Original Article

SERO-SUSCEPTIBILITY SURVEY OF RUBELLA INFECTION AMONG WOMEN ATTENDING ANTENATAL CLINIC AT FEDERAL MEDICAL CENTRE UMUAHIA, ABIA STATE

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Abstract

Background: Rubella is a common cause of childhood rash and fever. Acute rubella infection in the sero-negative pregnant woman in early pregnancy, is associated with risk of congenital rubella syndrome. Varying incidence rates of congenital rubella syndrome worldwide has been documented. Furthermore, vaccination programs exist in advanced countries unlike in developing world. The World health organization (WHO) recommends that countries determine their rubella prevalence and accordingly make plan for immunization against rubella.

Objective: To determine the seroprevalence of rubella infection among pregnant women attending antenatal clinic at Federal Medical Centre, Umuahia.

Materials and method: Two hundred and fifty-seven (257) pregnant women attending antenatal clinic of Federal Medical Centre, Umuahia who gave consent were consecutively recruited. Structured questionnaire was used to obtain required data from participants. Venous blood samples were taken from each woman. Rubella 1gG antibodies were determined in collected samples using fully automated ELECSYS 2010. Data analysis was done using SPSS version 20 statistical package**.**

Results: The average age of the participants in this study was 30.6 ± 4.9 years. Majority of the participants were married (98.4%), 83.7% in gainful employment and 71.2% had post-secondary education. All the subjects were Christians and none had previous rubella vaccination. Out of the 257 subjects, 237 had protective rubella 1gG antibody titre, hence sero-prevalence of 92%. This study did not show any association between rubella antibodies and socio-demographic characteristics.

Conclusion: This sero-prevalence rate suggests that one in ten pregnant women is susceptible, and the foetus at risk of congenital rubella syndrome.

Key words: Sero-susceptibility, Rubella, Pregnancy.

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INTRODUCTION

Rubella, commonly known as German measles is an infection caused by the rubella virus, a positive-sense RNA virus of the Rubiviridae family. It is an acute viral communicable disease mainly of children, young adults, women of reproductive age and pregnant population. The virus is transmitted via droplet infection from the upper respiratory tract of infected person.[1,2] Following an incubation period of 14-21 days, the disease which is usually mild, self-limiting and with usually no consequences develops.[2]

Rubella infection in the non-immune pregnant woman especially within the first twenty weeks is associated with 90% chance of trans-placental transfer to the foetus.[2,3] This can result in spontaneous abortion,

intrauterine growth restriction or in-utero foetal demise.[4] Furthermore, the new born can have congenital Rubella syndrome (CRS) which is a constellation of bilateral sensorineural deafness, cataract, mental retardation, microcephaly and congenital heart defects among others.[4,5,6]

The burden of CRS is not evenly represented in most countries.[3] In the USA, approximately 20,000 cases were reported between 1964-1965 during an outbreak.[3] The cost of the treatment is estimated to be 220,000 US Dollars per case.[7] To curb this ugly trend, concerted effort was made to forestall future epidemics via widespread vaccination campaign across USA, Latin America and Europe while the year 2010 was earmarked for elimination of rubella infection and fresh cases of CRS across these regions.[3] In contrast, data from the World Health Organization (WHO) estimates more than 100,000 cases of CRS per annum in developing countries alone.[8] Many of these countries are yet to imbibe prevention and vaccination programs against rubella. In addition, where such programs exist, the immunization cover is sub-optimal. Consequently, rubella infection in pregnancy still occurs with CRS often diagnosed in the post-natal life. In 2000, a WHO position paper on rubella vaccines recommended that all countries asses her rubella prevalence and accordingly make plan for the introduction of rubella vaccine.[9]

Screening and vaccination of women and children against rubella is neither part of routine antenatal tests nor among the vaccine-preventable diseases in the National Program on Immunization (NPI) in Nigeria.[10,11] Rubella infection and CRS are also not notifiable in the country yet it is preventable. The national prevalence of Rubella in pregnancy as well as of CRS is not known. However there has been pockets of report in the last two decades from a few centres across Nigeria.[10,11] Despite all these studies, information from the southeast is scarce.

