

Seroprevalence of varicella zoster and rubella antibodies among rural populations of the Chaco region, south-eastern Bolivia

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Summary

OBJECTIVE To determine the seroprevalence of antibodies against varicella zoster virus (VZV) and rubella virus among the population of two rural areas, Camiri and Villa Montes, Chaco region, south-eastern Bolivia.

METHODS In a cross-sectional study, serum samples from randomly selected subjects were screened for VZV- and rubella antibodies using enzyme-linked immunosorbent assay (ELISA).

RESULTS The prevalence of VZV antibodies was 80% (391 of 489). No significant differences were observed between genders and study areas. The prevalence increased with age with a seropositivity rate of 21.2% in the 1–4-year-old children, 56.9% in the 5–9 age group and 83.7% in the 10–14 age group, and reached 98.2% in over 45-year olds. The prevalence of rubella virus antibodies was 76.9% (377 of 490), without significant differences between genders and study areas. Similar to the trend observed for VZV antibodies, the seroprevalence increased with age with a seropositivity rate of 18.1% in the 1–4-year-old children, 53.9% in the 5–9 age group and 78.4% in the 10–14 age group, and reached 94.7% in over 45-year-old subjects. Among the 95 women of childbearing age (15–44 years) the susceptibility rate was 11.6%.

CONCLUSIONS A common seroimmunological profile was evidenced for the two infections. The age-specific profile of VZV seropositivity differs from that reported for other tropical countries where higher median age of seroconversion and lower seroprevalence among adults are observed. Data concerning the prevalence of immunity to rubella may be useful to evaluate the impact of the recently introduced rubella immunization programme.

keywords varicella-zoster virus, rubella virus, seroepidemiology, Bolivia, tropics

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Introduction

Varicella and rubella, caused by varicella zoster virus (VZV) and rubella virus, are common contagious diseases worldwide. Varicella is generally a benign childhood exanthematous disease, but when it occurs in older age groups or in immunocompromised hosts it tends to be more severe and the risk of serious complications, including pneumonia and encephalitis, is greater (Whitley 2000). The varicella epidemiology pattern differs from temperate to tropical and subtropical regions. In the latter

regions more cases are seen in adolescents and young adults (Maretic & Cooray 1963; Sinha 1976). A safe and efficacious varicella vaccine has been recently licensed in many countries, but vaccination policy is still a matter of debate (Krause & Klinman 1995; Plotkin 1996; WHO 2000a).

Rubella virus normally causes a mild, self-limited disease characterized by rash, fever and lymphadenopathy. Its public health importance is related to the effects on the foetus of primary rubella infection in pregnant women. Congenital rubella syndrome (CRS) can lead to deafness,

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heart disease, cataracts and a variety of other permanent manifestations (Gerson 2000). With the aim to prevent CRS by controlling postnatal rubella, vaccination programmes have been developed in many parts of the industrialized world. In those countries large rubella epidemics have stopped and the incidence of CRS declined (Plotkin *et al.* 1999).

The burden of disease from CRS is well documented in several developing countries, while data from many other such countries suggest that they have a risk of CRS at least as high as that in industrialized countries during the pre-vaccination era (Cutts *et al.* 1997). Rubella vaccine was incorporated in the Bolivian national immunization programmes starting from August 2000. Both rubella and varicella are notifiable diseases, but probably because of their benign course they are generally under-reported. Hence, the incidence and prevalence data about these diseases are considered unreliable. To our knowledge, neither clinical nor epidemiological study data about rubella and varicella in Bolivia have been published. To provide information about rubella and varicella immunity in the rural population of south-eastern Bolivia, we conducted a cross-sectional serosurvey at the end of 1997 with the agreement of the Bolivian National Department of Epidemiology of the Ministry of Social Welfare and Public Health and with the support of the Guaraní political organization (*Asamblea del Pueblo Guaraní*).

Materials and methods

The Chaco region lies in south-eastern Bolivia between longitude 64°30' and 58°50' east of the Greenwich meridian and latitude 17°58' and 22°20' south, and includes five provinces: Cordillera, Luis Calvo, Hernando Siles, Gran Chaco and O'Connor. The areas selected were located in the Cordillera and Gran Chaco provinces. The first province, with a population of 88 628 inhabitants (INE 1992), occupies the broad northern area (86 245 km²), whereas Gran Chaco is in the south with an area of 17 428 km² and a population of 17 612 inhabitants.

