Seroprevalence of Natural Rubella Antibodies among Antenatal Attendees at Moi Teaching and Referral Hospital, Eldoret, Kenya

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Abstract

Objective: This study was sought to determine the proportion of women susceptible to rubella among antenatal clinic attendees, and to assess risk factors for rubella infection.

Methods: Hospital based cross-sectional serosurvey. Four hundred and seventy antenatal clinic attendees (ANC) were randomly selected. Specimens were collected following routine procedures implemented at the clinic.

Setting: The study was conducted at the Prevention of Mother to Child Transmission (PMTCT) clinic of Moi Teaching and Referral Hospital, Eldoret, Kenya.

Results: The study captured pregnant women aged 15-46 years. This study showed that 7% of ANC attendees were susceptible to rubella, and the proportion decreased with advancing age. Clients who were over 30 years of age had a fourfold (OR-4.46, 95% CI 1.13-17.57) increase in the odds of rubella seropositivity compared to those below 20 years. Other variables that showed significance were multiparity in comparison to nulliparity (OR-2.9, 95% CI 1.35-6.26) and marital status (OR-2.6, 95% CI 1.18-5.74).

Conclusion: This study provides evidence that rubella is highly endemic and that there is a risk for contracting the infection in pregnancy. The data will be used by policy makers to decide on the way forward in the introduction of routine rubella vaccination, and will also justify the need to establish systematic surveillance for CRS in the country.

Background

Rubella is of public health importance because infection acquired during early pregnancy, often results in foetal abnormalities that are classified as congenital rubella syndrome (CRS). Congenital rubella syndrome occurs in up to 90% of infants born to women who are infected with rubella, during their first trimester of pregnancy [1,2]. Primary infection is associated with high risk of CRS [3,4]. The primary objective of rubella vaccine introduction is to prevent infection in pregnancy, which thus reduces the incidence of CRS. Whereas many developed countries have included rubella vaccine in their primary vaccine schedules, many developing countries are still undecided on the timing and modalities of introducing routine rubella vaccination. Like many other developing countries without rubella immunization policy, Kenya recognized the importance of rubella only after introduction of accelerated measles control activities, with a surveillance component that also captures rubella because of the case definition based on presentation of fever and rash. The country lacks a national policy on rubella immunization, although selected private hospitals offer measles, mumps and rubella (MMR) vaccine to their clientele.

The World Health Organization (WHO) advised and recommended that countries with measles control and elimination programmes consider the addition of rubella vaccine, as measles elimination creates an opportunity to control and eliminate rubella. [5,6]. Overall, addition of rubella control to a country’s measles elimination initiatives does not pose additional logistic challenges, in any significant way [7]. However, there is a risk if high childhood vaccination coverage is not achieved and sustained, as incidence will shift to older age groups where risk of CRS is confined. Therefore, it is important for countries to evaluate the burden of disease and assess programmes that are already in progress. The entire burden of rubella can be hard to estimate but given the inherent risk of rubella infection during pregnancy, many countries would make informed decision if the burden of disease were of importance to them. This study conducted among pregnant women provides evidence on specific profiles of immunity and sought to establish susceptibility rates, which indicate the risk of CRS case occurrence.

Methods

This cross-sectional, hospital based study involved 470 randomly selected pregnant women who gave informed consent, and were screened for rubella Immunoglobulin G (IgG) using the ELISA-based quantitative assay at the National Measles Laboratory, Kenya Medical Research Institute, Kenya.

Study site

This was hospital based study design conducted at Moi Teaching and Referral Hospital (MTRH). The hospital is government run and is one of the two classified within the Ministry of Health hierarchy as national hospitals. It is situated in the Rift Valley province, 310 km North of Nairobi. The catchment area of the institution covers the North Rift region, Western and Nyanza provinces. Prevention of Mother to Child Transmission clinic (PMTCT) created the point of entry for this study.

