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Seroprevalence of Rubella Virus Infection among Pregnant Women Attending Some Antenatal Clinics in Jigawa State – Nigeria

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Rubella, caused by the rubella virus, is an acute infectious disease posing a significant global public health challenge, particularly in developing nations where it annually results in 100,000 cases of congenital rubella syndrome (CRS). Despite its impact, there is limited data on rubella virus infection in the study area. This study aimed to assess the seroprevalence and molecular detection of the rubella virus among pregnant women attending some antenatal clinics in Jigawa State. The study, conducted as a cross-sectional, hospital-based analysis, involved 170 pregnant women. Socio-demographic information and risk factors were collected using a structured questionnaire. Blood samples were tested for Rubella virus IgG and IgM antibodies using enzyme-linked immunosorbent assay (ELISA). Data analysis was performed using SPSS version 20.0 for Windows. The study revealed an overall rubella IgM prevalence of 24.1% and a 94.7% prevalence of rubella IgG antibodies among the participants. The result of the study showed no statistical relationship between Rubella virus infection and socio-demographic parameters and risk factors. However, a relationship was observed between rubella virus infection and white blood cell (WBC) count, while no relationship was found with packed cell volume (PCV) and haemoglobin levels. The high prevalence of rubella virus among pregnant women underscores the importance of public awareness campaigns for prevention and control strategies to mitigate the disease's impact on morbidity and mortality.

Keywords: Rubella Virus, Antibodies, Seroprevalence, Pregnant Women, Jigawa State

1. Introduction

Rubella is a vaccine-preventable viral illness of the skin and lymph nodes that frequently results in minor rashes. It is also known as German measles or 3-day measles (Adewumi et al., 2013). One of the biggest global public health concerns is rubella virus infection, especially in developing countries where it can cause a variety of birth defects with grave health consequences (Remington et al., 2010).

The virus is transmitted via the respiratory route and replicates in the nasopharynx and regional lymph nodes from where it spreads to other parts of the body through the blood (Koki et al., 2014). It has an incubation period of 2-3weeks (Plotkin, 2021). The virus exhibits an acute febrile illness which is marked by a distinct macular rash, enlargement of the cervical posterior, cervical lymph node and lymphadenopathy that affects children and young adults (Olajide et al., 2015). 50% of Rubella virus infections in pregnant women and non-immunized members of the general population are subclinical, according to reports (Vueba, 2022). Rubella was formerly believed to only harm children, but it has now been shown that it may infect people of all ages and genders (Kolawaole and Adekeye, 2017).

While primary rubella infections during the first trimester of pregnancy have a high teratogenicity, leading to severe consequences, including birth defects, known as congenital rubella syndrome (CRS), which may occur in 80–85% of cases, postnatal rubella virus infection is typically mild and self-limited (Mawson and Croft, 2019). Congenital rubella infection (CRI) is the result of infection of many organ systems, including the heart, brain, endocrine system, eyes, and ears (Gubio et al., 2017). Early pregnancy acute infections have the potential to kill the fetus (Agbede et al., 2011).

Although there is no known cure for rubella, it can be prevented with a single dose of the MMR vaccination, which is more than 95% effective when administered in conjunction with the measles and mumps vaccines (Olajide et al., 2015). Over 100,000 babies worldwide are thought to be born with congenital rubella syndrome each year, despite the fact that there is a safe and effective vaccination to prevent the disease (Oyinloye et al., 2014; Priyanka et al., 2017).

Seroprevalence of rubella antibodies has been recorded in developed countries such as Europe and the United States and also in many developing countries including Africa, India, Middle and Far East, Jamaica, Malaysia, Panama, Sri Lanka (Isa et al., 2013). Before the vaccine to Rubella was introduced, sentinel studies have placed the incidence of rubella on a seasonal distribution, with an average of 5-9 years epidemic pattern that is highly variable in both developed and developing countries, mostly affecting children 5-9 years old (Isa et al., 2013; Yahaya et al., 2015). Approximately 80% of children have been found to be positive for rubella antibodies by the age of 10 years in some African countries. The prevalence of rubella antibody has been found to be 92% among pregnant women in Ghana (Kolawaole and Adekeye, 2017). A prevalence of 6.84% of anti-rubella IgM was recorded in Abia state, (Yahaya et al., 2015), 17.4% in Kano (Koki et al., 2014) and 16.3% in Ilorin (Agbede et al., 2011), South Eastern, Northern and Western Nigeria respectively with asynchronous epidemics (Agbede et al., 2011).

