Adult Males and Females in Osogbo, Osun State, Nigeria Manifest Extremely Low Level of Rubella Virus Susceptibility: Herd Immunity Implication

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Introduction: Despite the epidemic-prone nature of rubella and absence of its vaccine in routine immunization in Nigeria, there have been no reported cases of rubella outbreak in Osogbo, capital city of Osun State. We therefore hypothesized that susceptibility to rubella viral infection was low among males and females attending LAUTECH Teaching Hospital, Osogbo.

Methodology: To verify this, 89 sera of consecutively selected consenting males and females in the General-Out-Patient Department of LAUTECH Teaching Hospital were tested for presence of protective level of anti-rubella virus IgG antibody using ELISA. Relevant socio-demographic/clinical data were obtained with interviewer-administered questionnaires. The serologic results were analyzed vis-à-vis the participants’ data.

Results: The 89 participants were aged 3–85 years (mean age: 39.4 years) with 38.2% as males (mean age: 36.3 years). Overall rubella virus IgG seropositivity was 97.8%. Consequently, the rubella viral infection susceptibility rate was 2.2%, with group-specific susceptibility ranging from 0.0% to 4.2%. The susceptibility for males and females were 2.9% and 1.8% respectively. None of the participants’ variables was statistically associated with the susceptibility; this was mainly due to zero susceptibility of most groups of the participants. The 11 pregnant women and the 7 participants reporting skin rash had zero susceptibility to rubella.

Conclusion: The study concludes that males, as well as females, had very low level of susceptibility suggestive of herd immunity against the virus which apparently was responsible for absence of rubella outbreaks in Osogbo, Osun State. As the high positivity rate indicated rubella endemcity, we recommend inclusion of rubella virus-containing immunization in national routine immunization for children and young adults, as well as, public enlightenment regarding rubella in Osogbo, Osun State.

Keywords: rubella virus IgG, low susceptibility, herd immunity, male gender, Osogbo
1.0 INTRODUCTION

Rubella is a self-limiting, mild viral infection primarily of childhood but can affect adolescents/young adults and it is typically characterized by fever and skin rash [1,2]. It is caused by Rubella virus (RV), an enveloped virus with positive sense single stranded RNA genome belonging to the Genus Rubivirus in the family Togaviridae [3]. The virus is spread from infected to susceptible humans via respiratory droplets and direct contact [1]. It replicates in the throat of infected humans for about 2 to 3 weeks, and by the second week the viraemia is at the peak in the infected. About two-third of infected humans will show clinical rubella with signs like fever, lymphadenopathy, skin rash, arthralgia and arthritis [4]. In pregnant women with viraemic rubella infection, it infects the placenta and the developing fetus [5]. Rubella infection is usually devastating to the developing fetus when a woman contracts the virus in the first trimester of pregnancy. The viral replication causes lesions in the key organs resulting in a condition known as congenital rubella syndrome (CRS) typified by cataract, deafness, heart disease and mental retardation [5]. In immunocompetent humans however, the viraemic infection induces specific humoral immune response with appearance of RV-specific IgM and later IgG; while the presence of the former correlates with acute or ongoing infection [6], the latter correlates with previous rubella infection and resistance or immunity against same, otherwise a given individual is susceptible to rubella virus infection [5]. Therefore, absence of detectable rubella virus IgG in human’s blood is a marker of susceptibility to rubella viral infection.