Data collection

Structured pre-tested questionnaires were used for data collection. The main activity of the clinic was HIV counseling and testing, blood grouping, Hb determination and Venereal Disease Research Laboratory Test (VDRL). The study made use of the blood
that was drawn for these routine procedures. An aliquot of 0.5-2.0 ml of plasma was obtained and transferred to a sterile 1.8 ml cryovial, labeled with client code that corresponded to that on the form with socio-demographic data.

Plasma was stored at -20°C until the time of shipment to the laboratory, where testing was done.

Ethical Clearance was obtained from both KEMRI/National Committee of Ethics and Moi Teaching and Referral Ethics Committee.

Laboratory analysis used Dade Behring Enzygnost anti-rubella virus IgG. The assay is designed for qualitative and quantitative determination of IgG antibodies to rubella virus in human serum or plasma. In brief, the test wells were coated with antigen specific to IgG antibodies contained in the test samples. Upon reaction between antibody-antigen, anti-human conjugate was added which bound to the antibody complex, catalyzed a substrate producing a yellow colour on addition of acid solution. Intensity of the colour formed was proportional to the amount of rubella IgG. The absence of specific antibodies does not exclude the possibility of an acute infection in the incubation phase, therefore a limitation of the test assay.

**Sample size determination**

The sample size calculation was done using EPI INFO software and was based on 95% level of confidence, study power of 80% and anticipated seroprevalence of 83%. The estimate in prevalence was based upon previous studies in developing countries. Four hundred and seventy clinic attendees were sampled based on these criteria.

**Selection of subjects**

The subjects were selected during the period of June to December, 2005. The daily client flow to the clinic was erratic and indistinguishable, thus a ‘qualified’ random sampling technique was used to select subjects to be included in the study. This involved daily selection of clients without a full sampling frame of the total clinic attendees, over the study period.

**Inclusion criteria:** All ANC attendees regardless of age, presenting to the clinic for routine 1st visit procedures were taken into account.

**Exclusion criteria:** Patients not willing to participate in the study.

**Data management**

The data was entered, verified for consistency and analyzed using EPI INFO version 3.3.2. (CDC, Atlanta, Georgia, USA); all tests were at 5% probability level. Results are expressed as numbers and percentages. Odds ratios were computed for each potential determinant and those that showed associations were fitted into a final logistic regression model, to determine independence in contribution of each determinant.

**Results**

**Descriptive analyses**

The study population consisted of 470 ANC attendees recruited from the ANC of Moi Teaching and Referral Hospital. Age distribution of ANC attendees was near normal with a mean of 24.89 years (median 24 years, range 15-46 years). Majority (74%) were aged between 20-30 years.

The overall seropositivity rate was 92.9%. The presence of rubella-specific IgG antibody increased with age to 95.2% for women aged more than 30 years from 86.7% for those less than 20 years of age (Figure 1). Geometric Mean IgG Titre was 127 IU/ml (median 84 IU/ml, range 11-886 IU/ml). Geometric mean titres showed a decline in titre with increased age (Figure 2).

**Bivariate analyses**

The relationship between rubella seropositivity and its potential exposure determinants were assessed using odds ratio (OR) as a measure of association. Taking age category of below 20 years as baseline, there was a significant ($p=0.02$) difference in seropositivity, in comparison with those of age greater than 30 years (OR=4.46, 95% CI 1.13-17.57). Other variables that showed significance were multiparity in comparison to nulliparity (OR=2.9, 95% CI 1.35-6.26) and marital status (OR=2.6, 95% CI 1.18-5.74). Area of residence and level of education had no association with seropositivity (Table 1).

The three variables that showed significance in association
Interestingly, the high rate of seropositivity in this study conforms to previous reports in the region and no significant association was found, except for parity. Other factors have been identified as significant predictors of the rubella seroprevalence among women of childbearing age, other studies are recommended in different settings as local variations in susceptibility have also been identified [9,10]. Our findings showed that a high proportion of the population has immunity, confirming exposure to previous natural infections of rubella virus. Prevalence increased with age suggesting high natural transmission of wild virus in the maintenance of prevalence rates. There was significant association between rubella seropositivity and client’s age, parity and marital status (*p<0.05*). The bivariate analyses were fitted in a multivariate logistic regression model, to determine which of the factors contributed independently to the association. None of the variables showed significance at 95% level of confidence, signifying dependence of the three variables.

