SEROPREVALENCE OF VARICELLA-ZOSTER ANTIBODIES IN A THAI POPULATION

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Abstract. A stratified random sampling by age groups was conducted to determine seroprevalence of Varicella-Zoster virus (VZV) in a Thai population. In 2014, 2,218 serum specimens were collected from healthy people less than 60 years of age across four provinces from four regions of Thailand who attended pediatric and internal medicine units. Patients with chronic illness, undergoing immunosuppressive therapy or with clinical signs of infection with HIV or other immunodeficiency disorders were excluded. The overall seroprevalence of the sample population was 54.1%, with 27%, 50%, 89.6%, and 100% of those younger than 12, between 13 and 14, over 30, and over 50 years of age, respectively had anti-VZV antibodies. The proportion of VZV immunity increased rapidly in children from 5 to 9 years of age. The highest prevalence was among children attending kindergartens and primary schools. The findings were consistent with age groups reported in Thailand National Surveillance Database System. Because a significant proportion of teenage children currently susceptible to VZV could contract severe varicella and complications as adults, health-economic studies on cost-effectiveness and cost-benefit of VZV vaccine should be carried out to assist in decision making regarding introduction of such vaccines in Thailand.

Keywords: chickenpox, seroprevalence, seropositive rate, varicella antibody, Thailand

INTRODUCTION

Varicella is a highly infectious and contagious disease of the respiratory tract (CDC, 2007; Bureau of General Communicable Diseases, 2014; Hamborsky *et al*, 2015). The majority of varicella cases involves young children, especially kindergarteners (CDC, 2007; American Academic of Pediatrics and Pickering, 2009; Bureau of General Communicable Diseases, 2014; Hamborsky *et al*, 2015; Bureau of Epidemiology, 2015). Although varicella is usually a self-limiting viral illness, it remains latent in neural and intestinal ganglion, and can later become active as herpes zoster infection (CDC, 2007; Yawan *et al*, 2007; Hamborsky *et al*, 2015). Varicella disease in infants, adolescents, adults, and immunocompromised

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patients can cause severe complications and may even be fatal (Boelle and Hanslik, 2002; Yawan *et al*, 2007; Valentim *et al*, 2008; WHO, 2014; Hamborsky *et al*, 2015).

Varicella vaccine was developed approximately four decades ago (WHO, 2014). Although the vaccine is safe and quite effective for primary and secondary prevention, a number of countries recommended it as part of routine immunization protocol (Heininger and Seward, 2006; WHO, 2014). However, strong evidence of seroprevalence, immunity level, vaccine cost-effectiveness, and cost-benefit are needed before introduction of varicella vaccine (Apisarnthanarak *et al*, 2007; Bugaje *et al*, 2011; WHO, 2014). Accordingly, this study was carried out to evaluate the seroprevalence of Varicella-Zoster virus (VZV) in a Thai population, providing data towards a possible future introduction of VZV vaccination program in the country.

MATERIALS AND METHODS

Study population

Serum specimens were those remaining from previous projects on the impact of hepatitis B vaccine immunization program as part of an Expanded Program of Immunization (EPI) after 20 years of implementation and seroprevalence of hepatitis A, B, and C in Thailand, collected in 2014 (Posuwan *et al*, 2016; Sa-nguanmoo *et al*, 2016; Wasitthankasem *et al*, 2016). The participants were healthy children and adults who attended pediatric and internal medicine units. Patients with chronic illness, those undergoing immunosuppressive therapy and having clinical signs of infection with HIV or other immunodeficiency disorders had been excluded.

The study was approved by the Ethics Committee for Research in Human Subjects, Department of Disease Control, Nonthaburi, Thailand (FWA00013622, approved on April 20, 2015).

Serum specimens

Sera were stratified random samples according to age groups from approximately 6,000 to 2,218 specimens from four provinces (Khon Kaen, Lop Buri, Narathiwat, and Uttaradit) in four regions of Thailand, which were representative of the seroprevalence in the northeastern, central, southern, and northern region, respectively (Fig1). The serum samples were stored at -20°C until used.

Fig 1-Map of Thailand showing location of the four provinces from which serum samples were obtained.

Laboratory test

ELISA (Siemens Healthcare Diagnostics, Marburg, Germany) was employed for detecting anti-VZV IgG, with a positive cut-off point of ≥200 mIU/ml. Results are reported as geometric mean.

Statistical analysis

A chi-square test was used to compare differences, with statistical significance accepted at $p \leq 0.01$.

RESULTS

Of 2,218 serum specimens tested for anti-VZV IgG levels, 44.3% were collected from male subjects. Uttaradit, Khon Kaen, Lop Buri, and Narathiwat constituted 22.5%, 22.8%, 15.7%, and 39, 0%, respectively (Table 1).

