# The Prevalence of Varicella-Zoster Virus Infection in Normal Healthy Individuals Aged above 6 Months

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*The prevalence of varicella-zoster virus (VZV) infection was studied by determining the presence of IgG antibody to VZV (anti-VZV IgG) using ELISA method. Three hundred and fifty sera collected from Thai healthy individuals aged above 6 months (mean age ± standard deviation = 14.9 ± 11.4) were tested, the prevalence of VZV infection was 64.6% (225/350). All samples were randomly sampling from healthy children and blood donors who visited the hospital and clssified into 7 groups, 50 samples each, according to their age, i.e., group 1;6 months-3 years, group 2;4-6 years, group 3;7-9 years, group 4;10-14 years, group 5;15-19 years, group 6;20-24 years and group 7; above 25 years. The prevalence of VZV infection were 12%, 42%, 64%, 70%, 78%, 84% and 100% respectively. The mean amount of anti-VZV IgG among groups of positive VZV infection (225 samples) was 86.8 ± 29.7 unit/ml. The mean amount of anti-VZV IgG was highest in 6 months-3 years age group (113.6 ± 39.2 unit/ml). Significant difference of the mean amount of anti-VZV IgG was found between group 1, 3, 6 and other groups (*p-*value < 0.05). There was a correlation between history of varicella and the presence of anti-VZV IgG in the serum. 95.3% of individuals with positive history has already had the antibody. The important associated factors that might involve VZV infection were age, number of members in family and place of exposure to VZV infection. Other factors, such as sex and income did not show any association to VZV infection.*

***Keywords:*** *Prevalence, Varicella-zoster virus infection*

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Varicella-zoster virus (VZV) is a member in family herpesviridae, subfamily alphaherpesvirinae. The virus has linear double-stranded DNA. Icosahedral capsid is covered with an envelope, with size about 200 nanometre[1]. This virus has only one serotype. Human is the solely natural reservoir. Primary infection results in well-known exanthematous disease in children, called varicella or chickenpox. This is a highly contagious disease. Transmission of VZV is usually via respiratory droplets. This disease occurs worldwide with peak incidence in winter. Boys and girls are affected equally. Formerly, the disease was common in pre-school and school age. But in the past two decades, especially in the tropical region, it trended to occur in the older age group[2].

In a normal, healthy child, the incubation period is usually 14 to 16 days. The first appearance of exanthem is often preceded by one or two days of fever. The exanthem begins on the scalp, face, or trunk as erythematous macules, then evolve into virus-containing vesicles that begin to crust over after about 48 hours. While the first crop of lesions is evolving, new crops appear on the trunk and extremities. New lesions continue to appear over a period of up to six or seven days. Healing occurs without scarring. Complications are uncommon, such as pneumonia. Varicella is a more serious disease in healthy adults and immunocompromised patients. Varicella pneumonia is the most common serious complications with high fatality rate, but fulminant hepatitis and varicella encephalitis may also result. Primary infection of a pregnant woman may

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affect the fetus or neonate. Fetal infection early in pregnancy is uncommon, but can insult in mutiple developmental anomalies (congenital varicella syndrome). More commonly, a fetus infected near the time of delivery may exhibit typical varicella at birth or shortly thereafter (neonatal varicella). The severity of the disease depends on whether the mother has begun to produce anti-VZV IgG by the time of delivery. If the mother develops varicella 5 days before to 2 days after delivery, the infant is likely to develop more serious disease with high fatality rate due to absence of maternal immunity[1,3,4].

VZV causes latent infection. After the disseminated nature of primary infection, latency is established in multiple sensory ganglia[1]. Reactivation can occur with some stimuli, results in zoster (shingles)[4]. The virus spreads along sensory nerve and cause vesicles distributing in dermatome, usually unilateral. Burning sensation and pain at lesions are common. The disease is self-limited within 2 to 4 weeks. Zoster is common in the elderly age group, usually above 50 years of age.

Generally, the diagnosis of VZV infection can be made clinically without special investigations. However, there are several methods for confirmatory tests. Detection of infected cell can be done by immunofluorescense method using monoclonal antibody. This is a rapid test with high specificity and sensitivity[6]. Viral culture is time-consuming, cytopathic effect can be seen after 48 hours. Moreover, it has lower sensitivity so it is not in routine use[7]. In addition, detection of sera specific anti-VZV IgG and IgM is a useful test. It can be done by several techniques. For example, enzyme-linked immunosorbent assay (ELISA)[8,9], latex agglutination (LA)[10], fluorescent antibody to membrane antigen method (FAMA)[11].

