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ORIGINAL ARTICLE

Seroepidemiology of varicella among elementary school children in northern Taiwan



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Abstract *Background/Purpose:* In Taiwan, varicella vaccine was included in the expanded program of immunization since 2004. A seroepidemiologic study in the postvaccine era is helpful to evaluate the efficiency of current varicella vaccination strategies.

Methods: We used a multistage stratified systematic sampling design to classify 29 administrative districts of New Taipei City into five strata. In 2013, a total of 936 students from 14 primary schools were recruited and had blood drawn for serology tests for varicella-zoster virus-immunoglobulin-G via indirect chemiluminescence immunoassays. A history of clinical varicella and information on varicella vaccination status were obtained.

Results: Overall, the seroprevalence was 64.1%. For the five strata, the seropositive rate ranged from 54.2% (Stratum 5) to 71.7% (Stratum 2) with no significant difference. For each participating school, the seropositive rate ranged from 44.4% to 72.9% with a statistically significant difference ($p < 0.005$). For school children in each grade, seropositive rate increased significantly from 53.2% for Grade 1 to 71.8% for Grade 3 ($p = 0.005$) and increased steadily from 61.2% for Grade 4 to 71.2% for Grade 6 ($p = 0.17$). A positive correlation was observed between the seropositive rate and geometric mean titers ($p = 0.035$). Geometric mean titers and the rate of a history of clinical varicella were positively correlated with increasing class grades.

Conclusion: Nine years after the introduction of the varicella vaccine into the expanded program of immunization in Taiwan, around two-thirds of elementary schoolchildren were

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seropositive for varicella-zoster virus. Further surveillance studies on clinical varicella cases are worthwhile to determine whether a second dose of varicella vaccine is needed in Taiwan. Copyright © 2015, Taiwan Society of Microbiology. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Varicella, also known as chicken pox, is a highly contagious but vaccine-preventable disease caused by primary infection with varicella-zoster virus (VZV), which belongs to the *Herpesviridae* family.^{1–3} The incidence of varicella varies among regions with different climates, population densities and degree of economic-social development.^{4,5} The clinical course after primary infection in children is relatively mild and self-limited with fever and a characteristic skin rash that forms small and itchy blisters.⁶ However, varicella may occasionally cause severe complications including secondary skin and soft tissue infection, pneumonia, central nervous system disease, and even death in immunocompetent children.⁷

In Taiwan, the seroprevalence of varicella was ~83% in children aged 11–15 years in the prevaccine era.⁸ A live attenuated vaccine, that was developed from the Oka strain of the varicella-zoster virus, was first licensed for administration to children in Taiwan in 1997. Initially, the varicella vaccine was used in the private sector and people received the vaccine at their own expense. Since 1998, public health authorities of some local governments in Taiwan, including Taipei City, Taichung City, Taichung County, etc., started to provide free varicella vaccine to children younger than 2 years. Since 2004, varicella vaccine was included in the expanded program of immunization in Taiwan and was freely provided as a routine childhood vaccination nationwide.⁹ The incidence of varicella significantly declined from 66/1000 children aged 4–5 years between 2000 and 2003, to 23/1000 children aged 6 years in 2008.¹⁰ However, there was still a 2.1% varicella breakthrough infection among those vaccinees.¹¹

Seroepidemiologic data in the postvaccine era is helpful to understand the epidemiology of varicella and evaluate the efficiency of current varicella vaccination strategies. Therefore, we conducted this survey, which was supported by the Centers for Diseases Control of Taiwan (CDC-Taiwan), to evaluate immune status against VZV among school children aged 7–12 years in northern Taiwan.

Methods

We conducted a cross-sectional survey from September 2012 to June 2013 to investigate VZV-specific immunoglobulin (Ig)G antibody in the population of elementary school children aged 7–12 years in New Taipei City.

Study populations and the selection of participants

New Taipei City is the second largest directly controlled municipalities in northern Taiwan, which comprises 29

administrative districts and 3,921,580 people resided in. In total, 225,234 students resided in this city, which accounted for 16.5% of all primary school children in Taiwan in 2012. A multistage stratified systematic sampling design was employed to obtain samples. The 29 administrative districts of New Taipei City were arbitrarily classified into five strata based on 14 variables, which included six medical facilities' variables (nursing staff/10,000 people, medical personnel/10,000 people, all staff in health centers/10,000 people, number of colleges or universities/10,000 people, proportion of agriculture population, and proportion of population with college degree or above), four socio-educational variables (number of physicians, nursing staff, low-income households, and near-poor households per 10,000 people), and four demographic variables [population density (persons/km²), proportion of population older than 65 years, younger than 15 years, and younger than 6 years]. Elementary schools in each stratum were selected with selection probability proportional to their size. From each stratum, elementary schools were selected as the primary sampling unit, and then classes were selected as the second sampling unit. One class was drawn from each grade in a sampled school, that is, six classes in total were drawn from each sampled school. In each selected school, the numbers of students in each class were also selected with probability proportional to their size. Finally, students were randomly selected in each class. Accordingly, 558 students were selected from six schools in Stratum 1, 130 students from two schools in Stratum 2, 66 students from two schools in Stratum 3, 140 students from two schools in Stratum 4, and seven students from two schools in Stratum 5. In total, at least 901 students were obtained. Subsequently, we recruited a total of 936 students from the selected schools.

All participants were healthy without acute illness. Past medical history including clinical varicella was obtained using a questionnaire from each participant. The information on varicella vaccination status of students from Grade 1 to Grade 4 was obtained from the CDC-Taiwan since the recoding of administration of vaccines included in expanded program of immunization should be mandatorily transmitted to the CDC-Taiwan.

Determination of varicella-specific antibodies

Each selected students had 5–10 mL blood drawn and the sera was stored at –20°C before being measured. We used indirect chemiluminescence immunoassays (Liaison, DiaSorin, Italy), which is a quantitative test to determine the VZV-specific IgG antibody. Those with an antibody titer of > 160 mIU/mL were classified as positive, a titer between 140 mIU/mL and 160 mIU/mL was grouped as equivocal,

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