

# PREVALENCE OF CYTOMEGALOVIRUS ANTIBODIES AMONG VARIOUS AGE GROUPS OF THAI POPULATION

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**Abstract.** The prevalence of CMV antibody in various groups of Thai population was studied. Pregnant women and young children had been infected with CMV more than the other studied groups. Children of both sex had equal chance of getting CMV infection while the risk of CMV infection in adult between male and female was significantly difference ( $p < 0.001$ ). Pregnant women had higher chance to get CMV infection than normal women. Prevalence of CMV antibody at present was similar to previous studies.

## INTRODUCTION

Cytomegalovirus (CMV) can cause disease in all age groups. Transmission of the virus requires close interpersonal contact or direct transfer of infected cells or body fluids. The mother who has CMV infection may excrete virus in cervical excretion and urine of which the neonates may become infected during passing through the birth canal (Numazaki *et al*, 1970). Intrauterine infection of the fetus or post-partum infection during birth canal can lead to some form of physical abnormalities (Klein *et al*, 1976). In contrast, the infection in older children and adults is usually mild, except in immunological compromised hosts, in leukemia, in hypogamma- globulinemia, (Hill *et al*, 1964; Rifkind 1965; Kanich and Craighead, 1966, Craighead *et al*, 1967), and also in human immunodeficiency virus (HIV) patients. Our previous studies showed that CMV infection in Thailand had been found in infants and children as well as in adults with various occupations (Tantivanich *et al*, 1980, 1981, 1982, 1986). Infection of CMV in hospitality girls and pregnant women were about 8 to 9% (Tantivanich *et al*, 1982, 1986) indicated that transmission of CMV usually occur via sexual contact and infection in pregnant women can lead to congenital infection. In addition, changing of social environments and human behaviors at the present time may also have an effect on the transmission of CMV. Therefore, it is interesting to determine the prevalence rate of seropositivity for CMV among Thai population and to compare the prevalence of CMV infection at the present time with the past. The information obtained

would be useful for assessment of magnitude of problem, and would lead to an appropriate measure to prevent the spread of this virus in Thailand.

## MATERIALS AND METHODS

Sera were collected during April to November 1997 from 4 groups of Thai population. The first group comprised 380 healthy blood donors from Phra Mongkutklao Hospital. Their ages varied from 17 to 50 years. The second group was 153 pediatric patients who visited The Children's Hospital, Bangkok, with various diseases including congenital infection. Their ages varied from 1 day to 16 years. The third group was 209 normal pregnant women aged 15-45 years who attended the Out Patient Department at The Department of Obstetric and Gynecology, Faculty of Medicine at Siriraj Hospital, Mahidol University. The last group was 177 suspected HIV patients attending Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University. These patients were tested for the HIV antibodies by gel particle agglutination method. and confirmed by ELISA method.

The CMV antigens were prepared in our laboratory by infecting the confluence monolayer of human embryonic lung fibroblasts cells with CMV strain AD 169. After 24 hours with 3 + or 4 + of cytopathic effect were present, The infected cells were freezing and thawing in dry-ice alcohol bath for 3 times, then centrifuged at 1,000 rpm for 10 minutes to remove the cell debris. The supernatant was sonicated at 10 KC/second for 3 seconds by

using an ultrasonic liquid processor, (Heat Systems Inc, USA) then centrifuged at 2,000 rpm for 10 minutes and the supernatant were kept as the antigen. The dilution of the antigen of 1:2,000 was used to coat the plates.

The enzyme - linked immunosorbent assay test (ELISA) for measuring CMV antibodies was performed as described by Tantivanich (1980). The ELISA IgG and IgM antibodies were determined using peroxidase conjugated rabbit anti - human IgG specific for gamma chain and peroxidase conjugated rabbit anti - human IgM specific for Mu- chains (Dako). The dilutions of the conjugates were 1:2,000 as recommend by the manufacturer. ELISA was also used to study the prevalence of CMV antibody in the previous study. ELISA titers exceeding 1 : 80 or optical density value above 0.01 were considered positive for both IgG and IgM. The IgG and IgM antibody titers between each group of subjects were assessed by the Kruskal - Whitney one - way analysis of variance, then the Mann - Whitney U tests were done. The prevalence of CMV antibodies in each group of subjects were compared by the chi-square test on the Fisher's exact test as appropriate.

## RESULTS

The prevalence of CMV antibody in various groups of Thai population is shown in Table 1. The IgM antibody to CMV in children (13%) and IgG antibody to CMV in normal pregnant women (90.9%) was significantly higher than the other studied groups. The median antibody titers in each group is presented in Table 2. The median IgG antibody titer in normal pregnant women (> 1: 2,560) was significantly higher than that in the other studied groups (1 : 80 to 1 : 320) ( $p < 0.05$ ). In contrast, the median IgM antibody titer was significantly higher in children (1 : 160) than in the other studied groups (1 : 20 to 1 : 40) ( $p < 0.05$ ). Most of Thai population

had no significant difference of getting CMV infection among age groups by sex except in age group 18 to 30 years which had much difference in sample sizes between male and female. The analysis between normal and pregnant women in various age groups revealed significant difference in all age groups (Table 3.) and the prevalence of CMV infection in normal pregnant women increased with age. Analysis of IgM antibody between the present study and previous study was demonstrated in Table 4. Most of Thai population had no significant difference of IgM antibody titer to CMV except in age group 7 - 10 years, 18 to 30 years and over 31 years.

