Iranian Journal of Virology 2018;12(1): 25-31
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Original Article

The Difference in Levels of Cytomegalovirus Antibodies Among Women in Gestation Age

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Abstract

Background and Aims: Congenital cytomegalovirus (CMV) infection is one of the most common viral causes of congenital infection in different areas, and a leading cause of hearing impairment and a contributor to neurodevelopmental disablement in children. Reactivations and reinfections may occur conventionally in the herpes virus family group with the capacity to establish perennial latency in the host.

Materials and Methods: Through a cross-sectional study design, we studied fertile women in a public primary health care center in Karaj city in 1396. In this study, 360 volunteers from women of childbearing age were selected randomly. Then, 5 ml of blood was taken and after serum separation through centrifugation, the serums were frozen at -20°C for further ELISA test. The serums were examined for anti-CMV IgG and IgM antibodies.

Results: The results showed that 77% of the subjects (280 out of 360) had CMV infection and none of the participants had CMV-IgM antibodies. There was no significant difference between the educational levels, the age group of 30 and under 30 years of age and the infection rate with CMV.

Conclusions: The results of the present study on the high prevalence of positive CMV IgG antibodies were compatible with the results of other studies performed in Iran and elsewhere in the world indicating the previous confrontation of the individuals with cytomegalovirus and the widespread dissemination of this infection in the community.

Keywords: CMV, Cytomegalovirus, IgG antibodies, Childbearing age.

Introduction

Cytomegalovirus (CMV) is a double-stranded DNA virus subset in to the herpes virus family group with the capacity to establish perennial latency in the host (1) Human cytomegalovirus which is the largest known human herpesvirus HHV5, with a genome of around 230 kb (2) is engendered of nuclear as well as cytoplasmic inclusions and its perennial latency. Cytomegalovirus (CMV) is a prevalent cause of infections ecomenical. Like other herpes viruses, primary infection with CMV is followed by perennial latency, with episodes of reactivation when the virus can be transmitted against (3). The human cytomegalovirus (HCMV) or human herpesvirus is one of the significant reasons for inborn diseases transmitted against (4).

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Hiding and relapse of the disease. Re-activations and reinfections may occur conventionally in the herpes virus family group with the capacity to establish perennial latency in the host (1).

Like other herpesviruses, primary CMV infection is followed by the establishment of perennial latent infection from which periodic reactivation is prevalent (5). It isn't evident whether transplacental transmission of CMV in ladies with the previous seroimmunity is optional to virus reactivation or to infection with another or diverse CMV strain (reinfect-ion) during gestation (6).

Clinical symptoms. Congenital cytomegalo-virus (CMV) infection is one of the most common viral causes of congenital infection in different areas which leads to hearing impairment and a contributor to neuro-developmental disablement in children (1). CMV is the most well-known inborn infection, since it happens after primary and repetitive infection in life time which sometimes ends up in neurological debility (4).

Congenital CMV infection is most liable to occur following a primary infection in the mother during gestation.

The most essential weight of illness originates from CMV diseases during gestation that can cause contamination of the unborn kid. It is estimated that about 0.2% and 1.0% of all infants have an intrinsic CMV infection, which can cause serious and durable handicap including sensorineural hearing misfortune and psychological or deferred engine referrel (3).

5– 10% of intrinsically tainted neonates have side effects of irreversible CNS association as microcephaly, encephalitis, seizures, deafness (a single finding in 10% of cases), upper engine neuron issue, psychomotor impediment, and, once in a while, myopathy and choro-idoretinitis (7).

The course of infection in healthy individuals is mostly asymptomatic, yet CMV is a noteworthy reason for mortality in immuno-compromised people.

The range of illness articulation is expansive, with CMV recep-tivity of nearly all organs. (8)

CMV infection acquired by blood transfusion may lead to noteworthy confusions, in immunocompromised people. Serious infection including pneumonia, retinitis, hepatitis, encephalitis in immunocompromised patients have been accounted for (9).

In immunocompetent people, sufficient hum-oral and cell immunities are required to limit viral replication after essential disease to keep up HCMV in a long-lasting chronic state. Cytomegalovirus disease could prompt HCMV-related inflammation, which is detri-mental to adults, particularly in the elderly (10).

Furthermore, virus-associated disease and virus-associated post-transplant complications remain a vital financial deplete on singular transplantation programs (2).

Transmission. CMV is transmitted by close contact between individuals, through contami-nation from urine, saliva, semen, cervical secretions, and breast milk, while droplet contamination is less paramount (1).

