

The Role of Cytomegalovirus (CMV) Infection in Congenital Diseases in Malaysia

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Summary

A previous cross-sectional serological survey of various age groups (0-55 years) of the Malaysian normal population showed that cytomegalovirus (CMV) infection is highly endemic in Malaysia. A total of 1,688 infants (0-4 months) with congenital abnormalities were screened for evidence of congenital CMV infection and the rest of the TORCHES (TOxoplasmosis, Rubella, Cytomegalovirus, HErpes simplex, Syphilis) group of congenital infections. Congenital CMV infection was detected in 193 (11.4%) infants which is significantly higher than the prevalence of congenital syphilis (4%), congenital rubella infection (3.7%), congenital toxoplasma (1.0%) and congenital herpes simplex virus infection (0%). Of the 193 cases, 10.4 per cent had CNS defects. We concluded that 1) congenital CMV appears to be the most important cause of congenital infections among the TORCHES diseases in Malaysia; and 2) secondary rather than primary infections or reactivation is responsible for most of the intrauterine CMV infection in Malaysia, as primary infection is usually associated with neurological involvement.

Key Words: Congenital infection, Cytomegalovirus

Introduction

Cytomegalovirus (CMV) infection is endemic in Malaysia as shown by a serological survey of various age groups (0-55 yrs) carried out between 1961-1979¹. This serosurvey showed that 90 per cent of apparently normal newborns had antibody to CMV and more than 70 per cent of children in 5-11 month age group had antibody to CMV. This could reflect the high frequency of perinatal and post natal CMV infection originating from reactivated latent infection in the pregnant mother. Stagno *et al*² in 1977 showed that maternal humoral immunity may not protect the foetus against congenital CMV infections, and reactivation or secondary infection can cause congenital infection and abnormalities. This could occur in a population with a high prevalence of CMV infection as it is in Malaysia. This present study sought to determine the role of CMV in causing congenital abnormalities and diseases in Malaysia compared to the rest of TORCHES (TOxoplasmosis, Rubella, Cytomegalovirus, HErpes simplex and Syphilis) diseases, and to compare the congenital abnormalities with those of other countries.

Materials and Methods

A total of 1,688 infants (0-4 months) with congenital abnormalities ranging from CNS defects (like microcephaly, hydrocephaly, cerebral palsy), hepatosplenomegaly, hepatitis and neonatal jaundice (in ≤ 3 weeks old) were screened for CMV specific complementing fixing (CF) antibodies (US Department of Health, Education & Welfare Standard Method)³. All samples which had titres of ≥ 16 were tested for CMV IgM using the CMV IgM capture assay method (Organon Teknika). These samples were also screened for the rest of the TORCHES congenital infection using standard methods viz. the Haemagglutination inhibition test for Rubella specific HI antibodies⁴ and the haemadsorption immunosorbent technique (HIT) for Rubella specific IgM⁵. VDRL was used for syphilis, complement fixation test for herpes simplex and the indirect fluorescent antibody test (IFA) for detection of toxoplasma specific antibodies⁶.

Results

Of the 1,688 infants with congenital abnormalities tested, we detected CMV Infection (CMV IgM positive) in 193 infants which is significantly higher (95% confidence interval) than the prevalence of congenital syphilis (4.0%), congenital rubella infection (3.7%), congenital toxoplasmosis (1.0%) and congenital herpes simplex virus infection (0%).

Of the 193 cases, 80.0 per cent (155/193) had liver involvement and 10.4 per cent (20/193) had CNS defects. The remaining 9.5 per cent (18/193) had various other abnormalities which included skin rash and pneumonitis (Fig 1). The states of Selangor with 18.6 per cent (58/312) and Sabah with 20.7 per cent (50/246) had a significantly higher incidence of CMV infections as compared to the other states (95% confidence interval) (Fig 2).

There was no significant difference (95% confidence interval) of CMV infections among the various ethnic groups; Malays 10.7 per cent (109/1012), Chinese 9.0 per cent (20/227), Indians 10.7 per cent (14/132) and ethnic groups of East Malaysia 15.8 per cent (50/317) (Fig 3). There was also no significant difference between males 10.2 per cent (100/978), and females 12.3 per cent (82/708).

CNS involvement (which usually is used as a parameter of severe CMV infection) is significantly higher in developed countries like UK (20%), and USA (20%) compared to Malaysia (10.5%).

