Sero-prevalence of rubella-specific antibodies in pregnant women attending antenatal care in Maiduguri, north-eastern Nigeria

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Abstract

Context: Rubella is a disease caused by a virus – rubella virus. Major obstetrics concerns are profound effects of the virus on developing fetuses, which may result in multiple congenital malformations. Although vaccination has reduced the incidence of rubella virus substantially; the world health organization (WHO) estimated that more than 100,000 cases of congenital rubella syndrome occur each year worldwide, most of them in developing countries. Diagnosis of rubella cannot be made on clinical grounds alone due to lack of specific symptoms or signs that are unique to the disease. Laboratory confirmation of suspected cases is done based on the detection of the presence of immunoglobulin M (IgM) during the acute illness or a significant rise in rubella – immunoglobulin G (IgG) antibody titres in the serum of previously infected individuals.

Methodology: This is a descriptive cross-sectional study conducted at the antenatal clinic of the Department of Obstetrics and Gynaecology of the University of Maiduguri Teaching Hospital (UMTH), Maiduguri, Borno State, North-Eastern Nigeria. Eligible women who presented for booking for antenatal care at the hospital were recruited. Their bio-data, educational status, and history of vaccination with measles and previous obstetrics outcomes were obtained. Five milliliters of venous blood was taken and the serum obtained from the sample was analyzed for anti-rubella IgG antibodies. The samples that were negative for IgG were tested for IgM antibodies. Data obtained analyzed using the statistical package for social science SPSS v16.0.0 (Sept 13, 2007) Inc, Illinois, USA.

Results: There were 459 pregnant women who consented and participated in the study. Their age range is 17-43 years (mean= 25.8±5.3). There were 280 (61.0%) patients who were multiparous (mean=3.5±2.1) and women with secondary education accounted for 39.4%. Four hundred twenty-one women (91.7%) women tested positive for rubella-specific IgG antibodies, and of the remaining 38 women, 6 (15.8%) were positive for IgM rubella-specific antibody. Most of the patients (98.1%) with positive IgG had serum titers in the range of 51-150U/mL. All the patients with positive IgM antibodies were followed up till birth, all the pregnancies were carried to term and none of the neonates was found to have any congenital malformation. None of the socio-demographic characteristics were found to be significantly associated with presence of IgG antibodies. Past history of abortions and congenital cataracts were significantly associated with IgG sero-positivity.

Conclusion: The sero-prevalence of anti-rubella IgG sero-positivity is high in Maiduguri and this indicates high herd immunity. The number of pregnant women requiring rubella vaccination postpartum is also large. It is recommended that inclusion of rubella vaccination in the National programme on Immunization protocol will be cost effective in the control of rubella and CRS.

Keywords: Rubella; Pregnant women; IgG; IgM; Sero-prevalence

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1. Introduction

1.1. Occurrence
Rubella has a worldwide distribution [1-8]. Following introduction of vaccination against rubella in 1969, congenital rubella syndrome has become rare in industrialized countries [3,4,7,9], due to massive immunization of children and vulnerable non-immunized women of reproductive age [2,3,7]. Outbreaks are seen commonly due to vaccine failure or missed vaccination [6,11] in children between the ages of 3-10 years [8].

Among developing countries, only a few have included rubella vaccination in their national immunization programs [3,12]. This has contributed to a higher number of non-immunized women of reproductive age [4]. The sero-positivity of rubella antibodies increases with age [7] and parity [13-15], and has been reported to be higher in rural than in urban communities [5] and in people of low socio-economic status [12].

1.2. Reservoir
Rubella is a human disease [1,7]. There is no known evidence that animals can transmit the disease or act as reservoir [7]. Although infants with CRS may shed rubella virus for an extended period, a true carrier state has not been described [7,17-19].

1.3. Transmission
Rubella is transmitted by the respiratory route via airborne transmission or droplets shed from the respiratory secretions of infected persons [2-4,11,6,17-20]. There is no evidence other agents of transmission exist [6,19]. Transmission has been successfully minimized via mass vaccination programmes [21,22]. Vertical transmission has been well documented and associated with embayopathy [2,11,12,23-26], prevention of which has been the target of vaccination against rubella [2,23,27].

