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A population profile of measles susceptibility in Tianjin, China

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ABSTRACT

Background: Measles is a highly infectious illness requiring herd immunity of 95% to interrupt transmission. Measles is targeted for elimination in China, which has not reached elimination goals despite high vaccination coverage. We developed a population profile of measles immunity among residents aged 0–49 years in Tianjin, China.

Methods: Participants were either from community population registers or community immunization records. Measles IgG antibody status was assessed using dried blood spots. We examined the association between measles IgG antibody status and independent variables including urbanicity, sex, vaccination, measles history, and age.

Results: 2818 people were enrolled. The proportion measles IgG negative increased from 50.7% for infants aged 1 month to 98.3% for those aged 7 months. After 8 months, the age of vaccination eligibility, the proportion of infants and children measles IgG negative decreased. Overall, 7.8% of participants 9 months of age or older lacked measles immunity including over 10% of those 20–39 years. Age and vaccination status were significantly associated with measles IgG status in the multivariable model. The odds of positive IgG status were 0.337 times as high for unvaccinated compared to vaccinated (95% CI: 0.217, 0.524).

Conclusions: The proportion of persons in Tianjin, China immune to measles was lower than herd immunity threshold with less than 90% of people aged 20–39 years demonstrating protection. Immunization programs in Tianjin have been successful in vaccinating younger age groups although high immunization coverage in infants and children alone would not provide protective herd immunity, given the large proportion of non-immune adults.

1. Introduction

Measles has historically been a major cause of infectious childhood morbidity and mortality worldwide [1]. Over the last twenty-five years, however, childhood deaths from measles globally have decreased dramatically, from 631,200 in 1990 to 145,700 in 2013, in part due to an increased international focus on global eradication [2,3]. Measles has now been successfully eliminated in the Americas [4]. The other five WHO regions have also set a target for elimination by 2020 including China in the Pan Western Pacific Region [5,6]. Although China had originally established a national goal of elimination by 2012, the target was not met and the country instead has recently experienced year-on-year increases in the number of measles cases in 2013 and 2014 [7].

Measles is a highly communicable disease and at least 94% of the population needs to be immune to interrupt endemic transmission of disease [8]. Both active and passive immunity play important roles in protecting against measles. Following infection with the virus, an individual acquires both cellular and humoral immunity with the latter detectable by the presence of measles IgG antibodies in the serum which persist for decades [9]. Immunization with a live measles-containing vaccine (MCV) elicits an immune response similar to natural disease and both are forms of active immunity. Passive immunity results from transplacental transfer of measles

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antibody from mother to child generally during the third trimester of pregnancy [10]. Whether mother's immunity is derived from natural disease or immunization, the neonate's passive immunity from maternal antibodies theoretically protects against measles for several months after birth. The duration of protection depends on the quantity of antibody transferred and the rate of antibody decay in the infant [11]. Antibodies present from passive immunity may interfere with an active immune response and it is recommended that vaccines be given after maternal antibodies have waned.

The recommended age for administration of the first dose of MCV falls between 8 to 12 months but varies by country. The timing of the initial dose represents a trade-off between providing the vaccine early enough to prevent acquisition of disease, the age-dependent risk of which differs across countries, balanced against the potential for interference of the infant's immune response by maternal antibodies [12,13]. Moreover, young infants (i.e., aged ≤6 months) develop less of a humoral response to measles vaccination than older infants, no matter the mother's immune status [14].

In China, routine measles vaccination has been available for children as young as 8 months since 1966 [15]. However, the vaccine was not widely administered until 1978 when it was incorporated into the expanded program on immunization (EPI) and provided for free to all children. A second dose of MCV was added to China's EPI in 1986 with a recommendation for administration at age 7 years which was subsequently changed to age 18–24 months in 2005 [16]. Some regions of China, including the Tianjin Municipality, provide an additional third dose at age 5 years. Since 2004, most Chinese provinces have conducted at least two supplementary immunization activities (SIAs), which have targeted all children age 8 months through 14 years, regardless of their previous vaccination status, in an effort to reduce transmission of measles [7,17].

