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Seroprevalence Of Cytomegalovirus Infection In Women With Bad Obstetric History Visiting A Tertiary Care Hospital In Central India

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Abstract

Background: Human Cytomegalovirus (CMV) otherwise known as Human Herpes virus 5; is a member of herpes viridae family. It is a ubiquitous agent and one of the important causes of intrauterine infections. The infection is usually asymptomatic in adults. Prenatal infections of CMV have severe fetal consequences.

Aims & Objective: To detect seroprevalence of CMV in pregnant women with Bad Obstetric History**.**

Materials & Method: The present retrospective study was carried out from 1st January 2018 to 31st Dec. 2020 in the Serology section of the department of Microbiology of a teaching tertiary care hospital located in central India. The blood samples received from 92 women with Bad Obstetric History were tested for CMV IgG & IgM antibodies by ELISA method (Calbiotech Inc., USA)**.**

Results & Discussion: Out of 92 serum samples tested, 70.6% patients were IgG positive and 8.6% were IgM positive. Among these 8.6% patients were found to be positive for both IgG & IgM antibodies**.** Several studies have also quoted the seroprevalence of CMV ranging from 9% to 80-90% in different regions from India and abroad. It has mainly shown variations based on geographic, socioeconomic, and ethnic backgrounds and on child-rearing practices such as breast-feeding and use of day-care facilities.

Conclusions: The result indicates moderate prevalence of CMV in the women with Bad Obstetric History. It would be beneficial to screen women of reproductive age group for CMV IgG & IgM antibodies. It would help us to provide appropriate therapy and prevent intrauterine death or congenital fetal abnormalities.

Key Words: Cytomegalovirus, Bad Obstetric History, Seroprevalence, ELISA

Introduction

Human Cytomegalo Virus (CMV) otherwise known as Human Herpes virus 5 is a member of Herpes viridae family. [1] CMV was isolated in three laboratories simultaneously in 1956. CMV can potentially kill or be present silently in the body lifelong. [2] CMV infection is highly prevalent in both developed and developing countries and is an important health problem. [3, 4] It is an ubiquitous agent and one of the important cause of intrauterine infections. The infection caused by CMV in adult is usually asymptomatic but its significance is many times increased when it occurs during pregnancy. Prenatal infections of CMV have severe fetal consequences. CMV infection can be transmitted to the fetus after a primary or a recurrent infection. Infections *in utero* are associated with intrauterine death or congenital fetal abnormalities and intrauterine growth retardation along with the developmental delays, blindness, and deafness as a sequel after the birth. [5, 6] Infection in the first trimester leads to congenital malformation while infection in the second and third trimester may cause neurological impairment or growth restriction in the fetus. Other consequences of congenital CMV infection include hepatomegaly, chorioretinitis and sensorineural hearing loss in the newborn, thrombocytopenia with petechiae and purpura, hepatitis, pneumonitis, and faulty neurologic development consisting of microcephaly, optic atrophy, aplasia of various parts of the brain and microphthalmia. [7]

Bad obstetric history (BOH) implies previous unfavourable foetal outcome in terms of two or more consecutive spontaneous abortions, history of intrauterine foetal death, intrauterine growth retardation, still births, early neonatal death and/or congenital anomalies. Cause of BOH may be genetic, hormonal, abnormal maternal immune response and maternal infection. [3,8]

The presence of IgM antibodies in the serum of pregnant women may represent either a primary infection or a recurrent infection. High titers of IgG antibodies may represent a pre conceptional immunity to CMV infection

following a primary infection and has been associated with reduced risk of transplacental transmission of CMV infection. Therefore, accurate information of the serological status of the pregnant woman by the obstetricians could assist in identifying women at high risk of having foetuses with congenital malformation and institute measures to diagnose and undertake foetal surveillance of mildly affected foetuses or counsel the couples for termination of pregnancy in grossly affected foetuses. [2,3]

The present study was therefore undertaken to determine the prevalence of CMV IgG and IgM antibodies and the various factors affecting it in the women with Bad Obstetric History who visited our hospital.