Two specific antibodies are associated with rubella. The first to appear is Immunoglobulin M (IgM), which rises and peaks 7–10 days after infection and then reduces after several weeks. Immunoglobulin G (IgG) develops more slowly, but remains positive for life, hence conferring immunity against repeated infection. Therefore, the presence of IgM indicates a recent infection, while IgG indicates an old infection and immunity (Olajide et al., 2015).

2. MATERIALS AND METHOD

A. Study Design and Study Area

The study was a descriptive, cross sectional and hospital based study providing valuable insights into the prevalence of Rubella Virus infection among pregnant women attending some antenatal clinics in Jigawa State, contributing to our understanding of the epidemiology of the infection in the State. The research was aimed to cover different parts of Jigawa State by selecting one facility from each Senatorial District. Hadejia General Hospital represents Jigawa Northeast, Ringim General Hospital represents Jigawa Northwest and Dutse General Hospital represents Jigawa Southeast. This ensures a geographical spread across the State. These facilities were selected because the general hospitals are strategically located within their respective local government and served as a large catchment area that attracts a significant number of patients seeking medical care including pregnant women seeking antenatal care. This ensured a sufficient sample size for the research and increased the likely hood of obtaining representative data. Also the facilities that were used in this study have the necessary equipment and trained medical staff ensuring the quality and reliability of the data collected.

B. Study Population and Ethical Consideration

The study was carried out among 170 pregnant women attending some antenatal clinics in Jigawa State and the ethical clearance was obtained from the Ministry of Health Jigawa State with reference number MOH/SEC/I.S/638/V1 in order to have access to collect samples from the pregnant women. Informed consent was obtained from all pregnant women that were willing to participate in the study.

C. Sample Collection and processing

Prior to sample collection, data of each patient was collected using a structured questionnaire after obtaining their consent. The questionnaire had the following components: Socio-demographic data, gestational age, history of congenital malformation in previous pregnancies, history of still birth, history of vaccination with rubella vaccine, history of maternal rubella in the past. Five milliliter (5ml) of whole blood was aseptically collected from consenting pregnant women by venipuncture and transferred into a clean dry container. Serum was obtained by centrifuging at 3000 revolution per minutes for 10 minutes. Sera were kept frozen at -20^0C until analysis.

D. Sample Analysis

The serum samples was analyzed using Enzyme-Linked Immunosorbent Assay (ELISA) kits obtained from CALBIOTECH, to check for the presence of IgG and IgM antibodies to rubella virus respectively. It was carried out at Rasheed Shakoni Teaching Hospital Laboratory. The assay was carried out according to the manufacturer's instructions. The results were read in a micro-well reader and compared in a parallel manner with calibrators and controls. For rubella specific IgG and IgM antibodies the qualitative result was interpreted as, positive if the rubella IgG and or IgM index was >1.1, negative when the index was <0.9, and equivocal when the index was 0.9 – 1.1.

E. Statistical Analysis

All data generated were entered into Microsoft Excel spreadsheet and was analyzed using statistical package for social science (SPSS) version 20.0. The values were expressed as percentage. Chi-square test at 95% confidence interval and significance level of 0.05 was employed to determine the relationships between the data collected and prevalence rate. Results were presented in tables.

3. RESULTS

A total of 170 pregnant women participated in this study. They were recruited from antenatal clinics in 3 facilities in 3 Senatorial districts of Jigawa State in April 2022. During the course of the study, samples from Hadejia, Ringim and Dutse were collected, using General Hospital Hadejia, General Hospital Ringim and General Hospital Dutse as focal health facilities.