**Discussion**

In this study, the proportion of women with detectable antibodies against rubella was 92.9%, similar to several other published studies [9,10]. Our findings showed that a high proportion of the population has immunity, confirming exposure to previous natural infections of rubella virus. Prevalence increased with age suggesting high natural transmission of wild virus in the maintenance of prevalence rates. There was significant association between rubella seropositivity and client’s age, parity and marital status (Table 2). Inclusion of all the variables in the final logistic regression model which controlled for confounding effects gave no significant association, implying that these were dependent factors in a single pathway between exposure and outcome. Parity and marital status are likely proxy measures for age.

In this study, susceptibility rates decreased with increased age suggesting that immunization was induced by infection, given that no routine vaccination exists in this population. Other non-vaccinating countries have reported high seroprevalence rates with increase in age [11]. These findings point to high endemicity of rubella, thus individuals who remain susceptible up to child bearing age are at a high risk of contracting the disease in pregnancy.

Other factors have been identified as significant predictors of rubella seropositivity in other studies. These include schooling, place of residence and parity [12,13]. These factors were also assessed in this study and no significant association was found, except for parity. Interestingly, the high rate of seropositivity in this study conforms to surveys in countries with rubella vaccination programmes [14]. This suggests high natural transmission in this study population.

The finding on seroprevalence rate of 92.9% is similar to an earlier report in the early 1980 in Nairobi, Kenya, which found a rate of 92.7% [10]. The similarity suggests that virus epidemiology is still the same, as it was in the 1980s. The consistency is also replicated in our earlier study among school going children [15]. From the two studies, it is a fact that females start giving birth quite early in life, and that is why there is an overlap in age between primary school children and ANC attendees.

It is important to note that high proportion of seropositive women cannot be taken to mean, no risk of CRS. There are risks of CRS occurring even with low proportion of susceptible individuals [16]. A comprehensive review of literature revealed the incidence of CRS to be 0.5-2.2 per 1000 live births in developing countries. In Morocco alone, an incidence of 8.1-12.77 cases per 100,000 is there. In 1996, there were 110,000 cases of CRS in developing countries [5,17,18].

From our earlier publication, two risk factors were identified: age and socio-economic class predictors of rubella infection [15]. Age has also been identified as a risk factor in this current study, and a good control programme need to focus on these two categories that have increased risk of rubella infection.

The overall resulting findings of this study are reliable enough to support the main uses of the data. No major sampling errors were experienced, except a form of selection bias of the urban population. This occurred because rural clientele took advantage of a single market day within a week to attend antenatal clinic, and this resulted in more urban population being sampled during the other non-market days.

**Conclusion**

This hospital based cross-sectional study demonstrates that a large proportion of the ANC attendees have protective IgG antibodies. While this study is an important step in addressing the rubella seroprevalence among women of childbearing age, other studies are recommended in different settings as local variations in susceptibility profiles do occur. The low susceptibility rate in this study group...
could mask a significant national benefit from the introduction of routine rubella vaccination in the country. A large community-based serosurvey is recommended that will yield a big enough return information to justify introduction of routine vaccination, and to guide on the best strategy that guard against a possible age shift. This recommendation is based on the fact that it is now widely accepted that vaccination should be offered to all susceptible women of childbearing age [19].

If Kenya was to consider introduction of rubella vaccination, it is significant that the strategy chosen must be able to protect both adolescent girls who remain susceptible to rubella in the short term and curb the high transmission experienced in childhood, as described in our earlier study [15].

More importantly, these findings justify the need to establish systematic CRS surveillance programme in Kenya and also to develop models that estimate the effects of different CRS prevention and control strategies [20].

Competing Interests
The authors declare that they have no competing interests.

Author’s Contributions
Kombich JJ was the principal investigator, conducted the data analyses, wrote the first draft, and will act as guarantor for the paper. Borus PK substantially contributed to conception and design of the study and interpretation of data. Muchai PC was responsible for the laboratory analysis. All authors read and approved the final manuscript.

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