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Epidemiological characteristics of measles from 2000 to 2014: Results of a measles catch-up vaccination campaign in Xianyang, China

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ABSTRACT

This study was a cross-sectional case-control study aimed at (1) identifying risk factors contributing to the measles epidemic and (2) evaluating the impacts of measles-containing vaccines (MCVs), with the goal of providing evidence-based recommendations for measles elimination strategies in China. Data on measles cases from 2000 to 2014 were obtained from a passive surveillance system at the Center for Diseases Prevention and Control in Xianyang. The effectiveness of MCVs was evaluated in 357 patients with a vaccination history and 503 healthy randomly selected controls. Patient data were subjected to multivariable logistic regression modeling. From 2005 to 2014, the average incidence of measles in Xianyang was 5.42 cases per 100,000 people. The second MCV dose was highly protective in 8-month-old infants. MCVs in general have been highly protective in 8-month-old infants. Multivariable logistic regression modeling indicated that age (≥2 years vs. <2 years), MCV dose 2 vaccination, and MV vaccination were each independently associated with measles case status. In conclusions: A MCV should be administered on time to all age-eligible children, reproductive-age women, and migrant populations, to maximize herd immunity to measles.

Introduction

Measles is an acute highly contagious disease that is caused by the measles virus, which is transmitted mainly by droplets through the nose, mouth or throat of infected persons. A measles vaccine has been available in China since the 1960s, and China initiated its Expanded Program on Immunization in 1978 [1]. In China, measles has affected primarily children, especially after 1978 [2]. Although substantial decreases in the measles incidence rate and measles-related mortality have occurred, measles remains common in many countries around the world. According to the World Health Organization (WHO), more than 20 million people develop measles every year and 95% of measles deaths in recent years occur in developing countries with weak health infrastructures. An estimated 114,900 measles-related deaths were reported worldwide in 2014, with most of these deaths occurring in children under 5 years old [2].

Measles remains a leading vaccine-preventable cause of child mortality in China. According to the Chinese Health Statistics Yearbook, in 2013, the incidence rate for measles was 0.46/100,000 Chinese citizens, with a fatality rate of 0.13%. This incidence rate represents a marked improvement relative to 2001, when China saw a measles incidence of nearly 25/100,000 people. This improvement can be attributed to the introduction of routine measles immunization recommendations and supplementary immunization activities [2]. The Chinese government has committed to joining the global effort to eliminate measles [1–4], by implementing robust routine immunization services and a supplementary immunization activities (SIAs) program with the aim of achieving this goal. Many countries and regions have benefitted from WHO-recommended SIAs, including Xianyang. The measles incidence rate decreased dramatically in Xianyang after 2007, when SIA commenced in the region.

By 1989, measles had been nearly eliminated. However, in 2010, surveillance data detected a small measles epidemic in Xianyang, China. The number of reported measles cases in 2010

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(January–December) was nearly five times greater than that in 2009. We analyzed the epidemiological characteristics of the measles from 2001 to 2014, with the aim of identifying contributory factors, and evaluated the impacts of measles-containing vaccines (MCVs) with the aim of providing evidence-based recommendations for measles elimination strategies in Shaanxi province. For the purposes of this study MCVs included MCV dose 1 (first dose given at 8 months), MCV dose 2 (second dose at 1–2 years), and the measles and rubella vaccine.

Materials and methods

Study area, data collection, and management

Xianyang is a city in Shaanxi province located in the hinterland of the Guanzhong plains with a population of about 5.4 million people. Beyond its populous urban areas, Xianyang includes remote villages that can only be reached on foot.

Measles is a legally mandated notifiable disease in China. The National Notifiable Diseases Surveillance System (NNDSS) was established by the Chinese National Centers for Disease Control (CDC) in 2004 and updated to include the expanding variety of infectious diseases and more disease-related information (such as immunization history) of case investigations in 2008. This system requires physicians to report all suspected measles cases to the local CDC within 12 h. For each suspected case, the local health authorities are required to carry out an epidemiological investigation, which includes obtaining specimens for laboratory confirmation. The regional authorities reported the case report forms immediately to the Ministry of Health and the National CDC. The measles incidence rates for the population, and the vaccination schedule from the annual disease surveillance reports (2000–2014) were downloaded from NNDSS for analyzing. The Center for Disease Control and Prevention of Xianyang is responsible for data collection and case reports in the region. In this paper, two types of data were collected. First, the annual measles surveillance reports from 2001 to 2014 were downloaded from NNDSS. Second, the measles and rubella vaccine histories were recorded for 503 healthy individuals in 2013–2014. The ministry of health required that the CDC must carry out measles initiative monitoring at all geographic levels, and in 2013 proposed a mandatory measles reporting system to improve reporting rates and prevent omissions. The demographic data from 2000 to 2014 were acquired from the Xianyang Statistics Bureau. We were able to obtain detailed information about measles cases after 2005, following the 2004 NNDSS update. In 2012–2014, there was no measles cases reported. Therefore, the presently analyzed dataset encompasses 2005–2011.

