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Short Communication

Risk factors for measles among infants in Tianjin, China

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ABSTRACT

Objectives: Infants aged <8 months are ineligible for measles vaccination in China but represent a disproportionate number of cases. We examined the risk factors for measles among infants in Tianjin, China.
Study design: Case-control study.
Methods: Cases were enrolled from a surveillance system, and IgG-negative controls were sampled from registries at immunization clinics. A logistic regression model assessed for risk factors.
Results: Among 82 cases and 485 controls, exposure to a municipal hospital (OR [odds ratio]: 5.21; 95% confidence interval [CI]: 1.19–22.82) or a specialty hospital (OR: 13.22; 95% CI: 6.13–28.51) was associated with the disease, whereas visiting a township or district hospitals was not associated with increased odds of measles.
Conclusions: Hospitals were an important focal point of measles transmission for infants. Hospitals, particularly higher-level municipal and specialty hospitals, should enforce infection control programs to separate infants with highly communicable diseases to prevent transmission.

Measles elimination in China

Despite a global goal for measles eradication, measles still resulted in 134,000 deaths in 2015.[1] Vaccination is the key preventive intervention for measles, and global coverage of measles-containing vaccine (MCV) has increased from 72% in 2000 to 85% in 2015.[1] In China, children are administered MCVs at 8 months and 18–24 months. Some urban locales, like Beijing, Tianjin, and Shanghai, offer a third dose at 4–6 years. Infants <8 months of age are ineligible for vaccination and are at high-risk for disease given the rapid decay of maternal antibodies that we have seen in China.[2] In recent years, infants have constituted >30% of all measles cases within China.[3]

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Previous case-control studies have identified risk factors for measles in China—notably exposure to hospital settings.[4,5] However, the generalizability of these results is unclear because of small sample sizes, short study duration, and non-specific definitions of exposure (e.g. 'hospital' vs specific types of hospitals). In this case-control study in Tianjin, China, we enrolled cases and controls between 2011 and 2015 and examined risk factors for measles by comparing infant cases to a community sample of measles immunoglobulin G (IgG)-negative controls.

Study design

Tianjin is one of four province-level municipalities in China. Its 15.2 million residents live in urban, suburban, and rural districts. A finer administrative-level division in Tianjin is the urban community or rural village, with the entire Tianjin population registered as residents in one of over 5000 communities/villages within the municipality.

This case-control study samples are laboratory-confirmed cases from the infectious disease surveillance system in Tianjin. Each week, staff at the Tianjin Centers for Disease Control and Prevention (CDC) downloaded the list of measles cases reported within the proceeding week from the China Information System for Disease Control and Prevention web-based surveillance system and randomly selected cases to enroll into this study. The number selected into the study was based on overall measles caseload and staff availability to perform interviews.

Our community sample of controls was drawn from a population-based, two-stage cluster sample. At the first stage, 120 communities/villages were selected through a probability proportionate to size procedure with each district represented by at least one community/village. At the second stage, we took a sample from immunization clinics whereby infants <1 year of age and their mothers were found and selected in an age-stratified random selection within each community/village. This sample includes locals, those with a residency card or *hukou*, assigned to Tianjin, and non-locals, who are Tianjin residents whose *hukou* is from another province.

This manuscript's analysis only includes infants. Our original sample size calculations were based on the larger original study which encompassed a greater age range (0–49 years). In the original study, we wanted to select 500 cases and 500 controls, with similar age, neighborhood, and residency status. This sample size could detect associations between a risk factor and measles case status with 90% power if the risk factor had an odds ratio (OR) of at least 2.0.

Mothers of the infants consented to their participation before data collection. The mother was interviewed in-person. The interview included questions about sociodemographic characteristics, vaccination history, measles infection history, and exposure to various congregate settings in the prior 21 days (for non-cases) or 21 days prior to disease (for cases).

Mothers were asked if their child had gone to any hospital in the 21-day exposure period, which included township, district, and municipal hospitals. Specialty hospitals, such as infectious disease and pediatric hospitals, were aggregated in the analysis because of low counts.

Mothers who answered 'I don't know' to questions were recategorized as having missing information.

A blood spot from the participant's heel was collected using a single-use lancet and tested at the Tianjin CDC laboratory.[6] Measles IgG testing was done with a SERION ELISA classic Measles Virus IgG quantitative kit (Institut Virion/Serion GmbH, Würzberg, Germany). The IgG titers were categorized as positive if >200 IU/ml for positive, borderline if 150–200 IU/ml, and negative if <150 IU/ml.

Individuals who are measles IgG positive are presumably protected against future infection with measles, so our population of controls only includes those who are IgG negative (which excludes most children who had been vaccinated).

We present a logistic regression model adjusted for child's age, child's sex, urbanicity, and the mother's education. Given that age groups, urbanicity, and sex were related to the sampling design, the strength of association is not interpretable. We present the distribution of the number of children in the household and childcare use between cases and controls, but because of low cell counts, they were not included in the multivariable logistic regression. The precision of the ORs in all models was examined with 95% confidence intervals (CIs).

OpenClinica, version 3.3 (OpenClinica LLC, Waltham, MA, USA) database was used and data analyses were conducted using SAS software, version 9.3 (SAS Institute Inc., Cary, NC, USA).

Risk factors for measles in infants

Initially, 500 cases and 2818 controls aged 0–49 years were enrolled; 20 measles cases (3.8%) and 173 community members (5.8%) had refused to participate. There were 82 measles cases and 485 controls aged <1 year. Details of covariate distribution by case status among these infants are shown in Table 1.

In the adjusted model, household size was significantly related to measles case status, with infants in larger households (≥4 people) having 0.43 times the odds of measles compared to infants in smaller families (95% CI: 0.23–0.81). Although we did not collect information on household composition, it is possible that larger households represent multigenerational homes, whereas having ≤3 household family members represents a nuclear family. More people in the household may result in more socializing at home and reduced risk of community measles exposure. Future research could focus on the implications of different familial composition for differential exposure risk in the community.

Exposure to hospital settings within the past 21 days was highly related to measles case status. Infants who had visited township or district hospitals did not have significantly higher odds of measles compared to those who did not visit, but infants who had been at a municipal hospital (OR: 5.21; 95% CI: 1.19–22.82) or an infectious disease, pediatric, or other hospital (OR: 13.22; 95% CI: 6.13–28.51) had greater odds of measles. This association with municipal, but not township, hospitals is possibly reflective of the extended period an individual might spend in hospital settings prior to admission to higher-tier municipal hospitals. A 2006 study from Jilin province found the odds of measles to be 9.7 times higher for