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Measles in Bolivia: A 'honeymoon period'

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ABSTRACT

Background: Although measles is a highly infectious disease, the live measles vaccine provides protection for over 20 years, and immunity may be lifelong. This study assessed measles seroprevalence in schoolchildren in the Cochabamba region of Bolivia.
Methods: A seroepidemiological survey of measles immunity in 5–16-year-old schoolchildren ($n = 441$) living in the Cochabamba region of Bolivia was performed in March and April of 2010. Representative regional samples of school children from 14 schools were obtained. A parent-administered questionnaire collected sociodemographic and socio-economic status, and serum samples were tested for measles antibodies using an enzyme-linked fluorescent antibody test. The measles prevalence and corresponding 95% confidence intervals (CI) were calculated. A descriptive and bivariate analysis was performed using the ANOVA or the Kruskal–Wallis test according to whether the data were distributed normally (Kolmogorov–Smirnov test p-value < 0.05) plus the chi-square test or Fisher's exact test as needed.
Results: The global seroprevalence of measles was 69.61% (95% CI 65.32–73.90) and was higher in adolescents (84.16%, 95% CI 77.04–91.28) and Spanish speakers (74.74%, 95% CI 68.56–80.92). The seroprevalence did not differ according to socio-economic status, living area, or number of family members in the household.
Conclusions: This study found a high prevalence of measles susceptibility in Bolivian children. Thus, herd immunity may not have been established, and some outbreak could occur. Authorities should redress this situation before endemic measles transmission occurs nationally and regionally, and there is an urgent need to conduct more seroprevalence studies in the region.

1. Introduction

The Plurinational State of Bolivia is one of the poorest and least developed countries in Latin America, and historically Bolivia has had one of the highest mortality rates for children younger than 5 years old in the Americas [1]. Since the 1970s, there has been a huge effort to control the transmission of measles, which is one of the most highly infectious diseases. This effort has included training and surveillance in combination with national immunization programs and other organizations.

The measles immunization strategy that has been used to control the disease in accordance with the Expanded Programme on Immunization (EPI-WHO) has been used in Bolivia since 1979. All children aged 12–23 months are given a single dose of live attenuated vaccine as part of the routine childhood vaccination program [2]. In the 1980s, there was a dramatic decrease in measles incidence (4–69/100,000 people), despite a cluster of measles-related deaths ($n = 25$) in 1989–1990 [2]. Like other countries in the region,

Abbreviations: 95% CI, 95% confidence intervals; BMI, body mass index; ELFA, automated enzyme-linked fluorescent immunoassay; EPI, Expanded Programme on Immunization; IgG, immunoglobulin G; INE, Instituto Nacional de Estadística; IQR, interquartile range; MCV1, the first dose of measles-containing vaccine; MC V2, the second dose of measles-containing vaccine; MMR, measles, mumps and rubella-containing vaccine; MMR1, the first dose of measles, mumps and rubella vaccine; MMR2, the second dose of measles mumps and rubella vaccine MMR2; OR, odds ratio; SD, standard deviation; TVT, test value threshold; WHO, World Health Organization.

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in 1994 Bolivia set a goal of interrupting indigenous measles transmission by the end of 2000 [3]. A one-time national vaccination catch-up campaign targeting children <15 years old was conducted and achieved 96% vaccination coverage. In 1995–1997, measles cases declined, although routine coverage was quite low (<90%). There was a nationwide epidemic in 1998–2000 that involved 2567 people, most of whom had not been vaccinated. In 1999, the EPI second generation introduced some new vaccines (DTP-Hib-HepB) and replaced others, such as measles, by the MMR (measles, mumps and rubella) vaccine. At the end of the year, a national vaccination campaign was conducted that targeted areas with low coverage [4]. There were only 122 cases of confirmed measles in 2000, with the last confirmed case of indigenous measles occurring in October [2].

Since 2000, Bolivia has not reported any cases of measles to the World Health Organization (WHO) [5], even though the official immunization coverage rate has dramatically decreased from 99% in 2000 to 79% in 2010. Further, the percentage of districts that did not reach the herd immunity threshold increased from 69% in 2009 to 77% in 2010 [5]. In 2002, the Region of the Americas reported that measles transmission had been interrupted [6].

