Human cytomegalovirus and relationship with abortion among Iraqi females: a systematic review

Qabas Naser Kareem¹, Areej Atiyah Hussein¹, Shahad Khudhair Khalaf ¹

Abstract

Background: Human cytomegalovirus (HCMV) seroprevalence is a significant health problem, especially among pregnant women in lower socioeconomic societies. This study aims to explore the prevalence of HCMV infections among women in Iraq.

Methods: A systematic review was designed to collect and summarize articles concerning the relationship between HCMV infection and abortion in Iraq. We identified the titles and abstracts of the publications from 2008 to 2022. A pre-defined keyword was recruited to recognize the publications and filter the articles to eliminate duplication and remove irrelevant articles. In the reviewed studies, the HCMV was detected using diagnostic methods such as enzyme-linked immunosorbent assay and immunochromatography (rapid test) or molecular methods such as polymerase chain reaction.

Results: Twenty-four eligible articles have been included in this review sourced data from about 5442 patients covering 15 of 18 provinces in Iraq. The prevalence of HCMV IgG and IgM was (0%-100%) and (0%-93%), respectively. Many factors influenced the varied results, including the design of the study and sociodemographic and clinical aspects.

Conclusion: The high prevalence of HCMV infection indicates a causative relationship with repeated abortion among Iraqi females.

Keywords: Human Cytomegalovirus, Prevalence Rate, Congenital Infections, Abortion, Female, Iraqi

Background

Human cytomegalovirus (HCMV) is a widespread herpes virus. According to the Centers for Disease Control and Prevention (CDCs) and the World Health Organization (WHO), human cytomegalovirus infects people of all ages, and approximately one-third of children by the age of five in the United States are infected [1]. The prevalence of HCMV is about 100% in Africa and Asia and 80% in Europe and North America [2]. Germany recorded an infection rate of 56.7%, with a higher seroprevalence in women (62.3%) than in men (51.0%) [3]. Human cytomegalovirus is endemic in many countries, and the seropositivity of HCMV varies from 30-100%, depending on the region [4]. Human cytomegalovirus infection goes undiagnosed in healthy children and adults.

However, some high-risk categories, such as immunocompromised organ transplant recipients, hematopoietic stem cell transplant recipients, and HIV-positive individuals, are in danger of developing life-threatening and vision-threatening HCMV diseases [5]. In low- and middle-income countries, the prevalence of prenatal HCMV infection is estimated to range between 0.7% and 5% of all neonates [6]. Roughly 5-30% of children aged 5-6 years in high-income countries are human cytomegalovirus seropositive, compared to 85-95% in low- and middle-income countries, which renders it a national health threat to the latter countries [7].

The HCMV, commonly known as human herpesvirus 5 (HHV-5), is a member of the herpes viral family's beta herpes virus subgroup [8]. The transmission of the virus is mainly by vertical transmission from a mother to her fetus or infant [9], Then by infected persons’ breast milk, saliva, and urine [10]. However, transmitted through sexual activity in pregnant women and teenagers [11]. Congenital HCMV transmission rates are as high as 50.0% in women who get the HCMV

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infection during pregnancy and fewer than 2.0% in women who do not get primary HCMV infection [12]. Even though there are numerous causes of abortion, more than 50.0% of cases are still idiopathic. Most miscarriages occur in the first trimester of pregnancy, accounting for roughly 80.0% of unplanned fetal deaths, resulting from signs like bleeding and discomfort that increase maternal worry [13].

Several studies showed that viruses such as human cytomegalovirus; enterovirus, human herpes simplex virus (type 1 and type 2), human parvovirus B19, varicella-zoster virus, and adenovirus are causative agents of spontaneous abortion [14-16]. Human cytomegalovirus can infect and act in the cytoplasm and nucleus of infected cells, creating inclusions. It also can elude the immune system [8]. HCMV is the most common cause of intrauterine infection-induced congenital disabilities in humans. The HCMV infection can lead to abortion or stillbirth. Ventricular encephalitis and microglial nodular encephalitis are two distinct symptoms of HCMV infection [17]. Human cytomegalovirus can be pathogenic by direct organ damage that can make human cytomegalovirus dangerous by lowering host defenses against other microbes and/or increasing the body’s inflammatory response, as in acute respiratory distress syndrome [18].

