Cytomegalovirus seroprevalence in women with bad obstetric history in Kirkuk, Iraq

Zainab Khalil Mohamed Aljumaili a,b,*, Abdulghani Mohamed Alsamarai c,a,d, Wesam Suhail Najem e

a Department of Microbiology, Tikrit University College of Medicine, Tikrit, Iraq
b Kirkuk Health Authority, Iraq
c Department of Medicine, Tikrit University College of Medicine, Tikrit, Iraq
d Asthma, Allergy Centre, Tikrit Teaching Hospital, Tikrit, Iraq
e Department of Dermatology, Tikrit University College of Medicine, Tikrit, Iraq

Received 10 May 2013; received in revised form 8 July 2013; accepted 10 August 2013

KEYWORDS
Cytomegalovirus; CMV; BOH; Pregnancy; IgM; IgG; Kirkuk; Iraq

Summary The human cytomegalovirus (CMV) is a major cause of congenital infections. A case–control descriptive study was conducted in Kirkuk, Iraq to determine the seroprevalence of CMV in women with bad obstetric history (BOH) compared to women with a normal previous pregnancy. The CMV IgG and IgM seroprevalence was higher in women with BOH. The CMV IgG seroprevalence was significantly influenced by pregnancy, age, residence and level of education. In addition, the current CMV infection was significantly associated with pregnancy, age, residence and education. Large families (crowding index >3) exhibited higher seroprevalence for CMV IgM (8.3%) and IgG (98.3%), but odd ratio (OR) showed no significant association between family size and seropositivity. The CMV IgG seropositivity was higher in working women (100%) compared to housewives (95.4%). However, the CMV IgM (current infection) was 6.8% in housewives and was not detected in any working women (0%). The OR exhibited no significant association between occupation and both IgM and IgG levels.

© 2014 King Saud Bin Abdulaziz University for Health Sciences. Published by Elsevier Ltd. All rights reserved.

Introduction

The human cytomegalovirus (HCMV) is a major cause of congenital infections. This virus’s clinical manifestations range from asymptomatic forms (90% of cases) to severe fetal damage and, in rare cases, death due to abortion [1].
Cytomegalovirus (CMV) infection during pregnancy is far more complex than other infections because the virus can frequently be reactivated during the child-bearing years and can be transmitted to the fetus despite maternal immunity [2].

There are many confounding studies describing the association between CMV infection and pregnancy loss, which show that HCMV can result in abortion or stillbirth [3,4]. HCMV acts as an immune modulator by using an array of immune evasion strategies to avoid elimination from the host, and its viral proteins are involved in the regulation of cellular gene expression and the induction of pro-inflammatory cytokines [5] or an autoimmune response [6]. In another study in Wasit province, Iraq [7], women with a history of abortion showed 60.2% IgM seropositivity; however, this not significantly different from the control. A high percentage of repeated abortions (two and three or more) occurred in women seropositive for CMV IgM.

In Mosul, Iraq [8], 12% of women of child-bearing age were seropositive for cytomegalovirus (CMV); therefore, the majority cases of congenital CMV infection are likely a result of maternal re-infection. In Baghdad city, Iraq, IgM antibodies significantly correlate with a history of abortion [9]. In another study of women with habitual abortions in the Thi Qar Governorate, Iraq, 60 of 60 women (100%) had antibodies against CMV, with 9 women (15%) with IgM antibodies, 21 women (35%) with IgG antibodies and 30 women (50%) with both IgM and IgG antibodies [10].

Cytomegalovirus is frequently a causative agent of prenatal and perinatal infection and may lead to pregnancy complications [11]. The seropositivity of CMV varies widely worldwide [12]. A review of 40 global studies on CMV seroepidemiology indicated a range of seropositivity, from 30.4% in Ireland [13] to 98.9% in Turkey [14] in pregnant and/or child-bearing age women. In addition, the seroprevalence rate ranged from 14.2% in Iran [15] to 91.05% in India [16] in women with a bad obstetric history.

