

Rubella serosurveys at three Aravind Eye Hospitals in Tamil Nadu, India

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Objective To determine the susceptibility of female eye hospital staff to rubella infection and the potential risk for hospital-based rubella outbreaks.

Methods A prospective cohort study on the seroprevalence of rubella IgG antibodies was conducted at three large eye hospitals in Coimbatore, Madurai and Tirunelveli, Tamil Nadu, India, where young children with eye abnormalities attributable to congenital rubella are treated. A total of 1000 female hospital employees aged 18–40 years agreed to participate and gave written informed consent.

Findings The proportions of rubella-seronegative women were: 11.7% at Coimbatore, with a 95% confidence interval (CI) of 8.1–16.5; 15% at Madurai (95% CI = 12.3–18.1), and 20.8 at Tirunelveli (95% CI = 14.7–28.6). For the entire cohort the proportion seronegative was significantly higher among married women (21.5%) than among single women (14.0%) ($P = 0.02$). Rates of seronegativity were highest among physicians and lowest among housekeepers. All 150 seronegative women in the study sample accepted a dose of rubella vaccine.

Conclusion These are the first rubella serosurveys to have been reported from eye hospitals in any country. The relatively high rate of susceptibility indicated a risk of a rubella outbreak, and this was reduced by vaccinating all seronegative women. A policy has been established at all three hospitals for the provision of rubella vaccine to new employees. Other hospitals, especially eye hospitals and hospitals in countries without routine rubella immunization, should consider the rubella susceptibility of staff and the risk of hospital-based rubella outbreaks.

Keywords Rubella/epidemiology/immunology; Rubella syndrome, Congenital; Hospitals, Special; Personnel, Hospital; Cross infection; Rubella vaccine; Women; Seroepidemiologic studies; Prospective studies; Cohort studies; India (*source: MeSH, NLM*).

Mots clés Rubéole/épidémiologie/immunologie; Syndrome de rubéole congénitale; Hôpital spécialisé; Personnel hôpital; Infection hospitalière; Vaccin antirubéoleux; Femmes; Etude séroépidémiologique; Etude prospective; Etude cohorte; Inde (*source: MeSH, INSERM*).

Palabras clave Rubéola/epidemiología/inmunología; Síndrome de rubéola congénita; Hospitales especializados; Personal de hospital; Infección hospitalaria; Vacuna contra la rubéola; Mujeres; Estudios seroepidemiológicos; Estudios prospectivos; Estudios de cohortes; India (*fuente: DeCS, BIREME*).

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Introduction

If health-care workers are not immune to rubella they are at risk of contracting it, especially from their patients. This is particularly important in hospitals treating paediatric patients with congenital rubella syndrome (CRS) and in countries that do not include rubella vaccine in their national immunization programmes. Rubella has been a special concern of ophthalmologists for more than 60 years. In 1941, Gregg reported cataracts in 78 infants, many of whom were also affected by congenital heart disease and failure to thrive (1). Most of the mothers of

these children had contracted rubella during the early months of pregnancy, and Gregg therefore postulated that rubella virus was the cause of the infant malformations, later called CRS. Subsequent studies confirmed that the risk of rubella defects was high in infants whose mothers were infected by rubella virus in the first 16 weeks of pregnancy (2). WHO estimates that, worldwide, more than 100 000 children are born with CRS each year, most of them in developing countries (3). A study in southern India during 1993–94 found that CRS was the cause of 26% of cases of children born blind with congenital cataracts (4).

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The WHO-recommended case definition for probable rubella is a patient with fever, maculopapular rash and cervical, suboccipital or postauricular lymphadenopathy or arthralgia/arthritis (5). Because of the difficulty of clinical diagnosis of rubella, laboratory confirmation is required. This involves a rubella-specific IgM test on a serum specimen obtained within 28 days after the onset of rash.

The WHO-recommended case definition for clinically confirmed CRS is an infant with two of the complications described in (a) below or with one of those in (a) and one in (b) (5).

- (a) Cataract(s), congenital glaucoma, congenital heart disease, loss of hearing, pigmentary retinopathy.
- (b) Purpura, splenomegaly, microcephaly, mental retardation, meningoencephalitis, radiolucent bone disease, onset of jaundice within 24 hours after birth.

