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CMV Serovirulance in Mothers and Their Very Low Birth Weight (<1,500) Neonates in Tehran City, Iran, in a Year

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ABSTRACT

Background: Cytomegalovirus (CMV) is a pathogenic virus that is found everywhere. The serovirulance of this virus varies widely among different communities. The present study was conducted to investigate the frequency of CMV serovirulance in mothers and their very low birth weight (<1,500 g) neonates.

Methods: This descriptive cross-sectional study was conducted on 234 serum samples (117 maternal and 117 neonatal samples) for 12 months in Mahdieh Hospital, Tehran, Iran, from March 2019 to March 2020. The enzyme-linked Immunosorbent assay technique was used to evaluate specific antibodies (i.e., immunoglobulin G [IgG] and immunoglobulin M [IgM]) of CMV. Statistical analysis was conducted in SPSS (version 23).

Results: Based on the results, the seroprevalence of CMV IgG was 98.2% (115 cases) in mothers and 84.6% (99 cases) in neonates. The seropositivity rate of CMV IgM was reported at 1.8% (2 cases) in mothers and 0.9% (1 case) in neonates. It was found that the relationship between the mean scores of maternal CMV IgG and the number of live births was statistically significant (P=0.002). However, there was no statistically significant relationship between some maternal factors (e.g., age, occupation, living place, number of pregnancies, deliveries, abortions, and education) and maternal CMV IgM seropositivity. Furthermore, neonatal gender and gestational age showed no statistically significant relationship with maternal and neonatal CMV IgG and IgM seropositivity.

Conclusion: According to our findings, the serovirulance of CMV in mothers and their neonates was significant, whereas active CMV infection in both groups was highly unusual. Additionally, the transmission rate of CMV IgG and CMV IgM from the mother to her neonate was incomplete.

Keywords: Cytomegalovirus, Neonates, Serovirulance, Very low birth weight

Introduction

Cytomegalovirus (CMV) is a type of DNA virus that can infect humans at any age (1, 2). Cytomegalovirus grows and multiplies only in human fibroblasts in the laboratory; while in vivo, it first grows in epithelial cells (3, 4). This virus is present in the patient's saliva, urine, genital secretions, breast milk, and blood, and contact with any of these can transmit the virus (4, 5).

Congenital CMV infection is the most common congenital infection in the world with a prevalence of 0.3-2.4% of live births (1, 3). Perinatal transmission is the way 3-5% of infants get CMV through contact with vaginal or bloody secretions during childbirth (5). It is more likely that the primary infection of the mother during pregnancy transmits the infection to the fetus with the placental transmission, accounting for 30-40% of cases, whereas in re-infection or activation of a previous infection of mothers, only 1-3% of fetuses become infected (1, 3). It has also been

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reported that CMV transmission through breast milk leads to a sepsis-like syndrome in preterm neonates under 32 weeks of age (1, 3, 5).

Cytomegalovirus serovirulance in women of reproductive age is reported to be between 50-85% in developed countries and even up to 100% in developing countries (1). Approximately 85-90% of neonates with congenital CMV infection are asymptomatic at birth; however, there is a 15% chance of developing sequelae in these neonates (2, 3). Cytomegalovirus can cause systemic involvement in 10-5% of neonates, in which the central nervous system and reticuloendothelial system are more involved (3). Common clinical features in systemic CMV infection are jaundice, petechiae, hepatomegaly, splenomegaly, chorioretinitis, poor feeding, and lethargy. Prevalent laboratory findings are direct hyperbilirubinemia, increased liver enzymes, and thrombocytopenia (1). Congenital CMV infection is the most common cause of non-genetic sensory-neuronal hearing loss (1). For this reason, all neonates with congenital CMV infection, regardless of clinical signs at birth, should undergo periodic audiometric tests (1, 3).

This study was conducted because of the importance of the subject and the lack of knowledge about the incidence of CMV infection in pregnant mothers and their neonates in Tehran city, Iran. In this regard, the seroimmunological status of very low birth weight neonates (less than 1,500 g) and their mothers were evaluated in Mahdieh Hospital, Shahid Beheshti University of Medical Sciences, Tehran, within a year.

Methods

The current study was carried out on all very low birth weight newborns (less than 1,500 g) and their mothers over a year based on the general census without any exclusion criteria. Some conditions associated with severe CMV infections, especially congenital immunodeficiency disorders, were not excluded from our study. This descriptive cross-sectional limited unicentral study was conducted on 234 serum samples (117 maternal and 117 neonatal samples) for 12 months in Mahdieh Hospital (an educational hospital in the south of Tehran city) from March 2019 to March 2020.