In Arab countries, we reviewed 21 studies, which indicated a seroprevalence rate ranging from 77.8% in Babylon, Iraq [17] to 88% in Jordan [18] in pregnant women. The seroprevalence ranged from 4.8% in Baghdad, Iraq [19] to 95% in Jordan [18] in women with a bad obstetric history.

The objective of the present study is to determine the seroprevalence of CMV in women with a bad obstetric history and the sociodemographic characteristics that may influence seropositivity.

**Patients and methods**

**Setting**

Kirkuk General Hospital, Primary Health Care Centers in Kirkuk Governorate.

**Study design**

This study is a descriptive case—control study.

**Study area**

This descriptive case—control study was conducted at the antenatal clinic of the Kirkuk General Hospital and Primary Health Care Centre in Tessean. Women (pregnant or not pregnant) with a bad obstetric history were recruited from the outpatient Gynaecology Clinic Kirkuk General Hospital or the outpatient Clinic at Tessean PHC.

**Study population**

The study population comprises women of child-bearing age. The study population was recruited from the Primary Healthcare Centers located in urban and rural areas in Kirkuk Governorates. In addition, one study population group was recruited from pregnant women in labor to obtain the group of pregnant women with risky outcomes.

**Group 1:** Pregnant women aged 15–48 years with normal pregnancy.

**Group 2:** Non-pregnant women aged 15–48 years with normal pregnancy.

**Group 3:** Pregnant women with BOH depending on their previous pregnancy and/or delivery outcome, which includes pregnancy loss, intrauterine deaths, preterm deliveries and intrauterine growth retardation. Their ages ranged from 15 to 48 years.

**Group 4:** Non-pregnant women with BOH depending on their previous pregnancy and/or delivery outcome, which includes pregnancy loss, intrauterine deaths, preterm deliveries and intrauterine growth retardation. Their ages ranged from 15 to 48 years.

The demographic information of these groups is shown in Table 1. The target number recruited for each group was 150 women. However, the total number of women included in the study was 538, of which 293 (54.5%) had BOH and 245 (45.5%) had a normal pregnancy history. In the BOH group, 144 (49.1%) women were pregnant, whereas in the
normal pregnancy group, 117 women (47.7%) were pregnant.

Collection of data

The investigators visited the outpatient department daily, selected the study subjects and screened the patients using a predesigned, pretested schedule based on the inclusion and exclusion criteria to identify and recruit the study subjects. The next available age-matched multiparous antenatal woman without BOH was included in the control group subjects.

Clinical examination and laboratory investigations were performed for the study subjects to exclude other causes of abortion or fetal death, such as hypertension, diabetes mellitus, syphilis, Rh (rhesus) incompatibility, physical causes of abortion, and consanguinity. Subjects with known causes of fetal wastage were excluded from the study. All subjects were interviewed to ascertain age and medical and obstetric information.

Sample collection

For serological analysis, 5–10 mL of venous blood was collected from each study subject in a sterile container with strict aseptic precautions. The serum was separated and stored in numbered aliquots at −20 °C until it was assayed. All serum samples collected from the study and control groups were tested for CMV IgM and IgG antibodies using commercially available ELISA kits. The results were read with a microwell reader and compared to the controls. The optical density was read at 450 nm on an ELISA reader.

Ethical approval

The ethical committee of the institute approved the research protocol. The purpose and procedures of the study were explained to all study subjects, and informed consent was obtained. The study design was approved by the ethical committee of TUCOM registered in the USA [U.S. Department of Health and Human Services (HHS) & Registration of an Institutional Review Board (IRB)]. IORG #: IORG0006885.

Institution: Tikrit University College of Medicine [TUCOM] OMB No. 0990-0279.

Methods

ELISA was used to determine the IgM and IgG levels for HSV-2 and the test was performed according to the manufacturer’s instructions. The kit was purchased from BioCheck, Inc., 323 Vintage Park Dr., Foster City, CA 94404.

