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Original Article

Seroprevalence of Cytomegalovirus Infection in Pregnant Women Referred to Health Care Center of Khorramabad

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Abstract

Background and Aims: Cytomegalovirus (CMV) is a member of herpesviruses. It is one of the most common cause of congenital and prenatal infections. CMV infection of pregnant women, especially in the first trimester may lead to congenital abnormalities in the newborns. The prevalence of CMV infection in developed countries is about 40% and in developing countries may be 100%. Because there is no information related to the epidemiology of this infection in Khorramabad city, this study was done to determine the seroprevalence rate of the infection and its associated risk factors in pregnant women who referred to the health care centers of this city in 2008.

Materials and Methods: This cross-sectional study was done in 240 pregnant women. Demographic data were collected by a questionnaire. About 3 ml of blood was taken from each patient. Aliquots of serum samples were stored at -20°C until analyzed. The presence of anti-CMV Specific antibodies was assessed by enzyme immunoassays. Data were analyzed by fisher's exact test and χ^2 test using SPSS software version 11.5.

Results: Mean age of cases was 26 years and varied between 15-40 years. CMV IgG was found in 217 cases (90.6%) out of 240 cases. 97 people (86%) of the cases who were pregnant for the first time were positive regarding to CMV-IgG. In women who had 1-3 or more than 3 deliveries, this rate was 94% and 100% respectively. There was a significant relationship between the number of deliveries and the positive result of the test (CMV-IgG). There were no significant relationship between age, abortion history and number, education level and the stage of pregnancy with test result ($p>0.05$).

Conclusion: As in other developing countries, the prevalence rate of CMV infection in pregnant women in Khorramabad was high. Since the infection is prevalent and the potential abnormalities associated with it, it is highly recommended to expand preventive measures and inform population how to prevent the infection and associated consequences.

Keywords: Cytomegalovirus; Seroepidemiology Enzyme immunoassays; Khorramabad

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Introduction

Cytomegalovirus (CMV) is a member of β-Herpesviridae family. It is the largest member (150-200nm) of the family and it cannot be differentiated from other members morphologically. This pathogenic virus has a widespread distribution and can infect individuals at any age (1). CMV infection is one of the major causes of morbidity and mortality in immunocompromised patients such as newborns, AIDS patients and graft recipients (2, 3). Seropositivity for CMV

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infection ranges from 40 to 100 %(4). In different countries and is associated with socioeconomic status (4-6).

Infectious agents can threaten pregnant women and can cause fetus death and malformation (7). Infection during pregnancy, specially the first trimester, can cause acute fetal infections and neural and audiovisual abnormalities which has a great economic burden (5). CMV is one of these infectious agents which can cause unwanted clinical manifestations such as neural consequences and deafness in 10-14 % of infected fetuses. Infection of mothers can lead to preterm delivery in 34 % of cases (8). Fetus may be infected by this virus as a consequence of recurrent or primary infection of the mother (9). The exact natural history of intrauterine CMV infection ia not known, but it has been clearly demonstrated that it can cause irreversible damage to fetus (4). The rate of congenital infection as a result of primary infection is 30 % (15-50 %) and is 1-15 % following recurrent (active) infections (10).

CMV infection is essentially without clinical, symptoms or is associated with non- specific manifestations (10). Ninety percent of congenitally infected newborns have no symptoms at birth, and 5-17 % have clinical symptoms. Of these 20% will die and the remaining 80 % will suffer from unwanted consequences (11-13).

CMV infections are yet challenging for gynecologists and because maternal infection can cause acute fetus infection which is associated with neural, audio and dental abnormalities (14). These abnormalities have a considerable economic burden. The prevalence of infection in Lorestan province has not been studied so far. Therefore we decided to determine its prevalence rate in pregnant women in Khorramabad, and its association with abortion.

Methods

This research was a cross-sectional study which included 240 pregnant women who referred to health care centers of Khorramabad city. Written consent was taken from all cases. Demographic data such as age, job and education level was gathered by a questionnaire. A blood sample (3 ml) was taken from each patient and the sera were isolated and kept frozen at -20º C until used. The anti-CMV antibody in sera was assessed by ELISA method (Trinity Biotech plc, Ireland) and data analysis was done by χ^2 and exact Fisher test at p value <0.05 using SPSS version 15.

Patients and Participants

The mean age of participants was 26 years, ranging from 15 to 40 years. CMV-IgG was found in 217 sera samples (90.4%) of 240 samples. 94.2% of patients were housekeeper (Without any job) and 5.8% had a job. Fifteen percent of patients had at least one abortion in the past. 3.3% of cases were illiterate, 9.6% were at primary school level, 25 % were at guidance school level, 42.1% were at high school level and 20 % were at academic level. Of all cases, 32.8% were at first trimester, 33.2% were at second and 34% were at third trimester of gestational period. 47% of cases had one delivery, 49.2% had 1-3 delivery, and 3.8% had more than three deliveries.