A volume of 2 ml of cord blood was taken from the newborns and 2 ml of venous blood was collected from their mothers in test tubes without anticoagulation. Samples were obtained from the umbilical cord of newborns and peripheral veins of their mothers simultaneously during 24-48 h after birth. These samplings were performed in a sterile fashion with the permission of the mothers. Quality control of all testing stages was conducted according to the recommendations of the kit and the standards. Afterward, the samples were sent to the serology unit of the laboratory for the determination of CMV immunoglobulin M (IgM) and immunoglobulin G (IgG) values by enzyme-linked immunosorbent assay technique. A level of antibodies of more than 0.9% mg was considered positive. Sampling was performed after obtaining informed consent from the mothers. Mothers were fully assured of the confidentiality of their questionnaire information. The collected data were analyzed in SPSS software (version 23) using descriptive statistics. Mean and standard deviation (SD) were used to describe quantitative variables and frequency and percentage were employed to describe qualitative variables. T-test, Pearson, Chi-square, and Fisher's exact tests were used to measure the relationship between variables. A p-value of less than 0.05 was considered significant. However, none of the mothers and neonates had a history of receiving blood products. The lack of exclusion criteria was one of the limitations of our study.

Results

This study was conducted on 234 serum samples (117 maternal and 117 neonatal samples) for specific antibodies against CMV. The mean scores of maternal age and gestational age were estimated at 29.35±5.29 years and 29.35±2.46 weeks, respectively. The mean value of neonatal body weight was obtained at 1178.54±263.41 g. The information regarding the CMV IgG and IgM of mothers and neonates is presented in Table 1 and Figure1. Seropositivity of CMV IgG was 98.2% (n=115) in mothers and 84.6% (n=99) in their neonates. It was found that CMV IgM was negative in all positive CMV IgG mothers and neonates. Seropositivity of CMV IgM was 1.8% (n=2) in mothers and 0.9% (n=1) in neonates. Therefore, CMV IgM was positive in only one male neonate who was not intrauterine growth retardation, whose mother was CMV IgM positive. This seropositivity was confirmed by the urinary CMV polymerase chain reaction (PCR) test. The hearing level of neonates was not checked in this study. There was no statistical relationship between neonatal head circumference and seropositivity of neonatal and maternal CMV IgM in our study. Moreover, no statistically significant relationship was observed between some maternal factors (e.g., age, occupation, living place, and education)

and maternal CMV IgM seropositivity. In the same vein, no statistically significant relationship was found between the number of pregnancies, deliveries, abortions, gender, and gestational age of neonates with maternal and neonatal CMV IgG and IgM seropositivity. However, there was a statistically significant association between the number of live births and maternal CMV IgG; in this regard, an increase in the number of live births enhanced the chance of negative maternal CMV IgG increased by 62% (crude odds ratios=1.62, 95% confidence interval [CI]: 1.02-2.77). In fact, by adjusting the variables of gravid, abortions, deliveries, maternal education level, and maternal age, the chance of negative maternal CMV IgG was increased, and after controlling the effect of confounding variables, the chance of a negative maternal CMV IgG increased 2.35 fold with an increase in the number of live births (adjusted odds ratios=2.35, 95% CI: 1.04-5.34)

Table1. Characteristics of specific cytomegalovirus antibodies in subjects

Antibodies	Max (mg/dl)	Min (mg/dl)	Mean±SD
Maternal IgM	1.6	0.011	0.20±0.21
Maternal IgG	39	0.001	4.64±4.63
Neonatal IgM	2	0.000	0.23±0.23
Neonatal IgG	38	0.0001	3.77±3.82

