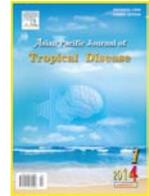




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Congenital cytomegalovirus infection: Experience from a tertiary health care centre of North India

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PEER REVIEW

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This is a good study in which the authors evaluated the prevalence of congenital CMV in a tertiary care set up. The results are interesting and suggested CMV is more prevalent than we think and the clinicians should be on lookout for the disease as early identification of the congenital or perinatal CMV infection can ensure adequate treatment and follow-up.

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ABSTRACT

Objective: To evaluate the prevalence of congenital cytomegalovirus (CMV) infection in a tertiary health care centre of North India.

Methods: In the present study over a period of one year and nine months (January 2011 to September 2012), the tests were put up by μ -capture ELISA for CMV IgM and IgG antibodies on the samples suspected of having congenital CMV infection.

Results: During the time period, we came across 10 cases among children, who were suspected with having congenital CMV infection. The case histories of these infants were studied retrospectively. Most of them had hepatitis with deranged liver enzyme levels and hepatosplenomegaly.

Conclusions: We conclude that congenital CMV is much more prevalent than we think and therefore, clinicians should be on lookout for the disease.

KEYWORDS

Congenital, CMV, North India, Neonates, Children

1. Introduction

Cytomegalovirus (CMV) is a major cause of congenital infection in humans. Most of the congenitally infected infants (85%–90%) are asymptomatic at birth but 5% to 15% of them develop sequelae mostly as sensorineural hearing loss, visual impairment or delay of psychomotor development. The prevalence of congenital infection ranges from 0.3% to 2.3% of all live births in different populations[1]. In developed countries, the disease is well-documented and is the most common congenital infection with about 0.6%–0.7% of all the infants infected with it[2]. Epidemiologically, the seroprevalence of CMV infection varies not only in different regions of the world but also between socioeconomic groups

and different age groups. Dense population, overcrowding, low literacy, poor sanitation, unhygienic conditions, *etc.*, are among the various reasons predisposing people of developing countries and even poorer society of developed countries to CMV infection and so high seroprevalence[3].

Various general population studies from India record a high seroprevalence rate in adults of upto 99%, making it a country with high seroimmune status[4]. Most of the studies done in females of reproductive age group in India have been done to know the possible association with pregnancy loss or congenital malformations in children born to them. The rate of CMV IgG incidence in women of reproductive age group vary from 80%–90%[5] while IgM seropositivity varies from 7%–20%[6]. In children suspected of having

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congenital CMV infection, the seroprevalence of CMV IgM has been found to be 12.5%–20% by various authors[6].

Review of literature shows that the increase in maternal seroprevalence increases the rate of CMV birth prevalence[7]. Therefore, in populations with a high seroprevalence, high rates of congenital CMV infection have been consistently demonstrated[8]. As a result, it is not advisable to simply extrapolate the knowledge acquired from populations of developed countries (with a low-to-intermediate CMV seroprevalence) to those of developing countries with high CMV seroprevalence[8].

2. Materials and methods

In our department, we routinely receive the blood samples for determining the IgG and IgM antibodies levels against CMV infection. The tests were put up by μ -capture ELISA for CMV IgM and IgG antibodies (kits supplied by LDN GmbH and company, KG) as per the manufacturer's instructions for qualitative detection. Interpretation of the results was done on basis of controls provided with the kits. A sample was said to be positive for IgM or IgG antibodies if the absorbance value was more than cut-off value. Positivity for IgM antibodies represents active infection, while IgG antibodies represent exposure to CMV infection in the past.

3. Results

Over the last one year and nine months (January 2011 to September 2012), we came across 10 cases among children, who were CMV IgM positive and were suspected with having congenital CMV infection. The case histories of these infants were studied retrospectively and the details of these children are given in Table 1. The age of the children varied from six weeks to one year. All these children were positive for CMV IgM antibodies. In addition, five of them were also positive for CMV IgG antibodies.

The standard diagnostic test for congenital infection with

CMV is viral culture within the first three weeks of life. Due to resource limitation, we could not attempt it in any of the cases.

4. Discussion

CMV infection to the foetus is transmitted either intrauterine, through birth canal or post-natally through breast milk or body secretions. The chances of infection are greatest if mother is affected during pregnancy for the first time *i.e.* primary infection. However, maternal CMV reactivation or reinfection with a different CMV strain can also lead to foetal infection. Congenital CMV infection is asymptomatic in the neonatal period in 85%–90% of the infants and only up to 10%–15% of intrauterine CMV infections result in symptomatic congenital disease at birth presenting with intra-uterine growth retardation, thrombocytopenia, petechiae, jaundice, hepatosplenomegaly or CNS disease including microcephaly and intra-cranial calcification. Among rest of asymptomatic congenital infections, 10% to 15% infants develop significant clinical sequelae like chorioretinitis and sensorineural deafness[9]. In most of the children in this case series had one or the other classic features of congenital CMV infection. Most of them had hepatitis with deranged liver enzyme levels and hepatosplenomegaly. Others presented with congenital malformations or congenital cataract or hematological abnormalities.