Laboratory confirmation of CRS involves a rubella-specific IgM test on a blood specimen obtained within the first year of life, preferably within the first six months. Where appropriate laboratory expertise is available, the detection of rubella virus in specimens from the nasopharynx or urine of an infant with suspected CRS may also provide laboratory confirmation. Infants with CRS shed rubella virus for long periods in nasopharyngeal secretions and urine, and close contact with such infants can therefore lead to rubella infection. In a large case series in the USA, rubella virus was isolated from nasopharyngeal secretions of 84% of infants with CRS during the first month of life and from 62% aged 1–4 months, 33% aged 5–8 months and 11% aged 9–12 months (6). Eye disease is a common sign of CRS: in a case series of 46 children with CRS at the Aravind Eye Hospital, Madurai, India, cataract was present in 81 eyes (7). A special risk occurs during cataract surgery for a child with CRS because the lens aspirate may contain live rubella virus. Rubella virus has been identified in lens aspirates from children aged up to 3 years (8).

Nearly 50% of rubella infections are subclinical, and an infected health care worker may therefore unknowingly transmit the virus to patients or other staff. This poses a risk of CRS if a woman becomes infected with rubella in the early months of pregnancy. Hospital-based rubella outbreaks have been reported from industrialized countries (9, 10). In India, such an outbreak was reported from the St John's Medical College and Hospital, Bangalore, in 1990 (11), and another occurred in 1996 among medical and nursing students and staff at the Christian Medical College, Vellore, Tamil Nadu (12).

This paper reports the results of a serological study to assess the rubella susceptibility of female employees at three Aravind Eye Hospitals.

Methods

From May to December 2002 a rubella serosurvey was conducted among female personnel at three Aravind Eye Hospitals in Coimbatore, Madurai and Tirunelveli, Tamil Nadu, India, with a total of 2675 beds. In 2002 these hospitals conducted approximately 190 000 operations and more than 1.3 million outpatient visits. All female personnel aged 18–40 years were eligible and were given background information about the study; those who provided voluntary and written informed consent to participate were enrolled. The study was approved by: the

Aravind Eye Hospital Ethics Committee, Madurai; the Indian Council for Medical Research, New Delhi; and the WHO Secretariat Committee for Research Involving Human Subjects. A standard questionnaire was administered on demographic characteristics, marital and vaccination history, and type and duration of employment. A 5-ml blood specimen was obtained from each participant. The serum was separated and stored at the study site at 4–8 °C before being transferred to the central laboratory at Madurai Hospital, where it was stored at –20 °C. Rubella-specific IgG antibodies were detected using a commercial IgG enzyme-linked immunosorbent assay (ELISA) kit (catalogue number 51208, Human Gesellschaft für Biochemica und Diagnostica mbH, Wiesbaden, Germany) in accordance with the manufacturer's instructions. The Enteric, Respiratory and Neurological Virus Laboratory of the Health Protection Agency, London, served as the reference laboratory for the study and provided on-site training of the laboratory technician. The London laboratory conducted quality control tests on the human rubella IgG ELISA kit every six months and performed a blinded proficiency test on the Aravind Hospital laboratory.

Seronegative women were offered rubella vaccine and, as recommended by WHO, were advised to avoid pregnancy for one month following vaccination (13). The RA 27/3 rubella vaccine (Serum Institute of India, Pune) was supplied in single-dose vials that were stored at 4–8 °C during the study. The vaccine was reconstituted with diluent supplied by the manufacturer and administered intramuscularly.

Data were double-entered in Epi Info, version 6.04 (Centers for Disease Control and Prevention, Atlanta, GA, USA and WHO, Geneva, Switzerland), and cleaned. Statistical analyses were performed using Stata, version 7.0 (Stata Corporation, College Station, TX, USA). Seroprevalence levels were compared by χ^2 tests.

Results

Of the 1038 female employees aged 18–40 years, 1000 (96%) consented to participate in the study, 248 of them at Coimbatore Hospital, 608 at Madurai Hospital and 144 at Tirunelveli Hospital. The age range of the participants was 18–40 years (mean, 21.7 years). Overall, 150 were negative for rubella IgG antibody (15%; 95% confidence interval (CI) = 13.3–16.7%). All the participants were informed of their test results and the seronegative women all accepted a dose of rubella vaccine. The seronegativity rates at the Coimbatore, Madurai and Tirunelveli hospitals were 11.7% (95% CI = 8.1–16.5), 15.0% (95% CI = 12.3–18.1) and 20.8% (95% CI = 14.7–28.6), respectively (Fig. 1). The differences between the hospitals were non-significant, nor were there significant differences in seronegativity rates between age groups (Table 1). However, the proportion of seronegative women was significantly higher ($P = 0.02$) among the 135 married women (21.5%) than among the 865 single women (14.0%).