Rubella is contagious and humans (males and females) are the only host or reservoir of the virus [1]. However, the devastating nature of the disease to the developing human fetus in infected pregnant women in the first trimester of gestation necessitated vaccine development. With the development of cell culture and RV isolation, effective live attenuated rubella vaccine was eventually developed. The vaccine induces protective immune response in vaccinees which is almost life-long thereby making rubella a vaccine-preventable disease [1]. The effectiveness of the vaccine and adequate vaccination coverage had led to regional elimination of rubella in some developed and developing countries [1,3]. The vaccine was able to achieve regional elimination due, in part, to herd immunity – which indirectly protects the few unvaccinated individuals by the 80.0% to 94.0% vaccinated (and immunologically protected) persons that obstruct successful transmission of rubella virus among members of a given community [7-9]. The herd immunity, described as the goal of vaccination, actually forestalls rubella outbreak when it is achieved [10]. Since the virus is especially significant in women of child-bearing age, research is somewhat biased at studying females for protective level of IgG and proportion having such antibody [11]. And knowing that, only on request would male (as well as female) children be vaccinated in Nigeria and that adult males do not go for ante-natal care where occasional testing of RV antibody or repeat of rubella vaccination is possible; it is worthwhile to include various age groups, especially adult males in seroepidemiologic study of rubella to monitor immunity to the virus. This study was therefore undertaken to assess level of serologic immunity and by extension susceptibility of males and females attending a tertiary health care facility in Osogbo (capital city of Osun State, Nigeria) to rubella infection. This is with the view to identifying proportion of susceptible males from whom susceptible women of child-bearing age may contract RV.

2.0 METHODOLOGY

2.1 Study area and Participants

The study participants were males and females attending Ladoke Akintola University of Technology (LAUTECH) Teaching Hospital, Osogbo, Osun State, Nigeria. The hospital is a tertiary health facility that provides medical care to people of the state and neighboring states (Oyo, Ondo, Ekiti, Kwara and Ogun).

2.2 Study Design

This is a descriptive, point-prevalence study that was health care facility-based. Rationale for choosing the hospital as study location is that many residents (more likely representative of residents of the city or the State) attend the hospital for medical care. Ethical approval to conduct the study was obtained from health Research Ethics Committee, College of Health Sciences, UNIOSUN, Osogbo. The essence and protocols of the study were explained to attendees at the general outpatient Department and only consenting individuals were consecutively enrolled in the study. Relevant socio-demographic/clinical data were obtained from each participant using interviewer-administered questionnaire form.

2.3 Blood Sample Collection and Serology

About 5 ml blood sample was aseptically obtained by venepuncture from the participants. Serum prepared from each blood sample was appropriately labeled and stored at -20°C in Microbiology laboratory, UNIOSUN until serologic analysis. The sera were tested for presence of rubella virus-specific IgG using ELISA kit (Dia. Pro.,
Milano, Italy) according to the kit manufacturer's instructions. The ELISA was conducted with automated ELISA washer and reader (Skanit® Thermoscientific), and results interpreted according to the kit instructions thus: Any sample with > 10 WHO IU/ml was considered positive for anti-rubella virus IgG and the corresponding participant regarded immunologically protected against rubella virus infection [12].

2.4 Data Analysis

Results obtained are presented with descriptive statistics (absolute figures, means and proportions). Inferential statistics to establish association or absence thereof between variables was done with student's t test, ANOVA, CHI square test and binary logistic regression analysis. The analyses were done in a two-tailed hypothesis using p value of ≤ 0.05 as indicator of statistical association/significance. SPSS 16.0 for Windows was used for the analyses.

3.0 RESULTS

A total of 89 participants (all from Osogbo) were studied; they were aged 3-85 years (yrs) (mean age: 39.4 yrs). They were categorized into 3 age-groups as shown in Table 1, the participants in the 19-50 yrs predominated with 64.0%. The mean age of the 3-18 (9.0%), 19-50 (64.0%) and 51-85 yrs (27.0%) were 10.8, 34.6 and 60.3 yrs respectively; these means were significantly different (p=0.001). The participants comprised 34 males and 55 females with mean age of 36.3 and 41.3 yrs respectively; these mean ages were statistically comparable (p=0.16).