Materials & Method

The present prospective study was carried out from 1st January 2018 to 31st Dec. 2020 in the Serology section of the department of Microbiology of a teaching tertiary care hospital located in the Central India. During the study period, a total of 92 blood samples were collected from women presenting with the Bad Obstetric History, for the detection of CMV IgM and IgG antibodies. Aseptically collected blood samples from the study subjects were kept at room temperature for 20 minutes. After clotting, the clot was retracted and centrifuged. Determination of Immunoglobulins (IgG and IgM) against CMV was done by using commercially available CMV ELISA kit (Calbiotech Inc, USA) following the manufacturer's instruction. Diluted serum was added to wells coated with purified lipopolysaccharide antigen from CMV. Antibodies, if present, binded to the antigen. All the unbound material was washed away by using wash buffer. The micro titer assay used peroxides conjugated IgG and IgM antibodies to bind to antigen antibody complexes. Again, the excess enzyme conjugate was washed off using wash buffer. After incubation with tetra methyl benzidine (TMB) substrate, the reaction was stopped by the addition of sulphuric acid (stop solution). The absorbance or optical density (OD) was read photometrically at 450 nm. by automated ELISA reader within 15 minutes. The intensity of the color generated was proportional to the amount of specific antibody in the sample. Optical Density was measured at 450 nm using automated ELISA microplate reader (Transasia Biomedicals Ltd, Mumbai, India). Result was interpreted as being seropositive, if the optical density (OD) value of samples was more than that of the cut off value (CV). Negative and positive controls provided with the kit were used during the each run. The antibody index value for a certain sample was considered as positive when it was greater than 1.1 and negative when it was less than 0.9. [9] Verbal consent was obtained from the patients & the present study has been approved by the institutional ethical committee.

Results & Discussion

In the present prospective study, a total of 92 samples from women with BOH were serologically tested for TORCH panel. Among them, 81 (88 %) serum samples tested positive for CMV antibodies (with or without the presence of other TORCH antibodies). Out of those, 08 (8.6 %) patients were IgM positive, 65 (70.6 %) patients were IgG positive and 08 (8.6 %) patients were found to be positive for both IgM & IgG antibodies. IgG antibodies were significantly found in larger number of women as compared to IgM ($p < 0.001$). All the women belonged to the reproductive age group with the average age of study population being 23.4. The seropositivity rates have been shown in Table/Fig. 1 & represented by pi-chart. (Fig 2)

Acute infection during pregnancy was noticed when IgM positivity was diagnosed. During our study 16 (17.3 %) women had acute infection. The results were in clinical correlation since 07 out of 16 women who had IgM seropositivity & 29 out of 65 women who had IgG seropositivity had the history of one or more abortions and eight women had the history of still birth. The differences were found to be statistically significant ($p < 0.001$). In rest of the women, cause of abortions & still birth could have been other organisms of TORCH complex. In the present study, seroprevalence of Cytomegalovirus was found to be higher as compared to those detected by Shrivastava *et al* during the study conducted in the same hospital in the year 2013. During their study, the seroprevalence came out to be 4.06% for IgM & 85.93% for IgG antibodies. [9] Our study results also showed higher levels of CMV IgM from those reported by Tamer *et al* [10] from Turkey that reported 3.6% for IgM & 96.4% for IgG antibodies. Our results were also high as compared those from the study conducted by Turbadkar *et al* which detected seroprevalence rate of 8.4% for CMV IgM in women with Bad Obstetric History [3] Our seroprevalence was also on the higher side as compared to the study done by Singh *et al* which reported the seropositivity of CMV IgM to be 12.5%. [10] However, our results resembled a recent study conducted by Khayyam et al. that detected CMV IgM equal to 19.2 %. [8] Our seroprevalence was also higher than those reported in a study done by kumar *et al* which shows seropositivity for IgM & IgG to be 9.46% and 83.24% respectively. [12] International studies has however reported IgG seropositivity of CMV in women with Bad Obstetric History as 39-94.7 % in the USA [13,14],56.8% in Australia [15] ,84% in Spain and 84.5% to 95% in Turkey [16,17] Wide range of variations have been detected in the seroprevalence rates based on different geographical regions at national and international levels. It has mainly shown variations based on geographic, socioeconomic, and ethnic backgrounds and on child-rearing practices such as breast-feeding and use of day-care facilities. It has been already

emphasized on knowing the epidemiology of the CMV infections, as it is an important aspect in the development of strategies for the prevention of congenital infections. Serological screening before pregnancy is important to diminish morbidity and mortality in both mother and child. [18]

