SEROPREVALENCE OF RUBELLA ANTIBODIES AMONG PREGNANT FEMALES IN SRI LANKA

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Abstract. The purpose of this study was to determine the seroprevalence of rubella antibodies among pregnant females in the Kalutara District of Sri Lanka, and to identify factors associated with susceptibility to rubella infection among pregnant females. A cross-sectional clinic-based study was conducted among 620 pregnant women attending antenatal clinics and residing in the district for more than one month. Data on the pregnant females and the socio-economic characteristics of the families were obtained using an interviewer-administered structured questionnaire. Three milliliters of blood was obtained to measure rubella-specific IgG antibody levels by ELISA (enzyme linked immunosorbent assay) tests. Overall, 76% of pregnant females were seropositive for rubella antibodies. Seropositivity in pregnant females increased with age. Susceptibility to rubella was significantly associated with rubella immunization status. Given the high susceptibility rate to rubella infection among pregnant females, it is imperative that any vaccination strategy in the short term should focus on reducing the number of susceptible women of child-bearing age.

INTRODUCTION

Rubella is a mild disease affecting children and adults. However, it can lead to disastrous consequences if acquired in early gestation, leading to fetal death, premature delivery and an array of congenital defects. Major epidemics of the disease have occurred in developed countries, such as Great Britain in 1940, Sweden in 1951 and the United States of America in 1964, and in developing countries, such as Panama in the mid 80's, and in Oman and Sri Lanka in the 1990s. In the United States alone, more than 20,000 cases of congenital rubella syndrome (CRS) have occurred (Anonymous, 1994; Basu *et al,* 1996; Robertson *et al,* 1997).

As the public health burden of rubella relates to the risk of infection of pregnant women, many countries have conducted serosurveys to determine the proportion of women of childbearing age who are susceptible to rubella (Cutts *et al,* 1997). A single cross-sectional survey of IgG antibody seroprevalence in women of childbearing age is of limited usefulness in demonstrating disease burden. Although a high level (*eg* >20%) of susceptibility is likely to indicate a high risk of CRS in that population, a low level of susceptibility cannot be taken to imply absence of risk of CRS. Even when susceptibility levels in women are below 10%, CRS can occur (Anonymous, 1996).

Immunity to rubella depends on a number of factors. There is an increase in the levels of immunity to rubella with age (Paul and Paul, 1983; Miller and Waight, 1990; Lin and Chen, 1994; Basu, 1996). Differences in rubella seroprevalence between urban and rural populations are diverse and contradictory (Rawls *et al,* 1967; Noah and Fowle, 1988; Yadav *et al,* 1995). A number of studies report an increase in the seroprevalence of rubella antibodies with parity, probably due to the relationship between parity and age (Miller *et al,* 1985; 1991; 1997).

In developing countries, the extent of maternal rubella infection remains unknown. There are very few clinical records of rubella infection and CRS cases. In Sri Lanka, Mendis (1989) tested immunity to the rubella virus in 534 women of childbearing age and found 228 (43%) to be susceptible, which was much higher than that found in most temperate countries.

Rubella was not a notifiable disease in Sri Lanka until 1996. Little has been done to determine

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the magnitude of the problem of rubella infection as a cause of embryonic and fetal damage in Sri Lanka. Hence, this study was conducted to determine the seroprevalence of rubella antibodies among pregnant females in a District of Sri Lanka and to identify factors associated with susceptibility to rubella infection among pregnant females.

METERIALS AND METHODS

Study setting

The study was conducted in the Kalutara District, Western Province of Sri Lanka, covering an area of 1,028 km^2 and having an estimated mid-year population of 1,031,480 in 1998. Twelve percent (12%) of the population live in urban areas. The district is divided into nine Medical Officer of Health (MOH) areas comprising 296 Public Health Midwife (PHM) areas and 763 Grama Niladhari (GN) divisions. The GN division is the smallest population unit identified for local government administrative purposes.

