Seroprevalence of Cytomegalovirus, Toxoplasma and Parvovirus in Pregnancy

A Wong, K H Tan, C S Tee, G S H Yeo

ABSTRACT

Aim of study: The aim of our study was to determine the seroprevalence of cytomegalovirus (CMV), toxoplasma and parvovirus infection in our local antenatal population, and to see the effects, if any, of age, race, parity and nationality on its seroprevalence.

Methodology: The sera of 120 consecutive antenatal women seen in KK Women's and Children's Hospital between the period of October 1997 and March 1998 were screened for cytomegalovirus (CMV) IgG, toxoplasma IgG and parvovirus B19 IgG and IgM. An antibody titer greater than 1:32 was regarded as positive.

Results: A total of 87.0% of patients were tested seropositive for CMV IgG, 17.2% seropositive for toxoplasma IgG and 30.0% seropositive for parvovirus IgG. There seemed to be a trend of increasing seropositivity with age in all three groups, however only parovirus B19 reached statistical significance. The incidence of all three infections were higher among the Malays, Indians and other races compared to the Chinese.

Conclusion: CMV is endemic in our population and hence the most common infection. Toxoplasmosis and parovirus is relatively low in our population but this implies that a large proportion of our antenatal women are still susceptible to these infections. Prevention of congenital CMV, toxoplasmosis and parovirus infection is mainly by educating the antenatal population.

Keywords: cytomegalovirus, toxoplasma, parvovirus B19, pregnancy, antenatal

INTRODUCTION

Congenital intrauterine infections have been associated with congenital abnormalities, intrauterine growth deficiency and intrauterine death of the fetus, as well as late sequelae such as developmental delay, blindness and deafness of the infected child. These can lead to a significant burden on our economic and social structure. Hence it would be relevant to determine the prevalence of these infections in our local population.

The aim of our study was to determine the seroprevalence of cytomegalovirus (CMV), toxoplasma and parvovirus infection in our local antenatal population, and to see the effects, if any, of age, race, parity and nationality on its seroprevalence.

METHODS

During the period between October 1997 and March 1998, 120 consecutive antenatal women seen in a clinic in KK Women's and Children's Hospital were recruited. A sample of blood was drawn and sent to Singapore General Hospital virology lab for serology for CMV IgG A b enzyme-linked immunosorbent assay and complement fixation test, toxoplasma A b IgG immunoflorescent test and parovirus B19 IgG and IgM enzyme-linked immunosorbent assay. A n antibody titer greater than 1:32 was regarded as positive.

The majority of the results were returned on a result slip and missing results were traced over the phone. A total of 12 CMV IgG results and 4 parovirus IgG results were missing or could not be traced.

The results were entered into the SPSS statistical package. Data was analyzed with the \( \chi^2 \) test and Fisher's exact test, where required, to see the relation between age, parity, race and nationality with regards to seropositivity. Statistical significance was assumed at the \( p < 0.05 \) level.

RESULTS

The mean age of the patients was 29.2 years. The mean gestation was 19.0 weeks and the mean parity was 0.95. The racial distribution were Chinese (81.7%), Indians (1.7%), Malay (13.3%) and other races (3.3%). A total of 89.2% were Singapore citizens and 10.8% were foreigners and permanent residents.

Up to 87.0% of patients were seropositive for CMV IgG, 17.2% were positive for toxoplasma IgG and 30.0% were seropositive for parovirus IgG (Fig. 1). Parovirus IgM was performed on all 120 patients and there were
no cases of acute parvovirus infection.

To determine the influence of age, the patients were divided into age groups less than or equal to 30 years and those that were above 30 years (Table I). Seropositivity increased with age in all 3 groups of infections. However this was not statistically significant for CMV or toxoplasma (p = 0.571 and 0.869 respectively). Only parvovirus showed a statistically significant increase in the seropositivity with age (p = 0.03).

Seropositivity was also analyzed with respect to parity (Table I). Patients were divided into primiparous and multiparous groups. There were no statistically significant relationship between seropositivity and parity (CMV: p = 0.629; toxoplasma: p = 0.993; parvovirus: p = 0.095).

Majority of the patients was Chinese (81.7%). They had lower seropositivity in all 3 groups of infections when compared to the other races which included Malays and Indians as well as the other races (CMV : Fisher’s Exact Test = 1.0; toxoplasma: p = 0.107; parvovirus: p = 0.714) (Table I).

When we compared the Singaporean citizens with the foreigners, there was no statistical significant difference in seropositivity rates for toxoplasmosis and parvovirus. However, 100% of the foreigners and permanent residents were seropositive for CMV IgG compared to 75.7% of the Singaporeans (p = 0.034).