Most of the participants had tertiary education; were married and without knowledge of rubella. Eleven of them were pregnant while only 7 self-reported having skin rash during sampling (Table 1). The proportion of samples with detectable anti-rubella virus IgG antibody was 97.8%; this means 2.2% of the participants had no detectable anti-rubella virus IgG antibody (i.e. < 10 WHO IU/ml of the antibody). It is noteworthy that the 2 participants negative for rubella virus antibody were aged 35.0 and 75.0 yrs, respectively male and female (not pregnant). Table 1 shows that the group-specific susceptibility to rubella virus infection among the participants ranged from 0.0% to 4.2%. The level of susceptibility of both the males and females were generally very low; though the susceptibility rate of the male participants was slightly higher, both groups were statistically comparable in susceptibility (p=0.73).

With regards to being pregnant, 44 females reported “no” to this variable; the remaining 11 women were pregnant (24-44 yrs; mean age: 31.4 yrs). Susceptibility of the latter was 0.0% and statistically comparable (p=0.61) to that of non-pregnant females, Table 1.

Seven participants reported having skin rash during sampling, while 80 reported “no”; the latter recorded susceptibility rate of 2.5%, Table 1.

Table 1: Group-Specific Seronegativity/Susceptibility to Rubella among Male and Female Participants in LAUTECH Teaching Hospital, Osogbo

<table>
<thead>
<tr>
<th>Variables</th>
<th>No Tested</th>
<th>No of Seronegative/Susceptible (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-18</td>
<td>8</td>
<td>0 (0)</td>
<td></td>
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<tr>
<td>19-50</td>
<td>57</td>
<td>1 (1.8)</td>
<td></td>
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<tr>
<td>51-85</td>
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<td>1 (4.2)</td>
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<td>Gender</td>
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<td></td>
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<tr>
<td>male</td>
<td>34</td>
<td>1 (2.9)</td>
<td></td>
</tr>
<tr>
<td>female</td>
<td>55</td>
<td>1 (1.8)</td>
<td>0.73</td>
</tr>
<tr>
<td>Educational status</td>
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<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>primary</td>
<td>6</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>secondary</td>
<td>20</td>
<td>0 (0)</td>
<td>Invalid</td>
</tr>
<tr>
<td>tertiary</td>
<td>57</td>
<td>2 (3.5)</td>
<td></td>
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<tr>
<td>Marital status</td>
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</tr>
<tr>
<td>married</td>
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<td></td>
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<tr>
<td>single</td>
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<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>widow</td>
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<td>Pregnant</td>
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<td></td>
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<tr>
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<td>11</td>
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<td>0.61</td>
</tr>
<tr>
<td>no</td>
<td>44</td>
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<td>Knowledge of rubella</td>
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<tr>
<td>yes</td>
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<td></td>
</tr>
<tr>
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<tr>
<td>no response</td>
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<tr>
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<td></td>
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<tr>
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<td>no response</td>
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</table>

#: Invalid statistical analysis was due to near 0.0% or 0.0% seronegativity rate.

4.0 Discussion

This study was undertaken to report susceptibility to rubella viral infection among males and females attending General-Out-Patient Department of LAUTECH Teaching Hospital, Osogbo. This is with the view to ascertaining, in part, the more likely reason for absence of report of rubella outbreak in Osogbo, Osun State, in spite of the fact that rubella is epidemic-prone and non-
inclusion of its vaccine in routine childhood immunization in Nigeria. The recent outbreak of rubella in two local government areas (Ipookia and Yewa North) in Ogun State, Nigeria corroborate the epidemic nature of the virus (www.afro.who.int/node/979).