1.4. Communicability
Rubella is moderately contagious [2,4,11,17-20]. The disease is most contagious during the three days (3-days disease) when the rash first appears, but the virus may continue to be shed from 7 days prior, to 5–7 days or more after rash onset [1,4,7]. Children usually recover from the infection more quickly [2,3,7] but may continue to shed large quantities of virus from body secretions [28].

1.5. The Rubella Virus (RV)
Rubella virus is an enveloped RNA virus with a single antigenic type and the only member of the Rubivirus genus [29] that does not cross-react with other members of the Togaviridae group [1]. The virus contains an RNA with 9762 nucleotides [1] and has a simple architectural structure of single stranded RNA genome enclosed by an icosahedral nucleocapsid, protected by a lipid bilayer membrane [1]. It is relatively an unstable virus inactivated by liquid solvents, trypsin, formalin, low pH, heat, and amantadine [29]. Its ectodomains –E1 and E2, are organized into extended rows of density separated by 9nM spaces on the viral surface [30]. The nucleocapsids often form a roughly spherical shell which lacks high density at its centre [1,31]. Rubella exhibits a large degree of pleomorphism [29,31,332].

Following infection with rubella, virus-induced cytopathic changes including cell detachments from monolayer and chromatin condensation occur on several cell lines [28-32]. Infected cells also exhibit acute and persistent alterations characteristic of apoptosis, including DNA fragmentation, reduced DNA content, and annexin V staining [33]. The signals involved in the RV-associated apoptosis are independent of P53 and the Bcl-2 gene family [33]. The cytopathic effects have been shown to be due to caspase-dependent apoptosis in the susceptible cells [30,32]. Infection is also associated with citron-K kinase (CK) functional perturbations and development of tetraploidy state in specific cell types [34].

Infection in adults is associated with development of acute and chronic disorder [27-30]. The acute disorders commonly seen are encephalitis and peripheral neuropathy and these are usually self limiting [30,32,35]. Acute encephalitis is seen during the viraemic period or the clinical eruption phase [32], and occurs at 1/6000 as a demyelinating disease [30]. About 80% of patients recover without sequelae [30]. The remaining will develop secondary encephalitis, postulated to be an autoimmune process and may be associated with mental retardation [29,30]. Chronic disorders following RV infection are CRS and progressive rubella panencephalitis [30].

Recently the World Health Organisation (WHO) recommended that all countries not routinely immunizing against rubella to quantify the burden of disease due to rubella and CRS and, consider universal rubella vaccination of children,
and ensure immunity of women of childbearing age [2,11]. In Nigeria like other countries in Africa, no single national study has been undertaken to study the burden of rubella, and prevalence reported has been from smaller local or regional studies, with many done in each of the other five geo-political regions of Nigeria. In North-Eastern Nigeria there had been only one study reported, and even this, is more than twenty (20) years ago, and was based on a small number of pregnant women. This study is imperative to reveal the burden of rubella from North-Eastern Nigeria.

The aim of this study is to know the current sero-prevalence of rubella antibodies in pregnant women who book for antenatal care in Maiduguri. The study will reveal the proportion of women at risk of carrying a pregnancy that could result in a child with CRS in Maiduguri. The data obtained could also be used to make an empirical evaluation of the need for the introduction of routine immunization against rubella in Maiduguri, Nigeria.

2. Material and methods

2.1. Study Design

This is a hospital based cross-sectional descriptive study conducted to determine the sero-prevalence of anti-rubella IgG and IgM antibodies in pregnant women attending the antenatal booking clinic at UMTH, Maiduguri, Borno State, Nigeria.