Study design

A cross sectional clinic-based study was conducted.

Selection of sample

The study population was identified as pregnant women who attended antenatal clinics in all MOH areas in Kalutara District and who resided in the district for more than one month. A sample of 620 pregnant mothers was studied. The study was conducted in 56 antenatal clinics. A systematic sampling technique was used to select pregnant females from each antenatal clinic. Twelve percent of the population (75 pregnant women) were from the urban sector and the rest of the population (545 pregnant women) was from the rural sector. Considering average clinic attendance, it was decided to sample every third pregnant female at each clinic after selecting the first female randomly.

Data collection

Data on the pregnant female and the socioeconomic characteristics of the family were obtained using an interviewer-administered structured questionnaire. Data obtained included obstetric information, clinical information on rubella infection and immunization, and serology results. Trained public health midwives of the area managing the antenatal clinics administered the questionnaire after explaining the objectives of the study to the participant and obtaining written informed consent.

Collection of blood samples

Blood for rubella antibodies was obtained from pregnant females at the antenatal clinics by medical officers under the supervision of the investigators. Three milliliters of venous blood was collected into a screw-capped bottle using a disposable syringe and needle under aseptic conditions. Bottles used for collection and transport of the samples were labeled and carried an unique link number which was also contained on the respective questionnaire. The collected bottles of blood were placed in ice and transported on the same day to the laboratory at the Department of Microbiology, Faculty of Medicine, University of Colombo.

Selection and training of interviewers

Forty (40) public health midwives from the Kalutara District were selected as interviewers and trained for 2 days in interviewing and administering the questionnaire. The questionnaire was pre-tested in a clinic in the Homagama MOH area in Colombo District, which was not selected for the study.

Processing of blood samples

Rubella-specific IgG antibody levels in the blood samples were determined by ELISA (enzyme linked immunosorbent assay), which were carried out at the Department of Microbiology, Faculty of Medicine, University of Colombo. Platelia Rubella IgG ELISA test kits (Pasteur Diagnostics Laboratories, France) were used. By comparing optical density readings of known concentrations for a range of standards, the serum concentration of rubella IgG antibody in the test sample was obtained in IU/ml. The validity of the test was assessed with the control panel of sera provided by the manufacturer. Test samples diluted 1/101 and exhibiting a titer <15 IU/ml were considered negative for the presence of rubella IgG antibodies. Subjects with these results were considered non-immune or susceptible to rubella infection.

Data processing and analysis

Data were coded and double-entered into a computer using the EpiInfo6 package. Univariate and bivariate analyses were performed to describe and determine associations between variables. Seropositivity rates were calculated for each age group. The significance of the difference in seropositivity rates between the different groups was

examined by the chi-square test.

Ethical considerations

Ethical clearance for the study was obtained from the Ethical Review Committee of the Faculty of Medicine, University of Colombo. Permission to conduct the study was obtained from the Deputy Provincial Director of Health Services, Kalutara and the Medical Officers of Health of the respective MOH areas. Pregnant females who were negative for rubella antibodies were informed and immunized at the termination of the current pregnancy.

RESULTS

A total of 620 pregnant females from 56 antenatal clinics in the Kalutara District of Sri Lanka were studied. All selected females agreed to participate in the study. Table 1 shows the characteristics of the study population. The majority of the pregnant females (79%) were in the age group 20-34 years. The ethnic and religious composition of the study population was similar to that of the Kalutara District. Five hundred and seventy-five (93%) pregnant females were currently married. Six hundred and fifteen (99.2%) pregnant females and 616 (99.4%) of their husbands/partners had attended school. Three hundred and thirty-seven (52.7%) pregnant females and 320 (51.6%) husbands/partners had studied up to Grade 10, indicating a relatively satisfactory level of education among the study group. Accordingly, almost 98% of the population was literate.

