

ORIGINAL ARTICLE

AFRICAN JOURNAL OF CLINICAL AND EXPERIMENTAL MICROBIOLOGY JULY 2016 ISBN 1595-689X VOL17 No. 3
AJCEM/1631 <http://www.ajol.info/journals/ajcem>
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AFR. J. CLN. EXPER. MICROBIOL. 17 (3): 213-218

RECENT RUBELLA INFECTION AMONG CHILDBEARING WOMEN IN A TERTIARY HOSPITAL IN NIGERIA: A SEROEPIDEMIOLOGICAL INDICATION FOR VACCINATION NEED

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ABSTRACT

Background: Congenital Rubella Infection can be prevented and future generation saved from disability by protecting women of reproductive age through vaccination. The study is aimed at determining serological evidence of recent rubella infection among women of childbearing age.

Method: A cross sectional study was carried out among 285 women aged between 15 and 49 years. Enzyme immunoassay method was used to detect and quantify human IgM and IgG antibodies with avidity for Rubella virus in sera of participants. Socio-demographic characteristics of the subjects, along with recent history of fever, rash and adverse pregnancy outcome among others were obtained using a questionnaire. Statistical analysis was carried out using the program statistical package for social sciences (SPSS) version 16.

Majority (78.3%) of the women recruited for the study were within 15-34 years age range. Of the 285 sera assayed for Rubella IgM antibodies, 23 (8.1%; 95% CI: 4.9%-11.3 %) was IgM seropositive, while the remaining 262 (91.9%) were seronegative.

A total of 7 (2.5%) of reproductive age women in Ilorin had a recent primary infection while 16 (5.6%) had a persistent Rubella infection or recent re-infection.

In conclusion, there is need for vaccination of susceptible women of reproductive age in Ilorin as a large number of women have Rubella in their reproductive age.

Keywords: Rubella, Immunoglobulin M, avidity, reproductive age, Ilorin, Nigeria

L'INFECTION DE LA RUBEOLE RECENTE LES FEMMES DE PROCREER DANS UN HOPITAL TERTIAIRE AU NIGERIA: UNE INDICATION SEROEPIDEMIOLOGIQUE POUR LA NECESSITE DE LA VACCINATION

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RESUME

Contenu : L'infection Rubéole congénitale peut être évitée et la future génération sauvée de l'invalidité en protégeant les femmes en âge de procréer par la vaccination. L'étude vise à déterminer la présence l'infection de rubéole récente chez les femmes d'âge de procréer.

Méthode : Une étude transversale a été réalisée parmi 285 femmes âgées de 15 à 49 ans. La méthode enzyme immunoassay a été utilisée pour détecter et quantifier les anticorps IgM et IgG humaines avec avidité pour le virus rubéole dans les sérums des participants. Les caractéristiques socio – démographiques des sujets, avec l'histoire récente de la fièvre, l'éruption cutanée, résultats défavorables de la grossesse entre autres choses ont été obtenus en utilisant un questionnaire. L'analyse statistique a été effectuée en utilisant le logiciel statistique pour les sciences sociales (SPSS) version 16.

La plupart des femmes (78,3%) recrutées pour l'étude ont été dans les 15 – 34 tranches d'âge. Sur les 285 sérums testés pour les anticorps IgM de la rubéole, 23 (8,1%; 95% CI : 4,9% - 11,3%) était IgM séropositive, alors que les autres 262 (91,9%) étaient séronégatives. Un totale de 7 femmes d'âge de procréer à Ilorin avaient une infection primaire récente alors que 16 (5,6%) avaient une infection de la rubéole persistante ou une ré-infection récente.

En conclusion, il est nécessaire de vacciner des femmes en âge de procréer qui ont sensibles à Ilorin comme un grand nombre de femmes a eu la rubéole leur âge de procréer.

Mots clés: Rubéole, immunoglobuline M, avidité, âge de procréer, Ilorin, Nigeria.

INTRODUCTION

Rubella is a significant cause of vaccine preventable birth defects. It is caused by *Rubella virus*, the only member of the *Rubivirus* genus of the *Togaviridae* family of RNA viruses (1). Rubella virus is spread mostly by droplets from upper respiratory tract (2). If acquired in pregnancy – especially in the first trimester - serious consequences may ensue in up to 90% of cases including miscarriage, foetal death, still birth and congenital rubella syndrome (3). Congenital Rubella Syndrome (CRS) affects virtually all organ systems and can lead to blindness, deafness, heart diseases and many others manifestations (4). Approximately the global burden of CRS is 110,000 cases annually (ranges between 14,000 and 308,000), with highest burden in the World Health Organization (WHO) South-east Asian (approximately 48%) and African (approximately 38%) regions (5). Although data on CRS in Africa are very limited and the true burden is largely unknown, the burden of the chronic disabilities from CRS is high as these disabilities incur high treatment costs thus increasing the public health importance of Rubella (6).