Rubella infection during the first and early second trimesters in the sero-negative is associated with deleterious foetal effects including CRS. Some antenatal women may present with rash, which may not be attributable to the infection. Furthermore, information on the prevalence of the infection in pregnant women is scarce especially in Umuahia and its environs. Nigeria is also a low resource country hence the dire need to judiciously use available scarce resources. To this end, obtaining government patronage for intervention should be evidence-based. Thus, the necessity to determine the sero-susceptibility of Rubella infection in pregnancy and the prospect of having an organized prevention program including Rubella vaccine is the justification for this study.

MATERIALS AND METHODS

Study area

The study was performed at the antenatal clinic of Federal Medical Centre (FMC), Umuahia and the serology department of MECURE diagnostic centre, Umuahia, South East Nigeria. MECURE diagnostic centre is in partnership with the Abia State Government. The Study population consisted of pregnant women who attended the antenatal clinic of the hospital who accepted on their volition to participate and were consecutively recruited. Pre-tested structured questionnaires were given to the participants and relevant data collected. The appropriate sample size was calculated using the formula below, which was suitable for cross-sectional studies with qualitative variables:

$N = Z^2 [P (1-P)]/x^2$. From the formula above, the appropriate sample size is 245. When we considered additional 10% for contingencies including participant withdrawal from the study and recording error, the sample size was 270. Approval was obtained from the Health Research Ethic Committee (HREC) of FMC Umuahia. This study was carried out over a four-month period between February and May, 2016.

About 5ml of venous blood sample was taken from the ante-cubital fossa of each participant under strict aseptic condition and were put in a plain container and left standing for at least 1-2 hours to allow for clot retraction or centrifuged at 1500 revolution per minute. The obtained sera were saved in the laboratory at 4-8^{0}C and analysed in batches within 10 days. Reagents for the analysis were ready to use and were manufactured and provided by ROCHE diagnostics. Rubella 1gG antibodies were determined in collected sera using fully automated ELECSYS 2010 (ROCHE diagnostics). The data was entered and analysed using the statistical package for social science (SPSS) version 20. Descriptive statistics which includes mean and standard deviation were used to summarize continuous numerical variables like age and 1gG level while categorical variables

were summarized using frequency and percent. The association between categorical variables was done using Chi-square testing. A P-value of <0.05 was considered statistically significant. Results were presented in tables and chart.

RESULTS

Two hundred and fifty-seven pregnant women took part in this study over a period of four months. Table 1 shows the socio-demographic characteristics of the subjects. The age range was 16-42 years, with a mean of 30.56 (± 4.86). Majority (68.5%) were between the ages of 25-34 years. Most (98.8%) were of the Ibo tribe. The participants in the urban area (51.4%) were almost equal in number to their rural counterpart (48.6%). The proportion of women seemed to decrease with increasing parity. Nulliparous subjects had 41.4% while grand multiparae made up 2.3% of cases. Most of the participants were in their second trimester (59.1%). A greater proportion was married (98.4%), public servants (42.4%) and had post-secondary education (71.2%). All were Christians and had no previous rubella vaccination.

The serum immunoglobulin G (1gG) level ranged from 0 - 512 IU/ml. The mean titre was 153.2 IU/ml (±142.2). Table 2 shows serum 1gG in the study subjects. Most of the women (92.2%) were seropositive for rubella 1gG antibodies with level greater than 10iu/ml while 7.8% were sero-negative with less than or equal to 5iu/ml. None of them had borderline assay. Figure 1 shows that the sero-prevalence of rubella 1gG antibody in this study is 92%. All those aged 19 years or below had rubella 1gG antibody (positive). The proportion was lowest among those at least 40 years old (85.7%) while other age groups had between 87.5% and 96.2% (Table 3). This was however not statistically significant (X^2 = 3.536, P=0.618).