2.2. Study Area

The study was carried out in the department of Obstetrics and Gynaecology of UMTH. The hospital is a tertiary centre located in a densely populated area, within Maiduguri metropolis (Latitude 11.85ºN, Longitude 13.156ºE), Borno State, North-Eastern Nigeria. The hospital is a 600-bed health institution serving Adamawa, Bauchi, Borno, Gombe, Taraba and Yobe states. About 3120 patients book for antenatal care annually. There are antenatal and gynaecological wards with 32 beds each.

2.3. Subjects

The subjects of the study were recruited from the population of pregnant women attending antenatal booking clinic at the centre.

2.4. Inclusion Criteria

All pregnant women who presented for booking for antenatal care at the hospital, who consented to take part in the study, were included.

2.5. Exclusion Criteria

- All other pregnant women who declined to consent for the study were excluded.
- Women who had vaccination against rubella during childhood, as adolescents or postpartum were excluded.
- Other women with a history of positive anti-rubella antibody test were excluded.
- Women who had known rubella infection were also excluded.

2.6. Sample

2.6.1. Sampling method

Convenience sampling method was used to recruit subjects until the sample size was obtained.

2.6.2. Sample Size

The minimum sample size was obtained using the Tailor DW formula [36]:

\[
 n = \frac{z^2pq}{d^2}
\]

Where:
- \( n \) - Desired sample size (when the population is greater than 10,000)
- \( p \) - Proportion of the target population estimated to have the particular characteristics (anti-rubella antibodies). Using prevalence of 54.1% from similar previous study done at the same hospital [14].

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Standard deviation was set at 1.96 confidence level, which corresponds to 95% confidence level. 

q = 1.0 – P 

d - Degree of accuracy desired, was set at 0.05

\[
\frac{(1.96)^2 \times 0.54 \times [1 - 0.54]}{(0.05)^2} = 3.8416 \times 0.54 \times 0.46 \\
= 0.0025 \\
= 3.8416 \times 0.2484 \\
= 0.0025 \\
= 0.9543 \\
= 0.0025 \\
= 382
\]

However, the population size was less than 10,000, therefore the desired sample size nf was calculated using Kish [37] formula (since the estimated population is 3120).

nf = desired sample size when population is less than 10,000. 

n = desired sample size when population is greater than 10,000.

N= estimate of the population size which in this case is the number of women who present for booking for antenatal care in the year before the study (3120).

\[
f = \frac{n}{1 + \frac{n}{N}}
\]

\[
f = \frac{382}{1 + \frac{382}{3120}}
\]

\[
= \frac{382}{1.12}
\]

\[
= 341
\]

To allow for attrition of up to 20% the obtained value was divided by 0.80.

\[
341/0.80 = 426.25 \approx 426
\]

Therefore, a sample size of 426, which satisfied the inclusion criteria was recruited. The sample size was increased to 459 pregnant women.

2.7. Data Collection

Venous blood samples from 459 healthy pregnant women who had no history of rubella immunization were collected. Their socio-demographic variables such as age, occupation, parity, and educational level were enquired and accurately recorded on to a questionnaire. Other information enquired included the couple social class status, history of vaccination with measles if known and the client past obstetrics outcome.

The data collection questionnaires were cross-checked to make sure all the relevant information was appropriately entered.
2.7.1. Blood Specimen Collection

The aim and the nature of the study were explained to the clients and their role in the study was clarified. They were informed that they have right not to participate in the study or withdraw from it anytime they want, without consequences.

Each client that consented was requested to sit on a chair comfortably and was informed that she might experience a little discomfort during the venipuncture. The site intended for the venipuncture at the forearm was cleansed with alcohol swab, and a selected vein from the forearm was pricked with a sterile needle attached to a Vacutainer bottle and 5 ml of blood was drawn. The needle was gently withdrawn and a dry cotton was applied on to the site with a gentle pressure applied to achieve haemostasis. The entire procedure was aimed to be of minimal risk to the clients. Each needle was used only once and properly discarded after use in to a sharps container. The blood sample bottle was labeled with the patients code, date of collection and specimen type. Samples were initially kept in the refrigerator at a temperature of about 4-8 °C, until clot formation and retraction were complete. The samples were then transported to the WHO Reference Laboratory for processing and freezing.