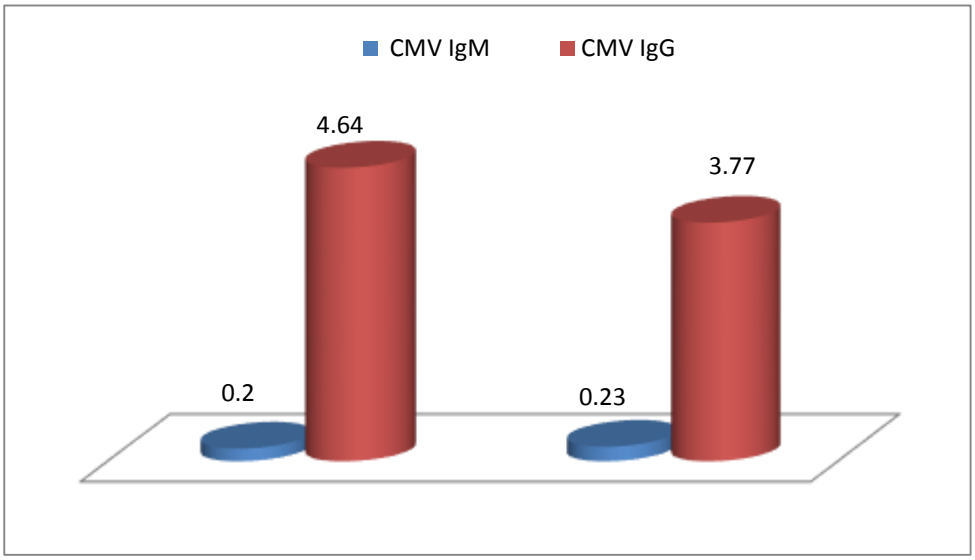

Figure 1. Diagram of mean values of maternal and neonatal cytomegalovirus antibodies (Right side is neonatal and left side is maternal data)

Discussion

Cytomegalovirus is a pathogenic virus that is found everywhere in the world. Serovirulance of this virus varies widely among different communities. Congenital CMV infection is the most common congenital infection worldwide with a prevalence rate of 0.3-2.4% of live births (1, 3, 4). Cytomegalovirus serovirulance in women of reproductive age is reported to be 50-85% in developed countries and even up to 100% in developing countries (1, 6). Our study was a limited unicentral small-size descriptive study and aimed at determining the serovirulance of CMV in pregnant mothers and their very low birth weight neonates. In the current study, the seropositivity rates of maternal CMV IgG and IgM were obtained at 98.2% and 1.8%, respectively. The results of a study by Jahan et al. (2017) in Bangladesh reported that the seroprevalence rates of maternal CMV IgG and IgM in pregnant women were 100% and 60%, respectively (2). In a study conducted by Mussi Pinhata et al. in Brazil, the seropositivity of maternal CMV IgG was estimated at 95.7% (7). Based on the findings of another study conducted by Wendy et al. (2004) in Canada, maternal CMV IgG seroprevalence was reported at 55% (8). This discrepancy with our results may be due to the high level of public health in Canada. Moreover, the seroprevalence of maternal CMV IgG was found at 94.9% in a study conducted in Turkey by Ocak et al. (9). In another study, Arabzadeh et al. reported maternal CMV IgG and CMV IgM in Kerman city, Iran, in 2007 as 91.9% and 33.8%, respectively (10). In the mentioned study, the serovirulance of mothers in Kerman was remarkable, and this difference with the results of our study was unjustifiable. Recently, Florin Gorun et al. reported that the seroprevalence of CMV IgG in Romania in 2020 was 91.8% (11). However, the seropositivity rate

of neonatal CMV IgM was obtained at 0.9% in our study. The seroprevalence of neonatal CMV IgM in a study in Bangladesh was estimated at 1.3%, which was similar to that in our study (2). Furthermore, Vaudry et al. reported that congenital CMV infection was 1.3% in very low birth weight neonates, which was similar to that in our study (8). This rate was calculated at 0.76% in the study conducted by Arabzadeh et al. in Kerman city (10). In a study in Paris conducted on 11,715 neonatal samples, the seroprevalence of CMV IgM was obtained at 0.38% (12). In another study in California, it was revealed that only 25% of CMV IgG-positive newborns were IgM positive (13). It was reported that the serovirulance of CMV increased with the aging of pregnant mothers (10, 14, 15). In two studies performed in Germany and Sweden, the seropositivity rates of neonatal CMV IgM were estimated at 0.1% and 0.5%, respectively (16, 17). In a recent study in Norway, the seropositivity of neonatal CMV IgM was calculated at 0.2%, which was confirmed by the positive CMV PCR of the umbilical blood sample (18). The relationship between maternal CMV IgG seropositivity and the number of live births was statistically significant. There was no statistically significant relationship between maternal age and neonatal CMV IgM (18).

It is recommended to diagnose congenital CMV infection through performing diagnostic tests, including neonatal CMV IgM, during the first two weeks after birth (19). Diagnosis of congenital CMV infection is impossible after three weeks of birth based on CMV IgM determination (20).

The limitations of our study were the small sample size, limited study time, and insufficient facilities to perform CMV PCR tests for all samples.

Conclusion

According to our findings, the serovirulance rates of CMV in mothers and their neonates were significant, whereas active CMV infection in both groups was highly unusual. Additionally, the transmission rate of CMV IgG and CMV IgM from the mother to her neonate was incomplete.

Acknowledgments

None.

Conflicts of interest

The authors declare that there is no conflict of interest in this study.