Furthermore, we found that all the women with a parity of four or more were Rubella-IgG positive (Table 4). This difference was not found to be statistically significant (X^2=3.125, P=0.681). There was no association between rubella antibody and gestational age of the subjects in this study as shown in table 5. The number of women in 2nd and 3rd trimester were similar (92.8% vs 92.3%) while 88.9% were in their first trimester. This again showed no statistical significance (X^2=0.481, P=0.786). Among those who were positive, 92% had secondary or more level of education as shown in table 6. Statistical testing was not significant (X^2=0.204, P=0.903). The rural subset of the population sample was almost equal to the urban counterpart (92%) as highlighted on table 7. There was also no significant statistical association (X^2=0. 016, P=0.899).

Table 1: Demographic characteristics of the subjects.

	Frequency	**Percent**
Age group		
≤19	5	1.9
20- 24	16	6.2
25- 29	86	33.5
30 – 34	90	35.0
35 – 39	53	20.6
40 – 45	7	2.7
Total	**257**	**100**
Ethnic group		
Igbo	254	98.8
Esan	1	0.4
Yoruba	1	0.4
Igala	1	0.4
Total	**257**	**100**
Locality		
Urban	132	51.4
Rural	125	48.6
Total	**257**	**100**

Parity		
0	109	42.4
1	59	23.0
2	43	16.7
3	26	10.1
4	14	5.4
≥5	6	2.3
Total	**257**	**100**
Trimester		
1st semester	27	10.5
2nd semester	152	59.1
3rd trimester	78	30.4
Total	**257**	**100**
Occupation		
Public servant	109	42.4
Housewife	42	16.3
Self employed	64	24.9
Undergraduate	28	10.9
Private company	14	5.4
Total	**257**	**100**
Level of education		
Post-secondary	183	71.2
Secondary	72	28.0
Primary	2	0.8
Total	**257**	**100**
Marital Status		
Married	253	98.4
Single	4	1.6
Total	**257**	**100**

Table 2: Serum IgG levels in study subjects.

Serum 1gG level (IU/ml)	Interpretation	Number	Percentage
0.0 – 5.0	Negative	20	7.8
5.1 – 10	Borderline	0	0.0
>10	Positive	237	92.2
Total		257	100.0