The categories of employees participating in the study included doctors, nurses, opticians/refractionists, laboratory staff, medical equipment production/repair staff, and housekeepers/caterers. The percentage of seronegativity was highest among doctors (26.7%) and lowest among housekeepers/caterers (11.1%) (Table 2).

Of the 1000 participants, only two physicians and one nurse reported previous receipt of rubella vaccine.

Fig. 1. Proportions of female employees seronegative for rubella IgG, by age group, Aravind Eye Hospitals at Coimbatore ($n = 248$), Madurai ($n = 608$), and Tirunelveli ($n = 144$), Tamil Nadu, India

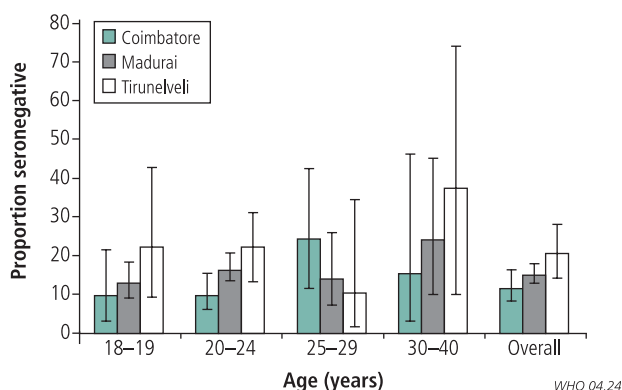


Table 1. Rubella IgG serosurvey among female employees by age group at three Aravind Eye Hospitals, Tamil Nadu, India, 2002

Age group (years)	No. examined	No. negative	95% CI ^a
18-19	292	38 (13.0) ^b	13.0-46.2
20-24	552	83 (15.0)	11.2-35.3
25-29	110	18 (16.4)	6.0-41.1
30-40	46	11 (23.9)	13.1-46.2
Total	1000	150 (15.0)	13.3-16.9

^a CI = confidence interval.

^b Figures in parentheses are percentages.

Discussion

These are the first rubella serosurveys reported from eye hospitals anywhere in the world. At the three hospitals, 12-21% of female health workers and 27% of female physicians were rubella seronegative. These are moderate-to-high rates. A WHO-sponsored global review identified more than 100 serosurveys conducted among women of childbearing age in 45 developing countries before the introduction of rubella vaccine (14). The proportion who were rubella seronegative was less than 10% in 13 countries, 10-24% in 20 countries and 25% or higher in 12 countries. A number of previous studies have demonstrated the potential risk of rubella to hospital employees, most commonly those working in obstetrics or paediatrics departments (15-18).

The high proportion of rubella-seronegative physicians is unexplained. However, only 30 physicians participated in the study, of whom 19 (63%) came to the Aravind Eye Hospitals from different states in India where their previous exposure to rubella virus may have differed from that of other hospital employees. The women employed at the Aravind Eye Hospitals who were not physicians came from the local areas and were possibly representative of working women in their respective cities, although they may have had additional exposure to rubella virus in the hospital work environment. Unmarried women employees at the three Aravind Eye Hospitals lived in dormitory residences. No outbreaks of rubella or measles had

Table 2. Results of rubella IgG serosurvey among female employees, by type of personnel, at three Aravind Eye Hospitals, Tamil Nadu, India, 2002

Type of personnel	No. examined	No. negative	Mean age (years)
Physicians	30	8 (26.7) ^a	28.9
Laboratory staff	22	4 (18.2)	23.2
Administrative staff	122	21 (17.2)	22.3
Medical equipment production/repair staff	174	28 (16.1)	20.8
Nurses/counsellors	407	58 (14.3)	21.3
Opticians/refractionists	164	22 (13.4)	21.2
Housekeepers/caterers	81	9 (11.1)	21.2
Total	1000	150 (15.0)	21.7

^a Figures in parentheses are percentages.

been reported among dormitory residents during the past eight years, although there were varicella outbreaks. We did not demonstrate an inverse relationship between age and the proportion of seronegative women, perhaps because of the small number of women aged ≥ 30 years. Previous studies indicated great variability in the proportions of women in given age groups who were susceptible to rubella, and some studies showed little decrease in susceptibility over the age range studied (19). A clearer picture of the community-based risk of rubella in the female population would be provided by an antenatal serosurvey with stratified sampling, ensuring a more even distribution of age groups. Such a study is planned.