Data analysis

The collected data were compiled in a Microsoft Excel spreadsheet. The proportions and odds ratios were computed for the appropriate analyses. To determine whether there was an association between the categorical data, a Chi square test was used with the SPSS software (Version 16.0, Licenced to TEAM EQX). If the sample size in the BOH group did not reach the targeted number, a power analysis will be performed to determine the accuracy of the findings. The study data are presented as the frequency ± SD and the 95% confidence interval. Bivariate regression line analysis was performed to calculate the odds ratio to determine an association between two variables. The determinants for CMV infection were determined by calculation of the odds ratio using a logistic regression line analysis. Confounding factors, such as age and socio-economic status were standardized when the serological determinants were calculated.
Table 2  Cytomegalovirus seroprevalence in women with bad obstetric history.

<table>
<thead>
<tr>
<th>Group [number]</th>
<th>Number positive [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IgM</td>
</tr>
<tr>
<td>Bad obstetric history</td>
<td></td>
</tr>
<tr>
<td>Pregnant [144]</td>
<td>12 [8.3]</td>
</tr>
<tr>
<td>$X^2$</td>
<td>0.579</td>
</tr>
<tr>
<td>$P$ value</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Total [293]</td>
<td>21 [7.2]</td>
</tr>
<tr>
<td>Normal pregnancy</td>
<td></td>
</tr>
<tr>
<td>Non-pregnant [128]</td>
<td>0 [0]</td>
</tr>
<tr>
<td>$X^2$</td>
<td>15.02</td>
</tr>
<tr>
<td>$P$ value</td>
<td>0.000</td>
</tr>
<tr>
<td>Total [245]</td>
<td>13 [5.3]</td>
</tr>
<tr>
<td>Grand total</td>
<td>[538]</td>
</tr>
</tbody>
</table>

Table 3  Cytomegalovirus seroprevalence in pregnant compared to non-pregnant women.

<table>
<thead>
<tr>
<th>Group [number]</th>
<th>Number positive [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IgM</td>
</tr>
<tr>
<td>Pregnant [261]</td>
<td>25 [9.6]</td>
</tr>
<tr>
<td>Non-pregnant [277]</td>
<td>9 [3.2]</td>
</tr>
<tr>
<td>$X^2$</td>
<td>9.093</td>
</tr>
<tr>
<td>$P$ value</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Table 4  Frequency of cytomegalovirus in regard to age.

<table>
<thead>
<tr>
<th>Age group in years</th>
<th>Number</th>
<th>HSV-2, number [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>IgM</td>
</tr>
<tr>
<td>15–19</td>
<td>74</td>
<td>1 [1.4]</td>
</tr>
<tr>
<td>30–39</td>
<td>172</td>
<td>7 [4.1]</td>
</tr>
<tr>
<td>40–48</td>
<td>54</td>
<td>2 [3.7]</td>
</tr>
<tr>
<td>Chi square</td>
<td>10.9</td>
<td>12.8</td>
</tr>
<tr>
<td>$P$ value</td>
<td>0.012</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Table 5  Odd ratio of cytomegalovirus in regards to age of women lower than 30 years.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odd ratio [95% confidence interval]</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMV IgM</td>
<td>2.1003 [0.9608–4.5911]</td>
<td>0.04</td>
</tr>
<tr>
<td>CMV IgG</td>
<td>2.7061 [0.9895–7.4008]</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Results

The overall CMV seroprevalence in our study population was 95.7% and was higher in women with BOH (96.6%) compared to women with normal pregnancy (94.7%) outcomes ($X^2 = 1.169$, $P > 0.05$). Furthermore, the current CMV infection was higher in women with BOH (7.2%) than in women with normal pregnancy (5.3%) outcomes ($X^2 = 0.7$, $P > 0.05$) (Table 1). However, there was a significant difference ($X^2 = 6.206$, $P = 0.013$) in the CMV IgG seroprevalence between pregnant (93.5%) and non-pregnant (97.8%) women. In addition, the current infection, as demonstrated by IgM positivity, was significantly higher ($X^2 = 9.093$, $P = 0.003$) in pregnant women (9.6%) compared to non-pregnant (3.2%) women (Table 2).