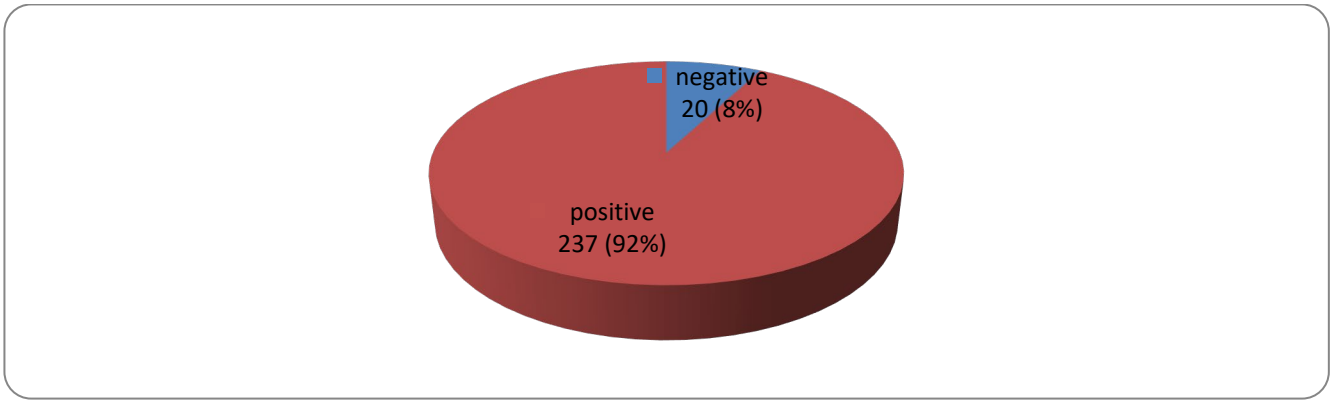

Fig 1: Proportion of seropositive and seronegative participants

Table 3: Age distribution of Rubella antibody

Age group	Immunoglobulin G		Total n (%)
	Positive n (%)	Negative n (%)	
≤19	5 (100.0)	0 (0.0)	5 (100.0)
20 – 24	14 (87.5)	2 (12.5)	16 (100.0)
25 – 29	77 (89.5)	9 (10.5)	86 (100.0)
30 – 34	84 (93.3)	6 (6.7)	90 (100.0)
35 – 39	51 (96.2)	2 (3.8)	53 (100.0)
≥40	6 (85.7)	1 (14.3)	7 (100.0)
Total	237 (92.2)	20 (7.8)	257 (100.0)

$\chi^2 = 3.536$, P = 0.618

Table 4: Parity distribution of Rubella antibody.

Parity	Immunoglobulin G		Total n (%)
	Positive n (%)	Negative n (%)	
0	98 (89.9)	11 (10.1)	109 (100.0)
1	54 (91.5)	5 (8.5)	59 (100.0)
2	41 (95.3)	2 (4.7)	43 (100.0)
3	24 (92.3)	2 (7.7)	26 (100.0)
4	14 (100.0)	0 (0.0)	14 (100.0)
≥5	6 (100.0)	0 (0.0)	6 (100.0)
Total	237 (92.2)	20 (7.8)	257 (100.0)

$\chi^2 = 3.125$, P = 0.681

Table 5: Gestational age distribution of Rubella antibody

Gestational age	Immunoglobulin G		Total n (%)
	Positive n (%)	Negative n (%)	
1st Semester	24 (88.9)	3 (11.1)	27 (100.0)
2nd Semester	141 (92.8)	11 (7.2)	152 (100.0)
3rd Trimester	72 (92.3)	6 (7.7)	78 (100.0)
Total	237 (92.2)	20 (7.8)	257 (100.0)

$\chi^2 = 0.481$, P = 0.786

Table 6: Distribution of Rubella antibody according to level of education

Level of education	Immunoglobulin G		Total n (%)
	Positive n (%)	Negative n (%)	
Post-secondary	169 (92.3)	14 (7.7)	183 (100.0)
Secondary	66 (91.7)	6 (8.3)	72 (100.0)
Primary	2 (100.0)	0 (0.0)	2 (100.0)
Total	237 (92.2)	20 (7.8)	257 (100.0)

$\chi^2 = 0.204$, P = 0.903

Table 7: Distribution of Rubella antibody according to locality.

Locality	Immunoglobulin G		Total n (%)
	Positive n (%)	Negative n (%)	
Urban	122 (92.4)	10 (7.6)	132 (100.0)
Rural	115 (92.0)	10 (8.0)	125 (100.0)
Total	237 (92.2)	20 (7.8)	257 (100.0)

$\chi^2 = 0.016$, P = 0.899

DISCUSSION

The sero-prevalence of Rubella in this study was 92%. This shows that a high proportion of the participants were positive for Rubella 1gG antibodies. This finding compares figures of 89.4%[12] and 90.6%[13] in Ibadan and Jos respectively. All were cross sectional studies. The Ibadan study recruited 273 pregnant women and assayed for only IgG rubella antibodies. The study from Jos on the other hand used 90 apparently healthy males and non-pregnant females and assayed for both 1gG and 1gM rubella antibodies. The over 95% seropositive rate documented for advanced countries that already have rubella vaccination policy[14,15,16] is also similar to the 92% documented in this study. On the contrary, the 53% and 63.3% seroprevalence reported from Benin[17] and Kaduna,[18] respectively are at variance with our finding. Although all were cross sectional studies, this disparity may be attributable to the different methods used for the detection of the rubella antibodies.