Rubella infections occur worldwide. The seroprevalence varies widely between countries, different parts of the same country and overtime within a particular region of a country. (7) The highest risk of CRS is found in countries with high susceptibility (low seroprevalence) rates among women of childbearing age, as presence of high circulating maternal antibody (minimum serum Rubella IgG level of 10-15 IUml⁻¹) indicates immunity to Rubella and virtually excludes the possibility of transmission of Rubella to the foetus (8).

Congenital Rubella syndrome occurrences are now rare in most developed countries, since the introduction of rubella vaccine (9). Various sero-epidemiological studies have evaluated the prevalence of rubella IgM in developing world. The rubella IgM seroprevalence among women of childbearing age is reported as 0.97% in Turkey and ranged from 5.1% to 9.6% in South African Province (10, 11) Five percent of all reported Rubella infection in Africa occur in women of reproductive age (12).

Rubella is endemic in Nigeria. Studies among women of child bearing age in Nigeria put IgM seroprevalence at 9.2% in Benin City, 3.9% and 3.26% in Markudi and Ilorin respectively (13, 14, 15). Unfortunately, routine screening of antenatal women for Rubella immunity is not available and there is no national surveillance on rubella in the country (14). Furthermore, alongside other 62 WHO

member states, Nigeria is yet to include Rubella-containing vaccines in their routine immunization programmes (16).

It has been estimated that to prevent CRS the percentage of susceptible women of child-bearing age must not exceed 5.0% (12). A recent study in this environment however put the seroprevalence of Rubella among pregnant women at 16.3% (15).

Rubella infection especially among women of reproductive age needs to be assessed with a view to ascertaining the risk of CRS. This study therefore aim to determine serological evidence of recent rubella infection among women of reproductive age, since this age group are important in determining those at risk of bearing babies with CRS.

MATERIAL AND METHODS

Study Population

All consecutive women of reproductive age (15-49 years) seen at the general out-patient department (GOPD) UIITH, Ilorin were enrolled. Patient who do not consent, pregnant women and those with history of previous Rubella immunization were excluded. Ethical clearance was obtained from the Ethics and research committee of UIITH Ilorin and informed consent was obtained from each participant

Method of data collection

Demographic and socio-economic information of participants such as age, marital status, religion, occupation, level of education and monthly family income were recorded in a questionnaire specifically designed for the study which was administered in an interview based manner.

Blood specimen collection and storage

The blood samples were collected by venepuncture under aseptic condition. The blood was allowed to clot and retract at room temperature. Sera were separated by centrifugation at 3,000 rpm for 5 minutes. The supernatant sera were aspirated into cryotubes using micropipette and stored at -20°C until analysis.

Laboratory tests

Rubella IgM, IgG and IgG-avidity were assayed for using RUB IgG (quantitative), RUB IgM (qualitative) and RUB Avidity (qualitative) kits

manufactured by Dia Pro. Diagnostic Bioprobes Srl Columella Milano, Italy (17). The tests were performed according to the manufacturer's instructions.

Interpretation of results

Rubella IgM: Any sera with values of >1.2 was considered positive for Rubella IgM antibody and values of <1.0 was considered negative for Rubella IgM antibody. Values between 1.0 and 1.2 were considered as equivocal.

Rubella IgG: Any sera with antibodies >10 WHO IUml⁻¹ were considered positive for Rubella IgG antibody and antibodies <10 WHO IUml⁻¹ were considered negative for Rubella IgG antibody.

Rubella IgG avidity test: Avidity index of > 0.4 was considered high avidity IgG antibodies and indicates past infection (> 3 months previous) or re-infection. Avidity index of < 0.4 was considered low avidity indicating a recent infection.

Data analysis

All data were entered into computer and analyzed using SPSS (Statistical Package for Social Sciences) version 16. Age of the participants was grouped into 15-24 years, 25-34 years, 35-44 years, and those above 44 years. Comparison of categorical data was done by Chi- square (χ^2) and Fisher's exact test. Results were presented in tables and figures where applicable.

RESULTS

Of the 285 subjects, only 23 participants were seropositive for Rubella specific IgM antibody. The seroprevalence of Rubella IgM antibodies was 8.1% (95% CI: 4.9%-11.3%). All the 23 participants with Rubella specific IgM antibodies also had Rubella specific IgG antibodies. Seven (2.5%) of the IgM seropositive participants had low-avidity IgG antibodies, implying recent primary infections while the remaining 16 (5.6%) had high-avidity IgG antibodies implying recent re-infections as shown in Figure I.

