## RESEARCH NOTE

# SEROPREVALENCE OF CYTOMEGALOVIRUS INFECTION IN PREGNANT WOMEN AND ASSOCIATED ROLE IN OBSTETRIC COMPLICATIONS: A PRELIMINARY STUDY

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**Abstract.** The objective of this study was to determine the seroprevalence of cytomegalovirus (CMV) infections through antenatal screening data and the association of this virus with obstetric complications. Serum samples from 125 apparently healthy pregnant women sent for antenatal screening from various hospitals in Malaysia between January 2007 and December 2008, were examined for CMV specific IgM and IgG antibodies using an enzyme-linked immunosorbent assay method. Of the 125 pregnant women tested, anti-CMV IgG antibody was found in 105 ( 84%) of the cases and anti-CMV IgM in 9 cases (7.2%). Both CMV IgM and IgG were also found in another 37 women whose serum samples were sent for investigation of various obstetric complications: 17 cases of spontaneous abortions, 15 cases of fetal anomalies detected during ultrasound examination, 1 case of incomplete abortion, 3 cases with premature delivery of infant with congenital anomalies and 1 case of infertility. Our preliminary data which only represented a small study group has shown the prevalence of CMV infection among the local population and the association of CMV in obstetric complications.

**Keywords:** cytomegalovirus, seroprevalence, antenatal, intrauterine infection

## INTRODUCTION

Primary infections caused by human cytomegalovirus (CMV) can lead to serious complications in pregnant women. Due to the latency following primary infection and periodic reactivation of CMV replication, *in utero* transmission of CMV may follow either primary or recurrent infections in pregnancy. Concerns on CMV infection in pregnant women have centered on the associated congenital abnormalities, intrauterine growth retardation and intrauterine death (IUD) of the fetus (Munro *et al*, 2005). Congenital abnormalities as well as late sequelae include mental retardation, developmental delay, blindness and deafness of the infected child. Serological surveys have shown the prevalence of CMV antibodies in adult population to be as high as 80-90% (Wong *et al*, 2000, Colugnati *et al*, 2007). CMV

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Table 1
CMV serology in asymptomatic healthy pregnant women and women with obstetric complications.

| Patient groups ($N$ = 158) | Number of samples | CMV IgM positive | Serology IgG positive |
|---|---|---|---|
| Spontaneous abortions (IUD) | 17 | 17 | 17 |
| Complications in pregnancy: | 19 | | |
| Fetal anomalies | | 15 | 15 |
| Congenital baby | | 3 | 3 |
| Incomplete abortion | | 1 | 1 |
| Infertility | 1 | 1 | 1 |
| Healthy pregnant women | 125 | 9 | 105 |

infection during pregnancy is common in developed as well as developing countries due to the ability of the virus to be frequently reactivated during the child bearing age and be transmitted to the fetus in spite of maternal immunity (Stagno *et al*, 1977). Primary CMV infection occurs in 0.15-2.0% of all pregnancies and may be transmitted to the fetus in up to 40% of cases. Up to 15% of intrauterine CMV infections result in symptomatic congenital disease at birth. However infected infants can be asymptomatic at birth with 10-15% of these subsequently developing late sequelae such as visual and auditory defects (Revello and Gerna, 2002).

## MATERIALS AND METHODS

In order to determine the seroprevalence of CMV in our Malaysian antenatal population, we analysed 125 serum samples received in our laboratory for routine antenatal screening from various government hospitals, during the period, January 2007 - December 2008. These samples and another 37 serum samples which were received for investigation of various obstetric complications were subjected to detection of CMV specific IgM and CMV specific IgG antibody by ELISA test. All the samples were sent with a request form complete with patient details and clinical history. All serum specimens for CMV specific IgM assay were tested using the DRG Anti CMV IgG antibody kit (DRG Instruments GmbH, Marburg, Germany). Anti CMV IgG antibody assay was tested using Axsym, automated analyzer (Abbott Laboratories, Abbott Park, IL). The test procedure, interpretation and validation of test results followed manufacturer's instructions.

## RESULTS

Seropositivity of CMV IgM antibody and CMV IgG antibody seen in apparently healthy asymptomatic pregnant women and those with obstetric complications is shown in Table 1. Of the 125 pregnant women tested, anti-CMV IgG antibody was found in 105 (84%) of the cases, while 7.2% of the subjects tested positive for anti-CMV IgM.

Thirty-seven serum samples were received from obstetric cases presenting with complications: 17 cases of IUD resulting in spontaneous abortion, 15 cases of fetal anomalies detected during ultrasound examination, 1 case of incomplete abortion, 3 cases with premature delivery

of infant with congenital abnormalities and 1 case of infertility. CMV specific IgM antibody and CMV specific IgG were positive in all these cases.

## DISCUSSION

A TORCHES study carried out by the Institute for Medical Research, Malaysia between 1974 and 1994, examined the role of *Toxoplasma*, rubella virus, CMV, herpes simplex virus and syphilis among 1,688 infants with congenital abnormalities. Congenital rubella was reported to be the commonest cause of congenital infection in Malaysian newborn before the implementation in 1986 of the National Rubella Immunization Programme. However the final phase of the study indicated that following the selective immunization of school girls and young women of child bearing age, using monovalent rubella vaccine in 1987, the incidence of rubella had been reduced drastically, while congenital CMV infection was emerging as the main cause of congenital disease in the TORCHES group.

In this study, which only represented a small study group, CMV specific IgG antibody was detected in 84% of all pregnant women tested, indicating the prevalence of infection in the local Malaysian population and also that 16% of this group tested, who were seronegative, were at risk for primary CMV infection during the course of their pregnancy. Out of the 125 asymptomatic pregnant women 7.2% tested positive for the CMV specific IgM antibody revealing primary infection and increasing the possibility of transmission of infection *in utero* to the fetus. It is recognized that primary CMV infections occurring at an early gestational age are more likely to cause fetal damage than recurrent infections. All the 17 serum samples from IUD cases were positive for both CMV specific IgM and IgG, suggesting intrauterine infection causing death of the fetus. However other risk factors such as smoking, alcohol consumption and drug history was not available in the clinical history of these patients. This study were based on the assumption that primary CMV infection can be demonstrated by the presence of CMV specific IgM antibodies. Since the definition of primary versus recurrent infection relies only on the presence or absence of IgM, the type of maternal infection remains uncertain without demonstration of seroconversion or documenting the immunity of the mother before pregnancy (Revello and Gerna, 2004). Our preliminary data has shown the prevalence of CMV infection among our local population and the association of CMV in congenital intrauterine infections.

## REFERENCES

Colugnati FAB, Staras SAS, Dollard SC, Cannon MJ. Incidence of cytomegalovirus infection among the general population and pregnant women in the United States. *BMC Infect Dis* 2007; 7: 71.

Munro SC, Hall B, Whybin LR. Diagnosis of and screening for cytomegalovirus infection in pregnant women. *J Clin Microbiol* 2005; 43: 4713-8.

Revello MG, Gerna G. Diagnosis and management of human cytomegalovirus infection in the mother, foetus and newborn infant. *Clin Microbiol Rev* 2002; 15: 680-715.

Stagno S, Reynolds DW, Huang ES, Thompson SD, Smith RJ, Alford CA. Congenital cytomegalovirus infection in an immune population. *N Engl J Med* 1977; 296: 1254-8.

Wong A, Tank KH, Tee CS, Yeo GSH. Seroprevalence of cytomegalovirus, toxoplasma and parvovirus in pregnancy. *Singapore Med J* 2000; 41: 151-5.