**DISCUSSION**

**Cytomegalovirus**

Cytomegalovirus infection is the most common congenital infection among the 3 organisms studied. The incidence of congenital CMV infection has been estimated to be between 0.2 to 2.2% of all live births in different parts of the world. In 1994, a study in neighbouring Malaysia involving 1688 infants with congenital abnormalities were screened for evidence of congenital CMV infection, and this was detected in 11.4% of the infants which was much higher than other intrauterine infections such as congenital toxoplasma (1.0%) and congenital rubella infection (3.7%)\(^1\).

Infection can occur any time throughout pregnancy and seroconversion does not protect against re-infection or reactivation. It is associated with congenital abnormalities like microcephaly, hydrocephalus, mental retardation, optic atrophy and sensorineural deafness. It can also cause intrauterine growth deficiency and intrauterine death. In our study, 13% of the antenatal population are susceptible to a primary CMV infection during pregnancy as 87% of the antenatal population were already seropositive for CMV IgG. In a primary CMV infection, about 40-50% of fetuses will become infected. Of these, 5-18% will be overtly symptomatic at birth and the mortality rate among these infants approaches 30%. The majority of congenitally infected infants will be asymptomatic at birth; about 10-15% of these children subsequently have late sequelae such as visual and auditory defects\(^2\). In contrast, in the majority of antenatal patients who are already CMV seropositive (87%), the risk of fetal infection is low (<1%) and hence risk of serious fetal injury is very low if recurrent or reactivated CMV infection develops during pregnancy. Currently, routine screening is not justifiable because seropositivity does not protect against re-infection, only a minority of fetuses will be damaged (total of <5%), and fetal blood sampling will detect fetal infection but does not predict which fetuses will be damaged.

Perinatal and early childhood CMV infections are common. Communal living and poor hygiene facilities facilitate early spread. Infected individuals may shed the virus in body fluids such as saliva, blood, cervical secretions, semen, and urine. The virus is not readily spread by casual contacts and close contact is required for transmission. Transmission can also occur venereally. CMV infection is endemic among school-going children and presents as a mononucleosis-like illness of fever, headache, myalgia, mild pharyngitis, cough, nausea and diarrhea. A dult infection is commonly asymptomatic. The main tactic to prevent congenital infection is to educate pregnant women about preventive measures, especially child-care givers and parents of children attending childcare centres. This includes strict hygiene...
practices such as handwashing, careful cleansing of children’s toys, kitchen utensils and environmental surfaces, and avoidance of contact with the saliva or urine of children.

CMV is endemic in Singapore. Our rates are higher than some parts of France (51.5%) \(^{(3)}\) and London (51.5%) \(^{(4)}\), but still lower than countries like Thailand where figures of 100% seroprevalence are reported \(^{(5)}\) (Table II). Our country’s high CMV seroprevalence reflects the high rates seen in the tropics, even though our lifestyle and hygiene standards are modern and Westernized. Most of the foreigners and permanent residents residing in Singapore come from neighbouring countries like Indonesia, Malaysia and Thailand, and the high rates among these foreigners likewise reflects the high rates seen in the tropics and their country of birth.

**Toxoplasma**

The classical features of congenital toxoplasma infection are chorioretinitis, hydrocephalus, intracranial calcification and convulsions. Congenital infection can also result in stillbirth. As opposed to CMV infection, an immunocompetent woman is considered immune and will not transmit the infection to the fetus. The low rates of toxoplasma seropositivity in our population suggest that a large proportion of our antenatal population (more than 80%) is susceptible to primary toxoplasma infection. The risk of fetal infection increases as the gestation advances, up to 60% in the third trimester; however, the risk of fetal damage inversely decreases as the gestation advances.

Infections in adults are mostly asymptomatic (90%). The most common clinical manifestation being cervical lymphadenopathy. Diagnosis of an acute maternal infection is suggested by a four-fold increase in IgG titers over a 3-week interval. IgM levels are produced 1-2 weeks after an acute infection but may be detectable for years after the acute infection \(^{(6)}\), and are thus not very useful in determining an acute infection.

Detection of fetal infection is recommended if an acute infection has occurred during or immediately preceding pregnancy. Tests designed to detect congenital infection include sonography, determination of the fetal immune response via percutaneous umbilical blood sampling, or identification of Toxoplasma gondii in fetal blood or amniotic fluid. Given the rapidity, accuracy, and diminished potential for pregnancy loss, amniotic fluid assessment using PCR is now the procedure of choice for diagnosing fetal toxoplasma infection \(^{(10)}\). Options available upon confirmation of a fetal infection include termination if infection occurred in the first trimester as this is often associated with greater fetal damage; or treatment with spiramycin, sulfadiazine and pyrimethamine which have been shown to decrease fetal transmission rates and fetal damage \(^{(13-14)}\).