The results of the IgM and IgG tests for the Rubella virus for 170 participants showed that 41(24.1%) tested seropositive for rubella IgM, while 129 (74.9%) tested Seronegative. There were 161 (94.7%) and 9 (5.3%) individuals that were seropositive and Seronegative for the rubella virus IgG, respectively (Table 1). The highest seropositive for the rubella virus was among participants from rural area 159 (93.5%) of which 40 (25.2%) were positive for Rubella IgM and 151 (95.0%) were IgG positive. 11(6.5%) of the participants lived in urban areas and have seropositive IgM 1 (9.1%), IgG 10 (91.0%). Analysis of the results also showed that 56(32.9%) participants are <20years of age, 95(55.9%) participants are between the age of 21 – 30years which have the highest prevalence IgM positive 18(19.0%) and IgG positive 90(94.7%). 16(9.4%) participants are between age 31-40years, and only 3(1.8%) participants are >40 years of age and has the lowest prevalence. The distribution of rubella virus positive antibodies to parity shows the highest prevalence was among participants with multi parity 121 (71.2%) with IgM 26 (21.5%) and 114 (94.2%) IgG positive.

All 170 (100.0%) participants were married, 110(64.7%) were from monogamous marriage and 60(35.3%) were from polygamous marriage. Education distribution in the population revealed that 23(13.5%) out of the 170 participants have primary education, 28(16.5%) have secondary education, 6(3.5%) have tertiary education and 113(66.5%) have informal education. Occupation of the participants was also taken note of and it shows only 2(1.2%) of the participants were civil servants, 99(58.2%) were entrepreneurs, and 69(40.6%) were full time housewives. All the observed socio demographical parameters showed no statistically significant relationship with the presence of the infection as p-value >0.05 (Table 2).

TABLE I SEROPREVALENCE OF RUBELLA VIRUS AMONG PREGNANT WOMEN ATTENDING SOME ANTENATAL CLINICS IN JIGAWA STATE (IGM AND IGG)

Parameters	Frequencies	Percentage (%)
IgM		
Positive	41	24.1
Negative	129	75.9
Total	170	100.0

IgG		
Positive	161	94.7
Negative	9	5.3
Total	170	100.0

TABLE III SEROPREVALENCE OF RUBELLA VIRUS INFECTION IN RELATION TO SOCIO-DEMOGRAPHIC FACTORS AMONG THE PARTICIPANTS

Socio-demographic factors	No. Examined	ELISA		Chi-Square (X^2)	P-value
		IgM	IgG		
Address					
Rural	159(93.5%)	40(25.2%)	151(95%)		
Urban	11(6.5%)	1(9.1%)	10(91.0%)	0.903	0.342
Total	170(100%)	41(24.1%)	161(94.7%)		
Age(Years)					
<20	56(32.9%)	15(26.8%)	53(94.6%)		
21-30	95(55.9%)	18(19.0%)	90(94.7%)		
31-40	16(9.4%)	6(37.5%)	15(93.8%)	3.099	0.377
>40	3(1.8%)	2(66.7%)	3(100.0%)		
Total	170(100%)	41(24.1%)	161(94.7%)		
Parity					
Null para	24(14.1%)	8(33.3%)	24(100.0%)		
Primi para	25(14.7%)	7(28.0%)	23(92.0%)	0.866	0.649
Multi para	121(71.2%)	26(21.5%)	114(94.2%)		
Total	170(100%)	41(24.1%)	161(94.7%)		
Marriage					
Monogamy	110(64.7%)	23(25.3%)	102(92.7%)		
Polygamy	60(35.3%)	18(30%)	59(98.3%)	0.729	0.393
Total	170(100%)	41(24.1%)	161(94.7%)		
Education					
Primary	23(13.5%)	3(13.0%)	22(95.7%)		
Secondary	28(16.5%)	10(35.7%)	27(96.4%)		
Tertiary	6(3.5%)	1(16.7%)	6(100.0%)	2.256	0.521

Non-formal	113(66.5%)	27(23.9%)	106(93.8%)		
Total	170(100%)	41(24.1%)	161(94.7%)		
Occupation					
Civil servant	2(1.2%)	0(0.0%)	2(100.0%)		
Entrepreneur	99(58.2%)	16(16.2%)	93(93.9%)	5.532	0.063
Housewife	69(40.6%)	25(36.2%)	66(95.7%)		
Total	170(100%)	41(24.1%)	161(94.7%)		

The distribution of rubella virus positive antibodies to possible risk factors showed that for Gestational, 54(31.8%) of the participants are in their second trimester and 116(68.2%) are in their third trimester, no participant in their first trimester was recorded. History of miscarriage and or obstetric loss showed that 73(42.9%) of the participants have had miscarriage/obstetric loss, while 97(57.1%) had none.