Measles diagnosis

All reported measles cases in this study were confirmed according to the WHO's criteria [5]. Specifically, diagnoses were based on the clinical case descriptions and laboratory confirmation criteria. A clinical measles case is defined as an illness characterized by all of the following signs: red skin rash; fever of 38 °C or higher; coughing, upper respiratory catarrhal symptoms, or conjunctivitis; measles spots (Koplik's spots); and extension of red skin from the ear to the whole body. A number of conditions have features that may resemble measles, including other viral infections (especially rubella), scarlet fever, Kawasaki disease, and toxic shock syndrome. These diseases need to be ruled out before making a definitive measles diagnosis.

For those cases in which the patients did not show typical symptoms, the following laboratory findings were considered indicative of a measles diagnosis: detection of anti-measles IgM antibodies in the serum (unless live attenuated measles vaccine received within the prior month); four-fold or greater increase in anti-measles serum IgG antibody; or antibody-negative in acute phase and antibody-positive in recovery phase; and isolation of confirmed measles virus (e.g. viral RNA identification) from nasopharyngeal secretions or blood. These cases should be categorized as laboratory-confirmed cases.

To ensure diagnosis reliability, confirmatory serological testing was performed on all patients with suspected measles (including clinical measles cases) by detecting specific measles IgG antibodies (detection threshold of 0.3 IU/L) with a commercially available ELISA kit (Yanhui Biotechnology Company, China), according to the manufacturer's instructions. When laboratory results contradicted clinical signs, we used the results of the laboratory diagnosis. In this study, we used data from all laboratory-confirmed and clinically diagnosed measles cases.

Case-control study

To evaluate the role of the MCVs in measles prevention, we conducted a case-control study from 2009 through 2014. The patients in the case group had been treated in one of 13 counties or districts in Xianyang between 2009 and 2014; their data were obtained from the NNDSS.

The subjects in the control group were healthy people who had not been infected with measles; they were confirmed to be serum-negative for measles-specific IgG antibodies. Firstly, five regions within Xianyang Province (Qin Du District, Wu Gong County, Chun Hua County, Jing Yang County, and Chang Wu County) were selected from the 13 counties and districts of Xianyang by simple random sampling. Based on the serum epidemiological characteristics of measles, infected patients (cases) and healthy control participants were divided into five age groups: <8 months, ≥8 months to <2 years, ≥2 years to <10 years, >10 years to <20 years, and ≥20 years.

To obtain a control group of at least 500 subjects, at least 20 subjects were selected randomly for each age group from each of the five selected regions. A total of 503 subjects were selected (with the extra 21st individuals coming from Qin Du District, Chun Hua County, and Chang Wu County). Control data including vaccination history and demographic characteristics were collected in 2009 and 2014 via a questionnaire. Our study protocol conforms to the ethical guidelines of the Declaration of Helsinki-Ethical Principles for Medical Research Involving Human Subjects adopted by the 18th World Medical Association General Assembly in Helsinki, Finland, June 1964, as revised in Tokyo 2004. The ethics committee at Xi'an Jiaotong University approved the protocol, and all participants gave informed consent for their inclusion in the study.

Data analysis

We calculated odds ratios (ORs) to examine the association between several independent variables (sex, community, age, MCV dose 2, and MCV dose 1) and measles case status. Individuals with unknown vaccination status were excluded from the analysis of how vaccination history relates to measles infection. The precision of the results was assessed with 95% confidence intervals (CIs). We used chi-square tests to evaluate significance, with a significance cut-off level of 0.05. All statistical analyses were performed using SPSS 20.0 statistical software. All significance tests were two-sided.

Results

Measles incidence and mortality, 2000–2014

With the implementation of a national routine program for immunization from 2000 to 2006, the measles incidence rate