30 years had no detectable IgM. A statistical relationship was observed between the age and the IgM seroprevalence (p= 0.000). The infection rates appeared to increase as pregnancy advanced for both IgG and IgM. In conclusion, there was a moderately high seropositivity of rubella IgG among the study population, leaving a significant percentage of the pregnant women at risk of congenital rubella infection. Hence, increasing rubella vaccination awareness among women of reproductive age and possible inclusion into the National Programme of Immunization in Nigeria is recommended to increase immunity coverage.

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Introduction

Infectious diseases remain a major cause of maternal and child morbidity and mortality in Sub-Saharan Africa (Pegha *et al.*, 2017). Rubella infections are among the principal blood borne viral infections that are transmitted transplacentally (Silasi *et al.*, 2015). Primary and secondary of these infections in pregnant women are often inconspicuous but may result into serious fetal damage (Albanna *et al.*, 2013). Rubella virus continues to be the main risk factor of women's health and their fetuses during pregnancy (Kassa *et al.*, 2020). Pregnant mother infected within the first 20 weeks of pregnancy has a 90% chance of having a foetus with CRS (Hamborsky *et al.*, 2015). Pregnancy outcomes as a result of maternal rubella infection include spontaneous abortion, fetal infection, stillbirths or fetal growth restriction, and CRS (Silasi *et al.*, 2015). Pregnancy has been described as an immunological condition which presents multiple challenges in diagnosis, prevention and management of infectious diseases (Mor and Cardenas, 2010).

Rubella virus in the genus Rubivirus belongs to the family Togaviridae. It is enveloped and has a single stranded ribonucleic acid genome (Frey, 1994). Rubella virus causes a disease called Rubella commonly referred to as German measles. The virus enters into the nasal epithelium through inhalation, reproduces in the nasopharynx, and multiplies in the cervical lymph nodes. Virus then gains entry into the bloodstream and is disseminated to other parts of the body (Louten, 2016). The disease has an incubation period of about 12-23 days, with infectious period being about 7 days before and 7 days after the onset of rash (Silasi *et al.*, 2015). Rubella often starts with the appearance of illness, mild fever and a maculopapular rash on the same day. The rash seldomly lasts more than 3 days and it starts on the face, extends to the body and extremities (Silasi *et al.*, 2015). Rubella can also present with symptoms such as lymphadenopathy, conjunctivitis, headache and joint pains (Edlich *et al.*, 2005).

Rubella virus is endemic in Nigeria. Different studies carried out among pregnant women puts seroprevalence at 87.5% in Osogbo (Kolawole *et al.*, 2014), 63.3% in Kaduna (Gubio *et al.*, 2015), 95.4% (Onwere *et al.*, 2014), 83.3% in Maiduguri (Oyinloye *et al.*, 2014), 53.0% in Benin (Onakewhor and Chiwuzie, 2011), 18.72% IgM in Abakaliki (Ekuma

et al., 2022), 97.9% in Zaria (Amina *et al.*, 2010), 3.9% IgM in Makurdi (Pennap *et al.*, 2009).

Rubella infections are often not symptomatic with uncertain clinical diagnosis. The diagnosis of acute infection in pregnant women is usually based on serological evidence, immunologic tests such as enzyme immunoassay (EIA) and the enzyme-linked immunosorbent assay (ELISA) involving the detection of specific IgG and IgM antibodies are the prominent and most sensitive protocols for the identification of these infections (Agbede, 2011).

Materials and Methods

Study area and population

This cross-sectional study was carried out among pregnant women accessing antenatal care at the State Specialist Hospital Asubiaro, Osogbo, Osun State.

Osogbo, the capital of Osun State, is located on latitude 7°46'E and 4°34'E with a land area of about 47 Km². The landscape of Osogbo is located on a raised land, well over 500 m above the sea level and is drained by River Osun and its tributaries. Agricultural activities such as poultry, gardening, cultivation of vegetables, yam and maize, fish farming are predominant in Osogbo.

Sample size

Sample size was calculated using Fischer's formula $n = Z^2P(1-P)/d^2$ with a prevalence of 87.5% from previous studies, at 95% confidence interval. A total of one hundred and seventy-one (171) samples were used for this study.

Inclusion and exclusion criteria

All pregnant women attending antenatal care and consenting to participate in the study were sampled while Antenatal respondents reporting for repeat visits during the study period were excluded.

Sample collection and analysis

A total of 171 venous blood samples were aseptically collected from the pregnant women. The samples were centrifuged, and the serum was separated carefully from the 5 mL venous blood and stored at -20 °C in sterile screw-capped cryovials.