Transmission is conceivable by means of blood, sexual contact, breastfeeding, and organ transplantation (11). Studies have distinguished two ways of maternal CMV infection: sexual rout and contact with infected youngsters (12).

Likewise, CMV can be transmitted vertically through the placenta. A few CMV transmission courses have been obviously illustrated.

During childhood, these routes include mother-to-child via breastfeeding, parents- or siblings-to-child via close contact, or child-to-child via close contact in out-of-home settings such as day care centers (3, 13).

Acquisition of the virus arises progressively from an early age, and the overall sero-prevalence is 30–70% in developed countries. Homosexual men, poor socioeconomic groups, and residents of developing countries, how-ever, have seroprevalence rates that can exceed 90% (2).

Epidemiology. CMV infection is endemic and lack seasonal variance. The seroprevalence is due to many factors such as hygienic circum-stances, socio-economic factors, breast-feeding and sexual contacts and it increases with age. The variation in the seroprevalence in different populations, including pregnant women, has been accounted for to be 35-95% (1).

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In population from low asset nations, most youngsters will catch a CMV infection amid the principal long stretches of life and the seroprevalence in kids from high financial populaces, breastfed for over half a year, is higher than in kids breastfed for shorter periods.

As a result of the variety in seroprevalence between nations, the pervasiveness of inborn CMV fluctuates between 0.15 - 2.0%(1)

Methods

Through a cross-sectional study design, we studied fertile women in a public primary health care center in Karaj city in 1396. The Inclusion criteria for enrollment in the study were: 1) reproductive women; 2) residing in Karaj City; 3) aged 15 years to 49 years; 4) who accepted to participate in the study.

Laboratory tests. In this study, the number of participants were 360 volunteers from women of childbearing age selected randomly. In this study, the formula for $n = z^2pq / d^2$ was used to calculate the minimum sample size ($z = 1.96$, $p = 80\%$, $q = 5\ \%$). For data analysis, SPSS software was used. Chi-square and Fisher were used to test the relationship between variables. First, a questionnaire including demographic data such as name, surname, age, place of birth, educational status, history of blood transfusion, history of transplantation, specific disease history, and information about CMV viruses were filled. Then, 5 ml of blood was taken and after serum separation through centrifugation, the sera were frozen and kept at -20°C till used for the ELISA test.

Serum samples were obtained from the whole blood taken from fertile women followed by low speed centrifugation. Sera were examined for anti-CMV IgG antibodies by a commercially available enzyme immunoassay "Cytomegalovirus IgG (CMV IgG)" kit (Acon Biotech Co .Ltd) and for anti-CMV IgM antibodies by a commercially available enzyme immunoassay "Cytomegalovirus IgM (CMV IgM" kit (Acon Biotech Co .Ltd).

The ELISA plates were subjected to the Acon-Biotech kit and the ELISA Reader Stat fax 4200. In this test, the cut-off kit was calculated, and those whose ODs were less than cut-offs were considered negative and those whose ODs were higher than cut-offs was considered positive.

The tests were performed according to the instructions of the manufacturer. The cut-off values for IgG and IgM seropositivity were obtained. A sample was considered positive for IgG or IgM when a CMV G index or a CMV M index was greater than 1.1, respectively.

Results

In this study, the total number of participants was 360 with the mean age of 28.26 ± 6.34 (14 and up to 48 years old). From these participants, 51 did not finish high school, 123 were high school graduates, and the rest had MsC and equivalent degrees. The evaluation of IgG concentration was indicated in Fig. 1 .

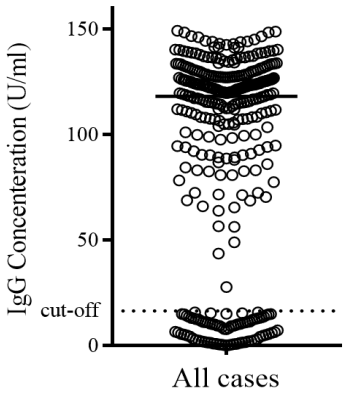

Fig. 1. The IgG concentrations in all samples

Table 1. The IgG prevalence in the specimens

	Positive	Negative	Prevalence	Lower CI	Upper CI
IgG	280	80	0.77	0.73	0.81

According to the cut-off determined by the kit, which is 16.5 (in the figure with the dotted line), 280 of tested specimens were IgG positive and 80 of them were IgG negative. The IgG prevalence in the specimens has been demonstrated in Table 1.