The survey was carried out in eight rural communities, four of them near Camiri (Cordillera province), and four near Villa Montes (Gran Chaco province). The communities near Camiri are distributed 5–10 km from the town on the Parapeti and Yuti rivers, at altitudes of about 800 m above sea level. The rural communities near Villa Montes are located at about 6 km from the town at an altitude of about 380 m. The study populations consist of Guaraní indians and mestizos. They live in poor dwellings with walls of sticks, straw and clay and thatched roofs. The local economy is based on agriculture (mainly

maize) and animal breeding (cattle, pigs, goats, chicken, etc.).

This survey was part of a more extensive study conducted to assess the prevalence of other infections [hepatitis A virus (HAV), hepatitis E virus (HEV), filari-osis] in the Chaco region (Bartoloni *et al.* 1999a, b). Data concerning notified cases of the studied diseases were requested from the local health authorities. Local physicians, nurses and health workers were asked about their perception of frequency and severity of VZV and rubella infection including infant evidence of CRS, such as blindness, deafness and mental retardation.

The number of inhabitants in the rural areas near Camiri and Villa Montes is about 3300 each. The sample size was determined considering an expected prevalence of rubella virus and VZV antibodies of 80% for both viruses, with a worst acceptable error of 5% and a confidence interval of 95%. A random cluster survey method was used, with each community constituting one cluster, and four communities in each area were selected at random. All the available inhabitants of the selected communities were included. The study populations consisted of 295 individuals (162 females and 133 males) from rural areas near Camiri and 292 individuals (147 females and 145 males) from Villa Montes. Their ages varied between 1 and 85 years.

A meeting with the inhabitants of the communities was organized to explain the purpose of the study and its procedures. Informed consent was obtained from all adult participants and from parents or legal guardians of minors. The study design, including its ethical aspects, was reviewed and approved by the Bolivian Ministry of Social Welfare and Public Health and the local health authorities.

Samples of 5 ml venous blood were taken from all available subjects of the selected communities. The sera were stored at -20 °C in Bolivia, transported to Italy in dry ice and then stored at -70 °C until tested. Serum samples were screened by commercial rubella virus immunoglobulin G enzyme-linked immunosorbent assay (IgG ELISA) and VZV IgG ELISA (Enzygnost[®], Behring, Marburg, Germany) according to the manufacturer's instructions. Data analysis, with adjustment for clustering, was carried out with Epi-Info6.

Results

Of the 587 people selected, 97 (16.5%) were excluded from the analysis: 88 (48 in the Camiri area and 40 in the Villa Montes area) who declined to provide a blood sample, and nine (seven in the Camiri area, and two in the Villa Montes area) whose age was not recorded. Because of the small amount of blood obtained from a 37-year-old

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woman, her serum sample was only tested for rubella virus antibodies.

The results on seroprevalence of antibodies to VZV are shown in Table 1.

The VZV antibodies were detected in 391 (80%) of the 489 tested sera. Females had a higher prevalence (215 of 265, 81.1%) than males (176 of 224, 78.6%) although this did not reach statistical significance ($P = 0.48$). There were no statistically significant differences between prevalences in the two areas ($P = 0.38$). The prevalence of VZV antibodies increased with age. The lowest seropositivity rate (21.2%) was observed in 1–4-year-old children. In this age group a higher rate was observed in children (5 of 14) from the Camiri area (35.7%) than those (2 of 19) from the Villa Montes area (10.5%), although this was not

statistically significant ($P = 0.09$). VZV seropositivity rate increased sharply in the 5–9 age group (56.9%) and then in the 10–14 age group (83.7%). The seroprevalence increased gradually in the older age group reaching 98.2% in over 45-year olds.

Rubella virus antibodies were detected in serum samples from 377 (76.9%) of the 490 subjects studied (Table 2). There were no statistically significant differences in seropositivity rate with regard to gender (174 of 224, 77.7%, in males and 203 of 266, 76.3%, in females; $P = 0.72$) or to geographical areas (77.9% in Camiri and 76% in Villa Montes; $P = 0.61$). Similar to the trend observed for VZV antibodies, the percentage of seropositive subjects increased with age. Among children aged 1–4 years, only 18.1% had detectable antirubella virus antibodies. This proportion

Table 1 Prevalence of antivariella-zoster virus antibodies by age, sex, and area, in the rural population of the Chaco region, south-eastern Bolivia