Anti-Rubella virus IgG antibody is protective for pregnant women and those of child bearing age as it guards them and their foetuses against acute rubella attack.[4,18] Immunoglobulin M (IgM) antibody denotes acute or recent infection. This study just like other Nigerian studies showed a high sero-positivity rate. Notably, none of the subjects received previous rubella vaccine. There is also lack of routine rubella immunization in the country. This indicates that all the anti-Rubella IgG positive women had natural exposure to the virus. Most local studies did not document statistically significant difference between places of abode. These observations suggest a well-supported and continuous transmission of endemic rubella virus in Umuahia and environs. A comparison of the mean serum IgG titres of women from urban and rural settings if done and found not to be significant would also suggest similar endemicity in both locations.[19]

A study in Ilesa/Ibadan[19] revealed higher prevalence of anti-Rubella IgG (95.9%) and IgM antibodies (8.1%) in women in their first and second trimesters. This was however discrepant to a study carried out in Ilorin where low rates were found (IgG: 7.0% vs IgM: 1.1%).[19] Regional differences in Rubella endemicity may probably explain these observations. Our study also recorded 8% sero-negative subjects who had no protective antibodies. These women are susceptible to this infection and also are at risk of having foetuses with CRS, should the infection occur early in pregnancy. This is in consonance with local data from Jos (9.4%).[13] It is however at variance with other studies at Ibadan (26.2%)[10] and Benin (47%).[17] However, the newer Elecsys 2010 employed in our study may also account for the discrepancy. The Ibadan study recruited smaller number of primigravid women only.

The sero-susceptibility obtained in this study is also similar to the less than 5% documented for advanced countries.[20] These countries have wide coverage of routine vaccination and the seronegative among them are likely unvaccinated immigrants. These women (non-immune) are at risk of acute Rubella infection and CRS. This is because the high rubella IgG sero-prevalence quoted in our local studies, in the absence of routine vaccination suggests endemicity.[18] They should benefit from vaccination in the postpartum period. In countries that have low Rubella susceptibility rate among women of childbearing age, it may be helpful to determine the burden of CRS.[21] If recent rubella outbreaks have taken place, then a high number of cases of CRS might have occurred.[3,8] This has been documented in the Americas and Europe.[22] Detection of rubella IgM antibodies in pregnancy suggests acute infection and potential CRS.[5] Rubella IgM antibody testing may be used for laboratory confirmation of CRS. However, this is most useful in children below 6 months.[8] The burden of CRS can also be assessed via a retrospective review of hospital

records or records of children in schools for the deaf and blind, looking out for those who meet the CRS clinical case scenario.[8,22]

Rubella vaccines (live attenuated rubella strains) were developed between 1965 and 1967.[6] Their use in the USA and other countries commenced in 1969 and thereafter.[8] However, none of the participants in our study had prior rubella vaccination as no vaccine model is currently available. The reasons may not be farfetched from lack of documentation of national burden of CRS, endemicity of Rubella virus transmission, lean resources and/or absence of political will. Where both Rubella-susceptibility among women of childbearing age and CRS burden is high, routine vaccine introduction would be a priority and vice versa. The sero-susceptible women (8%) in this study may benefit from postpartum rubella vaccination. Socio-demographic factors (age, parity, gestational age, educational level and locality) had no statistically significant association with maternal rubella IgG antibody in our study. A similar study in Ibadan documented that women living in rural areas had statistically significant higher prevalence of antibody than those in urban areas.[10] While in Maiduguri immune women increased significantly with increased maternal age ($P<0.05$),[23] However most studies did not find any association.[13,24,25]

CONCLUSION

The high sero-prevalence rate of Rubella IgG antibodies among pregnant women attending antenatal clinic at Federal Medical Centre Umuahia, in the absence of routine vaccination, suggests that the infection may be endemic. The 8% that are non-immune are at risk of CRS if the infection occurs early in pregnancy.

RECOMMENDATION

The sero-positive women should be assessed for evidence of recent infection and the burden of CRS determined while those who are sero-negative should be re-tested postpartum and if negative, offered Rubella vaccination.

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CONFLIT OF INTEREST

The authors declare that there are no conflicts of interest.

CONSENT

Written informed consent was obtained from every patient that participated in the research.

ETHICAL APPROVAL

The research work was examined and approved by the hospital research and ethics committee.

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