

Association between rubella seropositivity and parity among reproductive-aged women in Kenya

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Abstract

Background: Rubella virus infection in the first 12 weeks of pregnancy causes miscarriages, stillbirths or fetal anomalies known as congenital rubella syndrome. Factors associated with rubella immunity include age and parity. No studies have been done to isolate the association of parity independent of age.

Objective: To evaluate the association between rubella IgG seropositivity and parity among women of the same age group attending the Aga Khan University Hospital (AKUH), Nairobi, Kenya.

Methods: A cross-sectional study of women attending AKUH. Eligible participants were women aged between 30 and 34 years, recruited sequentially. The rubella IgG antibody was tested using a commercial ELISA Kit. Fischer exact test and Chi square was used to compare the two groups. Logistic regression was used to explore the association.

Results: A total of 300 women who fulfilled the inclusion criteria were enrolled into the study. The overall rubella seroprevalence was 87%. There was no difference in seropositivity by parity and place of birth. None of the socio-demographic and obstetrical factors included in the study questionnaire were associated with seropositivity for rubella in the univariate and multivariate analysis.

Conclusions: A significant number of women of childbearing age were susceptible to rubella virus and subsequent CRS. Seropositivity did not correlate with the socio-demographic and obstetrical factors. Regular rubella testing and promotion of wider coverage of vaccination is recommended since there seems to be no benefit in selective targeting of vaccination.

Keywords: Rubella, Congenital Rubella Syndrome, Sero-prevalence, Nairobi, Kenya

Introduction

Rubella Virus (RV) is the pathogenic agent that causes rubella; a mild febrile rash illness that is usually a self-limiting (1,2). Although rare rubella-related complications, such as encephalitis and thrombocytopenic purpura, have been reported, the public health significance of rubella prevention program is built on eliminating Congenital Rubella Syndrome (CRS) that occurs as a result of rubella infection in the first 16 weeks of pregnancy, leading to fetal demise and a wide range of intrauterine birth defects (3-5). The teratogenicity of RV begins when placental infection occurs during maternal viremia, causing dissemination of the virus throughout the fetus leading to miscarriages, stillbirths, or fetal anomalies (1, 5).

The trends and burden of rubella in Africa is unknown as there is no systematic rubella case-based surveillance. The majority of the available data on

rubella in Africa are from surveys done to assess the prevalence among risk groups of women of reproductive age and young children. Serosurveys among African women of childbearing age (15-35 years) have shown regional difference; while women in West and East Africa have a lower prevalence of 70-80%, women from North and Southern Africa have a slightly higher prevalence, 90-99% (6). Studies conducted in Kenya have shown similar seroprevalence range to western African countries. A study conducted in 2005 among school aged children in Moi's Bridge location, Uasin Gishu District, found overall rubella seropositivity rate of 79.9% that increased with age from 58.5% among those aged 4-6 years to 93.8% among those aged over 13 years (7). Although there are no recent studies conducted in Kenya among women of reproductive age, a study done in 1982 by Sequeira *et al* (8) found a rubella seropositivity rates of 92.3% and 85%, among African and Asian patients respectively at the time of delivery at the private Aga Khan Hospital; compared

with 96.4% among patients delivering at the public Kenyatta National Hospital, possibly reflecting a socioeconomic influence.

Taken together, the available African data indicate that there is wide variation in the rubella seroprevalence from low of 68% in Nigeria to 95% in South Africa. Studies have found no single factor that was significantly associated with rubella seropositivity. Furthermore, the epidemiology of communicable and vaccine-preventable diseases like rubella might change with population changes such as migration, urbanization and reducing fertility.

In Kenya, there is no routine vaccination of rubella and pregnant women are not routinely tested for immunity against rubella. The primary objective of this study was to determine the association between rubella IgG seropositivity and parity among women of the same age group attending the Aga Khan University Hospital, Nairobi.

Materials and Methods

Study design: A cross sectional study design was used to enrol sequentially eligible women aged between 30 and 34 years.