	Female			Male			Total		
	Tested	Positive	%	Tested	Positive	%	Tested	Positive	%
Age group									
1–4	20	5	25	13	2	15	33	7	21.2
5–9	54	34	62.9	48	24	50	102	58	56.9
10–14	34	30	88.2	40	32	80	74	62	83.7
15–24	36	30	83.3	31	28	90.3	67	58	86.6
25–34	31	29	93.5	18	16	88.8	49	45	91.8
35–44	27	26	96.3	24	24	100	51	50	98
> 45	63	61	96.8	50	50	100	113	111	98.2
Area									
Camiri	133	110	82.7	106	85	80.2	239	195	81.6
Villa Montes	132	105	79.5	118	91	77.1	250	196	78.4
Total	265	215	81.1	224	176	78.6	489	391	80

Table 2 Prevalence of antirubella virus antibodies by age, sex, and area, in the rural population of the Chaco region, south-eastern Bolivia

	Female			Male			Total		
	Tested	Positive	%	Tested	Positive	%	Tested	Positive	%
Age group									
1–4	20	5	25	13	1	7.7	33	6	18.1
5–9	54	28	51.9	48	27	56.2	102	55	53.9
10–14	34	27	79.4	40	31	77.5	74	58	78.4
15–24	36	32	88.9	31	27	87.1	67	59	88.1
25–34	31	28	90.3	18	17	94.4	49	45	91.8
35–44	28	24	85.7	24	23	95.1	52	47	90.3
> 45	63	59	93.6	50	48	96	113	107	94.7
Area									
Camiri	134	105	78.3	106	82	77.3	240	187	77.9
Villa Montes	132	98	74.2	118	92	77.9	250	190	76
Total	266	203	76.3	224	174	77.7	490	377	76.9

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rose sharply to 53.9% in 5–9-year-old children and then to 78.4% in 10–14-year olds. The seroprevalence rate continued increasing with age reaching 94.7% in people over 45. Among the 95 women of childbearing age (15–44 years), the susceptibility rate was 11.6%.

Both rubella and varicella are notifiable in Bolivia but data were available only for varicella in Villa Montes area, and limited to 1997. One hundred and one cases were notified in the survey year. Eighty-three per cent of all cases occurred in persons younger than 15 years, and 15% in adults between the ages of 14 and 49 years. No outbreaks of varicella or rubella had been reported in the surveyed areas. Varicella is perceived by local health personnel as a mild disease mainly occurring in persons younger than 15 years. Herpes zoster is known as a quite common disease in persons older than 50 years. No data on CRS were available, but anecdotal reports from the local health workers and physicians suggest that deafness and mental retardation in children are not rare events.

Discussion

A common seroimmunological profile was evidenced for the two infections, and no differences with respect to gender or to geographical area were observed. The seroprevalence rates, 80% and 77% for varicella and rubella, respectively, were similar, as well as the sharp increase of the seropositivity rate in the 5–9 age group and then in the 10–14 age group (Fig. 1).

In industrialized temperate countries primary VZV infection predominantly affects children with 90–100% seroconversion occurring by 15 years of age (Centers for Disease Control & Prevention 1996). A shift in the age of primary VZV infection to older groups was observed in the

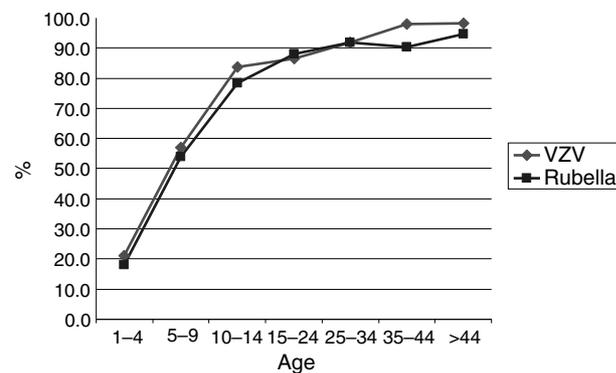


Figure 1 Age specific profiles of varicella zoster and rubella seropositivity in the rural population of the Chaco region, south-eastern Bolivia.

United Kingdom and United States (Gray *et al.* 1990; Sloan & Burlison 1992; Miller *et al.* 1993). However, a more recent study carried out in the United Kingdom and based on the analysis of the age-specific consultation rate for varicella showed an important decrease in the average age at infection that coincides with a significant increase in children attending preschool (Brisson *et al.* 2001).