Results

CMV-IgG prevalence was highest in cases older than 34 year old age group (100%). And lowest in 25-29 years old age group (Table 1). There was not any correlation between age and seropositivity for CMV-IgG.

The rate of seropositivity for CMV-IgG in employed women was 93% and in unemployed women was 90%. There was no significant relationship between employment status and CMV-IgG seropositivity. Thirty six cases (15%) had at least one abortion in the past, of these 34 (94%) were positive for CMV-IgG. Seropositivity rate in patients with no abortion history was 90%.So there was not any relationship between seropositivity rate and abortion history. Seropositivity rate for CMV-IgG in illiterate persons was highest (100%) and in cases with academic education level was lowest (92%). There was no significant relationship between seropositivity for CMV-IgG and education level (Table 2).

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Table 1. Frequency of CMV-IgG seropositivity in different age groups of pregnant women.

Age group	CMV-IgG +[a]	CMV-IgG -[b]	Total
15-19	23(92%)	2(8%)	25(100%)
20-24	65(89%)	8(11%)	73(100%)
25-29	71(87%)	11(13%)	82(100%)
30-34	41(95%)	2(5%)	43(100%)
34>	17(100%)	0(0%)	17(100%)
Total	217(90.4%)	23(9.6%)	240(100%)

a: CMV-IgG Positive b: CMV-IgG negative

χ^2=0.17

Table 2. Frequency of CMV-IgG in pregnant women with different educational level.

Educational level	CMV-IgG +[a]	CMV-IgG –[b]	Total
Illiterate	8(100%)	0(0%)	8(100%)
Primary School	23(100%)	0(0%)	23(100%)
Guidance School	55(92%)	5(8%)	60(100%)
High school	90(89%)	11(11%)	101(100%)
Academic	41(85%)	7(15%)	48(100%)
Total	217(90.4%)	23(9.6%)	240(100%)

a: CMV-IgG Positive b: CMV-IgG negative

χ^2= 0.29

There was not any significant relationship between gestational age and CMV-IgG seropositivity. Seropositivity rate in nulliparus(without parity) women was 89% and in women with 1-3 and more than 3 delivery was 94% and 100% respectively (Table 3). This relationship was statistically significant at p= 0.036 level.

Discussion

Some studies indicate that seropositivity of CMV-IgG is very high in healthy population in the world, so it seems like that CMV infection is one of the endemic infections of human beings (15, 16). In some of the countries it is believed that CMV infection is hyperendemic (17). Earlier researches proposed that prevalence rate of infection is depending on factors including race, age, the number of deliveries, sexual behaviors, breastfeeding, spread by children, population and job activity(kind of job) (4, 5 , 31).

In this study 217 (90.4%) out of 240 pregnant women's serum was detected as CMV-IgG positive. There was no significant relationship between age, abortion history, educational level and stage of pregnancy in this study (p>0.05), however the prevalence rate was increased mildly with age, but the CMV infection frequency have a meaningful significant relation (p=0.036) with parities (number of deliveries). This is probable that lacking of healthier behaviors in the time of delivery leads to increased contamination risk and high number of parities.

In recent years, many studies have been done on epidemiology, treatment and diagnosis of CMV infections (15). Seropositivity of infection is reported to be 24.6% to 97.14% in different populations (16). The prevalence of anti-CMV antibodies is correlated to socioeconomic status. Most preschool children in Asia and Africa are seropositive, but less than 20% of children in USA and England are seropositive (1).

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Table 3. Frequency of CMV-IgG seropositivity in women with different delivery numbers.

Number of Parities	CMV-IgG +[a]	CMV-IgG –[b]	Total
0	97(86%)	16(14%)	113(100%)
1-3	111(94%)	7(6%)	118(100%)
3>	9(100%)	0(0%)	9(100%)
Total	217(90.4%)	23(9.6%)	240(100%)

a: CMV-IgG Positive b: CMV-IgG negative

χ^2=0.036

Seroepidemiologic studies have shown that CMV infection is prevalent and rises with increased age (11, 12) Many acquired infections have no overt clinical symptoms (2, 6). Every year 30000 to 40000 neonates have been borne with congenitally acquired CMV infection in the united states, of these 10% have classic disease.(2,31) About 90% of newborns with symptomatic infection at birth will show neural consequences and reduced or lack of hearing (2,). 0.5 to 1 percent of neonates in the united states born with congenital CMV, that predisposes them to neurologic complications (4), Asher et al described in their review articles that: [in 0.2–2.5% of the newborn infants, there is evidence of intrauterine infection with CMV, but the rate of infection seems to be much lower in Europe and Australia, less than 0.5%] (6).