None among the participants have knowledge on rubella virus or MMR vaccine and have not been administered with the vaccine. The reason for non-vaccination is mostly because it is not a routine vaccine. Participants who had contact with measles patients are 58(34.1%), those that were not sure are 30(17.6%) and 82(48.2%) had no contact with measles or probable confirmed rubella patient. Among the 170 participants, only 4(2.4%) have a family history with congenital malformation. Only 3(1.8%) among the participants had sign or symptom of rubella virus, 14.7% of these participants have had blood transfusion at one point in their life.

All the observed possible risk factors showed no statistically significant relationship with the presence of the infection as p-value >0.05 (Table 3).

The distribution of rubella virus positive antibodies to hematological profile of the participants showed that pregnant women with <30 % PCV were 92(54.1%) out of which 24(26.1%) of them were IgM positive, 89(96.4%) tested positive for rubella virus IgG. Those with 30-38% PCV were 78(45.9%) with 17(21.8%) IgM positive and 72(92.3%) IgG positive.

Pregnant women with <10.5 Hb count has the highest count of 133(78.2%) with 23.3% and 94.7% IgM and IgG positivity respectively, those with 10.5-11 Hb count were 26(15.3%) with IgM 7(26.9%) and IgG 25(96.2%). Participants with >11 Hb count were only 11(6.5%) and 3(27.3%) were IgM positive while 10(91.0%) were IgG positive. For WBC count, pregnant women with <5.7 count had the highest prevalence 97(57.1%) with 33% and 95.9% IgM and IgG positivity respectively. Those with 5.7-13.6 WBC count were 73(42.9%) with 12.3% IgM and 93.2% IgG positives (Table 4).

TABLE IIIII SEROPREVALENCE OF RUBELLA VIRUS INFECTION IN RELATION TO POSSIBLE RISK FACTORS AMONG THE STUDY PARTICIPANTS

Possible Risk Factors	No. Examined	ELISA		Chi-Square (X^2)	P-value
		IgM	IgG		
Gestational age					
1st trimester	0(0.0%)	0(0.0%)	0(0.0%)		

2nd trimester	54(31.8%)	16(29.6%)	47(87.0%)	1.472	0.225
3rd trimester	116(68.2%)	25(21.6%)	114(98.3%)		
Total	170(100%)	41(24.1%)	161(94.7%)		
Miscarriage/obstetric loss					
Yes					
No	73(42.9%)	18(24.7%)	70(95.9%)	0.002	0.961
Total	97(57.1%)	23(23.7%)	91(93.8%)		
	170(100%)	41(24.1%)	161(94.7%)		
Reason for non-vaccination					
Not a routine vaccine					
Lack of awareness	166(97.6%)	39(23.5%)	159(95.8%)	2.226	0.136
Total	4(2.4%)	2(50.0%)	2(50.0%)		
	170(100%)	41(24.1%)	161(94.7%)		
Contact with measles/rubella patients					
Measles					
Rubella	58(34.1%)	12(20.7%)	52(89.7%)		
Not Sure	0(0.0%)	0(0.0%)	0(0.0%)	2.006	0.367
None	30(17.7%)	4(13.3%)	28(93.3%)		
Total	82(48.2%)	25(30.5%)	81(98.8%)		
	170(100%)	41(24.1%)	161(94.7%)		
Congenital Malformation					
Yes					
No	4(2.4%)	0(0.0%)	4(100.0%)		
Total	166(97.6%)	41(24.7%)	157(95.2%)	1.039	0.308
	170(100%)	41(24.1%)	161(94.7%)		
Blood transfusion					
Yes	25(14.7%)	5(20.0%)	23(92.0%)		
No	145(85.3%)	36(24.8%)	138(95.2%)	0.120	0.729
Total	170(100%)	41(24.1%)	161(94.7%)		

TABLE IVV SEROPREVALENCE OF RUBELLA RUBELLA VIRUS ANTIBODIES TO HAEMATOLOGICAL PROFILE OF THE STUDY PARTICIPANTS

Hematological parameters	No. examined	ELISA test		Chi-Square (X^2)	p-value
		IgM	IgG		
PCV (%)					
<30	92 (54.1%)	24(26.1%)	89(96.4%)		
30-38	78 (45.9%)	17(21.8%)	72(92.3%)	0.141	0.708