Age significant seroprevalence variation was demonstrated for both the IgG ($X^2 = 12.8$, $P = 0.005$) and IgM ($X^2 = 10.9$, $P = 0.012$) antibodies. CMV IgG seropositivity was 100% in women aged 20-29 years, and then declined in women 20–29 years of age, but subsequently increased to 100% in women aged 40–48 years. The CMV IgM seropositivity was lowest in women 20-29 years of age (1.4%), and highest (10.1%) in women aged 20-29 years. The CMV IgM seroprevalence then declined to 3.7% in women aged 40–48 years (Table 3). OR confirmed a significant association between the age and CMV IgM (OR = 2.1003, $P = 0.04$) and CMV IgG (2.7061, $P = 0.04$) seroprevalence (Table 4). OR confirmed the association between age >30 years and CMV IgG (OR = 2.7061, $P = 0.04$) seropositivity, whereas CMV IgM seropositivity was associated with age <30 years (OR = 2.1003, $P = 0.04$) (Table 5).
All women living in rural areas were seropositive for CMV IgG, whereas in urban areas, the seropositivity was 94.2% and was significantly difference ($X^2 = 8.45, P = 0.004$). However, the current infection was significantly ($X^2 = 12.76, P = 0.000$) higher in women from urban (8.5%) areas and was not detected in women from rural (0%) areas (Table 6). OR confirmed the association between residence and CMV seroprevalence for both IgM ($OR = 26.5967, P = 0.02$) and IgG ($OR = 17.5859, P = 0.04$) antibodies (Table 7).

CMV IgG seropositivity was higher ($X^2 = 1.98, P > 0.05$) in working women (100%) compared to housewives (95.4%). However, the CMV IgM seroprevalence (current infection) was 6.8% in housewives and was not detected in working women (0%). OR showed no significant association between occupation and both IgM ($OR = 0.1619, P > 0.05$) and IgG ($OR = 2.433, P > 0.05$) antibodies (Table 7).

### Table 6 Frequency of HSV 2 IgG and IgM in regard to sociodemographic characteristics.

<table>
<thead>
<tr>
<th>Variable</th>
<th>[Number]</th>
<th>Number positive [%]</th>
<th>IgM</th>
<th>IgG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Residence</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural [140]</td>
<td></td>
<td>0 [0]</td>
<td>140 [100]</td>
<td></td>
</tr>
<tr>
<td>Urban [398]</td>
<td></td>
<td>34 [8.5]</td>
<td>375 [94.2]</td>
<td></td>
</tr>
<tr>
<td>$X^2$</td>
<td></td>
<td>12.76</td>
<td>8.45</td>
<td></td>
</tr>
<tr>
<td>$P$ value</td>
<td></td>
<td>0.000</td>
<td>0.004</td>
<td></td>
</tr>
<tr>
<td>Working [41]</td>
<td></td>
<td>0 [0]</td>
<td>41 [100]</td>
<td></td>
</tr>
<tr>
<td>$X^2$</td>
<td></td>
<td>2.99</td>
<td>1.98</td>
<td></td>
</tr>
<tr>
<td>$P$ value</td>
<td></td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td></td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Housewife</td>
<td></td>
<td>5 [14.7]</td>
<td>34 [100]</td>
<td></td>
</tr>
<tr>
<td>Working</td>
<td></td>
<td>14 [4.2]</td>
<td>321 [97]</td>
<td></td>
</tr>
<tr>
<td>$X^2$</td>
<td></td>
<td>4.95</td>
<td>6.27</td>
<td></td>
</tr>
<tr>
<td>$P$ value</td>
<td></td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uneducated</td>
<td></td>
<td>14 [20.6]</td>
<td>55 [81]</td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td></td>
<td>1 [1]</td>
<td>105 [100]</td>
<td></td>
</tr>
<tr>
<td>Secondary</td>
<td></td>
<td>14 [20.6]</td>
<td>55 [81]</td>
<td></td>
</tr>
<tr>
<td>College and above</td>
<td></td>
<td>5 [8.3]</td>
<td>59 [98.3]</td>
<td></td>
</tr>
<tr>
<td>$X^2$</td>
<td></td>
<td>0.24</td>
<td>1.12</td>
<td></td>
</tr>
<tr>
<td>$P$ value</td>
<td></td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td></td>
</tr>
</tbody>
</table>