2.7.2. Sample Processing

In the laboratory, the sample was centrifuged at 1000 revolutions per minute (rpm) for 5 minutes to separate the serum. The serum was carefully removed using a fine bore pipette to avoid extracting red cells. The serum was frozen at -800°C until use.

Sera obtained were analyzed qualitatively and quantitatively for IgG antibodies with Rubella IgG Test kit (Genesis Diagnostics Ltd, UK. Kit Code GD82, LOT No: 54730), in accordance with manufacturer guidelines. Samples that tested negative for IgG were subjected to analysis for IgM using Rubella IgM Test kits (Genesis Diagnostics Ltd, UK. Kit Code GD83, LOT No: 58907), in accordance with manufacturer guidelines.

2.8. Principle of the Test

2.8.1. IgG Test

Diluted sera (1:100) are incubated for 20 minutes to allow specific antibodies to rubella to bind to the antigen-coated wells. After washing away unbound antibodies and other serum constituents, Rubella specific IgG is detected using rabbit anti-human IgG conjugated to horseradish peroxidase. After 20 minutes incubation, unbound conjugate is removed by washing, and TMB enzyme substrate is added for 10 minutes. A blue colour develops if antibodies to rubella are present. Addition of stop solution gives a yellow colour and the optical density of controls, standard(s), and samples are measured using a microplate reader.

2.8.2. IgM Test

The test sera are diluted with the sample diluents provided in the kit. Anti-human IgG is added to the sample diluents sample to eliminate the possibility of interference by antigen-specific IgG and rheumatoid factor, if present. The diluted sera (1:100) are incubated for 20 minutes to allow specific antibodies to Rubella to bind to the antigen-coated wells. After washing away unbound antibodies and other serum constituents, Rubella specific IgM is detected using rabbit anti-human IgM conjugated to horseradish peroxidase. After 20 minutes incubation, unbound conjugate is removed by washing, and TMB enzyme substrate is added for 10 minutes. A blue colour develops if antibodies to rubella are present. Addition of stop solution gives a yellow colour and the optical density of controls, 10U/ml standard and sample are measured using a microplate reader.

2.9. Validation of Results

The results were validated using a calibration curve plotted using the ODs of the ready to use standards provided in the kit (15U/mL, 25U/mL, 100U/mL). The graph produced was used to determine the equivalent serum antibody titers of IgG in the samples.

2.10. Interpretation of Results
Test results were interpreted as ratios of the sample OD at 450nm and the Cut-Off value. Samples with IgG antibody titers <10IU/mL was diagnosed as negative; 10-14IU/mL as borderline; and 15IU/mL or more as positives. All samples that tested negative for IgG antibodies were tested for IgM antibodies, and those with IgM titers <10U/ml were interpreted as negative, while samples with titers of 10U/ml or more were interpreted as positive.

2.11. Statistical Analysis

Data recorded on the questionnaires was transferred on to a proforma developed on and then analyzed using the statistical package for social science SPSS v16.0.0 (Sept 13, 2007) Inc, Illinois, USA). Percentages Pearson’s Chi-square were calculated and a p-value <0.05 was considered statistically significant.

2.12. Ethical Approval

Institutional ethical clearance was obtained from the Ethical Committee of the hospital. Informed written consent was obtained from the subjects after the purpose and the procedure of the study had been explained, stating clearly that they could withdraw at will at any time without any consequences. All non-consenting individuals were excluded from the study. Records were kept strictly confidential with code numbers used at the registration of each participant and records were accessible only to members of the immediate research team.

3. Results

A total of 459 patients consented and their data was obtained. The socio-demographic characteristics of the patients are as shown on table 1. Their age ranges between 17-43 years with mean of 25.8±5.3 years. Those with secondary education accounted for 39.4%, and majority of the women (73.2%) were unemployed. Women with professional occupation accounted for only 1.7%. Up to 280 (61.0%) patients were multiparous (Mean=3.5±2.1).