Nowadays, there is a live-attenuated vaccine against VZV infection. It derive from Oka strain. In children 1 to 12 years old, one dose of subcutaneous injection is recommended. In children over 12 years old and adults, two doses of injection are recommended with 1 month apart. Seroconversion rate is found over 95 percent and the immunity is longer than 20 years[12,13].

The epidemiologic data of VZV infection is useful. This study aims to find out the seroprevalence of VZV infection in Thai healthy individuals aged above 6 months. The specific anti-VZV IgG is detected by ELISA method.

## Material and Method

### *Study design*

This is a descriptive study. The sera of the population is tested for anti-VZV IgG in order to determine the prevalence of VZV infection.

### *Study population*

350 Thai healthy children 6 months to 14 years and blood donors who visited at Bhumipol Adulyadej Hospital during 1998-2000 were classified into 7 age groups, 6 months-3 years, 4-6 years, 7-9 years, 10-14 years, 15-19 years, 20-24 years and over 25 years. Each groups contained 50 samples.

### *Enzyme-linked immunosorbent assay (ELISA)*

Detection of specific anti-VZV IgG were done by using ELISA technique. The test kit is a product of Human, Germany. The principle is specific antibody against VZV will be form antigen-antibody complex with the VZV antigen coated at microwells. Then anti-human IgG conjugated with horseradish peroxidase is added. To detect the complexes, tetramethylbenzidine hydrogen peroxide (TMB/$H_2O_2$) is added. If there is the specific anti-VZV IgG in the sera, the color will change from blue to yellow. The intensity of the color is vary with the amount of the antibody. The intensity of the color is read at the wavelength 460 nanometre. The amount of antibody is calculated by comparing with the standard sera included in the test kit, reported in unit. In the qualitative interpretation, the result is read by comparing with cut-off value (COV). The result is considered as positive if it is greater than COV+15%. And the result is considered as negative if it is less than COV-15%.

### *Data analysis*

The qualitative data is presented in frequency and percentage. Statistic tests for difference between groups are done by using Chi-Square test. The quantitative data is presented in mean and standard deviation. Statistic tests for difference between groups are done by using ANOVA (Kruskal-Wallis test) and Mann-Whitney U test.

## Results

Sera of 350 Thai healthy individuals aged above 6 months who visited at Bhumiphol Adulyadej Hospital during 1998-2000 were tested for anti-VZV IgG, in order to study about the prevalence of VZV infection. The samples were divided into 7 groups by different age group. Each group contained 50 samples, Group 1; 6 months-3 years, Group 2; 4-6 years, Group 3; 7-9 years, Group 4; 10-14 years, Group 5; 15-19 years, Group 6; 20-24 years and Group 7; above 25 years. In

this study, the prevalence were 12, 42, 64, 70, 78, 84 and 100 percent, respectively (Table 1, Fig. 1). The prevalence of VZV infection in Thai people, average age 14.9 ± 11.4 years was 64.6 percent (225/ 350). The prevalence of VZV infection in male was 66.5 percent (135/ 203). In female, the prevalence was 61.2 percent (90/ 147) (Table 2). There were no statistically different between both sexes. There was a correlation between history of varicella and the presence of anti-VZV IgG in the serum, 95.3 percent of individuals with positive history has already had the antibody. But in case of the history of varicella was negative, 26.1 percent has aleready had the immunity (Table 3).

The average antibody level of 225 positive samples was 86.8 ± 29.7 unit/ ml (Table 4). Age group 6 months-3 years had the highest antibody level (113.6 ± 39.2 unit/ ml). The next orders were age group 7-9 years (98.2 ± 17.7) and 20-24 years (95.9 ± 33.4), respectively. Mean antibody levels in group 1, 3 and 6 were significant difference to other groups ($p$-value < 0.05) (Table 5).

In this study, the questionaires of 200 children were analysed (not include individuals whose age above 15 years) for determining association facters that might affect VZV infection (data shown in Table 5). The factors that associated with VZV infection were age, the number of member in the family and place of exposure to VZV infection ($p$-value < 0.05). The other factors, such as sex and income were not the associated factors.

