Seroprevalence of Epstein-Barr Virus Infection in Thai Children

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Abstract

A hospital-based cross-sectional survey was conducted in Bhumibol Adulyadej Hospital, Bangkok, Thailand between January and December 1997 to study the seroprevalence of anti-EBV IgG antibody in previously healthy hospitalized children aged 0-15 years. Of 589 cases, there were 327 boys and 262 girls with a mean age of 3.9 years. The seroprevalence of EBV infection was 50.4, 72.8, 92.3, 96.6 and 97.6 per cent in children at the age range of 0-2, 3-5, 6-8, 9-11 and 12-14 years, respectively. After excluding infants below 6 months of age, the total seroprevalence rate was 68.4 per cent. The age of children with positive anti-EBV IgG antibody was significantly higher than that of children with negative antibody. Children who were reared at home had lower seroprevalence rates. In conclusion, seroprevalence of EBV infection increased with advancing age and reached 90 per cent or more after 6 years of age.

Key word : Seroprevalence, Epstein-Barr Virus, EBV

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Epstein-Barr virus (EBV) is the most common cause of infectious mononucleosis (IM) which is manifested typically by fever, exudative pharyngotonsillitis, lymphadenopathy, hepatosplenomegaly, and atypical lymphocytosis. The outcome of EBV infection ranges from asymptomatic infection in infants and young children to more serious infection in older children and adults[1]. Infection frequently occurs early in life, particularly among lower socioeconomic groups. In 1969, two reports from developed countries showed that the seroconversion rate of EBV infection was 56 and 45 per

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Table 1. Demographic data of the subjects.

Characteristics	Anti-EBV IgG positive (n = 392)	Anti-EBV IgG negative (n = 197)	p-value
1. age (years) mean ± standard deviation	5.08 ± 4.33	1.66 ± 1.86	0.000
2. boys : girls sex ratio	1.19 : 1	1.37 : 1	0.446
3. income of family (baht per month)	12,842.17 ± 10,171.74	12,831.71 ± 9,742.16	0.991
4. number of children in the family mean ± standard deviation	2.07 ± 1.16	1.88 ± 0.93	0.173
5. place of rearing home : others	1.13 : 1	3.35 : 1	0.000

Table 2. EBV seropositivity of the study children as classified by age-group.

Age-group (years)	Number tested	Number positive anti-EBV IgG	%
0-2	331	167	50.4
3-5	92	67	72.8
6-8	65	60	92.3
9-11	59	57	96.6
12-14	42	41	67.6
Total	589	392	66.6

cent in 0-4 and 0-2 year old children respectively (2-3). In 1980, Puthavathana et al[4] reported that the seroprevalence rate of EBV infection was 48, 30, 83, 90 and 93 per cent in Thai children aged 0-6 months, 6-12 months, 1-5 years, 5-15 years and more than 15 years respectively. In 1999, Pancharoen et al[5] studied 143 children whose sera were tested for antibodies against viral capsid antigens (anti-VCA antibodies) for any reasons and found that among 124 children with negative anti-VCA IgM, 64.5, 50.0, 66.7, 83.3 and 100.0 per cent of children aged 0-2, 3-5, 6-8, 9-11 and 12-14 years had positive anti-VCA IgG antibodies. However, a number of children in this study had underlying diseases. Therefore, we conducted this research in order to obtain current data on seroprevalence of EBV infection in different age groups of previously healthy Thai children.

MATERIAL AND METHOD

Study subjects

The study was carried out at Bhumibol Adulyadej Hospital, and the research was a hospital-based cross-sectional survey. The eligible study subjects were children aged 15 years or younger who were hospitalized between January and December 1997.

Those who were diagnosed with primary immunodeficiency, HIV infection including perinatally HIV-exposed infants, cancers, chronic hepatic or renal diseases, and those who received blood or blood components in the past three months and who were admitted to the nursery or intensive care unit, were excluded.

Data collection

After the subjects' parents completed the informed written consents, information was obtained by interviewing them with structured questionnaires which included the children's age and sex, parental income, number of children in the family and place of child rearing. Two milliliters of blood was obtained and the serum was tested for anti-EBV IgG antibody.

Detection of anti-EBV IgG

All sera were determined for the presence of anti-EBV IgG by using Enzygnost anti-EBV IgG kit purchased from Behring, Germany. The principle of the test was indirect enzyme-linked immunosorbent assay. The EBV antigens, prepared from lymphoblastoid cells infected with EBV, consisting of VCA, EBV cell nucleus-associated antigens (EBNA) and early protein (EA-D) were coated on microtiter plate. The IgG antibodies present in the test serum would bind specifically to the antigens coated on the well. The antigen-antibody complexes were detected by using anti-human IgG conjugated with peroxidase enzyme. After adding TMB substrate, the reaction was terminated by stop solution. The developed color was measured by spectrophotometer. The control wells coated with normal lymphoblastoid cell antigens were run in parallel

Table 3. Difference in demographic data of the subjects who had or had no anti-EBV IgG.

Characteristics	Anti-EBV IgG positive (n = 331)	Anti-EBV IgG Negative (n = 153)	p-value
1. age (years) mean ± standard deviation	6.00 ± 4.09	2.04 ± 1.95	0.000
2. boys : girls sex ratio	1.22 : 1	1.22 : 1	0.938
3. income of family (baht per month)	12,768.46 ± 10,152.86	13,487.68 ± 10,273.01	0.497
4. number of children in the family mean ± standard deviation	2.11 ± 1.17	1.90 ± 0.88	0.148
5. place of rearing home : others	0.82 : 1	2.54 : 1	0.000

Table 4. Comparison of antibody activity among anti-EBV IgG positive subjects, classified by age-group.