There were 421 (91.7%) women who tested positive for rubella-specific IgG antibodies, and sero-negative women accounted for 38(8.3%). Of those negative patients, 6 women tested positive for rubella-specific IgM antibodies. IgG sero-positivity ranged between 82.4-96.7% across all age groups ($\chi^2=13.761, p=0.184$), with a gradual rise in prevalence as the age increases up to the age of 39 years, after which it decreases. Women with tertiary education had the highest proportion of IgG sero-positivity among all the other groups. Multiparous women had the highest proportion of positive IgG test. However, the differences within socio-demographic factors were not statistically significant.

Table 1 The distribution of IgG antibody by socio-demographic characteristics

<table>
<thead>
<tr>
<th>Socio-demographic factor</th>
<th>Rubella IgG Antibody</th>
<th>$\chi^2$</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive (%)</td>
<td>Negative (%)</td>
<td>Total</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15-19</td>
<td>87 (87.9)</td>
<td>12 (12.1)</td>
<td>99 (100)</td>
</tr>
<tr>
<td>20-24</td>
<td>141 (92.8)</td>
<td>11 (7.2)</td>
<td>152 (100)</td>
</tr>
<tr>
<td>25-29</td>
<td>99 (92.3)</td>
<td>6 (7.7)</td>
<td>105 (100)</td>
</tr>
<tr>
<td>30-34</td>
<td>51 (91.1)</td>
<td>5 (8.9)</td>
<td>56 (100)</td>
</tr>
<tr>
<td>35-39</td>
<td>29 (96.7)</td>
<td>1 (3.3)</td>
<td>30 (100)</td>
</tr>
<tr>
<td>≥40</td>
<td>14 (82.4)</td>
<td>3 (17.6)</td>
<td>17 (100)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>54 (94.7)</td>
<td>3 (5.3)</td>
<td>57 (100)</td>
</tr>
<tr>
<td>Primary</td>
<td>117 (90.7)</td>
<td>12 (9.3)</td>
<td>129 (100)</td>
</tr>
<tr>
<td>Secondary</td>
<td>163 (90.1)</td>
<td>18 (9.9)</td>
<td>181 (100)</td>
</tr>
<tr>
<td>Tertiary</td>
<td>54 (96.4)</td>
<td>2 (5.6)</td>
<td>56 (100)</td>
</tr>
<tr>
<td>Islamic only</td>
<td>33 (91.7)</td>
<td>3 (8.3)</td>
<td>36 (100)</td>
</tr>
</tbody>
</table>

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Among 141 patients who were immunized for measles, as shown on figure 1, 90.1% were sero-positive for rubella-specific IgG, and the corresponding figure for non-measles immunized is 96.5% ($\chi^2=5.565$, $p=0.232$). Majority of the patients (98.1%) had moderate to strong immunity with IgG serum titers ranging from 51-150U/mL. Only one patient who is a grand-multiparous woman had a serum titer above 150U/mL (see figure II).

Table 3 showed the relationship between previous obstetrics performance and IgG sero-positivity. There were 36 patients who had history of abortions of which 83.3% had positive serum IgG ($\chi^2=6.44$, $p=0.040$). Three had given birth to babies with congenital cataracts, and 2 were positive for rubella-specific IgG ($\chi^2=12.44$, $p=0.001$). Congenital deafness occurred in 3 children of the patients and all their mothers were positive for rubella IgG ($\chi^2=0.27$, $p=0.873$). Relationship between IgG sero-positivity and history of having had a child with congenital heart disease, stillbirths, or other congenital anomalies (spina bifida, limb anomalies) was not statistically significant.
Table 3 Relationship between IgG antibodies and previous obstetric performance