A breakdown of the Rubella IgM seropositive participants with respect to their age groups is shown in table I. It revealed that the age groups 35-44years had the lowest IgM seropositivity rate (5.4%). There is no significant association between age and Rubella specific IgM seropositivity (p=0.689).

As shown in table II, 49 women had a recent history of rash and fever (within the past 2 months), 3 (6.1%) of them had Rubella specific IgM antibodies. Among the remaining 236 participants with no history of fever and rash, 20 (8.5%) had Rubella specific IgM antibodies. Therefore, no significant relationship was found between recent Rubella infection and recent history of fever and rash (p=0.776).

TABLE I: STRATIFIED-AGE DISTRIBUTION OF RUBELLA IGM ANTIBODIES

Variable	Rubella IgM Positive (%)*	Negative (%)*	χ^2	p-value
Age (years)				
15-24	8(7.5)	98(92.5)		
25-34	11(9.4)	106(90.6)		
35-44	3(5.4)	53(94.6)		
>44	1(16.7)	5(83.3)	1.472	0.689

*Row percentage

TABLE II: RECENT HISTORY OF FEVER AND RASH BY RUBELLA-SPECIFIC IGM ANTIBODIES

History of fever & rash	Rubella specific IgM		OR(95%CI)	p-value**
	Positive (%)	Negative (%)		
Yes	3(6.1)	46 (93.9)		
No	20(8.5)	216(91.5)		
Total	23(8.1)	262 (91.9)	0.72(0.22-2.34)	0.776

OR- Odd ratio at 95% Confidence interval

** - Fisher exact test

Rubella specific IgM seropositivity of participants in relation to their specific occupation and level of education is presented in table III. The highest number of IgM seropositivity was observed among

students and those whose highest level of education was secondary education. There was however, no significant association between Rubella IgM seropositivity and level of education and occupation.

TABLE III: SERUM RUBELLA IGM BY SOME SOCIO-ECONOMIC VARIABLES

Variables	Rubella IgM		χ^2	p-value
	Positive (%)*	Negative (%)*		
Level of education				
None	1(100.0)	13(0.0)		
Primary	1(3.7)	26(96.3)		
Secondary	13(8.0)	149(92.0)		
Tertiary	8(9.2)	4(90.2)	1.025	0.795
Occupation				
Trading	4(5.6)	67(94.4)		
Students	12(9.2)	118(90.8)		
Civil servants	6(9.5)	57(90.5)		
Skilled labourers	1(6.3)	15(93.7)		
House wife	0(0.0)	1(100.0)		
Unemployed	0(0.0)	4(100.0)	1.494	0.914

*Row percentage

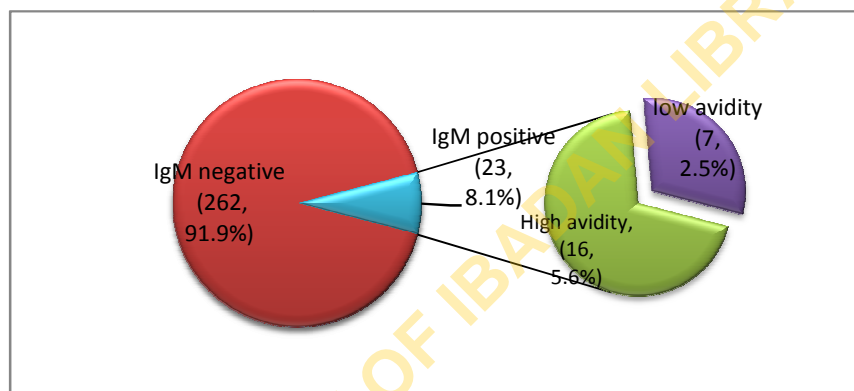


FIGURE I: SEROPREVALENCE OF RUBELLA IGM ANTIBODIES AND IGG AVIDITY AMONG IGM SEROPOSITIVE SUBJECTS

DISCUSSION

Congenital Rubella Syndrome is a devastating consequence of maternal Rubella infection during early pregnancy. Thus women of reproductive age with recent primary rubella infection could be at risk of having CRS children, if they were to be pregnant.

Detection of IgM antibody is well established as a means of diagnosing recent Rubella/CRS and is recommended by WHO as the primary test for laboratory confirmation of Rubella Infection (18).