In France and Austria, where rates of approximately 50% seropositivity are reported, antenatal screening programs are in place. Nearly 1% of all pregnancies in France are infected by toxoplasma, making the frequency of neonatal infection 0.1 - 1 per 1,000 births \(^{(6)}\). Seropositivity is still low in our population compared to countries such as France (53.6%) \(^{(7)}\), but comparable to countries such as United States (20%) \(^{(8)}\) and Thailand (13-15%) \(^{(5)}\) (Table III). Seroprevalence of toxoplasma has not changed since earlier seroprevalence studies in other groups in Singapore which found a 17.2 - 18.8% seropositivity rate among healthy adults suggesting a steady rate of transmission over the last 15 years \(^{(9,10)}\). A higher rate among Malay and Indian races compared to the Chinese is similarly found in their studies as well as other local studies \(^{(11,12)}\).

In our country, screening is not routinely performed. Further studies are needed to determine the incidence of acute toxoplasmosis in pregnancy and the prevalence of congenital toxoplasmosis among our newborns, in order to determine if screening is worthwhile among our local population.

The cat is the main host and infection occurs via eating raw or undercooked foods infected with the tissue cysts, or vegetables contaminated with cat faeces. The higher incidence of seropositivity in the Malay and Indian races may be related to their preference for cats as pets. There is no evidence of direct human to human transmission, other than the mother to fetus. Prevention of congenital toxoplasmosis is again by educating the pregnant woman to avoid contact with cat litter and to avoid eating undercooked pork, beef or lamb.

**Table II. CMV seropositivity**

<table>
<thead>
<tr>
<th>Country</th>
<th>Seropositive (%)</th>
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<tbody>
<tr>
<td>Thailand</td>
<td>100%</td>
</tr>
<tr>
<td>Singapore</td>
<td>87%</td>
</tr>
<tr>
<td>London, UK</td>
<td>54.4%</td>
</tr>
<tr>
<td>France</td>
<td>51.5%</td>
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</tbody>
</table>

**Table III. Toxoplasmosis seropositivity**

<table>
<thead>
<tr>
<th>Country</th>
<th>Seropositive (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>53.6%</td>
</tr>
<tr>
<td>United States</td>
<td>20%</td>
</tr>
<tr>
<td>Singapore</td>
<td>17.2%</td>
</tr>
<tr>
<td>Thailand</td>
<td>13-15%</td>
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Parvovirus
Parvovirus B19 causes exanthem erythema infectiosum or fifth disease in children and susceptible adults, giving rise to a ‘slapped-cheek’ appearance. Adults may more commonly present with arthropathy as the sole symptom and many may be asymptomatic. Transmission occurs most commonly through respiratory droplets but may also be acquired via contaminated blood products. Vertical transmission to the fetus occurs during an acute infection and transmission rates are estimated to be approximately 33% (18). In two large cohort studies the incidence of acute B19 infection during pregnancy was 3.3% to 3.7% (16-17).

The first case of hydrops associated with acute B19 infection was reported in 1984 (18). Since then several reports have been written and much more data has been established. It has been found to be the cause of up to 16% of the cases of non-immune hydrops (19). Other pathological conditions caused by this virus in pregnancy include fetal anemia and fetal death. The pathogenesis for fetal damage seems to be inhibition of fetal erythropoiesis, leading to severe aplastic crisis followed by hydrops. A recent prospective cohort study in UK involving 427 pregnant women with B19 infection estimates that the fetal loss rate with parvovirus B19 averages about 9% and was confined to the first 20 weeks of gestation (20). They observed a 2.9% risk of fetal hydrops following maternal infections between 9-20 weeks of gestation. No other fetal abnormalities attributable to parvovirus B19 was found in the other surviving infected gestation. No other fetal abnormalities attributable to parvovirus B19 were found in the other surviving infected infants and no late sequelae was found up to 10 years of follow-up. Fetal treatment is controversial. Several cases of spontaneous resolution of fetal hydrops have been reported (21-22). Successful intrauterine blood transfusion with a decrease in fetal deaths has also been reported (23).

This is the first published report of parvovirus seroconversion as well as cases of non-immune hydrops and in patients presenting with fever and arthralgia.

CONCLUSION
This study is the first published report on the seroprevalence of CMV, toxoplasmosis and parvovirus in pregnancy in our local population. In this study, CMV being endemic in Singapore is the commonest infection. Toxoplasma seropositivity is still low in our country but this implies that a large proportion of our antenatal women are susceptible to a primary infection in pregnancy. Immunity to parvovirus B19 is also fairly uncommon among our population and similarly this implies that many pregnant women are susceptible to infection. Prevention of congenital infection is primarily through thorough antenatal education on prevention. Universal screening is currently not carried out among our antenatal population but selective screening is recommended for parvovirus in the case of exposure to parvovirus, in cases of non-immune hydrops and in patients presenting with fever and arthralgia.

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REFERENCES