Limited seroprevalence surveys carried out in tropical countries identified a different epidemiology with a higher median age of seroconversion and lower seroprevalence among adults than in temperate countries. In Sri Lanka 71.5% of varicella infections occurred in adults aged 20 years or over (Maretic & Cooray 1963), in Somalia 46% of infections were in people over 15 years of age (Jezek *et al.* 1981), in Thailand 26% of 15–29-year-old adolescents and young adults were seronegative for specific VZV antibodies (Migasena *et al.* 1997), and in India only 26% of rural adult Bengalis were immune by the age of 25 (Mandal *et al.* 1998).

The occurrence of varicella outbreaks in immigrants from the tropics confirms the lack of immunity of young adults to VZV infection (Hastie 1980; Kjersem & Jepsen 1990; Longfield *et al.* 1990). Some possible reasons have been suggested to explain the different VZV epidemiology including climate conditions (White 1978; Iyun 1984; Venkitaraman & John 1984; Lee 1998), cross-immunity between VZV and herpes simplex virus (Lee 1998; Edson *et al.* 1985), competition with other viruses (Bang 1975; Sinha 1976), social and cultural factors (Mandal *et al.* 1998; O'Grady *et al.* 2000), and population mobility, but no conclusive evidence for or against these hypotheses has been obtained. The difference in epidemiology pattern suggests that human populations from tropical countries are at risk of greater morbidity and mortality, and vaccination has been considered beneficial in reducing the public health impact of VZV in these countries (Lee & Tan 1995; Migasena *et al.* 1997; Lee 1998).

In the surveyed rural communities of south-eastern Bolivia we did not find the age-specific seroprevalence of antibodies to VZV reported for other tropical countries. We found a progressive increase in seroprevalence with age, with 84% seropositivity by 15 years of age, and an overall 80% seroprevalence. The limited data of notified cases of varicella available only from one of the two studied areas show that 83% of the cases occurred in children under 15 years of age, the majority of them being in the 5–14 age group. The high VZV-seropositivity levels we found in these rural communities might be explained by the regular visits of both adults and children to the near urban areas (Camiri and Villa Montes). Although our findings do not allow to estimate the public health and socioeconomic impact of varicella in the study area, a

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varicella vaccine does not seem to have a high priority for routine introduction into the immunization programme.

Rubella serosurveys are useful particularly to determine the proportion of women of childbearing age who are susceptible to rubella. There is great variation in the age-specific seroprevalence of rubella between countries (Cutts *et al.* 1997). Considering the age-specific profiles of rubella seropositivity in some Latin American rural populations in the pre-vaccination era, rubella is predominantly a childhood disease in Brazil, Chile and Argentina with over 60% of seropositive subjects in the younger age group (5–9 years), while in other countries, like Panama and Trinidad, only about 10% of the children in the same age group was seropositive (Dowdle *et al.* 1970).

Regarding rubella susceptibility in women, a recent review of 45 low-income countries prior to introduction of rubella vaccine reported proportions of susceptible women of < 10% in 13 countries, 10–24% in 20 countries and > 25% in 12 countries (Cutts *et al.* 1997). In the surveyed rural areas of south-eastern Bolivia 12% of women of childbearing age remained susceptible to rubella. Considering that no outbreak was observed recently, the presence of rubella antibodies in the majority of women might be explained by the frequent migration between rural and urban areas. The lack of surveillance data does not allow to estimate the real burden of CRS in the surveyed area. In 2000, Bolivia introduced rubella vaccine in the national childhood immunization programme by vaccinating children of 12 months of age with measles–mumps–rubella vaccine (MMR) (WHO 2000b). Childhood immunization poses a risk of an increase in susceptibility in women of childbearing age, with the potential of an increased number of cases of CRS, unless at least 80% coverage is achieved (Robertson *et al.* 1997). In fact, inadequate levels of coverage may be slow, but does not interrupt rubella transmission, thus increasing the average age at infection. Recently, an outbreak of CRS was reported in Greece after several years of low MMR coverage (Panagiotopoulos *et al.* 1999). In Bolivia, according to recent national immunization reports, 100% of children were vaccinated against measles by their first birthday in 2000 (Ministerio de Salud y Previsión Social, La Paz, Bolivia, unpublished data). Our study, carried out prior to introduction of rubella vaccine, may provide a point estimate to monitor trends in the proportion of adult women who are susceptible and to evaluate the effects of the current rubella immunization strategy (WHO 1999).

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