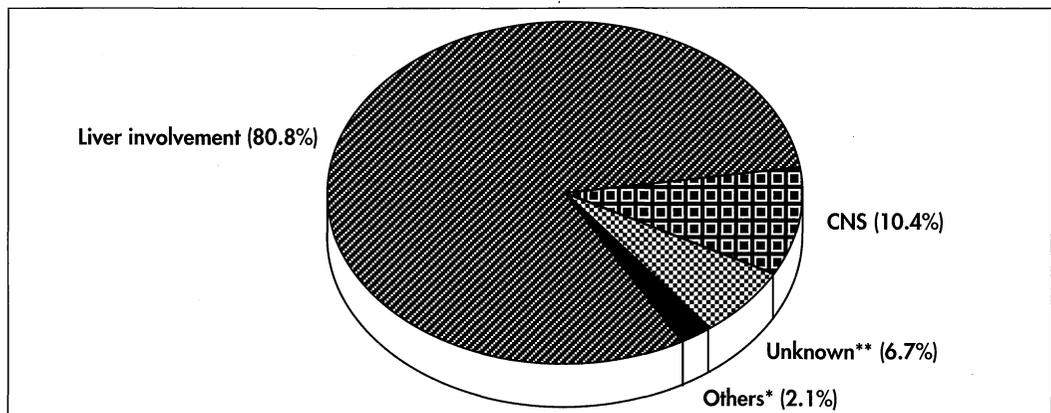


Fig. 1: Congenital abnormalities in CMV infected infants in Malaysia

* Rash, pneumonitis, myocarditis

** No clinical data provided

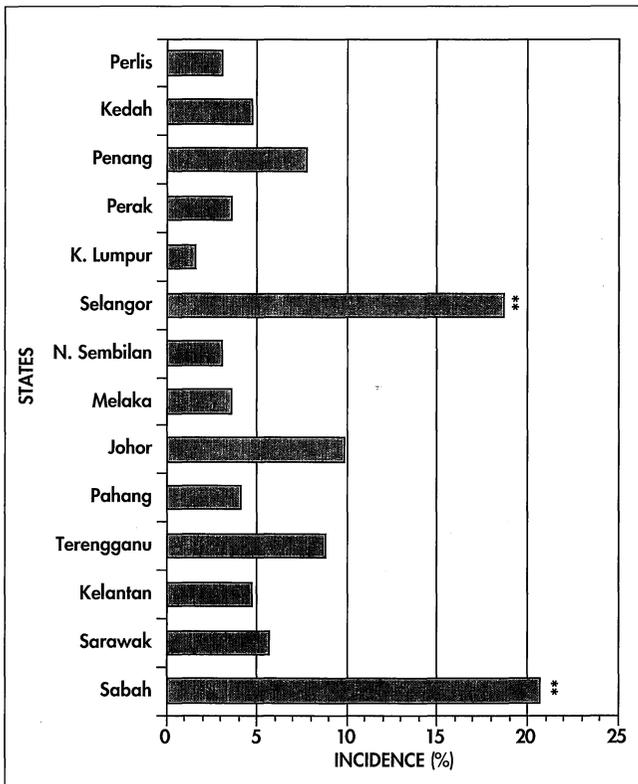


Fig. 2: Incidence of CMV infection in Malaysian states

** Significantly higher than the other states

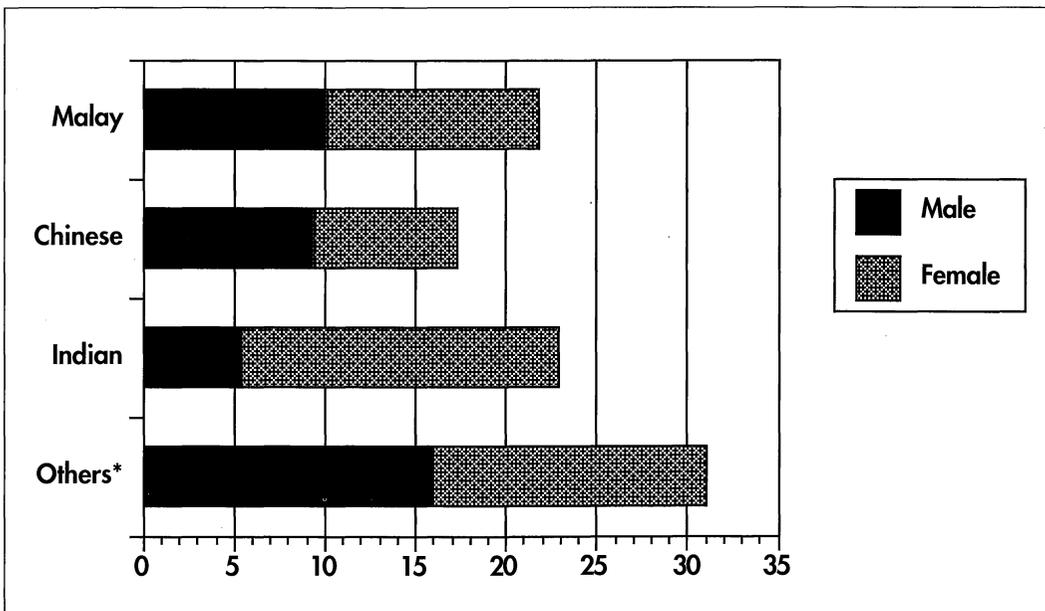


Fig. 3: Prevalence of CMV positive cases according to race and sex in Malaysian infants

* Others: Ethnic in East Malaysia, Siamese, aborigines and foreigners

Discussion

Our study has shown that congenital CMV infection is the most common congenital infection among the TORCHES group of congenital diseases. This is similar to the situation in the rest of the world². However, the severity of the disease varies. Primary infection unlike reactivation can cause severe foetal brain damage⁷⁻¹¹ and CMV infection is a major cause of brain damage in countries where 40-60 per cent of women of childbearing age are seronegative. In Malaysia, we have shown that only about 10 per cent of women of childbearing age are seronegative for CMV antibodies¹². Our study showed that liver involvement accounted for 80 per cent of the congenital abnormalities and CNS defects only for 10.4 per cent. At the time of the survey, severe CMV infection was detected in only 10.5 per cent of the cases. We can conclude that secondary rather than primary infection is responsible for most of the intrauterine CMV infection in Malaysia.

However as Malaysia progresses economically the population of CMV seronegative mothers will increase. Continuous surveillance, therefore, is imperative.

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