Rubella serosurveys in India

A review of the literature identified 15 rubella serosurveys in women of childbearing age in India (20-28, Table 3). However, the data should be viewed with caution because of the diversity of the laboratories and assays in question. Almost all the studies carried out in 1990 and subsequently involved the use of rubella IgG ELISA assays, whereas earlier studies employed haemagglutination inhibition assays. Nevertheless, a review of rubella test methods indicated general agreement between these assays (29). The 15 serosurveys from India showed that susceptibility ranged from 5% to 45%, reflecting the large size of the country and the pattern of rubella virus circulation. A larger proportion of women can be expected to be susceptible during periods when rubella virus circulates at an endemic level than during periods following rubella outbreaks. There is evidence that the proportion of susceptible women in Tamil Nadu has increased gradually from 4% in the 1980s to the 15% found in the present study, suggesting endemic levels of virus circulation with no major outbreaks.

Study limitations

A major limitation of our study was the lack of background rubella surveillance data that would provide an understanding of the local endemic-epidemic cycles of rubella virus. In the future such data should be increasingly available from countries in the South-East Asia Region of WHO. During 2002-03, staff from one or more laboratories in Bangladesh, Bhutan, India, Indonesia, Maldives, Myanmar, Nepal, and Sri Lanka attended

Table 3. Summary of rubella serosurveys among women, India, 1970–2002

State/Territory	Location	Year	Age group (years)	No. studied	% negative	Laboratory assay and cut-off titre ^a	Reference
Andhra Pradesh	Hyderabad	1991	Antenatal	274	5	ELISA	20
Chandigarh	Chandigarh	1973	16–40	325	19	HI, 1:10	21
Delhi	Delhi urban	1970	15–34	137	15	HI, 1:10	22
Delhi	Delhi rural	1970	15–34	124	28	HI, 1:10	22
Delhi	Delhi	1989	Antenatal	603	31	HI, 1:16	23
Delhi	Delhi	1994	Teens + Childbearing	200	45	HI, 1:8	24
Kerala	Trivandrum	1981	Antenatal	536	26	HI, 1:16	25
Tamil Nadu	Vellore	1984	Antenatal	132	4	HI, 1:8	26
Tamil Nadu	Vellore	1990–91	Antenatal	931	11	ELISA	D. Brown, personal communication, 2000
Tamil Nadu	Vellore	1997–98	Antenatal	765	13	ELISA	D. Brown, personal communication, 2000
Tamil Nadu	Coimbatore Madurai Tirunelveli	2002	18–40	248 608 144	12 15 21	ELISA	Present study
Uttar Pradesh	Lucknow	1981	Antenatal	300	22	HI, 1:8	27
West Bengal	Calcutta	1972	15–25	176	43	HI, 1:10	28

^a ELISA = enzyme-linked immunosorbent assay; HI = haemagglutination inhibition.

a one-week workshop in Bangkok, Thailand or Pune, India. Participants received training in the IgM ELISA tests for measles and rubella, and their laboratories were subsequently enrolled in a proficiency-testing scheme. To complement the laboratory training a surveillance and data management workshop was held during September 2003 in New Delhi for countries of the South-East Asia Region. The surveillance and reporting of measles and rubella are expected to benefit from the experience gained in the highly successful surveillance of acute flaccid paralysis in this Region.

Risk groups and rubella vaccination

Our study identified physicians as the employee group at highest risk. The vaccination of seronegative individuals can help to lower the institutional risk of hospital-based rubella outbreaks. In addition, a new policy is planned for vaccinating hospital physicians and nurses against rubella at the start of their employment, without serological screening. This is consistent with the WHO recommendation that the health of employees, including

their immunization history, be reviewed at recruitment (30). Rubella vaccination is important for doctors and nurses working at eye hospitals anywhere in the world, and for obstetricians, midwives, paediatricians, neurologists, cardiac surgeons, ear, nose and throat surgeons and other specialists who see children with congenital rubella. Moreover, the provision of rubella vaccine to both medical and nursing students before they entered the hospital environment would help to prevent hospital-based outbreaks and would protect female health personnel before their first pregnancies. ■

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Conflicts of interest: none declared.

Résumé

Enquêtes sérologiques sur la rubéole dans trois hôpitaux ophtalmologiques Aravind au Tamil Nadu (Inde)

Objectif Déterminer la sensibilité du personnel féminin des hôpitaux ophtalmologiques à l'infection rubéoleuse et le risque potentiel de flambées hospitalières de rubéole.