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In order to study the relationship between the prevalence of CMV IgG and the level of education, the samples were examined and the results of which was demonstrated in Fig. 2.

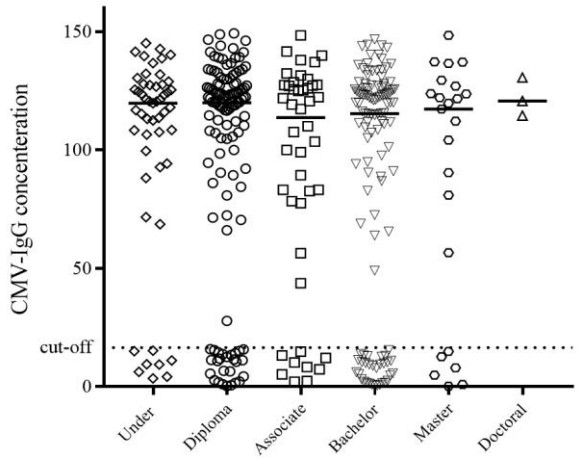

Fig. 2. The relationship between the prevalence of CMV IgG and the education levels.

Chi-square test used to compare CMV IgG among educational levels reported a non significant difference. (P=0.59).
The IgM prevalence in the specimens was zero which is shown in Table 2.

Table 2. IgM prevalence

	Positive	Negative	Prevalence	Lower CI	Upper CI
IgG			0	0	0.013

Fisher's comparison test was used to compare IgG CMV between two age groups. The results showed that the observed difference between the two age groups was not statistically significant (P=0.79). (Fig. 3).
In order to find the association between the prevalence of the IgG and the age of CMV, the samples were divided into two groups of 30 and over 30 years of age and were evaluated for IgG prevalence. Table 3.
Chi-square test was used to compare CMV IgG between educational levels and the results showed that the observed difference between groups was not statistically significant (P=0.59). (Table 4).

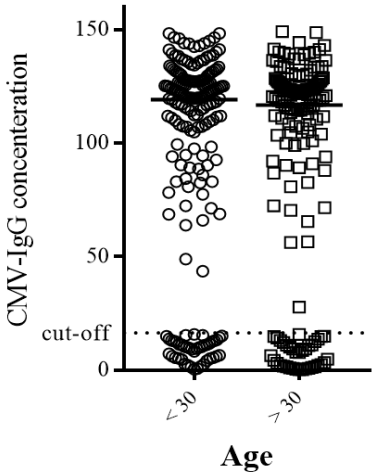

Fig. 3. Distribution of CMV seropositive women according to two age groups.

Table 3. Campare CMV IgM between two age group

	Positive	Negative
< 30	156	43
> 30	124	37

Table 4. Anti- CMV IgG Seropositivity rate by educational levels.

	Positive	Negative
Associate	35	9
Bachelor	85	31
Diploma	97	26
Master/Doctoral	20	6
Under g.	43	8

In the present study, the mean age of the members was 26 to 28 years, out of a total of 360 participants, 51 under-diplomas, 123 diplomas, 44 Associate students, 116 Bachelor, 23 Master, and 3 Ph.D. The results show that 77% of the subjects (280 out of 360) had CMV infection and none of the participants had CMV-IgM antibodies. There was no significant difference between the educational levels and the age group of 30 and under 30 years of age and the infection rate with CMV.

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Discussion and Conclusion

This study revealed that the prevalence of CMV in reproductive women was very high. It was also found out that anti-CMV IgG antibodies were detected in 280 of the cases, while 0 of the subjects tested positive for anti-CMV IgM.

The detection of CMV IgG indicated that the reproductive women had previously been infected with CMV. After CMV infection, IgG remains in the body for alifetime and protects against the next infections considerably. This indicates that a negative result of the CMV IgG test means the woman has not been infected with the virus.