Surveillance of the measles immunization coverage rate has frequently been used as an outcome of a vaccine program, even though not all immunization coverage data are reliable or precise. The sources used to determine the measles immunization coverage rate include administrative records and surveys of households, and there is a mean difference of ~9% in the rates found by these two methods, probably due to ambiguity in the studied age group, a lack of complete medical records, pressure to achieve target coverage rates, counting the doses distributed rather than doses administered, or sampling errors [7]. In Bolivia there were large differences in the coverage rates as determined by the two methods: in 1994, the rate was 90% using administrative records and 64% using survey data, and in 1998 the rate was 98% using administrative records and 51% using survey data [7]. This suggests that there is cause for concern in terms of measles susceptibility in children.

To maintain herd immunity and prevent measles outbreaks, the immunization coverage rate should be at or above 83–95% [8,9]. In this range, the spread of measles from person to person is unlikely. When a high proportion of the community is vaccinated against a contagious disease, the endemicity of the disease declines [10], and there is an increase in the susceptibility of individuals that escape immunization or in whom the vaccine failed. This may lead to a delayed epidemic after several years of few or no measles cases, which is known as a "post-honeymoon period epidemic." This typically involves older age groups than are traditionally affected by measles [9].

Determining the immunization coverage rate does not provide information about the susceptibility of a population to a specific disease in a population. To determine the measles susceptibility, we need to consider both vaccinees and naturally occurring cases of a specific disease and the seroprotected population. Measles immunization has been demonstrated to be protective for more than 20 years, and immunity is thought to be lifelong [11,12]. The development and persistence of serum antibodies following measles vaccination are lower than but parallel the response following wild measles infection, so we can not distinguish the disease origin by examining the circulating antibodies to measles [12].

Bolivian children may have received a single vaccine dose (MCV1 or MMR1) or two doses (MCV2 or MMR2), depending on which campaign they were part of (i.e. catch-up, keep-up, or follow-up campaign). Thus, the susceptible population is unknown. Current recommendations specify that every child receive a first dose of the measles vaccine (MCV) before the age of 2 years and a booster dose before the age of 5 years. Even when these recommendations are followed, some children will lack protective levels of circulating measles-specific neutralizing antibodies [13], and the protection may be insufficient at the population level [14]. Notably, cellular immunity for measles can protect against infections despite waning measles-specific antibodies [15].

Given the paucity of data about measles susceptibility in childhood in Andean Latin American and specifically in the Cochabamba region of Bolivia, and keeping in mind the great differences between survey and official immunization coverage rates, we carried out a seroepidemiological survey in Bolivian children. The aim of the study was to assess the seroprevalence of measles, and thus community susceptibility, as determined by a lack of persistence of measles antibodies induced by vaccine or wild measles infection in childhood. The seroprevalence data was analyzed to identify associations with birth cohort, sociodemographic characteristics, and socio-economic status. We also sought to determine whether a post-honeymoon period could be identified in order to prevent a delayed (post-honeymoon period) epidemic.

2. Methods

2.1. Study design

This population-based cross-sectional study was conducted by surveying 5–16-year-old schoolchildren ($n = 441$) in the Cochabamba region of Bolivia. The children attended public and private schools (n = 14) in 6 different municipalities. Participation was voluntary, and there was no financial incentive. The institutional ethical review board (Universidad Mayor de San Simon/Universitat de Barcelona) approved the study protocol, as did the Bolivian Health and Sports Ministry, the Bolivian Education Ministry, and the directors of the selected schools.

2.2. Setting

The Cochabamba regional health and nutrition examination survey, entitled Bolkid, is a region-wide, population-based, cross-sectional study conducted in the Cochabamba region in eastern Bolivia in March and April of 2010.

2.3. Sampling

By accepting an alpha risk of 0.05 and a beta risk of 0.20 for a precision of ±0.04 units in a two-sided test for an estimated measles seroprevalence of 86% and a replacement rate of 30%, we determined that 413 subjects should be selected randomly.

The sampling technique included stratification according to population size of municipalities, geographical area, and type of school, and randomly selecting the primary sampling units (schools) and the final sample units (schoolchildren).

2.4. Bolkid survey/questionnaires

The Bolkid survey was initiated in March 2010 and ended in mid-April 2010. It consisted of a physical examination and a questionnaire. The physical examination determined anthropometric measures, and a blood sample was collected to determine the level of antibodies to measles.

A global questionnaire was provided to the school directors, who completed the questionnaire after meeting with the children's parents or guardians and obtaining their consent. Each child's parents or guardians filled in the questionnaires at home regardless of the age of the child. If the parents or guardians were not able to read or understand the survey by themselves (<5% of the sample), the questionnaires were filled out the day that the physical examination was conducted. At that time, assistance was provided by teachers in the native language of the parent or guardian.