**Bold values indicated a significance difference.**

### Table 7 Association of HSV 2 seropositivity with sociodemographic characteristics using bivariate analysis.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odd ratio [95% confidence interval]</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occupation [housewife versus official]</td>
<td>IgM 0.1619 [0.9997—2.6882]</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>IgG 0.2433 [0.0145—4.0777]</td>
<td>NS</td>
</tr>
<tr>
<td>Crowding index [&lt;3 versus &gt;3]</td>
<td>IgM 0.7105 [0.2641—1.9112]</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>IgG 0.3513 [0.0465—2.6544]</td>
<td>NS</td>
</tr>
<tr>
<td>Education</td>
<td>Uneducated [26] 16.7800 [0.9665—291.471]</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>Primary [331] 7.5870 [3.1700—18.1580]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>Secondary [105] 51.3240 [2.9950—87.9660]</td>
<td>0.006</td>
</tr>
<tr>
<td></td>
<td>College and above [68] 16.7838 [0.9665—291.471]</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>Uneducated versus educated [478] 2.8240 [1.0179—7.835]</td>
<td>0.04</td>
</tr>
<tr>
<td>Residence [rural versus urban]</td>
<td>IgM 26.5967 [1.6195—436.7827]</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>IgG 17.5859 [1.0610—291.4844]</td>
<td>0.04</td>
</tr>
</tbody>
</table>

**Bold values indicated a significance difference.**
and IgG seroprevalence (OR = 0.2433, P > 0.05) (Tables 6 and 7).

The education level significantly influenced the CMV seroprevalence for both IgM ($X^2 = 49.95, P = 0.000$) and IgG ($X^2 = 62.77, P = 0.000$) in our study population. OR confirmed this association for IgM (OR = 2.824, $P = 0.04$) and IgG (OR = 7.58–16.78, $P = 0.05$ to <0.0001) (Tables 6 and 7). Large (crowding index >3) families had higher seroprevalence for CMV IgM (8.3%) and IgG (98.3%), but OR showed a significant association between the family size and seropositivity (Tables 6 and 7).

Discussion

The present study shows a high overall seroprevalence of CMV IgG (95.7%), with no significant differences between the rate in women with BOH and those with normal pregnancy. Therefore, the susceptibility rate in our study population was 4.3%, which was higher than that reported for Turkey [14,20–23], Nigeria [24,25] and Brazil [26]. However, our study susceptibility was lower than that reported for Nepal [27], India [28], Switzerland [29], Croatia [30], Malaysia [31], Iran [15,32,33], Poland [34], Ireland [13], Russia [35], Germany [36], Azerbaijan [37], Bangladesh [38], and Brazil [39]. Compared to Arab countries, the study susceptibility rate was lower than that reported for Egypt [40], Sudan [41], Saudi Arabia [42], Syria [43], Jordan [18], Baghdad, Waset, Mosul, Al-Anbar, Al-Hila, Thi Qar, Kirkuk, Diwaniya, and Babylon [7,8,17,18,44–50].

Both the present study and global reports show a high seroprevalence of CMV IgG antibodies; however, preconceptional immunity against CMV provides incomplete protection against intrauterine transmission, and adverse outcomes can occur in infected children born to women who were seropositive prior to pregnancy [51–55].

Transplacental transmission of CMV in women with preexisting seroimmunity may occur secondary to virus reactivation [56] or to infection with a different CMV strain (reinfection) [57] during pregnancy.

Previous immunization with CMV is not absolutely protective against either reinfection or vertical transmission of infection from mother to fetus [23]. In a recent study, approximately one third of the study seroimmune women had CMV reinfection during the follow-up visit [57]. A recent review of the literature indicated that the incidence of congenital CMV infection increases with increasing maternal CMV seroprevalence [56]. The positive correlation between higher maternal seroprevalence and high birth prevalence may seem paradoxical because this suggests that a fewer number of pregnant women are at risk for primary infection. However, in a population with high seroprevalence, the number of pregnancies at risk for reactivation is also increased. In addition, the high seroprevalence may be due to a higher prevalence of risky behaviors in the population. In a population with high seroprevalence, a pregnant woman has a higher likelihood of exposure to CMV-infected people. Therefore, in a high risk population, seropositive women have a higher risk of reactivation and seronegative women have a higher risk of primary infection [58]. Preventive measures should be taken to decrease perinatal mortality and morbidity related to CMV infection and to ensure that women are not infected with CMV during pregnancy. Pregnant women should be consulted and encouraged to implement these preventive measures. Routine nationwide screenings for CMV should be considered, although serious cost effectiveness issues must be evaluated before the implementation of such screenings.