References

1. Marsico C, Kimberlin D. Congenital Cytomegalovirus infection: advances and challenges in diagnosis, prevention and treatment. Ital J Pediatr. 2017; 43:38.
2. Jahan M, Sultana N, Asma R, Tabassum S, Islam MN. Birth prevalence of congenital cytomegalovirus (CMV) infection in a cohort of pregnant women in Bangladesh. Bangladesh Med Res Counc Bull. 2017; 43(2):77–81.
3. Fanaroff& Martin, S. Neonatal-Perinatal Medicine, Diseases of Fetus and Infant. Eleventh Edition; 2020.
4. Cloherty and Stark, S Manual of Neonatal Care. Eight Edition. 2017.
5. Malm G, Engman M. Congenital cytomegalovirus infections. Semin Fetal Neonatal Med. 2007; 12(3):154-9.
6. Rawlinson WD, Boppana SB, Fowler KB, Kimberlin DW, Lazzarotto T, Alain S, et al. Congenital cytomegalovirus infection in pregnancy and the neonate: consensus recommendations for prevention, diagnosis, and therapy. Lancet. 2017;17(6):e177–88.
7. Marisa M. Mussi-Pinhata, Aparecida Y. Yamamoto, et al. Britt. Birth prevalence and natural history of congenital cytomegalovirus infection in a highly seroimmune population. Clin Infect Dis. 2009; 49(4):522-8.
8. Vaudry W, Rosychuk R, Lee BE, Cheung PY, Pang XL, Preiksaitis JK. Congenital cytomegalovirus infection in high risk Canadian infants: Report of a pilot screening study. Can J Infect Dis Med Microbiol. 2010; 21(1):e12-e19.
9. Ocak S, Zeteroglu S, Ozer C, Dolapcioglu K, Gungoren A. Seroprevalence of Toxoplasma gondii, rubella and cytomegalovirus among pregnant women in southern Turkey. Scand J Infect Dis. 2007; 39(3):231-4.
10. Arabzadeh AM, Mosavat SA, Eftekhari N. Seroepidemiology of Human Cytomegalovirus in Pregnant Women and their Neonates in Kerman City during 2005. J. Kerman Univ. Med. 2007;14(4): 279-288.
11. Gorun F, Motoi S, Malita D, et al. Cytomegalovirus seroprevalence in pregnant women in the western region of Romania: A large-scale study. EXP Ther Med. 2020;20(3):2439-2443.
12. Leruez-Ville M, Magny M J, Couderc S, Pichon C, et al. Risk factors for congenital cytomegalovirus infection following primary and non primary maternal infection: a prospective neonatal screening study using polymerase chain reaction in saliva. Clin Infect Dis. 2017; 65(3):398-404.
13. Kharrazi M, Hyde T, Young S, Amin MM, Cannon MJ, Dollard SC. Use of screening dried blood spots for estimation of prevalence, risk factors, and birth outcomes of congenital cytomegalovirus infection. J Pediatr. 2010;157(2):191–7.
14. Mirzaie F, Arabzadeh S.A.M, et al. Comparison of the frequency of CMV and Parvo B19 infections in Intrauterine Fetal Death and normal Pregnancy. J Kerman Univ Med. 2008; 15(4): 273-281.
15. Sanjideh M, Naeimi S, Morady Nasab M, Moradi R,

Vahdat K. Cytomegalovirus infection in NICU admitted neonates in Boushehr. ISMJ 2016; 18(6):1171-1178.
16. Gaytant MA, Galama JM, Semmekrot BA, Melchers WJ, Sporken JM, Oosterbaan HP et al. The incidence of congenital cytomegalovirus infections in The Netherlands. J Med Virol. 2005;76(1):59-71.
17. Ahlfors K, Iverson SA, Harris S. Report on a long-term study of maternal and congenital cytomegalovirus infection in Sweden. Review of prospective studies available in the literature. Scand J Infect Dis. 1999;31(5):443-57.
18. Barlinn R, Dudman S G, Trogstad L, Gibory M, Muller F, Magnus P, Rollag H. Maternal and congenital cytomegalovirus infections in a population-based pregnancy cohort study. APMIS. 2018;126(12):899-906.
19. Enders G, Bäder U, Bartelt U, Daiminger A. Cytomegalovirus (CMV) prevalence and frequency of CMV primary infections in pregnant women. Pol J Microbiol. 2003; 46:426-32.
20. Ross, S.A, Novak Z, Pati S, Boppana SP. Diagnosis of Cytomegalovirus Infections. Infect Disord Drug Targets. 2011:11(5):466-474.