Cytomegalovirus is in the Herpesviridae family and most people have an experience of contact with it. Intrauterine infection by cytomegalo-virus virus is common in some countries such as America and various studies have reported the prevalence rate of this infection to be 0.4 to 2.4%. Young mothers who are negative for CMV infection are at increased risk and mothers who are infected by Cytomegalofor the first time during their gestation usually transmit the virus to the fetus, which can have teratogenic effects. The prevalence of this virus depends on the economic factors, age and geographical location of the population and the prevalence of infection is reported to be 40-100% in the studied populations. (14)

Seroepidemiological studies have shown that Cytomegalovirus infection is common and the prevalence of infection increases with age. The distinction between primary and secondary infection is very important because the acute primary infection is transmitted to the fetus almost in 40% of cases and can lead to severe complications, while recurrent infection causes infections of the fetus in 0.1-10% of cases. Moreover, since IgM might be found in primary and recurrent infections, measurement of IgG binding incline (IgG avidity) is a valuable method for confirming the initial infection of Cytomegalovirus(15)

Concerning the necessity for pregnant mothers' health and the role of CMV virus in the emergence of fetal abnormalities and major central nervous system disorders such as deafness, mental retardation, ocular disorders and etc., the aim of this study was to determine the seroprevalence of Cytomegalovirus infection in women of fertility age referring to Sabze Parvar clinic of Karaj. The results of this study showed that from most women of fertility age who participated in this study, 77% of them had positive antibody titers against cytomegalovirus and all of them were negative in respect to IgM antibody titers. Several studies have been carried out on the association of Cytomegalovirus and recurrent abortions in different parts of the world. In Orang Ilami et al study (2013) in Yasuj, 98.9% of women of fertility age had positive IgG antibody titer against cytomegalovirus and all were negative in respect to IgM (15).

In Arabzadeh et al study in 2007 in Kerman, the prevalence of IgG antibody against cytomegalovirus was 91.94% positive and the prevalence of IgM antibody against Cyto-megalovirus of 33.8% of samples was positive (16).

In Skild et al study in 2005 on the relation between anti-cytomegalovirus IgM and IgG antibody and intrauterine fetal death, it was found that 72% of the patient's group and 69% of the control group were positive for IgG antibodies (16)

the results of the present study on the high prevalence of positive CMV IgG antibodies were compatible with the results of other studies performed in Iran and elsewhere in the world indicating the previous confrontation of individuals with cytomegalovirus and the widespread dissemination of this infection in the community.

The presence of an anti-cytomegalovirus IgG antibody indicates that the individual has been infected by this virus at a time after birth and this antibody would remain in the human body for his whole life. It should be noted that the antibody cannot prevent a recurrence, re-activation of being infected by an infection with the external and congenital origin. However, in cases of the previous infection of mother and acquired immunity, the risk of incidence of congenital infection by cytome-galovirus and the infection of an infant is greatly reduced.

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The prevalence of CMV infection in this study was determined to be 77%, which is close to studies conducted in Iran and elsewhere in the world, especially in developing countries. Given the clinical importance of the diseases caused by cytomegalovirus and lack of comprehensive information on the seroepidemiology of this virus, as well as the prevalence of congenital infections of cytomegalovirus in Iran, it is required to perform more cross-sectional studies. Moreover, performing studies with molecular methods such as PCR could be a useful and beneficial method for virus identification.

In the mentioned questionnaire, in addition to demographic information of the subjects, a question was asked about the familiarity or rate of information, the participant's posses about the disease that could be considered as one of the variables of health literacy. However, health literacy is a collection of cognitive and social skills that determines the motivation and ability of individuals to obtain, access understand and use the information to promote and maintain the health of individuals. Nowadays, health is introduced as a global issue and due to its significant role on the decision making of individuals on areas related to health, it has been considered by policymakers as an essential instrument for the promotion of the health level of community and increasing the quality of presented health care service. Although it is still not clear how health literacy affects health outcomes, many undesired outcomes concerning the health could be due to inadequate health literacy such that researchers believe that health literacy is a stronger predictor of an individual's health compared to variables such as age, income, employment status, education level, and race. Individuals usually have little knowledge about the methods for preventing diseases and they rarely participate in health care programs against chronic diseases. The global health organization has identified health literacy as one of the greatest determinants of health. In definitions of health literacy, its multi-dimensionality is usually mentioned and the ability of individuals in understanding and interpreting the meanings and concepts of health information is defined in various forms. Concerning what has been mentioned, measurement of health literacy can be useful and necessary and through designing special interventions to increase it, it becomes possible to prevent the risk resulting from limited literacy since people with lower health literacy are more likely to evaluate their own health as weak after conforming age, gender, race and indicators of economic deprivation. 31 In our study, one of the questions was to measure how informed the individuals are about cytomegalovirus and the resulting diseases, however no participant had information about it. Moreover, the participants were asked some questions about the history of blood transfusion, the transplantation, and special disease and none of the participants responded positively to the above questions.

Acknowledgement

Hereby, I thank Dr. Ali Ehsan Heydari and everyone who voluntarily participated in this study.

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