Over half (54.1%) of the specimens had anti-VZV IgG levels above the cut-off value. Seroprevalence among provinces was 47.5%, 54.7%, 59.2%, and 62.6% for Lop Buri, Khon Kaen, Uttaradit, and Narathiwat, respectively; among females and males was 57.9% and 49.4%, respectively; and among age groups was 10.4%, 11.7%, 32.3%, 46.2%, 63.3%, 79.1%, 89.6%, 94.8%, and 100% for subjects <1, 1-4, 5-9, 10-14, 15-19, 20-29, 30-39, 40-49, and >50 year(s) of age, respectively. Overall, seroprevalence of varicella is significantly different with respect to each category, namely, province, gender and age group ($p<0.001$). Seroprevalence of varicella among age groups in each province had the same pattern (Fig 2). For the infant group, maternal anti-VZV IgG was absent after 3 months of age (Table 1).

The geometric mean titer (GMT) among positive anti-VZV IgG samples was 579.8 mIU/ml. Anti-VZV IgG GMT rose sharply in 1-4 year old compared to <1-year-old age group, and thereafter, remained unchanged (Fig 3). In order to obtain a picture of the trend of varicella incidence over the previous ten years, median incidence of 2005 (Bureau of Epidemiology, 2005) and this study was calculated, revealing outbreak usually occurring before 10 years of age and incidence in children <10 years old of 441.9/100,000 population (range 295.3-608.7/100,000) (Fig 4). Overall incidence of varicella cases in 2005 is 106.6/100,000 population (range 76.4-137.0/100,000).

DISCUSSION

Our study finds half of the tested Thai population in 2014 were seropositive for anti-VZV IgG, indicating the country continues to be at risk of varicella out-breaks as half of the population still does not have immunity to VZV. Varicella seroprevalence of the 2005 survey (Bureau of Epidemiology, 2005) stratified according to age groups is consistent with the current study, both highlighting the major risk to kindergarteners and primary school-aged children, in agreement with previous studies demonstrating low seroprevalence (27.2%) in children <12 years of age (Migasena *et al*, 1997; Lolekha *et al*, 2001). Although our study included only 77 infants, which was not large enough to be statistically significant, seroprevalence data suggest transplacental maternal varicella immunity might be absent before the age of 4 months, as noted by others (Gershon *et al*, 1976; Pinquie *et al*, 2009; Waaijenborg *et al*, 2013). A majority of the Thai population is at risk of contracting severe varicella infection and complication, high proportion of susceptibility among adolescent and adult, a phenomenon similar to other Asian tropical countries, such as India, Indonesia, Philippines, and Singapore, but different from that of temperate countries where risk is mainly occurs among children 1-9 years of age

Table 1
Varicella seropositive rate and anti-varicella-Zoster virus IgG titer according to province, gender and age group, Thailand 2014.

Category	Sample size (%)	Seropositive rate (%) (95%CI)	GMT (mIU/ml) (95%CI)
Province			
Lop Buri	866	47.5 (44.1-50.8)	597.1 (548-646.2)
KhonKaen	506	54.7 (50.3-59.1)	546.8 (504.2-589.3)
Uttaradit	498	59.2 (54.8-63.6)	602 (551.9-652.1)
Narathiwat	348	62.6 (57.3-67.7)	590.3 (525.4-655.3)
Gender			
Male	983	49.4 (46.3-53.6)	533.9 (533.9-612.3)
Female	1,235	57.9 (55.1-60.7)	584.4 (551.7-617.2)
Age (year)			
<1[a]	77	10.4 (4.6-19.4)	341.4 (174.8-508)
<1-month-old	6	83.3	-
1-month-old	2	50	-
2-month-old	3	33.3	-
3-month-old	1	100	-
1-4	239	11.7 (7.9-16.5)	691.5 (500.5-882.5)
5-9	415	32.3 (27.9-37.1)	640.8 (564.5-717.3)
10-14	418	46.2 (41.3-51.1)	533.8 (478.6-589.0)
15-19	349	63.3 (58.0-68.4)	606.8 (536.9-676.7)
20-29	359	79.1 (74.5-83.2)	573.8 (525.8-621.4)
30-39	241	89.6 (58.1-93.2)	545.5 (489.3-601.8)
40-49	58	94.8 (85.6-98.9)	586.8 (483.8-689.7)
>50	62	100 (100-100)	616.5 (493.5-739.5)
Total	2,218	54.1 (52.0-56.2)	579.8 (554.7-605)

[a]Separated into <1-month-old, 1-month-old, 2-month-old, and 3-month-old. CI, confidence interval; GMT, geometric mean titer.

(Migasena *et al*, 1997; Lee , 1998; Lokeshwar *et al*, 2000; Wutzler *et al*, 2001; Fatha *et al*, 2014; Rimseliene *et al*, 2016; Bollaerts *et al*, 2017; Chen *et al*, 2017).