Study setting: The study was conducted at Aga Khan University Hospital, a private teaching facility with specialist and referral services. Eligible participants were recruited from outpatient clinics.

Study population: Nulliparous and multiparous women aged 30 to 34 years attending outpatient obstetrics and gynaecological clinics at the hospital were approached and assessed for eligibility. Women who work with small children (e.g. day-care, nursery school, paediatricians), those acutely ill with febrile rash illness and those participating in other ongoing studies were excluded.

Data collection and management: An online statistical software package, Open Epi (www.OpenEpi.com), was used to estimate the minimum sample size required to provide 80% power to detect a 10% increase in seropositivity among multiparous ('cases') compared with nulliparous women ('controls') assuming 85% rubella seropositivity in the latter, based on unmatched case-control design. A 1.2 ratio of nulliparous to multipara was used based on data from a previous study of the hospital obstetric population. Intergrowth-21st indicated (9) that among a sample of 5,000 participants, among those aged 30-34 years the ratio of nullipara to para 2 was 1.2. This ratio was therefore used for sample size estimation in the present study.

A commercially available indirect Rubella IgG Enzyme-Linked Immunosorbent Assay, Elecsys

Rubella IgG assay was used for the detection and qualitative determination of IgG antibody to rubella virus in serum specimens. The tests and interpretation of results were done in accordance with the manufacturer's instructions while optical signals generated were read at 450nm with ELISA plate reader (Cobas®, 2010). According to the kit protocol, serum samples with anti-Rubella IgG concentrations <10 IU/mL were considered seronegative and those ≥10 IU/mL were considered seropositive. In a recent study, the Elecsys Rubella IgG assay exhibited a relative sensitivity of 99.9–100.0% and specificity of 97.4–100.0% in samples from routine antenatal screening (10).

Data analysis approach: Data were entered and analysed on a password protected personal computer using Microsoft Access 2010 (Microsoft, Seattle, WA, USA) and SAS 9.2 (SAS Institute Inc., Cary). The personal identifiers were removed from the main database to keep participant information confidential.

Pearson chi-square or Fisher exact tests were used to compare categorical variables including the rubella immunity among the two groups; $p < 0.05$ was considered statistically significant. The exact 95% confidence intervals were determined by the mid-P Exact method using SAS. Logistic regression was used to explore potential associations. *Ethics:* The study was approved by the Research and Ethics Committees at the Aga Khan University Nairobi (2013/REC-18). Written consent was taken from all study participants.

Results

A total of 300 women who fulfilled the inclusion criteria and signed the informed consent were enrolled into the study. The mean (standard deviation) of age and gestational week were 31.7 (1.7) years, and 32.9 (8.9) weeks, respectively. Almost half the participants were born in Nairobi and Central province; few participants were born outside of Kenya (Table 1).

The majority of the participants were married (92%). Ninety one percent of the participants were college or university graduates and 87% of their spouses were graduates of college or university as shown in Table 1. There were 202 pregnant study participants (67%), of which 80% were in the third trimester. Only 32% of the study participants were aware of rubella. However, 86% were willing to receive rubella vaccination at their own cost, if offered.