**Table 1.** The prevalence of VZV infection in different age groups

| Group | Range of age (years) | Mean age ± SD (years) | Prevalence (%) |
|---|---|---|---|
| 1 | 0.5-3 | 2.2 ± 1.1 | 12 |
| 2 | 4-6 | 5.9 ± 0.8 | 42 |
| 3 | 7-9 | 7.8 ± 0.9 | 64 |
| 4 | 10-14 | 11.7 ± 1.3 | 70 |
| 5 | 15-19 | 18.7 ± 0.5 | 78 |
| 6 | 20-24 | 21.5 ± 1.3 | 84 |
| 7 | ≥ 25 | 36.6 ± 8.1 | 100 |
| Total | | 14.9 ± 11.4 | 65 |

**Table 2.** The prevalence of VZV infection in both sexes

| Sex | No. of seropositive (%) | No. of seronegative (%) | Total |
|---|---|---|---|
| Male | 135 (66.5%) | 68 (33.5%) | 203 |
| Female | 90 (61.2%) | 57 (38.8%) | 147 |

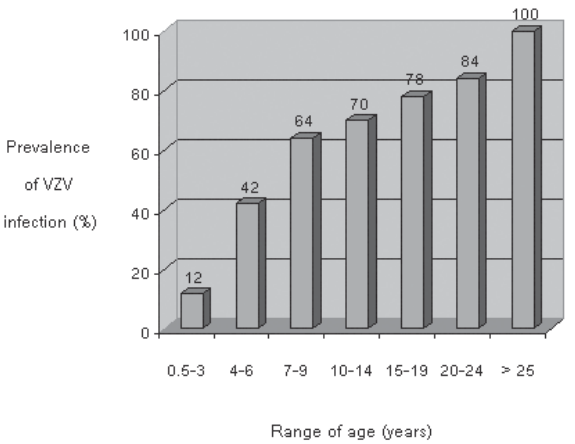


**Fig. 1** The prevalence of VZV infection in different age groups

## Discussion

Primary VZV infection leads to varicella (chickenpox) which is common in children. It usually occurs in 5 to 9 years of age. But in the past two decades, it trended to occur in the older age group. The number of cases in adolescents and adults is increased, especially in the tropical area[2].

In this study, the prevalence of VZV infection in Thai population aged above 6 months in Bangkok was determined by detection of anti-VZV IgG in sera of 350 Thai healthy people. In children 6 months-3 years

**Table 3.** The correlation between the history of varicella and the presence of anti-VZV IgG in serum

| History of varicella | No. of seropositive (%) | No. of seronegative (%) | Total |
|---|---|---|---|
| Yes | 163 (95.3%) | 8 (4.7%) | 171 |
| No | 40 (26.1%) | 113 (73.9%) | 153 |
| Unknown | 22 (84.6%) | 4 (15.4%) | 26 |

**Table 4.** Mean anti-VZV IgG level in different age groups

| Group | Range of age | Mean anti-VZV IgG level ± SD (HU/ ml) |
|---|---|---|
| 1 | 0.5-3 | 113.6 ± 39.2* |
| 2 | 4-6 | 83.7 ± 27.8 |
| 3 | 7-9 | 98.2 ± 17.7* |
| 4 | 10-14 | 87.5 ± 29.3 |
| 5 | 15-19 | 76.7 ± 28.1 |
| 6 | 20-24 | 95.9 ± 33.4* |
| 7 | ≥ 25 | 77.6 ± 28.1 |
| Total | | 86.8 ± 29.7 |

* statistically different with other age groups, $p$-value < 0.05

**Table 5.** Factors associated with VZV infection

| Factors | Anti-VZV IgG | | *p*-value |
|---|---|---|---|
| | Positive (N=225) | Negative (N=125) | |
| Age (years): mean ± SD | 19 ± 11.6 | 7.5 ± 6.0 | 0 |
| Male:Female | 135:90 | 68:57 | 0.31 |
| Income (Baht) ± SD | 18,220 ± 16,125 | 18,562 ± 30,187 | 0.92 |
| Number of children | 2.4 ± 1.3 | 2.0 ± 1.1 | 0.02 |
| Place of exposure (1:2:3:4)* | 5:0:0:89 | 36:1:1:68 | undetermined |

* 1 = home, 2 = neighbour, 3 = nursery, 4 = school

old, anti-VZV IgG was presented in 12 percent. In children 4-6 and 7-9 years old, anti-VZV IgG was presented in 42 and 64 percent, respectively. The seropositivity was rising to 100% at age above 25 years old (mean age was 36.6 ± 8.1 years). It seems that Thai population is likely to have peak infection at age 4 to 9 years (52% of VZV infection in all age group) which is similar to the previous epidemiologic data, that showed peak of VZV infection in children 5 to 9 years old.

In 1985, Kositanont U et al[14] reported that children 3 to 13 years old, 25.8% had the immunity to VZV. Whereas adults 17 to 27 years, 64.8% had the immunity to VZV. In 1996, Bhattarakosol P et al[15] reported that the prevalence of VZV infection in 74 undergraduate students (mean age 21 years old) was 74.3 percent. In 1997, Migasena S et al[16] reported that children 1 to 14 years, 41.8% had the immunity to VZV. In this study, 47% of children 6 months to 14 years have the immunity to VZV and 78% of individuals aged 15 to 19 years have the immunity. Note that in this study, the prevalence is slightly higher in both age groups.