In Kirkuk, the CMV seroprevalence is as high as 95.7%. Routine CMV screening in such a population is unnecessary, but there are exceptions. Pregnant women who had contact with a patient with a proven acute CMV infection, as well as patients with upper respiratory system infection-like symptoms, hepatomegaly, elevated liver enzymes, lymphadenopathy and immunocompromised statuses should all receive screening [23]. Therefore, a routine screening test is usually justified only for conditions with an expected high rate of infection, conditions that have a proven mode of prevention and conditions for which the screening method is safe and inexpensive. Currently, routine screening for CMV is not recommended because of the high prevalence of seropositivity. Because there is no consistently effective treatment for congenital CMV infection, testing is clinically useless and expensive. However, Nigo et al. [59] recently reported promising results for passive immunization against congenital CMV infection.

In the current study, there was no significant difference in the CMV seroprevalence between pregnant (97.2%) and non-pregnant (96%) women with bad obstetric history. However, there was a significant difference between the pregnant (88.9%) and non-pregnant (100%) women with a previous normal pregnancy ($X^2 = 15.02, P = 0.000$). Furthermore, the CMV IgG seroprevalence was significantly ($X^2 = 6.206, P = 0.013$) higher in non-pregnant (97.8%) compared to pregnant (93.5%) women, and OR confirmed the association between rubella IgG seropositivity and pregnancy.
CMV IgG seroprevalence in our study population ranged from 92.4% to 100% across age groups and showed no significant trends with age. However, there was a significant \( (X^2 = 12.8, \ P = 0.005) \) difference in seroprevalence among the age groups. In addition, the women aged 30 years and above had the highest prevalence of CMV IgG (97.7%, 221/226) compared to women in aged <30 years (94.2%, 294/321). This difference was significant by OR calculation (OR = 2.7061, \( P = 0.04 \)). This could be because as women age, their interactions and encounters with risk factors increase [60]. Our finding was consistent with that reported for other geographical areas [23,41,60–62]. The seroprevalence of CMV in women between the ages of 15 to 19 years was high (100%). This high seroprevalence may be attributed to the wide practice of breastfeeding during infancy [63]. Breastfeeding is a significant source of CMV transmission to children and plays an important role in the epidemiology of CMV infection because the virus is reactivated during lactation in nearly every seropositive mother [64]. In addition, close contact and crowdedness in primary and secondary schools may contribute to this increase in CMV seroprevalence [65]. The antibody prevalence was reduced (92.4%) in 20–29-year-old age group. This finding is not consistent with that reported for the USA, in which the seroprevalence increased steadily with age [66]. However, this result was consistent with that reported for Portugal [62]. Studies with similar age groups conducted in other countries, such as the USA, Japan, France, England, Poland, and Russia, report seroprevalences ranging between 51.5% and 78% [35,67–72].

The seroprevalence of women with CMV IgG gradually increased in the two oldest age groups, with values of 97.1% and 100%, suggesting that sexual transmission was an important route of viral transmission [73]. Another recognized source of adult CMV infections are children. CMV infected children shed virus in their saliva and urine for years, providing an opportunity for continued spread to other children and susceptible adults, such as close relatives and teachers [74,75].

It should be noted that in our study, 6.5% of the pregnant women were susceptible to CMV and 9.6% of the pregnant women had a current infection that led us to conclude that there is considerable risk for congenital infection caused by maternal primary CMV infection, which leads to fetal infection in approximately 40% of cases (6% congenital infection in our cohort) [76]. In this risk group, we must use approaches to prevent congenital CMV infections, which include the improved hygiene of seronegative women and the administration of hyperimmune globulin to pregnant women with primary infection or pregnant women with previous infections who have CMV antibody titers or low IgG avidity [77].