<table>
<thead>
<tr>
<th>Rubella IgG Antibody</th>
<th>Total</th>
<th>X²</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>Positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abortion</td>
<td>6</td>
<td>30</td>
<td>6.44</td>
</tr>
<tr>
<td>Stillbirths</td>
<td>4</td>
<td>14</td>
<td>4.88</td>
</tr>
<tr>
<td>Congenital cataracts</td>
<td>1</td>
<td>2</td>
<td>12.44</td>
</tr>
<tr>
<td>Congenital deafness</td>
<td>0</td>
<td>3</td>
<td>0.27</td>
</tr>
<tr>
<td>Mental retardation</td>
<td>0</td>
<td>2</td>
<td>0.181</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>0</td>
<td>4</td>
<td>0.364</td>
</tr>
<tr>
<td>Other congenital anomalies</td>
<td>2</td>
<td>3</td>
<td>8.80</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
<td>58</td>
<td>70</td>
</tr>
</tbody>
</table>

Figure 2 Serum IgG titres in sero-positive pregnant women

4. Discussion

The sero-prevalence of rubella-specific IgG antibodies (rubella immune) found in this study of rubella vaccine naïve pregnant women is 91.7%, which indicates that the patients have had previous infection with wild rubella virus. This demonstrate high sero-prevalence with marked increase over the prevalence of 54.1% reported in 2002 from Maiduguri [14]. The current prevalence rate compares well with those reported from Zaria (97.9%) [38] and Ibadan [39] but higher those reported from Ilorin (16.3%) [97] and Benin (53%) [13], all in Nigeria. It also compares with sero-positivity reported elsewhere [41]. Although the proportion of rubella immune pregnant women is high, the number of sero-negative women is still large. These are the group that are at risk of acquiring the infection whether during or outside pregnancy, and therefore will require rubella immunization in the post-partum period.

An IgM sero-prevalence of 15.8% was found in this study among the pregnant women who were sero-negative for IgG antibodies. This rate is higher than rates reported from Benin (10%) [13], Jos (6.8%) [41], and Makurdi (3.9%) [42], and indicates a recent infection with rubella virus, as none of the women had a history of recent vaccination. Management of these women will include counseling and close monitoring of their pregnancies. All the IgM positive pregnant women in this study presented for antenatal booking at 26-32 weeks of gestation. Infection acquired after 20 weeks of gestation has not been associated with any risks of CRS [3], but the fetuses may suffer variable degree of growth restriction, fetal death or mental retardation [43,44]. The high incidence of IgM sero-positivity could be as a result of an asymptomatic outbreaks, which occurs in a seasonal pattern, with epidemics every 5-9 years [10,12,45].
None of the socio-demographic characteristics of the population of pregnant women significantly relates to the risks of having had a previous infection with rubella in this study, as the p-values were all higher than the predetermined level of significance (p-value <0.05). Nonetheless, these findings are similar to findings from other previous studies [13-16,39,40]. This study found a decreasing prevalence after the age of 39 years, and this may result from waning immunity [46], which is commonly seen following childhood vaccination with MMR vaccine, but has also been reported to develop in women who developed immunity as a result of infection with the wild virus during childhood [46,47]. This group of women have increased risks of re-infection during pregnancy with consequent transmission of the virus to their fetuses, and a CRS rate of up to 8% [48-50].

Nulliparity although not shown to be significantly related to IgG sero-positivity in this study, has been reported to be a significant risks factor in other studies [13]. This particularly occur in countries where children immunization policies do not include rubella vaccination [28]. Other studies reported this association to be a chance finding as pregnancy is not known to be protective against rubella infection.

History of measles vaccination has not been shown to be significantly associated with the presence of rubella-specific IgG antibodies. Previous studies showing this relationship may have resulted from false positive tests due to cross-reacting specific IgG produced following infection with other non-common viruses, such as CMV, EBV, and human parvovirus B19 [51-55].

Serum IgG titers were found to be in the range of 51-150U/mL in 98.1% in this study, with only one woman having a titer of 168U/mL. These titers are lower than that reported by Adewumi et al from Ibadan, where a median titer of 165U/mL was found with a range of <10-250U/mL [39]. The titers in this study are also lower than that reported by Kaushal et al in an Indian population, where serum IgG titers were above 200U/ml in 11.11% of the study population [42]. Nevertheless, the finding in this study shows that 98.1% of the pregnant women studied had moderate to strong protection against re-infection with the wild type rubella virus. The other 1.9% have weak protection and may still benefit from rubella vaccination once made available by the Federal Government of Nigeria, as this has been shown by many studies to boost immune strength [56,57].