The trend of natural VZV infection in the current study differs from an earlier study, which could be attributed to differences in geographic location of the test population and season during which the survey is conducted, factors known to affect prevalence of varicella infection (Migasena *et al*, 1997). Lolekha *et al* (2001) reported the coldest regions of northern Thailand have the highest seroprevalence,

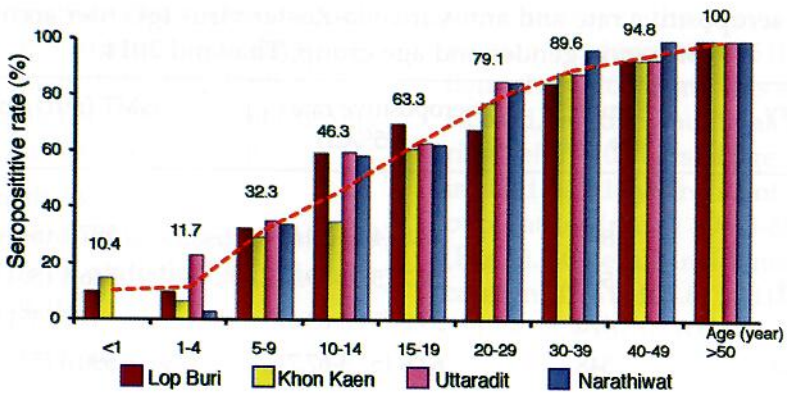

Fig 2-Varicella seropositive rate in four provinces of Thailand, 2014 according to age group (n = 2,218). Presence of anti-Varicella-Zoster virus IgG was determined by ELISA. Number above each set of bars indicates seropositive rate in each age group.

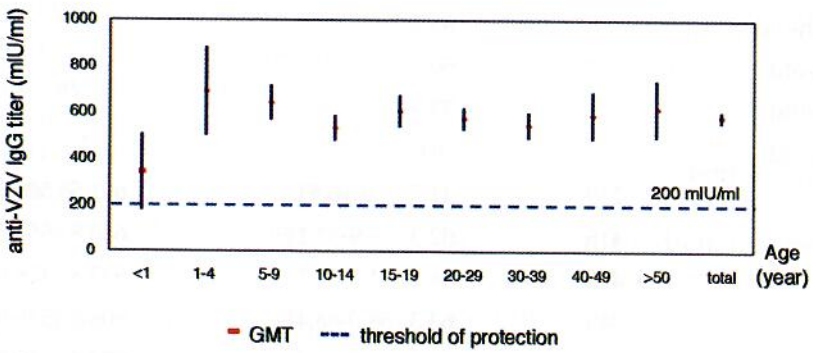

Fig 3-Anti-Varicella-Zoster virus (VZV) IgG titer according to age group in a Thai population in 2014 (n = 2,218). Anti-Varicella-Zoster virus IgG titer was determined by ELISA and presented as geometric mean titer (GMT). Vertical line denotes 95% confidence interval.

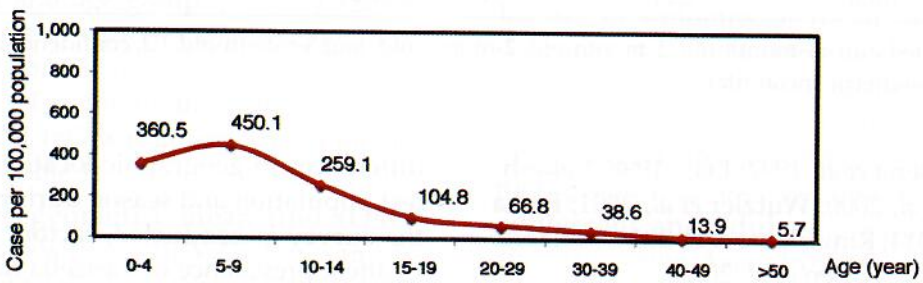

Fig 4-Median incidence of varicella according to age group in a Thai population, 2005 (R506 surveillance report, 2005) and 2014 (this study).

whereas in the current study it was the southern region, in agreement with the R506 surveillance report (Bureau of Epidemiology, 2005) indicating Narathiwat Province is among the top three southern provinces with highest incidences. Consequently, the result of this study used the specimens collected in 2014. Unfortunately, there were no data in the records of the history of chickenpox infection and varicella immunization.

In conclusion, the study shows nearly half of the Thai population have no immunity against varicella infection, and those at highest risk were infants and children below the age of 5 years. Vaccine is an important means of preventing and control of disease, although it is expensive. This study indicates that vaccination should be considered among those most susceptible, namely, infants and primary school children. However, further health-economics studies should be conducted to guide informed decision on any possible future varicella vaccine introduction.

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