CMV-IgG is an indicator of post or current infection. This antibody remains in the body for a long time and can protect person for the rest of his/her life. IgG seronegativity is a sign of no CMV infection in the past and present. Because of high prevalence of CMV-IgG, it detection has a minimal diagnostic value, but it can be very useful for identification of seronegative people (2).

Seroprevalence rate of CMV infection has been determined 91.94% in a study in Kerman (17). This rate has been determined to be 98% in less than 20 years-old women and 100% in over 40 years-old, and on average 99.1% in Tehran (18). In a study on pregnant women in Kermanshah, the seroprevalence rate of CMV-IgG has been reported 23%. All cases were negative for CMV-IgG (5).

Spano etal have reported that the prevalence rate of anti-CMV antibodies is 98% in pregnant women and 98.3% in non-pregnant women (9).

Seroepidemiologic studies in rural areas of Egypt in 1996 showed that 98% of pregnant women were CMV positive and 96% of their newborns were also seropositive (19). In another study in Brazil, 87% of pregnant women and 85% of their newborns were CMV-IgG positive (20). In a study by Stein et al which was done in Israel in 1997, the prevalence rates of CMV-IgG in pregnant women has been reported to be 84.3% and of CMV-IgM was found in 0.7% of them. The mortality rate of infection has been estimated 280 case/years and the number of symptomatic newborns has been reported 56 case/year (21).

The rate of CMV-IgG seroprevalence in pregnant women with a history of abortion has been 37% in comparison with 15% of controls in Tabriz conducted in 1997 (22). In a study which was done in Tabriz on asymptomatic women's, the rate of anti-CMV IgG has reported to be 82% (23). This rate has reported to be 89.6% in another study on healthy blood donors in Tehran transfusion center (24). In the other study in Tabriz 87% of pregnant womens of first trimester was reported as seropositive for CMV-IgG (10).

Seropositivity for CMV-IgG has been reported to be 97.14% in healthy blood donors in France (25). In a similar study in India, the prevalence rate of CMV-IgG has found to be 95 %(26). In

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a study which was done in Spain in 1993-1994 on 2-60 year age groups, the prevalence rate of CMV-IgG has found to be 62.8%(27). In another study which was done in Spain in 1999 on 31-40 years old people, the prevalence rate of CMV-IgG has been found to be 79.1% (28). Seropositivity for CMV-IgG has been reported to be 41% in Finland children's under 8 years old (29). The prevalence rate of CMV-IgG in Turkey was reported 90.6% and 99% in 1 day - 15 and 15 - 49 years old women's respectively (30). In the United State the prevalence rate of CMV-IgG estimated 36.3% in a 6 year period of 6-11 years old group. The authors emphasized that the prevalence rate increases in accordance with age of studied groups (31). In the other study, researchers estimated that 27000 new cases of CMV infections occurring in pregnant seronegative womens (8). In a study in Tehran the prevalence rate of CMV-IgG was reported to be 100% on pregnant women (33). Arabpour et al in a cohort study in Fars province of Iran indicate that 764 (93%) out of 844 pregnant women were positive CMV-IgG (9), but in a similar study in Saudi Arabia it was reported 92.1% (34). In a pilot study 297(87.4%) out of 340 pregnant women in India have been reported as seropositive for CMV-IgG (2 new).

Conclusion

The prevalence rate of CMV-IgG is high in a population of pregnant women in Khorramabad (one of the western provinces of Iran). High prevalence in our study is in accordance with others in Iran and developing countries (2, 3). Because of clinical complications of CMV infections especially in newborns, lack of sufficient seroepidemiologic data, and high frequency of congenital CMV infections in Iran, it is necessary to be cross-sectional studied in our country. Because of CMV excretion in urine of most infected pregnant women, it is proposed recently that detection of CMV in urine of patient by PCR could be a useful method for identification of primary infections in pregnancy period (11, 12). Differentiation between primary and non-primary infection of CMV by avidity index (AI) of anti-IgG is important, because of severe complications in primary infections (1, 6). In addition it is probable that CMV in association with other pathogens could have a role in creation of cervical neoplasia (13). Since the prevalence of congenital infection of CMV is not clear in Iran, identification, epidemiology and clinical impacts of CMV infections should be included as important priorities of health ministry professionals.

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