Occupations were categorized according to the occupational categories used in the Annual Employment Return to the Commissioner of Labor by the Department of Census and Statistics, Sri

Table 1
Characteristics of pregnant females.

Variable	No.	%
Age (years)		
≤ 19	65	10.5
20-24	145	23.4
25-29	202	32.5
30-34	143	23.1
35-39	56	9.0
40-44	9	1.5
Marital status		
Currently married	575	92.7
Unmarried	42	6.8
Separated/Divorced/Widowed	3	0.5
Educational level		
No schooling	5	0.8
Grades 1-5	34	5.5
Grades 6-8	104	16.6
Grades 9-10	327	52.7
Grade 11-12	139	22.4
University education	11	1.8
Educational level of partner		
No schooling	4	0.7
Grades 1-5	38	6.1
Grades 6-8	118	18.9
Grades 9-10	320	51.6
Grade 11-12	129	20.9
University education	11	1.8
Monthly family income (SL Rs, 1 US$=90.00 SL Rs)		
≤ 1,000	24	3.9
1,001-2,000	95	15.3
2,001-5,000	282	45.5
> 5,000	219	35.3
Social class		
I	3	0.5
II	10	1.6
III	304	49.1
IV	292	47.0
V	11	1.8
Number of persons in household		
2	71	11.4
3	161	26.0
4	145	23.4
5	102	16.5
≥ 6	125	22.7
Employment status of pregnant female		
Employed	75	12.1
Housewife (full time)	545	87.9
Employment status of partner		
Professional/Technical	14	2.3
Clerical and related workers	94	15.2
Sales workers	131	21.1
Skilled/semi-skilled/unskilled	373	60.1
Unemployed	8	1.3
History of symptoms suggestive of rubella		
Had symptoms	7	1.1
Did not have symptoms	613	98.9
Rubella immunization status		
Immunized	245	39.6
Non-immunized	375	60.4
Parity		
Primiparous	277	44.7
Multiparous	343	55.3
Period of amenorrhea at enrollment (weeks)		
≤ 12	75	12.1
13-28	241	38.9
≥ 29	304	49.0
Total	620	100

Lanka, 1997. Approximately 12% of pregnant females were currently employed outside the home, the rest being housewives, while almost 99% of the husbands/partners were employed. Two hundred and nineteen families (35%) had a monthly family income of more than 5,000 Sri Lankan rupees per month (1 USD = 90.00 Sri Lankan Rupees). Social class was ascertained using the method recommended by Sewell (1994), and Hollingshed and Redlich (1958). Ninty-six percent of pregnant females belonged to social classes III and IV. Seventy-seven percent of the households had five or fewer persons.

Six hundred and thirteen (98.9%) pregnant females did not have recent symptoms suggestive of rubella. Only one mother had acquired a rubella-like illness during the current pregnancy. Two hundred and forty-five (39.6%) pregnant females were immunized, of whom the majority (81%) were immunized in 1997 and 1998. Two hundred and seventy-seven (44.7%) pregnant females were primiparous. Only 11% of the pregnant females were in their 1st trimester of pregnancy.

Age-specific seroprevalence data of pregnant females are given in Table 2. Overall, 76% of pregnant females were seropositive for rubella antibodies. Seropositivity in pregnant females increased with age. The proportion of pregnant females under 20 years of age seropositive for rubella was 0.71, while among 25-29 year-old pregnant females it was 0.79. Thirty-five to forty-four year-old pregnant females had the lowest susceptibility (0.18). However, the differences in the proportions were not statistically significant (χ^2_4 =4.15; p=0.3866).

Table 3 gives the susceptibility of pregnant females to rubella infection by selected variables. Susceptibility to rubella was significantly associated only with rubella immunization status, with susceptibility being significantly less in the immunized group. Of the unimmunized females, 141 (37%) were susceptible to rubella. Although not statistically significant, a higher percentage of females resident in rural areas (25%) was susceptible to rubella, compared to those resident in urban areas (16%). Almost 25% of housewives were susceptible to rubella infection. Susceptibility to rubella infection appeared to be greater if the households were small, but the association was not statistically significant.