Child-to-mother transmission of CMV during pregnancy in seronegative women may be controlled or prevented by simple hygiene, such as frequent hand washing, wearing gloves for specific childcare tasks and avoiding intimate contact with their child, including sharing utensils, food or towels, and kissing on or near the mouth [78–80].

Despite advances in the diagnosis of maternal–fetal CMV infection and approaches to prevent congenital CMV, an effective prenatal therapy is unavailable. A prospective, non-randomized study of pregnant women who acquired CMV infection during pregnancy and who received passive immunization with CMV HIG, showed that this therapy was associated with a significantly reduced risk of congenital CMV disease and infection and had no adverse effects [77,81,82]. Recent case reports support the safe administration of oral ganciclovir to mothers of CMV-infected fetuses, with no teratogenic side effects when administered during the early stages of pregnancy [77,83,84]. The efficacy of ganciclovir remains to be defined in controlled trials. Other studies regarding the treatment of intrauterine CMV infection using maternal oral administration of valaciclovir showed that it significantly decreased the viral load in fetal blood and could potentially reduce the morbidity of prolonged intrauterine infection [85]. The absence of adverse effects or teratogenicity with valaciclovir is compatible with its clinical use, but a well-designed, randomized controlled trial is necessary. Currently, there is no approved vaccine for CMV, but two vaccines are in phase II studies. One vaccine is a recombinant vaccine containing the major envelope glycoprotein B of the virus with the adjuvant MF59 (gB/MF59) that induces high levels of neutralizing antibodies and is safe and immunogenic in adults and infants, and also prevents maternal CMV infection [86,87]. The other vaccine is the live attenuated CMV Towne strain that stimulates neutralizing antibodies comparable to those induced by the wild type virus and protects renal transplant patients from severe CMV following transplantation [81,88].

The primary intervention for the prevention of CMV infection should be aimed at women who wish to become pregnant, women who care for children and immunocompromised individuals. These individuals to whom CMV exposure is the most detrimental are the target groups for possible administration of a future vaccine [62].

In this study, rural residents had the highest CMV IgG prevalence of 100%, whereas for urban
residents, the CMV IgG seroprevalence was 94.2% ($X^2 = 8.45, P = 0.004$). The association between CMV IgG seroprevalence and residence was confirmed by OR calculation (OR = 17.5859, $P = 0.04$), which is consistent with observation that low socioeconomic status is a strong risk factor for CMV infection [89]. Our finding was consistent with that reported for other geographical areas [60,90].

In relation to educational status, the CMV IgG seroprevalence was higher in uneducated (100%), primary (97%) and secondary (100%) educated women, whereas it was lower (81%) in women with college level and higher education ($X^2 = 62.77, P = 0.000$). OR confirmed the association between CMV IgG seroprevalence and uneducated women (OR = 16.78, $P < 0.05$), primary educated (OR = 7.587, $P < 0.0001$), secondary educated (OR = 51.324, $P = 0.006$) and college level and higher educated (OR = 16.7838, $P = 0.05$) women. This finding is consistent with that reported for other countries [41,60]. Illiteracy and low education levels were previously observed as risk factors for increased susceptibility to CMV infection, perhaps through direct contact with contagious secretions from their own children and poor hygiene practiced by these women [89,91–93].

Likewise, low socioeconomic status is a strong risk factor for CMV infection [89]. However, in Iraq, it is difficult to investigate the socioeconomic status of these pregnant women because the culture is based on an attitude of generous hospitality toward guests and family members who usually live in extended families.

There was a higher prevalence of CMV IgG among working women compared to housewives, but this difference was not significant. Using bivariate analyses, OR showed no significant association between occupation and CMV IgG seroprevalence. This finding is consistent with that reported by others [60]. By contrast, a previous study indicated that CMV IgG seropositivity occurred more often in housewives compared to women with other occupations [38].