A glandular fever (mononucleosis) condition marked by flu-like symptoms, or a prolonged fever, are clinical symptoms of primary infection. Elevated lymphocyte counts and liver transaminase levels may be detected in laboratory tests [19]. The infection might be asymptomatic or produce severe problems at delivery in pregnant women. 10-15% will have intrauterine growth retardation, microcephaly, retinitis, jaundice, and hepatosplenomegaly, and 20-30% will die, causing irreversible harm. Mental retardation, deafness, and blindness account for 50-80% of the cases [20, 21].

In approximately 10% of infected neonates, signs involve unilateral or bilateral deafness, loss of vision, optic atrophy, strabismus, chorioretinitis, hydrocephalus, enlargement of the liver and spleen, decrease in platelet number, and jaundice [22]. About 15% of asymptomatic infected newborns develop neurological sequelae before five years of age [23]. The method of diagnosis depends on the presence of IgM, and low IgG avidity in the urine and saliva is used to diagnose acute maternal HCMV infection. Fetal infection is often confirmed using polymerase chain reaction (PCR) of the amniotic fluid and viral culture of the urine and saliva [24]. The polymerase chain reaction has been recognized as the gold standard for identifying systemic HCMV infections by blood samples, with a sensitivity of 80.1% and specificity of 93.0% [25].

The treatment of the virus by using Valganciclovir to start treatment in AIDS patients with HCMV retinitis [26]. The nucleoside analogs Valganciclovir and Ganciclovir (GCV) block the viral DNA polymerase. Cidofovir and foscarnet, both second-choice medicines, block the viral polymerase over the polymerases of the cells [27]. Letermovir (Prevymis) is a new antiviral against human cytomegalovirus that targets the HCMV terminase complexes [28]. Maribavir is another favorable anti-HCMV drug, which is taken orally and targets the viral kinase [29], which has a vital role in the formation of the viral structure, assembly complex, and viral release [30]. In the profile of Iraq, human cytomegalovirus infection was under the eyes of Iraqi researchers over the last three decades. Various studies have been conducted depending on the study objective and the population involved [31-54]. Lazim and Kadhim [55] reviewed 46 CMV-related articles published in Iraq between 2007-2015. Most of the reviewed articles discussed the relation of CMV to abortion among pregnant women. In this study, we systematically reviewed the HCMV-related articles to identify the seropositive anti-HCMV IgG and IgM rates among Iraqi women.

Methods
Design and Protocol
This systematic review was conducted according to PRISMA (The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions: Explanation and Elaboration) Guidelines and Guidance [56]. However, the current review has no pre-published protocol and is not registered in any systematic review registers.

Criteria for inclusion and exclusion
All research (original research, case report, systematic and meta-analysis) designed to estimate the prevalence of HCMV infection among Iraqi females who suffered from repeat abortion were considered for inclusion. Articles should be published in peer-reviewed English journals. All studies articles not written in English designed to estimate other causes of abortion with HCMV infection as co-infection; the studies conducted in females younger than 18 years and HCMV seronegative were excluded.

Search methods for eligible literature
The highly-indexed electronic databases (PubMed, Elsevier, science direct, Google Scholar, and academic scientific Iraqi journals website) have been searched for literature on women suffering from abortion in Iraq. The database search was restricted to English to make it easier for all authors who took part in the literature search to understand. The last date of the database search was July 31, 2022. The keywords used for the search are described here: ‘aborted women’, ‘ women with abortion’, ‘ prevalence of HCMV’, ‘ HCMV with abortion’, ‘ infectious agent caused abortion’, and ‘ abortion in Iraqi women’. Eligible literature was also selected from the reference list of articles that met the inclusion criteria.