DISCUSSION

In developing countries, the extent of maternal rubella infection is largely unknown. There are very few clinical records of rubella infection and/or CRS. Clearly, the first step in determining an appropriate immunization policy for a given population is to carry out a serologic survey, in order to determine the seroprevalence of rubella antibodies (Hizel, 1995).

This study comprised a clinic-based cross-sectional study of pregnant females attending antenatal clinics in the Kalutara District of Sri Lanka. Pregnant females are the most suitable group for assessing susceptibility to rubella infection among women of child-bearing age. They are at risk and are easily reached through routine screening at antenatal clinics (Noah and Fowle, 1988).

The seroprevalence of rubella antibodies among pregnant women in this study was 76%. In an earlier study done in Sri Lanka, 43% of women of child-bearing age were found to be susceptible to rubella infection (Meudis, 1989). This study was done among female medical students and some females selected from some districts at a time when rubella immunization was not offered on a national scale to women of child-

Table 2
Rubella seroprevalence among pregnant females by age.

Age group (years)	Sample size	No. sero-positive	No. sero-negative	Proportion sero-positive	95% confidence interval
<20	65	46	19	0.71	0.71 - 0.82
20 - 24	145	106	39	0.73	0.66 - 0.79
25 - 29	202	160	42	0.79	0.73 - 0.85
30 - 34	143	106	37	0.74	0.72 - 0.92
35 - 44	65	53	12	0.82	0.67 - 0.81
Total	620	471	140	0.76	0.73 - 0.79

Table 3
Association between susceptibility to rubella infection and selected variables.

Variable	Susceptibility to rubella infection				Odds ratio (95% CI)
	Yes		No		
	No.	%	No.	%	
Marital status					
Married	135	23.5	440	76.5	0.68
Single	14	31.1	31	68.9	(0.34-1.39)
Area of residence					
Urban	12	16.0	63	84.0	0.57
Rural	137	25.1	408	74.9	(0.28-1.12)
Employment status of mother					
Employed	13	17.3	62	82.7	0.63
Housewife (full time)	136	25.0	409	75.0	(0.32-1.22)
Parity					
Primiparous	66	23.8	211	76.2	0.98
Multiparous	83	24.1	260	75.9	(0.66-1.44)
Number of persons in household					
≤ 5	118	24.6	361	75.4	1.16
> 5	31	22.0	110	78.0	(0.72-1.87)
Social class					
I, II, III	68	21.5	249	78.5	0.75
IV, V	81	26.7	222	73.3	(0.51-1.10)
History of symptoms suggestive of rubella					
Yes	2	28.5	5	71.5	1.27
No	147	23.9	466	76.1	(0.12-7.84)
Rubella immunization status					
Immunized	8	3.0	237	97.0	0.06
Non-immunized	141	37.0	234	63.0	(0.02-0.12)

bearing age, and was probably a reflection of natural infection in the community. Although the sampling technique was not clearly outlined, and other methodological issues existed in this study, the results of the former study may be compared with the present one, to look at trends over the long term. However, differences in susceptibility to rubella infection between the two studies may be due to the protection offered by immunization of women of child-bearing age, on a national scale, since 1996. The reduction in susceptibility, from 43% to 24%, also suggests that the vaccination program, which targeted women of child-bearing age, has not been very successful and that a significant proportion of women of child-bearing age are still susceptible.

