

Seroprevalence of rubella antibodies among antenatal patients in the Western Cape



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Objectives. To determine the seroprevalence of rubella virus infection among antenatal patients aged between 15 and 45 years in the Western Cape province of South Africa, in order to provide data to determine the need for vaccination to protect women of childbearing age.

Design. A cross-sectional study.

Setting. Virology laboratory, Groote Schuur Hospital, National Health Laboratory Service (NHLS), South Africa.

Subjects and methods. One thousand two hundred provincial serum specimens from participants in the 2003 Department of Health antenatal HIV/syphilis serosurvey were selected from the 4 districts of the Western Cape. The specimens were age-stratified and screened qualitatively for rubella immunoglobulin G (IgG) antibodies by means of a commercial immunoassay during October 2004.

Results. Within the Western Cape a total of 95.3% of women in the 15 - 24-year age group, 97.5% in the 25 - 34-year group and 98% in the 35 - 45-year age group were immune to rubella. There was no statistically significant difference in the rate of rubella susceptibility between the 4 districts tested.

Conclusions. The study is an important step in addressing the seroprevalence of rubella infection in women of childbearing age in South Africa. Further information is needed on rubella seroprevalence from the other provinces in South Africa as well as formal implementation of rubella and congenital rubella syndrome surveillance to determine the feasibility of routine rubella immunisation.

Rubella virus is a common cause of childhood fever and rash. It is of public health importance largely owing to the teratogenic effects of primary or secondary rubella infection in the first trimester of pregnancy.¹ Rubella acquired in the first 12 weeks of pregnancy is associated with a nearly 90% risk of congenital malformations.² A highly effective vaccine has been available since 1969 and vaccination programmes have eliminated or greatly reduced the incidence of rubella and congenital rubella syndrome (CRS) in developed countries.³ Information on the epidemiology of rubella in South Africa is somewhat lacking. An article published in the December 1977 issue of the *SAMJ* by Kipps *et al.* entitled 'The epidemiology of rubella in Cape Town' began as follows: 'Information on the epidemiology of rubella in the Republic of South Africa is woefully incomplete. The disease is not notifiable and there are no available reports of nationwide epidemics or of the incidence of congenital rubella infections in the general population.'⁴ Regrettably little has changed in the subsequent 28 years. Currently there is no national rubella immunisation programme, rubella is

not notifiable, there are no surveillance programmes for congenital rubella, and the percentage of non-immune women of childbearing age is largely unknown. The 1977 study by Kipps *et al.* showed that 8.5% of females aged between 15 and 25 years living in Cape Town were not immune to rubella. A small study in 1983 from Tygerberg Hospital⁵ showed that 10.5% of female hospital staff were susceptible to rubella. Data collected by Johnson *et al.*⁶ in 1985 from the former Witwatersrand area on random serum specimens submitted to the former National Institute for Virology showed that a worrying 18.4% of women of child-bearing age were non-immune. In other developing countries the proportion of women of childbearing age susceptible to rubella varied from 4% in China to 70% in Trinidad and Tobago.⁷

This study was prompted by a retrospective view which revealed that our virology laboratory at Groote Schuur Hospital confirmed 20 cases of congenital rubella syndrome over the 30 months from April 2002 to October 2004. In addition we are frequently asked

to investigate cases of probable primary rubella or rubella reinfection in early pregnancy. Knowledge of rubella seroprevalence would allow one to model the incidence of CRS, thus providing an indirect measure of the burden of CRS. This is essential information for health policy makers when considering the inclusion of the rubella vaccine in the routine Expanded Programme for Immunisation in South Africa (EPI (SA)) schedule. We investigated the prevalence of immuno- globulin G (IgG) antibodies to rubella virus in 1 200 serum samples obtained from the 2003 Department of Health antenatal HIV/syphilis serosurvey within the Western Cape, South Africa.⁸ The present study is the first systematic study of rubella seroprevalence in pregnant women to have been performed in South Africa.