In this study, there is a correlation between history of varicella and the presence of anti-VZV IgG. 95.3 percent of individuals who had the history of varicella have had the immunity to VZV. The result is similar to the previous study which reported that 97.7 percent of individuals who had the history of varicella have had the immunity to VZV[15,16]. In contrast to the negative history of varicella, it was not well correlate to the presence of anti-VZV IgG (Table 3).

Because of using the ELISA method, the average antibody level in each age groups can be defined (Table 4). The highest antibody level is found in children 6 months to 3 years old. In general, the highest antibody level reflect peak infection, but it does not correlate with the results as above that found peak infection in children 4 to 9 years old. In this study, we excluded children under 6 months old because in this age group, maternal antibody can be found in the infants. Owing to detection of the highest antibody level in children 6 months to 3 years old, but the incidence of infection was low. It might be that some part of detected antibody is maternal antibody. So the further study about how long the maternal anti-VZV IgG will be presented in infants should be done.

About the factors that might be associated with VZV infection, sex and income did not show any association to VZV infection. The important associated factors that might affect VZV infection were age, number of members in family and place of exposure to VZV infection (p-value < 0.05, Table 5).

## Conclusion

In Thailand, VZV infection is common. Peak incidence is in children 4 to 9 years old. Most of the infection occurs in children, but 30 percents occur after 15 years old. The past history of varicella is reliable and has a correlation with immunity against VZV.

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## *ความชุกของการติดเชื้อไวรัสอีสุกอีใสในคนปกติอายุตั้งแต่ 6 เดือนขึ้นไป*

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*การศึกษาความชุกของการติดเชื้อไวรัสอีสุกอีใสทำได้โดยการตรวจหาแอนติบอดีจำเพาะต่อเชื้อไวรัสอีสุกอีใสชนิด IgG ด้วยวิธี ELISA จากการตรวจน้ำเหลืองประชากรไทยที่มีสุขภาพแข็งแรงอายุตั้งแต่ 6 เดือนขึ้นไป (อายุเฉลี่ย 14.9 ± 11.4 ปี) จำนวน 350 ราย พบมีความชุกของการติดเชื้อไวรัสอีสุกอีใส ร้อยละ 65 (225/350) ตัวอย่างทั้งหมด เก็บสุ่มมาจากผู้ที่มาตรวจสุขภาพและผู้ที่มาบริจาคโลหิตที่โรงพยาบาล โดยแบ่งตามช่วงอายุเป็น 7 กลุ่ม กลุ่มละ 50 ตัวอย่าง คือ กลุ่มที่ 1; 6 เดือน-3 ปี, กลุ่มที่ 2; 4-6 ปี, กลุ่มที่ 3; 7-9 ปี, กลุ่มที่ 4; 10-14 ปี, กลุ่มที่ 5; 15-19 ปี, กลุ่มที่ 6; 20-24 ปี และกลุ่มที่ 7; ตั้งแต่ 25 ปีขึ้นไป พบความชุกของการติดเชื้อไวรัสอีสุกอีใส ร้อยละ 12, 42, 64, 70, 78, 84 และ 100 ตามลำดับ ค่าเฉลี่ยปริมาณแอนติบอดีจำเพาะต่อเชื้อไวรัสอีสุกอีใสที่อ่านผลบวกจำนวนทั้งสิ้น 225 ตัวอย่าง เท่ากับ 86.8 ± 29.7 ยูนิต/ มล. โดยค่าเฉลี่ยปริมาณแอนติบอดีในกลุ่มที่ 1, 3 และ 6 มีความแตกต่างจากกลุ่มอื่น ๆ อย่างมีนัยสำคัญทางสถิติ (p-value<0.05) มีความสัมพันธ์กันระหว่างประวัติการเป็นโรคอีสุกอีใสและการตรวจพบ แอนติบอดีต่อเชื้อไวรัสอีสุกอีใส โดยร้อยละ 95.3 ของผู้ที่มีประวัติเคยเป็นโรคอีสุกอีใสตรวจพบว่ามีภูมิต้านทานต่อเชื้อแล้ว ปัจจัยที่เกี่ยวข้อง กับการติดเชื้อไวรัสสุกใสที่สำคัญคือ อายุ, จำนวนสมาชิกในครอบครัว และสถานที่ที่มีโอกาสสัมผัสโรค ส่วนปัจจัยอื่น ได้แก่ เพศและเศรษฐฐานะ ไม่พบมีความสัมพันธ์กับการติดเชื้อ*