The seroprevalence of rubella antibodies in pregnant females increased with age, as expected, except for the 25-29 year-old group with a seroprevalence of 79%, which was higher than that for the 30-34 year group. This probably indicates that the younger age groups may have accepted the rubella vaccination offered since 1996 more than the older age groups. These findings are consistent with studies carried out in other developing countries such as India, where the reported susceptibilities ranged from 37-47% (Khare *et al,* 1987; 1990), and Korea, where 27% susceptibility was reported (Park and Kim, 1996). In contrast, lower susceptibilities in comparable populations have been reported from developed countries, such as the United Kingdom (3-5%) (Noah and Fowle, 1988), United States of America (10.5%) (Allen *et al,* 1985) and Switzerland (6%) (Zuffery *et al,* 1995). Trends in seroprevalence with age are consistent with vaccination coverage among different age groups, as reported in this study. Vaccine coverage in the district was high among the younger age groups. The coverage for 25-29 year-old females was the

highest, reported to be 45%. Increased seropositivity among the older age groups was probably due to acquired immunity through natural infection.

Rural pregnant females were more susceptible to rubella than urban females but the difference in susceptibility was not statistically significant. Dowdle *et al* (1970) and Yamamoto *et al* (1995) found an urban/rural difference, with rural mothers being more susceptible than urban mothers. However, Gomwalk and Ezeronye (1985) found no difference between urban and rural pregnant mothers in Nigeria. The urban/rural difference observed in this study may be due to less overcrowding and exposure, and the greater observance of specific exposure-reducing cultural practices such as the isolation of persons with communicable diseases in rural areas.

There were no ethnic differences in seroprevalence of rubella antibodies. In Britain, it has been reported that susceptibility was higher in Asian women than in non-Asian women (Miller *et al*, 1987; 1990). Zufferey *et al* (1995) reported women of Swiss nationality were less susceptible to rubella than women of other nationalities. The equal accessibility of immunization services provided by the Department of Health to all ethnic groups in the Kalutara District, and the common cultural patterns of the different ethnic groups in the district, may have been why no single ethnic group was more susceptible to rubella.

This study found that susceptibility to rubella infection was not significantly associated with the socio-economic status of the mother. However, the number of pregnant females in the higher social classes was too few to make inferences. Given the characteristics of the population in the Kalutara District, the sample selected for this study is comparable. Studies done in Delhi revealed that females of low socio-economic status had a higher seroprevalence of rubella antibodies then women of higher socio-economic status.

In this study, both primiparous and multiparous women were equally susceptible to rubella. Miller *et al* (1985) and Kadoya *et al* (1998) found that nulliparous women were more susceptible to rubella than parous women. They also observed in parous women that there was no difference in susceptibilities to rubella between those in their second and those in subsequent pregnancies.

As expected, susceptibility to rubella infection was significantly associated with immunization status. Very few immunized mothers (3%) were susceptible to rubella. Given the characteristics of the Kalutara District, which are similar to the rest of the country, the findings of this study may be considered representative of the entire country.

The decision to start a vaccination policy against rubella needs careful local epidemiological studies to determine whether such a policy is necessary and, if vaccination is incompletely implemented, whether the incidence of CRS will increase (Hizel, 1995). Given the relatively high median age of infection estimated by Palihawadana (2000), it is imperative that any vaccination strategy should focus on reducing the number of women of child-bearing age susceptible to rubella in the short term.

Miller *et al* (1987) confirmed the Manchester experience, that even with individual follow-up of non-immune women, total vaccination of the target group cannot be achieved. The risk of infection among the remaining susceptible population is directly dependent on the prevalence of rubella, particularly among children. Hence, to eliminate congenital rubella, selective vaccination policies must be augmented by the additional rubella vaccination of children of both sexes.

The policy of selectively vaccinating females 12-14 years of age and child-bearing age in Sri Lanka was introduced to reduce the number of susceptible women of childbearing age. In order to reduce the circulation of wild rubella virus in the community, an additional strategy, such as immunizing all children at 3 years of age is required. This strategy was implemented in Sri Lanka, in April 2001. A supplement to this strategy could be the incorporation of a 'pulse rubella' strategy for all women of child-bearing age, to be conducted within a year. This would significantly reduce the number of current rubella-susceptible women of reproductive age.

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