Our finding are well supported by a recent study[10] which reported 18.75% of babies with congenital anomalies to be positive for CMV IgM antibodies using μ -capture ELISA, demonstrating a significant rate of congenital CMV infection in infants born to seroimmune women.

Mandatory screening for CMV by serology has always been a debated issue. Currently, there is no effective and safe immunization against CMV. Even effective prenatal treatment options are not yet available. Fetal loss or elective termination can cause significant emotional distress for a family. Prenatal testing offers an opportunity for health education of women about precautionary measures or lifestyle changes.

Table 1

Details of children presenting with suspected congenital CMV infection.

Age	Sex	Clinical picture	Laboratory investigations	CMV IgM/ CMV IgG
6 weeks (2nd Twin)	Male	Preterm, birth weight 995 g, APGAR 5 at 1 min and 7 at 5 min, neonatal hepatitis	Raised bilirubin, Alkaline phosphate, SGOT and SGPT	Positive/Positive
1 year	Female	HSM, rickets, global neurodevelopmental defect with storage disorder, ascites	Raised Alkaline phosphate, SGOT and SGPT	Positive/Negative
10 weeks	Male	Jaundice, fever	--	Positive /Positive
12 weeks	Female	Fever, cleft lip, right eye corneal opacity, micro-ophthalmia, depressed nasal tip, multiple congenital malformations	–	Positive/Positive
12 weeks	Male	Jaundice, hepatosplenomegaly, biliary atresia	Raised liver enzymes	Positive/not done
1 year	Female	Congenital cataract	–	Positive/Negative
6 weeks	Male	Fever	–	Positive/Negative
10 weeks	Female	Fever, jaundice, hepatosplenomegaly	–	Positive/Positive
6 month	Male	Hemolytic anemia, thalassemia, thrombocytopenia, CCF	Raised alkaline phosphatase levels	Positive/Negative
12 weeks	Male	Birth weight 1.5 kg, fever, hepato-splenomegaly, anaemia, optic disc oedema, pneumonia, respiratory distress	Raised alkaline phosphatase levels	Positive/Positive

Our findings clearly document the importance of congenital CMV infection as a cause of morbidity even in populations with a high maternal CMV seroprevalence. Most of the females are unscreened for CMV infection in our country and therefore, the total impact of the congenital CMV infection remain under appreciated. Similarly, in about 90% of CMV infected newborns, clinical examination is clueless in diagnosis, resulting in the majority of infants with infection going unidentified. As congenital CMV generally cannot be diagnosed retrospectively, the majority of infants who are suffering/will suffer from CMV-related disabilities will not be properly diagnosed in the absence of a universal laboratory screening program.

In conclusion, our observation raises two main issues. One is that congenital CMV is more prevalent than we think and the clinicians should be on lookout for the disease as early identification of the congenital or perinatal CMV infection can ensure adequate treatment and follow-up. Second is that what should be the stance if the case has been identified and confirmed by viral culture or molecular methods too along with positive serology. Till date no treatment protocol for infected patients with CMV exist in our country.

Conflict of interest statement

We declare that we have no conflict of interest.

Comments

Background

CMV is a virus of paradoxes and can be a potential killer or a silent companion lifelong. CMV poses an important public health problem as it may cause serious morbidity and mortality in congenitally infected newborns and immunocompromised patients. The magnitude of this problem in India and the various diagnostic modalities used have not been adequately investigated and, hence, CMV infection is still a major health problem warranting strong preventive measures.

Research frontiers

Study is being performed in order to determine importance of congenital CMV infection as a cause of morbidity even in populations with a high maternal CMV seroprevalence

Related reports

Data about seroprevalence of congenital CMV are in agreement with study done by Gandhoke I *et al.* (2006) which reported 18.75% of babies with congenital anomalies to be positive for CMV IgM antibodies using μ -capture ELISA.

Innovations & breakthroughs

CMV is a major cause of congenital infection in humans. Most of the congenitally infected infants are asymptomatic at birth but 5% to 15% of them develop sequelae. Data regarding

the prevalence of congenital CMV in Northern India are scarce so such studies are useful in changing the clinicians outlook regarding the disease. As the magnitude of this problem in India warrants strong preventive measures.

Applications

It is important to estimate and to monitor the presence of congenital CMV. The facts presented in this article conclude beyond doubt that CMV infections cause considerable burden on society, especially in a developing country like ours, and we truly need to develop and implement consensus strategies for prevention of CMV infection.

Peer review

This is a good study in which the authors evaluated the prevalence of congenital CMV in a tertiary care set up. The results are interesting and suggested CMV is more prevalent than we think and the clinicians should be on lookout for the disease as early identification of the congenital or perinatal CMV infection can ensure adequate treatment and follow-up.

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