In this study, of the 285 subjects, 23 (8.1%) were seropositive for Rubella IgM antibodies, which indicate recent Rubella infections. In Nigeria, Rubella is currently not a notifiable disease and there is no routine surveillance for Rubella, thus pattern of wild Rubella virus circulation are not known (12). Five percent of all reported Rubella infection in Africa is said to occur in women of reproductive age (12). Similar Rubella IgM seropositivity of 9.2%, 6.8% and 6.5% among women of reproductive age group were reported by

Onakewhor *et al*, Singla *et al*. and Raveenran *et al* (13, 19, 20). The 8.1% Rubella IgM seropositivity obtained in this study however differs from the 3.26% and 3.90% observed in previous study among pregnant women in Ilorin and Makurdi respectively (14, 15). The observed difference might be due to differences in study population and sample size.

Reliable serological diagnosis of rubella infections requires discrimination of specific IgM induced by primary rubella from persistent, reinfection or non-specific IgM reactivity. To distinguish participants with reinfection or persistent infection from those with primary infection, since there were no pre-screening sera available, the rubella IgG avidity were determined. Sera from cases of recent rubella primary infection have low IgG avidity, while sera taken from participants with distant infection, including cases of rubella reinfection, have higher avidity (21).

Among the 23 participants with Rubella specific IgM antibodies only 7 (2.5%) had low-avidity Rubella IgG implying recent primary infections. Of this 7 participant only 3 (42.9%) had a recent history of fever and rash which might be due to the fact that more than 50% of Rubella infection can be subclinical (8). This particular proportion of women in their reproductive age had a chance of having a child with CRS if they were to be in early stage of pregnancy.

Furthermore, because this study is hospital based, it an indication that primary Rubella infection is presented to the hospital and hospital personnel might be at risk of acquiring infections. This supports the fact that emphasis should be placed on vaccinating susceptible hospital personnel especially women.

The remaining 16 IgM seropositive participants had high-avidity Rubella IgG implying reinfection or persistent IgG in 5.6% women of reproductive age. Although reinfection poses approximately 8% risk (symptomatic reinfection may have a greater risk) of foetal infection following asymptomatic reinfection in the first 16 weeks of pregnancy, foetal malformations are rare (22). However, the distinction between reinfection and persistent Rubella infection could not be made in this study as further assay is required.

Seroprevalence of Rubella virus in different communities is notably related to age (23). In this study, the influence of age on the seroprevalence of Rubella IgM among women of reproductive age was assessed. Rubella IgM Seropositivity rate increased with increasing age, but this was not statistically significant. Studies by Dayan *et al* and Palihawadana *et al* found significant increasing seroprevalence of Rubella with increasing age (24, 25). Study by among Turkish women however, reported no significant relationship between age and Rubella seroprevalence (26).

Although fever and rash are known symptoms of rubella infections, only three (8.7%) of the 23 participants with rubella specific IgM antibody had a recent history of fever and rash. There was no significant association between Rubella IgM seropositivity and recent history of fever and rash. ($p=0.776$). This may be due to the fact that more than 50% of rubella infection may be asymptomatic

(8). However, Pennap *et al* reported significant association between rubella infection and fever and rash (14).

Seroprevalence of Rubella virus in different communities is notably related to age, and socioeconomic status (23). Socio-economic class (SEC) is an economic and sociological combined total measure of an individual based on the level of education, occupation and family income (27). In this study, the influence of highest level of education and occupation on the IgM seroprevalence of rubella among women of reproductive age was assessed.

The highest number of recent rubella infection observed among students could be due to high exposure with a wider population. The participants whose highest level of education was secondary education also recorded the highest number of recent rubella infection. This is similar to study by Eleazu *et al* (28). The rubella IgM seroprevalence however had no significant association with level of education and occupation of participants.

CONCLUSION

Prevalence of recent rubella infection among women of reproductive age in Ilorin was 8.1%. The seroprevalence of recent primary rubella infection was 2.5%. No significant association was found between age and rubella IgM seropositivity. There is therefore a need for rubella vaccination among women of childbearing age when rubella vaccination is eventually introduced in the national programme on immunization (If the WHO recommended 80% measles vaccination coverage before rubella vaccine introduction is achieved).

COMPETING INTERESTS

The authors declare that they have no competing interests.

AUTHORS' CONTRIBUTIONS

All authors participated in the study. All authors read and approved the final manuscript.

ACKNOWLEDGEMENTS

We do acknowledge the efforts of Dr. Saka Aisha, Mrs Lawal Mariam and Dr. Wahab of University of Ilorin Teaching Hospital, toward the successful completion of this work.

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