Table 1: Demographic characteristics of study participants, Nairobi, Kenya

Variable	No. (%)	
Place of birth	Abroad	17 (6)
	Kenya	283 (94)
	Central	65 (22)
	Coast	17 (6)
	Eastern	34 (11)
	Nairobi	97 (32)
Province of birth	North Eastern	4 (1)
	Nyanza	16 (5)
	R.Valley	36 (12)
	Western	14 (5)
	Abroad	17 (6)
	Central	64 (21)
Childhood province	Coast	18 (6)
	Eastern	35 (12)
	Nairobi	100 (33)
	North Eastern	4 (1)
	Nyanza	16 (5)
	R.Valley	33 (11)
Rural/Urban-Kenyan	Western	15 (5)
	Abroad	15 (5)
	Nairobi	98 (35)
	Outside-Nairobi	185 (65)
	ANC	140 (48)
	Others	114 (39)
Clinic	GOPC	40 (14)
	Primary education/basic education	2 (1)
	Secondary education	24 (8)
Education level	University/higher degree	273 (91)
	Secondary education	13 (4)
	University/higher degree	260 (87)
Husband's education	Not Applicable	25 (8)
	Non-pregnant	98 (33)
Gestation	Pregnant	202 (67)
	Multiparous	136 (45)
Parity	Nulliparous	164 (55)
	No	203 (68)
Aware of rubella	Yes	97 (32)
	No	41 (14)
Willing to pay for vaccine at cost	Yes	259 (86)

There was no difference in seropositivity rate between the nulliparous and multiparous group,

88% and 87% respectively. The overall rubella seroprevalence was 87%. Seroprevalence did not vary by place of birth and age (Table 2).

Table 2: Seroprevalence of rubella antibodies among women attending AKU clinics by selected variables (n=300)

	Category	Positive No. (%)	P-value
Place of birth	Overall	261 (87)	0.87
	Abroad	15 (88)	
	Kenya	246 (87)	
	Central	58 (89)	
	Coast	14 (82)	
	Eastern	28 (82)	
Province of birth	Nairobi	84 (87)	0.81
	North Eastern	4 (100)	
	Nyanza	14 (88)	
	R.Valley	30 (83)	
	Western	14 (100)	
	Abroad	15 (88)	
Childhood province	Central	60 (94)	0.19
	Coast	14 (78)	
	Eastern	28 (80)	
	Nairobi	88 (88)	
	North Eastern	4 (100)	
	Nyanza	12 (75)	
Rural/Urban-Kenyan	R.Valley	27 (82)	0.76
	Western	15 (100)	
	Abroad	13 (87)	
	Nairobi	86 (88)	
	Outside-Nairobi	160 (86)	
	Gestation	Non-pregnant	
Pregnant	177 (88)		
Parity	Multiparous	119 (88)	0.81
	Nulliparous	142 (87)	
	Primary education	2 (100)	
Education level	Secondary education	20 (83)	0.74
	College/higher degree	238 (87)	
	Secondary education	11 (85%)	
Husband's education	University/higher degree	226 (87%)	0.73
	Not Applicable	23 (92%)	

The socio-demographic and obstetrical factors included in the study questionnaire were country of birth, where participants spent most their childhood, gestational age and educational level of the participant and her spouse. These factors were not associated with seropositivity for rubella in the univariate, and bivariate analysis (Table 2 and 3). Multivariate regression model including place of residence and parity, did not identify any further associations (Table 3).

Table 3: Risk factors of rubella seropositivity among women attending AKU clinics by selected variables (n=300)

Variable	Bivariate analysis		Multivariate analysis	
	Odd ratio (95% CI)	P-value	Adjusted Odd ratio (95% CI)	P-value
Multiparous vs nulliparous	0.92 (0.47–1.82)	0.81	0.79 (0.35–1.75)	0.55
Rural vs urban	0.89 (0.43–1.87)	0.76	0.86 (0.41–1.82)	0.69
Secondary education vs university/higher degree	1.36 (0.44–4.21)	0.98	1.06 (0.29–3.86)	0.98
Non-pregnant vs pregnant	1.18 (0.58–2.39)	0.64	1.06 (0.51–2.21)	0.87

Among the 202 participants who were pregnant at the time of study, 25 (12.4%) were rubella seronegative. Two of the women in their first trimester of pregnancy were seronegative compared to five second trimester and 18 third trimester women. There were no significant differences between seronegative and seropositive women in trimester of pregnancy, place of birth, education, parity or gravidity.