Materials and methods

Study population

One thousand two hundred provincial serum samples from participants in the 2003 Department of Health antenatal HIV/syphilis serosurvey were analysed for rubella IgG antibodies. These samples had been stored at -20°C following testing for HIV and syphilis. The Western Cape covers an area of roughly 129 370 km² and has a population of approximately 4.5 million people.⁹ For the purposes of the annual antenatal survey the province is divided into 4 districts, namely the Metropolitan, West Coast/Winelands, South Coast/Klein Karoo and Boland/Overberg districts (Fig. 1). The

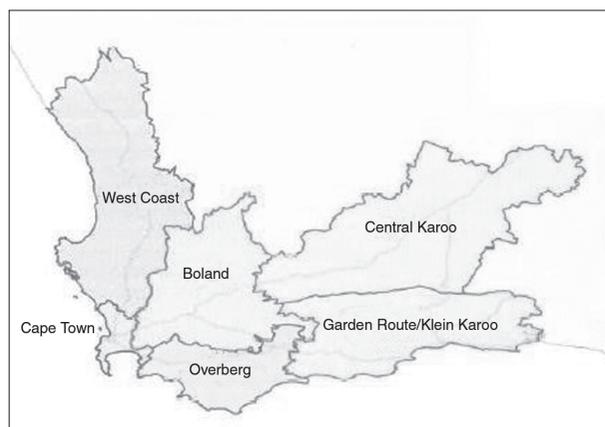


Fig. 1. Districts of the Western Cape as in the HIV/syphilis antenatal survey.⁸ (Source: Migration Study in the Western Cape 2001, Provincial Government of the Western Cape.¹²)

Central Karoo district is not included in the Western Cape for the HIV/syphilis serosurvey and was therefore not included in this study. Three hundred anonymously collected serum specimens from women from each of the 4 districts were stratified according to age and tested for rubella IgG antibodies. The study was approved by the Research Ethics Committee of the University of Cape Town.

Enzyme-linked immunosorbent assay (ELISA) for measuring antibodies to rubella

Rubella-specific IgG antibodies were screened for qualitatively using a commercial immunoassay (Dade Behring, Marburg, Germany). The procedure and the interpretation of the results were performed according to the manufacturer's instructions. Specimens with equivocal results were re-tested in duplicate. An optical density reading of > 0.2 at 450 nm was interpreted as positive for rubella IgG. Women with negative or equivocal results were regarded as being non-immune to rubella.

Results

A total of 1 200 serum specimens (300 from each district) were tested and included in the analysis. The combined results from all 4 districts tested are shown in Table I.

| Age group (yrs) | Number tested | Number immune (%) | 95% confidence interval (%) |
|-----------------|---------------|-------------------|-----------------------------|
| 15 - 24 | 600 | 572 (95.3) | 93.33 - 96.88 |
| 25 - 34 | 400 | 390 (97.5) | 95.45 - 98.79 |
| 35 - 45 | 200 | 196 (98.0) | 94.96 - 99.45 |
| Total | 1 200 | 1 158 (96.5) | 95.30 - 97.47 |

The age-stratified results from each district are shown in Table II. Combining the results from the 4 districts, a total of 95.3% of women in the 15 - 24-year age group, 97.5% in the 25 - 34-year group and 98% in the 35 - 45-year age group were immune to rubella. Using the chi-square test no statistically significant difference in the rate of rubella susceptibility was found between the 4 districts tested.