The samples were assayed for rubella IgG and IgM antibodies using Enzyme Linked Immunosorbent

Assay (ELISA) manufactured by Calbiotech, 1935 Cordell Ct., El Cajon, CA 92020 USA. The statistical analysis was carried out using the SPSS version 20, the Chi square test was performed at a p-value of 0.05 significance level.

Results and Discussion

A total of 171 pregnant women were enrolled in the study. The study affirm that majority of the respondents are between the ages of 26-30 years with only 1 person under 20 years and 25 people reported 36 years and above. Most of them were married (97.6%), with very few (1.8%) being single and only 1 person reported divorce. Table 1 also reveal that majority of the respondent administered (42.7%) has not given birth before (Nulliparity), 33.9% reported primiparity while 23.4% reported Multiparity. However, most of them (37.3%) are traders.

A total of 90 (52.6%) and 12 (7.0%) women were seropositive to Rubella IgG and IgM respectively (Figure 1). It can also be observed that 10 of the women were positive to both IgM and IgG antibodies. This is likely because IgG takes over as IgM declines, suggests a resolving primary infection.

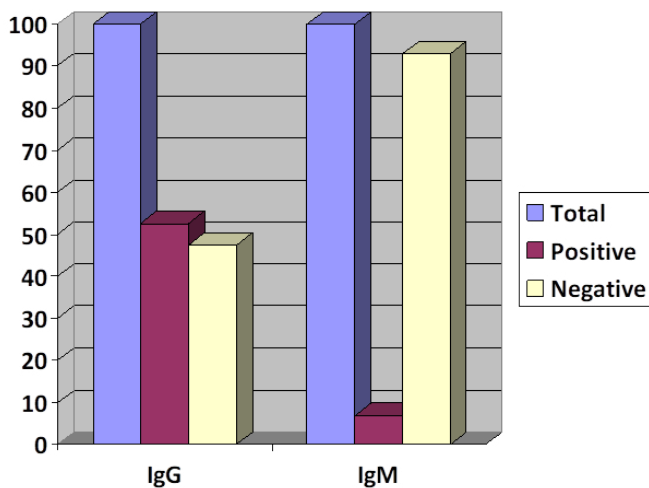


Figure 1: Overall prevalence of IgG and IgM among the pregnant woman.

Table 2: Educational background against Rubella IgG and IgM.

Educational back-ground	Total	IgG result		p value	IgM result		p value
		Positive	Negative		Positive	Negative	
Tertiary	117(68.8)	63(70.8)	54(66.7)	0.332	7(58.3)	110(69.6)	0.494
Secondary	48(28.2)	25(28.1)	23(28.4)		5(41.7)	43(27.2)	
Primary	5(2.9)	1(1.1)	4(4.9)		0(0.0)	5(3.2)	

Among the age groups, majority of the respondents who showed evidence of past infection or immunization to Rubella (38.90%) were within 26–30 age groups (Table 2). It can also be deduced that all participant between 26 to 30 age group were seronegative to Rubella IgM. There was a significant association between the proportions of seroprevalences of Rubella (IgM) among the age groups (P = 0.000). However, no significant association was observed between the Rubella (IgG) and the age distributions as reflected on Table 2.

Table 1: Socio-demographic characteristics of the pregnant women against IgG and IgM.

Variable	Frequency	IgG positive	IgM positive
Age			
Less than 20	1(0.6)	0(0.0)	1(8.3)
20 to 25	35(20.5)	22(24.4)	7(58.3)
26 to 30	72(42.1)	35(38.9)	0(0.0)
31 to 35	38(22.2)	21(23.3)	2(16.7)
36 and above	25(14.6)	12(13.3)	2(16.7)
Marital status			
Single	3(1.8)	2(1.2)	1(0.6)
Married	166(97.6)	87(51.2)	11(6.5)
Divorced	1(0.6)	0(0.0)	0(0.0)
Educational background			
Tertiary	117(68.8)	63(70.8)	7(58.3)
Secondary	48(28.2)	25(28.1)	5(41.7)
Primary	5(2.9)	1(1.1)	0(0.0)
Parity			
Nulliparity	73(42.7)	36(40.0)	5(41.7)
Primiparity	58(33.9)	32(35.6)	4(33.3)
Multiparity	40(23.4)	22(24.4)	3(25.0)
Occupation			
Civil servant	37(22.3)	22(13.3)	2(1.2)
Trader	62(37.3)	30(18.1)	6(3.6)
Self employed	22(13.3)	13(7.8)	0(0.0)
Artisan	32(19.3)	16(9.6)	2(1.2)
Others	13(7.8)	11(6.6)	2(1.2)

Table 3: Associated factors of respondents against Rubella IgG and IgM.