Discussion

There is evidence of no difference in the rubella seroprevalence between nulliparous and multiparous women of the older reproductive age group in this relatively well-off urban reproductive-age population. Twelve percent of pregnant women were susceptible to rubella infection with potential risk of infection and subsequent congenital rubella syndrome. Rubella IgG antibodies can be formed naturally after an infection by the rubella virus or after vaccination. Since rubella-containing vaccine is not included in the public routine immunization schedule in Kenya, although it is increasingly used in the private sector, was assumed in this study that many of the positive results were due to natural infection (2). None of the socio-demographic and obstetrical factors including parity were significantly associated with rubella seropositivity. The distribution of seronegative study participants was fairly random, reducing any potential programmatic benefit of focusing one group of women or the other for interventions.

The seroprevalence of 87% among women aged 30-34 years in our study is lower than in a previous report from Kenya where rubella seroprevalence was 93.8% among those aged over 13 years (7) and 96.7% in women above 30 years of age (11). In that study, ownership of a television set reduced the odds of rubella seropositivity and this factor showed significance at 95% level of confidence in the multivariate analyses. This was considered as a proxy measure for socio-economic status of a family in that study (7) and implied that children from lower socio-economic backgrounds were infected much earlier in life than their counterparts who lived in better conditions in the same area and even attended the same schools. The likely reason for increased risk among low socioeconomic group can be attributed to crowding and this has been cited elsewhere (7).

The present study did not identify significant differences in rubella seroprevalence by parity. Lower rubella susceptibility rates in parous women have been reported in England (12) and in never-married women after a live birth in the United States (13). In Switzerland rubella seropositivity was identical in primiparous and in multiparous women (14). Unlike measles which has significantly higher seroprevalence among women with more than four pregnancies, rubella is not so contagious, reducing the chance of women getting infected even if they have contact with more children (15). Our results were similar to those reported in a recent study from Algeria, which did not find correlation between the level of IgG and the parity of the mothers (16). In contrast, a study in Nigeria found a gradual increase in rubella seroprevalence from 43% amongst primigravidae to 59% and 78% in multiparous and grand-multiparous women respectively (17). A 1995 study from India in the absence of universal rubella immunization showed a higher seroprevalence rate in females of low socioeconomic status (63%) than those from a higher socioeconomic class (40%) (18), suggesting that those from lower socioeconomic status had greater exposure to rubella infection. Living at or above the poverty line or in a non-crowded household and a greater level of education of the head of household has been associated with rubella and measles susceptibility (15). Although income information was not collected, previous studies have shown strong correlation between education and income. Linking the level of education to the socio-economic status suggests that our study participants are of middle or upper class status. Furthermore, with the burgeoning economic middle class, families in urban areas live as nuclear families in relative isolation so the assumed exposure from other children might not be there.

Although the annual incidence of CRS in Kenya is unknown, five cases of CRS have been documented at AKUHN in the last five years, including two within

the last year (hospital registers, unpublished data). Since there are approximately 3000 deliveries per year, that suggests a rubella incidence rate of at least 33 per 100,000 births in the AKUHN population despite the lack of active surveillance.

In assessing attitude of our participants towards the idea of taking the vaccine at a cost since it was not provided by the government, 86% of the participants were willing to take the vaccine at a cost. The patient readiness to pay for vaccines should encourage policy makers and clinicians to facilitate the introduction of rubella-containing vaccine in the public immunization program as the majority of Kenyans cannot afford to pay for vaccines.

A limitation of our study is that the hospital, in which the study was conducted, serves predominantly the middle and upper social economic class. Therefore, the results may not be representative of the general population in Kenya hence not generalizable. Secondly the vaccine was available in AKUHN, but a history of rubella vaccination or rubella disease was not included in the study questionnaire; therefore, it is hard to differentiate the role of vaccination or natural infection among the seropositive group. However, the uptake of rubella vaccine among reproductive-age women was low at the time of the study low. Thirdly, the study suggested no association of rubella seropositivity with any of the tested socio-demographic factors, but there may have been some differences that the study was not powered to detect.

Conflict of interest

The authors have no conflict of interest.

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