| Age group (yrs) | Number tested | Metropolitan (%) | 95% confidence interval (%) | West Coast/Winelands (%) | 95% confidence interval (%) | South Coast/Klein Karoo (%) | 95% confidence interval (%) | Boland (%) | 95% confidence interval (%) |
|-----------------|---------------|------------------|-----------------------------|--------------------------|-----------------------------|-----------------------------|-----------------------------|------------|-----------------------------|
| 15 - 24 | 150 | 141 (94.0) | 88.92 - 97.22 | 142 (94.7) | 89.76 - 97.67 | 145 (96.7) | 92.39 - 98.91 | 144 (96.0) | 91.50 - 98.52 |
| 25 - 34 | 100 | 96 (96.0) | 90.07 - 98.90 | 97 (97.0) | 91.48 - 99.38 | 100 (100) | 96.38 - 100* | 97 (97.0) | 91.48 - 99.37 |
| 35 - 45 | 50 | 48 (96.0) | 86.29 - 99.51 | 49 (98.0) | 89.35 - 99.95 | 49 (98.0) | 89.35 - 99.95 | 50 (100) | 92.90 - 100* |

* One sided, 97.5% confidence interval.

Discussion

Rubella vaccine is not part of the EPI schedule in South Africa and rubella virus continues to circulate freely. This study shows that by the time women in the Western Cape reach childbearing age, taken to be 15 years, 95.3% are immune to rubella. Similar prevalence rates were seen in all 4 districts sampled. This study was not powered to assess differences in rubella susceptibility among different racial groups in the province or to look for 'pockets' of increased rubella-susceptible women. At first glance the high level of immunity may seem reassuring; however, at the time of reaching childbearing age nearly 1 in 20 women in the Western Cape (4.7%) remain susceptible in an environment with freely circulating wild-type rubella. These patients are at substantial risk of primary rubella infection. Although there was no statistically significant difference in rubella susceptibility between the age groups ($p = 0.085$), using the non-parametric test for trend the observable increase in rubella immunity from 95.3% in the 15 - 24-year age group to 98% in the 35 - 45-year age group could be indicative of primary rubella infection occurring in women of childbearing age ($p = 0.04$). However, this interpretation is limited by the cross-sectional nature of the study. The data from this study are corroborated by data 'mined' from Groote Schuur Hospital's infertility clinic, which showed a rubella susceptibility rate of 4.97% among 1 139 patients screened from April 2002 to October 2004. These patients are routinely tested for immunity to rubella as part of their initial assessment.

Rubella infections tend to occur in late spring/summer and our laboratory has seen a consistent peak in the number of new congenital rubella cases during the winter months (6 - 9 months after seasonal peaks).

An additional point to consider is that exposed pregnant women with low-level immunity to rubella can be reinfected in the face of circulating wild-type rubella. The risk of fetal infection is approximately 8% following reinfection in the first 16 weeks of pregnancy, but fetal malformations are rare.¹⁰

Rubella vaccine has not been recommended for inclusion in the EPI in many developing countries because where sustained high coverage cannot be guaranteed, its introduction could paradoxically increase the number of susceptible young women by slowing but not interrupting virus transmission and thus shifting the age of first exposure into the reproductive years.¹¹ Private-sector MMR vaccination in South Africa creates the same potential hazard.⁶

Vaccination, however, is the only way of preventing congenital rubella. Two vaccination strategies may be implemented. A selective vaccination programme prevents CRS by vaccinating adolescent girls and women while allowing rubella to continue circulating. Universal vaccination of children has the aim of eliminating both rubella and CRS and has been shown to be the more successful strategy. Initially a combined approach would be the most prudent in South Africa as the impact on CRS prevention would be immediate.

Before authorities can consider including rubella vaccine in the EPI (SA), more information is needed on rubella seroprevalence in women of childbearing age in other provinces in South Africa. In addition, formal rubella and CRS surveillance need to be implemented. This information will provide a more scientific foundation for recommending that rubella vaccine be included in the national schedule. The magnitude of congenital rubella is underappreciated in South Africa and a concerted effort needs to be made to provide the data that will assist in its control. Even with the limitations of this small cross-sectional study, it is an important step in addressing the issue of seroprevalence of rubella antibodies in South Africa and in beginning to deal with this public health problem.

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