Variable	Total	IgG result			IgM result		
		Positive (90)	Negative (81)	P value	Positive (12)	Negative (159)	P value
History of miscarriage							
Yes	48(28.1)	26(28.9)	22(27.2)		1(8.3)	47(29.6)	
No	123(71.9)	64(71.1)	59(72.8)	0.802	11(91.7)	112(70.4)	0.115
Information/knowledge on rubella							
Yes	13(7.6)	9(10)	4(4.9)		1(8.3)	12(7.5)	
No	158(92.4)	81(90)	77(95.1)	0.212	11(91.7)	147(92.5)	0.921
Vaccination							
Yes	1(0.6)	1(1.1)	0(0.0)		0(0.0)	1(0.6)	
No	160(93.6)	84(93.3)	76(93.8)	0.628	11(91.7)	149(93.7)	0.897
Not sure	10(5.8)	5(5.6)	5(6.2)		1(8.3)	9(5.7)	
Rash during pregnancy							
Yes	13(7.6)	9(10.0)	4(4.9)		1(8.3)	12(7.5)	
No	158(92.4)	81(90)	77(95.1)	0.212	11(91.7)	147(92.5)	0.921
Ultrasound scan							
Yes	1(0.6)	1(1.1)	0(0.0)		0(0.0)	1(0.6)	
No	160(93.6)	84(93.3)	76(93.8)	0.628	11(91.7)	149(93.7)	0.897
Not sure	10(5.8)	5(5.6)	5(6.2)		1(8.3)	9(5.7)	
Overcrowding							
Yes	5(2.9)	2(40.0)	3(60.0)		1(20.0)	4(80.0)	
No	166(97.1)	88(53.0)	78(47.0)	0.757	11(6.6)	155(93.4)	0.139

Majority of participants (68.6%) reported tertiary education (Table 3). All participants that had primary education were seronegative to IgM antibodies. Most of the respondents who were seropositive to IgG (70.8%) and IgM (58.3%) of Rubella are individual with tertiary education. There were no significant association between the IgG and IgM Rubella antibodies among educational background.

In this study 52.6% seropositivity to rubella IgG was observed which is similar to the 53% reported in the seroprevalence survey among pregnant women at University of Benin Teaching Hospital in Nigeria (Oyinloye *et al.*, 2014) and 63.3% rubella seropositivity reported among pregnant women in Kaduna, Nigeria (Kolawole *et al.*, 2014). Furthermore, in this study, 7% seropositivity to rubella IgM was observed which is comparable to the reported 9.4% and 4.3% by Onakewhor and Chiwezie (2011) and Gubio *et al.* (2015), respectively. Nevertheless, this finding is in contrast with the reports of Agbede (2011) (84.8% IgG) from Ilorin, Koki *et al.* (2014) (17.4% IgM) from Kano, Oyinloye *et al.* (2014) (83.3% IgG) from Borno State and even Kolawole *et al.* (2014) (87.5%) in 2014 done in same locality- Osogbo, Osun State

in Nigeria. To the best of my knowledge, there is no known published data on IgM seroprevalence carried out in Osogbo. The disparity observed in the findings of Kolawole *et al.* (2014) (prevalence of 87.5% for IgG) and this study despite being carried out in the same locality may be as a result of the public health measures against covid-19 such as the use of facemasks and hand sanitizers, physical distancing and isolation being enforced in the year 2021 when this study was carried out as the route of transmission of rubella is via respiratory droplets. There have been reports of public health measures during covid-19 pandemic reducing the spread of other respiratory viruses (Hu *et al.*, 2021).

Notably, 10 (5.9%) of the pregnant women that participated in this study had both IgG and IgM which may be because of a resolving primary infection, the IgM is waning off at the same time the IgG is increasing in circulation. This is similar to a study that reported 5 (5.6%) pregnant women with both IgG and IgM (Obijimi *et al.*, 2013) It therefore implies that the fact that a person has IgG does not mean such a person cannot still be positive to IgM.