Méthodes Une étude de cohorte prospective sur la séroprévalence des anticorps antirubéoleux de la classe des IgG a été réalisée dans trois grands hôpitaux ophtalmologiques (Aravind Eye Hospitals) à Coimbatore, Madurai et Tirunelveli, dans le Tamil Nadu (Inde), où sont traités de jeunes enfants atteints d'anomalies oculaires dues à la rubéole congénitale. En tout, 1000 femmes faisant partie du personnel hospitalier et âgées de 18 à 40 ans ont accepté de participer à l'étude et ont donné par écrit leur consentement éclairé.

Résultats La proportion de femmes séronégatives pour la rubéole était de 11,7 % à Coimbatore, avec un intervalle de confiance (IC) à 95 % de 8,1-16,5 %, 15,0 % à Madurai (IC 95 % : 12,3-18,1 %) et 20,8 % à Tirunelveli (IC 95 % : 14,7-28,6 %). Au niveau de la cohorte entière, la proportion de femmes séronégatives était

significativement plus élevée chez les femmes mariées (21,5 %) que chez les femmes célibataires (14,0 %) ($p = 0,02$). Le taux de séronégativité le plus élevé a été observé chez les médecins et le plus faible chez les intendantes. Les 150 femmes séronégatives de l'échantillon étudié ont accepté de recevoir une dose de vaccin antirubéoleux.

Conclusion Ces enquêtes sérologiques sur la rubéole sont les premières rapportées au niveau mondial pour des hôpitaux ophtalmologiques. Le taux de sensibilité relativement élevé observé indiquait un risque de flambée de rubéole, que l'on a réduit en vaccinant toutes les femmes séronégatives. Les trois hôpitaux ont établi une politique consistant à vacciner les nouvelles employées. D'autres hôpitaux, en particulier les hôpitaux ophtalmologiques et les hôpitaux des pays qui ne pratiquent pas la vaccination systématique contre la rubéole, devraient prendre en compte la sensibilité de leur personnel à la rubéole et le risque de flambées de rubéole en milieu hospitalier.

Resumen

Estudios serológicos sobre la rubéola en tres hospitales oftalmológicos Aravind de Tamil Nadu (India)

Objetivo Determinar la vulnerabilidad del personal femenino de hospitales oftalmológicos a la infección rubeólica, así como el riesgo potencial de brotes de rubéola en los hospitales.

Métodos Se llevó a cabo un estudio de cohortes prospectivo sobre la seroprevalencia de anticuerpos IgG contra la rubéola en tres grandes hospitales oftalmológicos de Coimbatore, Madurai y Tirunelveli, en el Estado de Tamil Nadu, India, donde reciben tratamiento los niños pequeños que sufren anomalías oculares causadas por la rubéola congénita. Un total de 1000 empleadas de hospital de 18-40 años respondieron positivamente a la invitación de participar y dieron por escrito su consentimiento informado.

Resultados Las proporciones de mujeres seronegativas para la rubéola fueron las siguientes: 11,7% en Coimbatore, con un intervalo de confianza (IC) del 95% de 8,1%-16,5%; 15% en Madurai (IC95% = 12,3%-18,1%), y 20,8% en Tirunelveli (IC95% = 14,7%-28,6%). En el conjunto de la cohorte la proporción

seronegativa fue significativamente mayor entre las mujeres casadas (21,5%) que entre las solteras (14,0%) ($P = 0,02$). Las tasas de seronegatividad fueron máximas entre las médicas y mínimas entre las trabajadoras de los servicios de limpieza. Las 150 mujeres seronegativas aceptaron una dosis de la vacuna antirrubéolica.

Conclusión Estas son las primeras encuestas serológicas de que se informa sobre la rubéola en los hospitales oftalmológicos en país alguno. La tasa relativamente alta de vulnerabilidad mostró que existía el riesgo de que se produjera un brote de rubéola, riesgo que se redujo vacunando a todas las mujeres seronegativas. Se ha instaurado en los tres hospitales una política destinada a suministrar la vacuna antirrubéolica a las nuevas empleadas. Otros hospitales, especialmente los hospitales oftalmológicos y los hospitales de los países sin inmunización sistemática contra la rubéola, deberían estudiar la vulnerabilidad del personal a esta enfermedad y el riesgo de brotes de rubéola en los hospitales.

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