China has had notable success in controlling measles since the introduction of the vaccine. Although it has an annual birth cohort of roughly 16 million children, the second largest in the world, vaccination coverage among children is generally high and at a level that exceeds herd immunity thresholds [18,19]. Measles vaccines are provided free to both local residents and to internal migrants who relocate from rural to urban areas with SIAs reaching the majority of both local and migrant children [20]. Moreover, in most areas in China, governmental public health authority now has access to comprehensive notifiable disease surveillance systems and immunization information systems to monitor measles cases, detect outbreaks, and assess vaccine uptake [7]. Tianjin, located approximately 110 km southeast of Beijing in the northern part of the country, is one of the most populous municipalities in China and serves as an important center of trade and economics. In 2014, 14.7 million people lived in Tianjin's 16 districts, which span from urban and suburban to rural areas. The dense population of urban districts reside in historical business areas, whereas suburban districts and rural counties are more industrial and have less access to public services [21,22]. Below the district/county level, residents are registered to live in either a rural village or an urban community, with a total of 5073 villages/communities throughout the municipality. In Tianjin, the municipal Centers for Disease Control and Prevention (CDC) is responsible for serving the entire municipality and directs staff at district and local CDCs who carry out much of the work in investigating outbreaks and evaluating immunization programs.

Given the challenges in the control of measles in China, assessing population susceptibility is an important step in developing a better understanding of the epidemiology of measles and in advancing an effective elimination strategy. Using information from a population-based study of measles immunity in combination with case data from China's public health surveillance system, we developed a population profile of measles immunity among residents aged 0 through 49 years in Tianjin, and compared this profile to the distribution of measles cases across different age groups. We anticipate that measles immunity will be low in both infants and adults between 20 and 40 years since cases predominantly occur in these two age groups [23].

2. Methods

The targeted sample size consisted of 2800 individuals aged 0–49 years, with 200 individuals in each age category (groups of 3 month blocks for infants <1 year of age, and 10-year age blocks, thereafter). This sample size would allow us to generate age-stratified confidence intervals of <14%, which is sufficient to compare measles immunity across age groups given immunity levels reported in previous literature [24]. Women aged 20–39 were oversampled in order to generate more precise confidence intervals and because we concomitantly enrolled mothers of every infant <1 year of age. The study enrolled participants between November 2011 and April 2015 using a two-stage cluster sample design. In the first stage, 120 villages/communities were selected through a probability proportionate to size procedure while insuring that each district was represented by at least one village/community. In the second stage, which was conducted within each village/community, 12–32 people aged 1–49 years from the village's population registry were selected using an age-stratified random selection procedure. The enrollment age cutoff date was selected to be age 49 years old to correspond with introduction of the measles vaccine in China in 1966 [25]. Because of a systematic delay in listing infants in the village/community registry, infants age <1 year were selected from records housed at local immunization clinics. An age-stratified random sample of infants was drawn from the clinic list although the number of infants from each village/community varied because some small rural villages had relatively few infants. The mother of each infant was also enrolled in the study.

Prior to data collection, informed consent was obtained from adult participants and the parents of minors enrolled in the study were required to give their consent for the minor's participation. Study enrollees completed an in-person interview administered by Tianjin CDC staff that required approximately 10 min to complete; parents or guardians were included in the interview for any participant <18 years of age. The interview included questions about socio-demographic characteristics, vaccination history, measles infection history, and exposure to congregate settings. Five bloodspots from the participant's finger were collected using a single-use lancet, dropped onto filter paper, and dried. After transport to the Tianjin CDC laboratory, dried bloodspots were tested for measles IgG antibodies [26]. Measles IgG testing was conducted using SERION ELISA classic measles IgG (quantitative) Institut Virion/Serion GmbH, Würzberg, Germany. The laboratory results were interpreted according to the guidelines from the Standardization Administration of the People's Republic of China [27]. Threshold levels for IgG antibody test results were >200 IU/ml for positive, 150–200 IU/ml for borderline, and <150 IU/ml for negative.

Each village/community was classified as either urban, suburban or rural based on which of the 16 districts it was located in; the urban districts included Heping, Hedong, Hexi, Nankai, Hebei, Hongqiao, and Binhai New Area; suburban districts were Jinnan, Dongli, Xiqing, and Beichen; and rural districts comprised Baodi, Wuqing, Ji, Jinghai, and Ninghe.

We compared the seroprevalence data to measles cases recorded in the national notifiable disease registry, the China Information System for Disease Control and Prevention (CISDCP). From this source, we tabulated the age of all 12,466 measles case-patients reported from 2005 to 2014 in Tianjin.

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