>38	0 (0.0%)	0(0.0%)	0(0.0%)		
Total	170(100%)	41(24.1%)	161(94.7%)		
Hb (g/dL)					
<10.5	133(78.2%)	31(23.3%)	126(94.7%)		
10.5-11	26(15.3%)	7(26.9%)	25(96.2%)	0.141	0.932
>11	11(6.5%)	3(27.3%)	10(91.0%)		
Total	170(100%)	41(24.1%)	161(94.7%)		
WBC ($\times 10^9$/L)					
<5.7	97(57.1%)	32(33.0%)	93(95.9%)		
5.7-13.6	73(42.9%)	9(12.3%)	68(93.2%)	5.700	0.017
>13.6	0(0.0%)	0(0.0%)	0(0.0%)		
Total	170(100%)	41(24.1%)	161(94.7%)		

4. DISCUSSION

Using a serological approach, this study assessed the seroprevalence of rubella virus infection in pregnant women who visited certain antenatal clinics in Jigawa State, Nigeria. ELISA was used to identify Rubella antibodies (IgG and IgM) against the Rubella virus.

According to the results, approximately 94.7% of the expectant mothers had rubella virus IgG antibodies. This figure is comparable to the prevalences of 95.0%, 90.1%, and 96.2% in Burkinafaso, Senegal, and Iran, respectively, as reported by Zanga et al. (2017), and 93.1% in Zaria, as reported by Olajide et al. (2015). A prolonged infection and the formation of rubella virus antibodies may have contributed to the high incidence seen. Given that the majority of participants had not received the rubella vaccine and that it is not a routine vaccination in Nigeria, this indicates that the virus is common in the research area and that most pregnant women had previously been exposed to it. The results of this study, however, are significantly greater than the prevalences of 58.97% in Congo reported by Zanga et al. (2017), 53%, 7%, and 58.33% in different regions of Nigeria reported by Onakewhor and Chiwuzie (2011), Agbede et al. (2011), and Rabiu et al. (2020) in Benin City, Ilorin, and Kano, respectively. This suggests that there are variations in the rubella virus's dissemination throughout Nigeria for perhaps climatic reasons. The immune system's attempt to neutralize the virus is reflected in the production of IgG antibodies. This antibody provides immunity against reinfection and extends life. As a result, it is reasonable to believe that pregnant women with IgG antibodies might be more immune. This also implies that the spread of the rubella virus varies across Nigeria, maybe due to climatic factors. The generation of IgG antibodies is a reflection of the immune system's effort to neutralize the pathogen. This antibody prolongs life and offers immunity against reinfection. A clearer picture emerged, nevertheless, when the seroprevalence of IgM antibodies to the rubella virus was also considered. Among the subjects, an IgM antibody prevalence of 24.1% was found. The same proportion of these expectant mothers also, to some extent, showed IgG antibodies, which may indicate reinfection or the resolution of the first infection (still in recovery stage). Since almost all infected individuals should have produced IgG antibodies by 30 days postinfection, the fact that the majority of

these women were in their second and third trimesters of pregnancy suggests that they were infected earlier in pregnancy (Olajide et al., 2015). Therefore, the fetuses of these pregnant women shouldn't be eliminated from the risk of congenital rubella.

The 24.1% prevalence achieved is significantly greater than the 1.1% prevalence reported by Agbede et al. (2011) in Ilorin, the 7.87% prevalence recorded by Yahaya et al. (2015) in Kano, and the 10% prevalence reported by Onakewhor and Chiwuzie (2011) in Benin City. Given that rubella outbreaks may not always be identified in underdeveloped nations like Nigeria and that rubella-induced rashes are frequently misdiagnosed, the high incidence found in this study points to the possibility of an outbreak occurring during the study period that may have gone undetected. Pregnant women in the 21–30 age range had the highest frequency in this research (95, or 55.9%), while those over 40 had the lowest frequency (3, or 1.8%). This was in line with the findings of Koki et al. (2014), Yahaya et al. (2015), and Mangga et al. (2017), who found that the age group of 21–25 years had the greatest seroprevalence, while the age group of 41–45 years had the lowest. This finding emphasizes the need of vaccinating women of childbearing age and for the country to begin monitoring trends in the incidence of CRS and rubella susceptibility.