The present study shows a higher CMV IgG seroprevalence in large families (crowding index >3) (98.3%) than in small families (95.4%), but the difference was not significant. In addition, OR showed no association between the crowding index and CMV-IgG seropositivity, which was consistent with other reports [92]. Housing crowdedness and family size are imperfect measures of the transmission dynamics that actually determine an individual’s risk of exposure [93]. No significant association was found between the prevalence of congenital CMV and a mean household size of more than 3.0 persons. Previous studies suggest a positive correlation of congenital CMV with a household size of more than three persons and low socioeconomic status [75,58,94,95].

CMV IgM seroprevalence in the women included in this study was 6.3% and varied significantly between pregnant (9.6%) and non-pregnant (3.2%) women ($X^2 = 9.093, P = 0.003$). Although the CMV IgM seroprevalence was higher in women with bad obstetric history (7.2%) compared to women with a normal pregnancy (5.3%), the difference was not significant. However, the current infection of 9.6% and 6.5% in seronegative and pregnant women, respectively, represents a high rate of risk for fetal infection.

Globally reported CMV IgM seropositivity ranges from 0% for Turkey [22] to 13% for Poland [34] in pregnant women and from 0% for India [28] to 8.42% for India [6]. In Arab countries, the range of CMV IgM seropositivity was from 2.3% for Jordan [18] to 57.2% for Babylon, Iraq [17] in pregnant women, whereas in women with BOH, it ranged from 1.4% for Jordan [18] to 60.2% for Waset, Iraq [7]. Therefore, the findings of the present study for women with normal pregnancy and with BOH are within the reported ranges worldwide and for Arab countries. However, the current CMV infection rate in our study was similar to that reported for Waset [7], Babylon [17], Diwaniya [50], Mosul [8], Baghdad [44,49,96], and Al-Hila [45]. In addition, the rate was similar to that reported for Thi Qar [47] and Kirkuk [48].

The CMV IgM seroprevalence varies significantly by age ($X^2 = 10.9, P = 0.012$), with the highest rate of current infection (8%) in young women (<30 years) compared to older women (>30 years) (4%, $X^2 = 3.6, P = 0.05$). This finding is consistent with previous studies, which showed that elderly persons appear to be protected against CMV infection because of the accumulation of CD28 effector cytotoxic T lymphocytes [60]. This is a characteristic feature of all age groups but is most pronounced in elderly persons [97]. However, there is considerable debate regarding maternal age and CMV infection. Many investigators have observed that elderly women were at a higher risk of CMV infection [60,89], whereas others have reported the reverse [98] or absence of variation by age [66]. All the above findings are consistent with the understanding that CMV IgM can be produced over the course of a lifetime after primary infection or as the result of reinfection or reactivation [99,100]. This suggests that some older cohorts may be as likely to have recurrent episodes of CMV as younger people are to have a primary infection [66].

Risk factors based on residence (OR = 26.5967, $P = 0.02$), education (OR = 8.5842, $P = 0.0001$), age (OR = 2.1003, $P = 0.04$) and pregnancy (OR = 3.1544,
However, Staras et al. [67] reported that age was not a risk for CMV IgM seropositivity, but confirmed that age was a risk for CMV IgG seropositivity. The lack of identifiable risk factors for CMV IgM may be because of the relatively small number of observations, and because over 80% of the IgM reactivity in the tested sample was with high avidity and therefore presumably from a non-primary CMV infection, which may be less associated with identifiable risk than a primary infection [66]. In addition, a portion of the IgM positive sera may have been false positive determinations, which is known to occur with CMV IgM testing [101].

The current CMV infection was more predominant in urban women (8.5%), and this finding was not consistent with previously reported studies [60,96,102]. In addition, there were no significant differences for the current CMV infection with regard to occupation; however, the current infection was significantly different between poorly and highly educated women ($X^2 = 5.53, P < 0.0001$). Kolo et al. [60] reported a high prevalence of CMV IgM in pregnant women with primary education, which is consistent with reports from the United States and Western Europe.

In conclusion, maternal CMV infection in Kirkuk, Iraq population still represent a health problem that should be considered by local healthcare providers.

**Conflict of interest**

No conflicts of interest.

**Financial support**

Kirkuk Health Authority.

**References**