## DISCUSSION

Cytomegalovirus can cause infection all over the world. The rate of infection varies in different population and different age groups (Numazaki *et al*, 1970; Klein *et al*, 1976). In this study, variable seropositive rates were found in different population and different age groups with the highest positive rates in age group of 3-6 years. This finding was similar to the previous study by Tantivanich *et al* in 1981. The only difference was in age group of 7-10 years. Our results indicate that the pattern of transmission of CMV in Thailand remain the same eventhough the time has been passed for more than ten years. The results of IgM antibodies in age group of 18 - 30 and over 31 years were also significant difference but the sample sizes in the past were quite small compared to the present study. Therefore, it is difficult to make conclusion.

The high prevalence rate of CMV infection in young children (0 - 5 months) may due to congenital infection or post natal infection from the environments including sexual contact of their mothers. In this study, the seropositive rate of congenital infection (33.3%) was similar to the previous study (32.5%) (Tantivanich *et al*, 1981), and the study in

Table 1  
Prevalence of CMV antibodies in various groups of Thai population.

Group No.	Group	Total no.	IgG (%)	IgM (%)	IgG and IgM (%)	Neg (%)
1	Healthy adult	380	273 (71.8)	0 (0)	5 (1.3)	102 (26.8)
2	Children	153	45 (29.4)	20 (13.1)	63 (41.2)	25 (16.3)
3	Normal pregnant women	209	190 (90.9)	0 (0)	16 (7.7)	3 (1.4)
4	HIV positive	89	29 (32.6)	0 (0)	0 (0)	60 (67.4)
5	HIV negative	88	47 (53.4)	0 (0)	1 (1.1)	40 (45.5)

Table 2  
Median (range) IgG and IgM antibodies titer to CMV in various groups of Thai population.

Group No.	Group	Total no.	IgG Median (Range)	IgM Median (Range)
1	Healthy adult	380	320 (20->2,560)	40 (20-160)
2	Children	153	160 (20->2,560)	160 (20->2,560)
3	Normal pregnant women	209	> 2,560 (0->2,560)	40 (0-160)
4	HIV positive	89	80 (20-1,280)	20 (20-40)
5	HIV negative	88	160 (40->2,560)	20 (20-160)

Table 3  
Comparison of IgM antibodies from blood donors and pregnant women by age group.

Age group (year)	Normal women		Pregnant women		p-value
	No. pos/No. tested	%	No. pos/No. tested	%	
11-17	7/9	77.8	0/14	0	0.000
18-30	0/22	0	10/148	6.8	0.000
> 30	2/64	3.1	6/47	12.8	0.006

USA (30 - 40 %) (Raynor, 1993), but higher than in Italy (0.57%) (Natali *et al*, 1997). The high rate of congenital infection may due to the sexual activity of the mothers and or reactivation of the virus while the post natal infection may depend on the socioeconomics, hygiene, sexual activity, and reactivation of the virus. Frequent sexual activity usually begin in the teenager. In this study, the rate of CMV infection of teenage girls (11 to 17 years) was higher than boys and also higher than teenage girls in Sweden (Anderow-Ellstrom *et al*, 1995) which was only 45%.

The seropositive rate of CMV infection in adult was similar to the study in Italy (71.8%) (Natali *et al*, 1997), and India (72.7%) (Chattopadhyaya *et al*, 1997) which suggested that the transmission of CMV among these countries were similar.

The risk of CMV infection between male and female was not difference except in the age group of 18 to 30 years. Lower percentage of female than male might be due to the difference in sample sizes. Therefore, further study is needed to compare the different rate of CMV infection in this group. Since most of Thai population have been infected with CMV, therefore the high rate of recurrence infection during pregnancy must be found because of depressed immunity. Seropositive rates of CMV in pregnant women of this study were high and similar to the previous study (Tantivanich *et al*, 1981) but higher than the study in Italy (2.34%) (Natali

*et al*, 1997) and other developing countries (0.4 - 7%) (Raynor, 1993).

CMV can cause opportunistic infection in HIV patients which usually result in severe disease. The presence of IgG but not IgM antibodies of CMV in HIV positive patients suggested that these patients had been infected with CMV before having HIV infection or the patients were infected with CMV and the levels of IgM antibody were already diminished. The lower percentage of IgG antibody in HIV positive patients than HIV negative patients might be due to the number of CD<sub>4</sub> in some HIV positive patients were destroyed by the HIV. Since CD<sub>4</sub> act as T helper cells to produce antibody, therefore, lower number of CD<sub>4</sub> will result in lower antibody production. The results of this study seems to show that CMV did not play role in HIV patients but the number of the patients in this group is too small to come to conclusion.

From this study, it can be concluded that the problem of CMV infection was found quite often in pregnant women and the newborns. Therefore, education about this virus is strongly needed in order to minimize the rate of congenital infection.

#### ACKNOWLEDGEMENT

The authors would like to express our sincere thanks to Mr Somchai Pooudong and Miss Benya

Table 4  
Comparison of IgM antibodies to CMV among various age groups of Thai population between the previous and the present studies.

Group No.	Age	Present study		Previous study		p-value
		No. tested/No. positive	%	No. tested/No. positive	%	
1	0-5 months	11/33	33.3	13/40	32.5	1.000
2	6-24 months	17/35	48.6	17/28	60.7	0.212
3	3-6 years	29/40	72.5	29/45	64.4	0.248
4	7-10 years	16/28	57.1	12/34	35.3	0.019
5	11-17 years	10/17	58.8	8/19	42.0	0.481
6	18-30 years	2/244	0.8	27/83	32.5	0.000
7	> 31 years	3/163	2.2	14/45	31.1	0.000

Supnithasanaporn for their kind assistance in operating the instruments.

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