The study found that pregnant women in the second and third trimesters had seroprevalence rates of 29.6% and 21.6%, respectively. Given that there was no incidence throughout the study's first trimester, this is in contrast to the findings of Rabiu et al. (2020) regarding prevalence. According to reports by Agbede et al. (2011) and Olajide et al. (2015), the highest prevalence was seen among pregnant women in their first and second trimesters, which increases the risk of the virus spreading from infected pregnant women to their fetuses. These data also contradict those reports. The fact that the majority of pregnant women who came to the prenatal clinic were in their second or third trimester may have contributed to the highest prevalence seen in those trimesters.

There was a greater prevalence of both antibodies among multipara subjects 121 (71.2%), primipara 25 (14.7%), and nullpara 24 (14.1%), according to the findings. This greater frequency was also observed in research by Olajide et al. (2015), who found that prevalence rose with parity. However, a study by Agbede et al. (2011) found that prevalence was higher in primipara women. In terms of educational background, the study population had very little awareness and understanding about rubella and how it spreads; 113 (66.5%) of the pregnant women who took part in the study had non-formal education, while only 6 (3.5%) had completed higher education. This lack of awareness was also observed in the study conducted in Zaria by Olajide et al. (2015). This is a significant issue since prevention and control of a disease depend on understanding its mode of transmission.

In addition, IgM antibodies were found in every group of women examined in terms of profession, with the exception of two government servants. The largest incidence, 99 (58.2%), was observed in women who were listed as entrepreneurs. There was no significant correlation ($p>0.05$) between the individuals' employment position and the prevalence of rubella antibodies. There is no statistical relationship between individual's reproductive condition, employment, or educational attainment and rubella virus infections, according to the study's conclusion. The results of previous investigations conducted by Zanga et al. (2017) and Olajide et al. (2015) are consistent with this.

Some of the typical clinical signs and symptoms of rubella virus infection were noted in the expectant mothers. Among them were sore throat, headache, and low fever. Tender, swollen lymph nodes were not reported by any of the pregnant women. Olajide et al. (2015) noted the clinical symptoms of moderate fever, headache, and arthralgia (painful joints), whereas Agbede et al. (2011) noted that just one pregnant lady complained of enlarged lymph nodes. The pregnant women who reported symptoms predominantly of fever, sorethroat and headache however, were negative for rubella infection (IgM antibody), suggesting that the fever, sore throat and headache were related to other sources. This data demonstrates that most of the infected individuals were asymptomatic, and none of the clinical signs was substantially related with the likelihood of infection.

The results of the study also showed that the greatest prevalence rate was 92 (54.1%) for pregnant women with less than 30% PCV and 78 (44.9%) for pregnant women with 30–38% PCV. With a frequency of 133 (78.0%), pregnant women with a Hb count of less than 10.5 are the most common, followed by those with a count of 10.5–11 (15.3%) and those with a count of more than 11 (6.5%). A p-value of >0.05 indicates that there was no significant correlation between PCV and Hb. The largest frequency of WBC count was seen in pregnant women with a count of less than 5.7 (97, or 57.1%), who also had IgM and IgG positive of 33% and 95.9%, respectively, whereas pregnant women with a count of 5.7–13.6 had a count of 73 (42.9%). There were no pregnant women recorded with WBC count of >13.6 and statistical analysis showed an association between rubella virus infection and WBC as P-value is <0.05.

5. CONCLUSIONS

Out of 170 pregnant women screened 24.1% were IgM positive, 94.7% IgG rubella virus positive. Specifically, the study shows serologic evidence of previous exposure and/or recent infection by rubella virus among the studied women. The antibodies of Rubella virus were detected by ELISA (IgG and IgM). The study showed no statistical relationship with tested socio-demographic and possible risk factors but showed a statistical relationship with White Blood Cell (WBC) count. Findings from the study corroborate reports of previous studies in the country and further showed that elimination of rubella virus in Nigeria is feasible since the definite susceptible population is defined.

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