There is a statistical significance between the different age groups in the seroprevalence of IgM ($p= 0.000$) with more acute infections found in those less than 25 years and lower in those above. This is similar to the findings by [Gubio *et al.* \(2015\)](#), which recorded higher IgM prevalence (51.3%) in subjects between the ages of 21-25 years but is in contrast with reports by [Ekuma *et al.* \(2022\)](#) carried out in Abakaliki, Ebonyi state which reported the highest IgM prevalence (26.15%) among the 26-30 age group ([Ekuma *et al.*, 2022](#)). The non-significant difference associated with the age and rubella IgG ($p= 0.498$) observed in this study among < 35 years, could suggest that most infections were probably acquired before that age. In a study to determine the prevalence of rubella antibodies and age of exposure to rubella among 323 Yemeni schoolgirls of age 11-21 years reported 91.64% rubella IgG antibody seropositivity ([Sallam *et al.*, 2013](#)), indicating that a majority of the girls were naturally immune by age 11-21 years. It is noted in this study that rubella infection declines as the age advances (> 40 years), also in line with the findings by [Ekuma *et al.* \(2022\)](#) (0.0%). This is not unexpected because the population of women getting pregnant at that age is reduced.

The highest seroprevalence rate for IgG (38.9%) among different age groups is within the age group 25–30 years which is also similar to the findings by [Kolawole *et al.* \(2014\)](#) (34.5%) carried out in Osogbo. This is likely because this age group accounts for the largest percentage (42.1%) of participants studied; hence, it is not surprising the lack of statistical significance between the age groups despite the high percentage.

The lowest prevalence for both IgG (1.1%) and IgM (0%) is seen in those with primary level of education, this is likely a result of the fact that they account for the least proportion of study population (2.9%). The highest prevalence for IgG (70.8%) and IgM (58.3%) is found in those with tertiary level of education, as they constitute the largest proportion of study participants. This is also exemplified with the absence of a statistical significance between the different levels of education.

Women with one previous pregnancy represents the largest proportion of study population and represent the largest with seroprevalence of IgG antibodies, however, primigravida represents the

largest proportion of those with IgM, this may be because majority of respondents fall in the lower age group (<25 years) and may have recently acquired the infection and have not all seroconverted to IgG. There is however no statistical association between the number of previous pregnancies and seroprevalence to both IgG and IgM antibodies.

The largest percentage of study participants are those in the last trimester of pregnancy and not surprising to find them representing the highest group with seroprevalence to both IgG and IgM.

Conclusions and Recommendations

It can be drawn from this study that there was a moderately high seroprevalence of rubella IgG among the pregnant women that participated in this study. The seemingly lower prevalence observed in this study as compared with previous studies may indicate a high susceptibility level in women of reproductive age. This implies that quite a number of these subjects are at risk of primary infection that may lead to possible abnormalities in newborns. Also, ten (5.9%) of the pregnant women had both IgG and IgM antibodies suggesting a resolving primary infection. There was a 7% seroprevalence of rubella IgM among the study population while most of the risk factors considered were not significantly associated with the acquisition of rubella virus. However, it was observed in this study that women less than 25 years were more at risk of acute infections to rubella virus.

This study revealed a high susceptibility level of 47.4% among pregnant women which indicates a high percentage of the pregnant women are at risk of primary infection which poses a great threat to the unborn fetus and newborns, hence there is a need for increasing vaccination awareness campaigns, and the inclusion of Rubella vaccination in the National Programme of Immunization in Nigeria for children and women of child-bearing age especially the seronegative ones. However, a multicentre study with a larger sample size should be carried out so as to determine the susceptibility level in the state. Furthermore, a follow-up prospective study would be necessary to evaluate pregnancy outcome and congenital anomalies in newborns of seropositive pregnant women especially those seropositive to rubella IgM. Screening and monitoring of pregnant women less than 25 years is also recommended as

they are at risk of acute infections.

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Novelty Statement

This study determined the prevalence of both rubella IgG and IgM in pregnant women, which enabled detection of pregnant women who have been acutely infected and now seroconverting. This underscores the need for screening of women of reproductive age for Rubella infection.

Author's Contribution

BOA conceptualized the work, collected samples and wrote the manuscript.

KOA also conceptualized the work, assisted with samples collection, did statistical analysis and reviewed the manuscript.

SAO assisted with samples collection, reviewed and corrected the manuscript.

JAO and ATO assisted with samples collection, data analysis and manuscript review.

OOO supervised the work from conception to reporting.

Ethical clearance

Ethical approval was obtained from the Committee on Human Research, Publications and Ethics (CHRPE) (HREC/27/04/2015/SSHO/687) at the State Specialist Hospital Asubiaro Osogbo.

Conflict of interest

The authors have declared no conflict of interest.

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