Age-group (years)	Number of positive anti-EBV IgG subjects with quantitative analysis	Antibody activity (u/ml) mean ± standard deviation
0-2	120	216.60 ± 265.92
3-5	63	286.98 ± 248.85
6-8	52	296.13 ± 267.61
9-11	53	273.57 ± 229.07
12-14	39	193.59 ± 150.60

Note : The antibody activity is not different among groups (p-value > 0.05).

with the test wells. A positive result was determined when the difference between O.D. of the test well and the control well was greater than 0.2, as recommended by the manufacturers. In addition, quantitative evaluation of anti-EBV IgG was measured by Behring ELISA Processor II (BEP II) and expressed as antibody activity (unit/ml). The limit of detection of the test was 25 unit/ml.

Data analysis

Demographic data were presented by using mean, range and percentage. Categorized variables were analyzed by Chi-square test and noncategorized variables were analyzed by Student *t*-test. The level of significance was set at the alpha = 0.05.

RESULTS

A total of 589 cases were enrolled. Of these, 327 were boys and 262 were girls, with the mean age of 3.9 years: and 392 (66.6%) of them were positive for anti-EBV IgG antibodies. The study children with positive anti-EBV IgG were significantly older and were reared at home significantly less than those with negative anti-EBV IgG (Table 1).

Seroprevalence of EBV infection was 50.4, 72.8, 92.3, 96.6 and 97.6 per cent in children in the age range of 0-2, 3-5, 6-8, 9-11 and 12-14 years respectively (Table 2).

After excluding 105 infants whose ages were under 6 months, the seroprevalence rate was 68.4 per cent. The children's age and place of rearing were significantly different between the group with positive and negative anti-EBV IgG (Table 3).

Quantitative analysis was done in 327 anti-EBV IgG positive samples and it was found that there were no significant differences among children of different age-ranges (Table 4).

DISCUSSION

To our knowledge, there were three previous studies on seroprevalence of EBV infection among Thai children. Puthavathana et al[4] (1980) revealed that the seroprevalence rate in children aged 6 months to 15 years was 67.4 per cent and the rate increased with advancing age, reaching 90 per cent by the age of fifteen. Poovorawan et al[6] (1997) studied the seroprevalence of EBV antibody among 4- to 14-year-old school children of the low to middle socio-economic class in Bangkok and found a very high seroprevalence rate of 97.3-100.0 per cent. Pancharoen et al[5] (1999) reported that the rate of previous EBV infection in children whose sera were tested for anti-VCA IgG for any reasons was 70.2 per cent. Comparing the data in 1980, the seroprevalence rate found in our study was not much different. Moreover, our data were also not different from that among Chinese children in 1986[7].

Half of the children with positive antibody tests and three-quarters of those with negative antibody tests were reared at home. This may be explained by the increased opportunity of children reared in crowded families to contract EBV infection. However, there were no statistical co-relations between seroconversion and other risk factors, including sex, number of children in the family and family incomes. Cross-sectional analytic studies with controlling confounders may yield more reliable possible risk factors of EBV infections.

In conclusion, the seroprevalence rate of EBV infection in 6 month to 15 year old children who were admitted to Bhumibol Adulyadej Hospital, Bangkok, Thailand between January and December 1997 was 68.4 per cent. The seroprevalence rate increased with advancing age and was above ninety per cent after the age of six. Children who were reared at home had a statistically lower seroprevalence rate.

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ความชุกของภาวะติดเชื้อไวรัสเอ็ปสไตน์บาร์ในเด็กไทย

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การศึกษานี้เป็นการสำรวจภาคตัดขวางเพื่อหาความชุกของภาวะติดเชื้อไวรัสเอ็ปสไตน์บาร์ โดยการตรวจหาแอนติบอดีย์จำเพาะในเด็กไทยอายุ 0–15 ปีซึ่งเคยแข็งแรงดีมาก่อนและรับไว้รักษาในโรงพยาบาลภูมิพลอดุลยเดช ระหว่างเดือนมกราคม–ธันวาคม พ.ศ.2540 จำนวน 589 คน เป็นเพศชาย 327 คน เพศหญิง 262 คน มีอายุเฉลี่ย 3.9 ปี พบว่าความชุกของการติดเชื้อไวรัสเอ็ปสไตน์ในเด็กกลุ่มอายุ 0–2, 3–5, 6–8, 9–11 และ 12–14 ปี เท่ากับร้อยละ 50.4, 72.8, 92.3, 96.6 และ 97.6 ตามลำดับ หลังจากคัดเด็กอายุน้อยกว่า 6 เดือนออกไป พบว่าอัตราการติดเชื้อเฉลี่ยในทุกกลุ่มอายุ คิดเป็นร้อยละ 68.4 เด็กที่มีแอนติบอดีย์ต่อไวรัสเอ็ปสไตน์บาร์มีอายุเฉลี่ยสูงกว่าเด็กที่ไม่มีแอนติบอดีย์อย่างมีนัยสำคัญทางสถิติ เด็กที่ถูกเลี้ยงดูที่บ้านมีโอกาสติดเชื้อน้อยกว่าเด็กที่ถูกเลี้ยงดูนอกบ้านอย่างมีนัยสำคัญทางสถิติ สรุปได้ว่าอัตราของการติดเชื้อเอ็ปสไตน์บาร์สูงขึ้นตามอายุของเด็กและสูงถึงร้อยละ 90 หรือมากกว่าเมื่ออายุ 6 ปีขึ้นไป

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