Table/Fig. 1: Prevalence of CMV antibodies among women with BOH

CMV Antibody / Total no. of serum samples tested positive for CMV antibodies	IgM Positive		IgG Positive		Both IgM & IgG Positive	
	No. of Patients	%	No. of Patients	%	No. of Patients	%
92	08	8.6	65	70.6	08	8.6

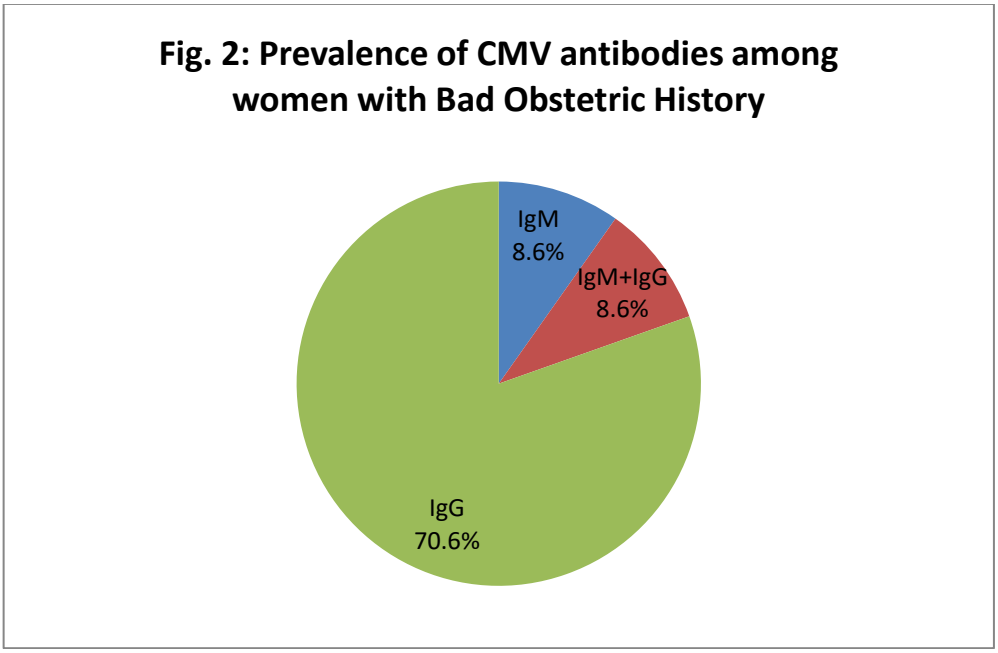

Fig. 2: Prevalence of CMV antibodies among women with Bad Obstetric History
IgM
8.6%
IgM+IgG
8.6%
IgG
70.6%

Conclusions

The result indicates moderate prevalence of CMV in the women with Bad Obstetric History in our study. CMV is an important cause of congenital infection and is liable to cause significant perinatal morbidity. It would be

beneficial to screen women of reproductive age group for CMV IgM and IgG antibodies. We recommend that pregnant women especially with Bad Obstetric History should be advised to be more attentive to personal hygiene, especially hand hygiene after handling diapers or oral secretions. The three important tips to decrease exposure to the most common sources of CMV, which are to be given as advice, especially to seronegative mothers, is as follows: not to share food, drinks, straws, or eating implements with young children; not to kiss young children on or around the mouth or lips; and thorough washing of hands after changing diapers (wet with urine or dirty with stool) and wiping runny nose or mouth drool. We also recommend that high risk pregnant women or health workers should undergo mandatory screening for CMV that will result in reduction in the risk of primary CMV infection and subsequent fetal transmission. Effective screening would help us to provide appropriate therapy and prevent intrauterine death and congenital fetal abnormalities.

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