The manufacturer of ELISA kit used in this study and few studies stipulate that presence in blood of an individual of anti-rubella virus IgG antibody of > 10 WHO IU/ml protects such against rubella viral infection [12, 13]. In the same vein, herd immunity against a given infection indicates community protection against such infection, and in this wise against rubella [7-9, 14]. In this study, detectable and protective level of rubella virus IgG antibody was observed among 97.8% of the study participants with group-specific rubella susceptibility of 0.0% to 4.2%. The herd immunity threshold for rubella has been variously reported to be between 80.0% and 94.0% in countries with high rubella virus transmission [7-9, 15], this implies that with such very low rubella susceptibility (or high level of protection), extrapolating this to the city of Osogbo, would mean there was epidemiological interruption of sustainable transmission of the virus among the population (i.e. suggestive of rubella herd immunity). In addition, such high antibody positivity in an environment where routine rubella vaccination is absent suggests natural exposure of the people to rubella virus; and implies that Nigeria still remains endemic to the virus. A study earlier reported endemicity of Nigeria for rubella virus [16]. The high rate of positivity observed in this study agrees with the observation that urban dwellers show higher rate of immune response to rubella virus which reflects natural infection rather than rubella immunization as Nigeria has no rubella vaccination policy [17]. In addition, report has it that by 15 years of age, most Nigerian children have immunity to rubella due to natural infection [18, 19]; this might explain the very low susceptibility rate among the study participants.

It has been observed that women of child-bearing age usually contract the virus from infected males; in congruence with this, a high proportion of young male adults were reportedly infected in Poland [20]. In this study, males with immunological protection against rubella virus recorded 97.1% prevalence rate. In a rubella-endemic country like Nigeria where rubella is not included in routine immunization, this observation corroborates natural rubella viral infection of most of the males. Therefore, vaccination of identified susceptible males against rubella is suggested to reduce or eliminate human reservoirs of rubella virus as once observed [21].

It was observed that only 2 individuals were seronegative for protective levels of rubella virus IgG; one of these was a female of 75 yrs old who had passed child-bearing age and probably had had her rubella virus IgG decayed to undetectable level. In this study, we observed no significant difference (p=0.73) between seronegativity of males and females regarding rubella virus IgG as observed in a similar study with large sample size of Tanzanian children and adolescents, though the study participants, unlike ours, spanned a large age range [22].

With regard to pregnancy, the 11 women that reported being pregnant had zero susceptibility to rubella viral infection. This implied protection of the developing fetus against rubella and its attendant congenital rubella syndrome (CRS); this is in agreement with observation of Saito et al. [10] that elevating herd immunity level against rubella is essential to prevent CRS. A study [23] observed that rubella susceptibility among 422 pregnant women in two public hospitals in Hawassa City, Southern Ethiopia was 13.7% (higher than ours); a possible reason for the higher rate compared to ours might be low number of pregnant women in our study. In the same study, [23] observed highest and higher rubella susceptibility among widowed/divorced and singles respectively; we reported zero susceptibility for both categories. Our small sample size however, requires caution in interpreting our findings.

The observation that all the 7 participants with report of skin rash had zero susceptibility to rubella virus might imply recent transition from rubella virus IgM (with skin rash) to rubella virus IgG [24]. These were not likely infectious to in-contact susceptible as the virus usually spreads 7 days before and about 5-7 days after rubella virus-induced rash [25, 26]. It is also possible they were incubating other rash-inducing viral infections like chickenpox, erythema infectiosum, roseola infactum, enteroviral infections or a drug rash [25, 27].

In conclusion, the very low level of susceptibility to rubella viral infection was apparently due to natural infection at childhood or later age as there is no prevention or routine vaccination policy to reduce rubella in Nigeria [2]. The rubella herd immunity therefore was responsible for absence of report of rubella outbreak in Osogbo in spite of epidemic-prone nature of the disease. Adequate and wide-coverage routine rubella virus-containing vaccination is suggested for children and young adults in Osogbo (and Nigeria) to sustain the rubella virus herd immunity and to swing with WHO plan for rubella elimination by 2020 [28]. A way of achieving this plan is by integration of rubella
surveillance with measles surveillance and investigation of pregnant women either eposed to or with suspected rubella [28].

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Conflict of interest

The authors declare that there is no conflict of interest

Authors’ Contributions

MAA collected samples, performed ELISA, read and revised the manuscript; WFA conceived and designed the study, analyse data, wrote the the manuscript. All authors approved the final version of the manuscript

References