This study showed significant relationship between the presence of diagnostic serum IgG titers in the pregnant women studied, and a history of previous abortion (p=0.040), congenital cataracts (p=0.001), and occurrence of other congenital abnormalities (p=0.012). No significant relationship was found with previous history of stillbirth, congenital deafness, congenital heart disease, and mental retardation in this study. Previous studies have shown that infection with rubella early in pregnancy is associated with increased risk of development of CRS in the infant, and pregnancy complications such as abortions, growth restriction, and stillbirth [3,54,55]. There is no evidence that any treatment in the mother reduced the incidence of these complications [56,57].

All the IgM sero-positive pregnant women presented for antenatal booking at 26-32 weeks. Generally, after 20 weeks of gestation, acquired rubella infection in pregnancy is not associated with increased risk of CRS or malformations in the fetus [3], fetal growth restriction is the major complication during this period, particularly when the infection occurs in the third trimester [43,44]. Therefore, managing these pregnancies will involve counseling as to the development of such complications and need for intervention therein. They will also require close monitoring with frequent visits and serial sonographic evaluation. These women were counseled adequately and referred to the feto-maternal unit for growth monitoring and continued counseling.

Like in most developing countries, in Nigeria, vaccination against rubella is not part of the National Program on Immunization (NPI) protocol and neither is it part of the information given to women during antenatal health talks in ANC clinics [13]. All the women in this study had no prior knowledge of the existence of a virus called rubella, or the attendant complication it could lead to if acquired during pregnancy.

It is important and desirous to vaccinate all the sero-negative women after delivery with a potent rubella vaccine, together with their children after the first year of age. However, rubella vaccine is not available in Nigeria and attempt to procure the vaccine failed. It is generally the responsibility of the Federal Government of Nigeria to procure and distribute, and administer vaccines [13]. Until such a time when immunization against rubella is included in NPI for children and adults, getting the vaccine for those women at risks will continue to be hampered by none availability, costs of the vaccine, poverty and lack of awareness from the population. A change of pattern from the current measles vaccine to MR or MMR vaccine for all children, and monovalent rubella vaccine for selected adults will ensure high herd immunity [23,60,61] in our population, and prevent acquiring rubella in pregnancy and its related complications. The sero-negative women were educated on the existence of a rubella vaccine, although not widely available, and the need to be vaccinated.
5. Conclusion

It is concluded from the fore-going that the sero-prevalence of rubella specific antibodies has remarkably increased and the current herd immunity level is high. But, even then, the number of women (sero-negative) requiring rubella immunization in the post-partum period is still many. The number of new infection during pregnancy are higher than those previously reported by other studies. The null hypothesis is therefore rejected.

Limitation

It is a limitation of this study that IgM antibodies to other viruses such as EBV, CMV, or parvovirus B19, that could cross-react with rubella antigens were not screened. However, anti-human IgG against rheumatoid factor which is the commonest cause of false-positives was added to the serum/diluents samples to neutralize the rheumatoid factor and increase the sensitivity and specificity of the test kits.

Compliance with ethical standards

Acknowledgments

I appreciate the contribution of the nurses/midwives working in the ANC clinic for their assistance during the data collection, and the staff of Hematology Laboratory for assisting to take some of the blood samples from the patients, Dr. David Bukbuk of Microbiology Department and WHO Reference Laboratory for running the procedure of ELISA, and Mohd Ali for reading the microplate reader. I appreciate all my patients that participated in this study and those that could not participate due to the strict exclusion criteria.

Disclosure of conflict of interest

I declare that there is no conflict of interest in this study

Statement of ethical approval

Ethical approval for the study was obtained from the Human Research Ethics Committee of the University of Maiduguri Teaching Hospital. HREC No: 25052014-01.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study. (See 2.12)

References


Global Distribution of Rubella Virus

Prevalence of rubella


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