Article screening and selection
We used the databases mentioned above and the search mentioned above criteria to find articles. For the study, we used a four-stage technique (Figure 1).

Step 1: A total of 97 articles were retrieved for the identification of articles using mentioned search criteria.

Step 2: After reading the titles and abstracts in accordance with the goals of the study to identify possibly pertinent papers, 33 articles were excluded due to duplication.

Step 3: We evaluated the complete texts using the eligibility and inclusion standards. Due to mismatched content, 22 articles were omitted.

Step 4: When the predetermined exclusion criteria were applied, 18 articles were disqualified. As a result, we included 24 articles in the comprehensive final review.
Authors’ role
The review authors carefully searched the literature and evaluated the pertinent material for inclusion and eligibility. Assessment bias has decreased due to group discussions that led to decisions. In other situations, a second party’s opinion was required.

![PRISMA 2009 diagram](image)

Results
Scope of this review
The database search showed ninety-seven citations. Duplication was detected in twenty-three articles. Further, thirty articles were excluded due to non-matching and ineligibility criteria. Figure 1 presents the steps used in the selection process. In this systematic review, we included twenty-four matching the inclusion and exclusion criteria and were conducted from 2008 to 2022. These articles sourced data from 5442 aborted or repeatedly aborted Iraqi females covering 15 of 18 Iraqi provinces. The reviewed articles reported information about the design of the study, population, when and where the study was conducted, and the prevalence of HCMV IgG and IgM among the aborted females (Table1).

Maternal HCMV Seroprevalences in Iraqi Women with Abortion
The current review was designed to determine the prevalence rate of HCMV among aborted women in our population. Basically, the reported HCMV IgG and IgM among the studied sample in each study were considered the base to indicate the prevalence rate of HCMV infection. In our review, some studies reported low HCMV infection rates, and others reported high HCMV infection rates among aborted women based on the immunological methods. The immunological techniques included latex agglutination test, immune chromatography (Rapid test), enzyme-linked immunosorbent assay (ELISA), or molecular methods such as PCR and RT-PCR. Depending on the study design, population, sociodemographic and clinical characteristics, the rates of IgG and IgM in the reviewed studies vary between 0%-100% and 0%-93%, respectively. Compared to a review study by Lazim and Kadhim [55], the number of articles discussing the HCMV seroprevalences and their relationship with abortion among Iraqi women significantly increased. The HCMV has attracted the interest of Iraqi researchers. Many articles have been published after 2007 referring to improvement in research activity in Iraq. AL-Jurani [31] conducted a serological test among 92 pregnant women attending primary healthcare centers in Baquba city, Diyala province. The author did not find any positive cases for anti-HCMV IgM. A descriptive correlational study conducted by Ghailani and Mohammed [32] among 100 women with...
pregnancy loss at the General Kirkuk Hospital, Azadi Teaching Hospital, and Al-Nasr Hospital in Kirkuk city reported 37.0% for IgG and 1.0% for IgM, respectively. A brief report published by Hussein and Balatay [33] in the north of Iraq reported a seroprevalence rate of 2.27% (29 out of 1275 aborted women) for anti-HCMV IgM antibodies among 1275 women with early pregnancy loss. The authors recruited an ELISA test to examine 575 women from Duhok province, 189 women from Sulaimania province, 201 women from Zakho city, 150 women from Akra city, and 160 samples from Amedi city, respectively. Another study by Yaser et al. [34] reported a 60.63% (97/160) prevalence rate of HCMV among pregnant women using an Enzyme immunoassay and PCR amplification test in the Al-Najaf Public Health Laboratory. The authors reported positive IgG antibodies among 59.38%, indicating the presence of chronic HCMV infection, compared to two cases (1.25%) with positive IgM antibodies referring to acute HCMV infection. An interesting study was conducted by Al-Mishhadani and Abbas [35] among women who attended Al-Gailani Medical Laboratory (private laboratory) in Al-Anbar Governorate (west of Iraq). The authors found that ‘seropositivity rates of anti-CMV IgG (90.4%) and IgM (6.1%)’ were higher among the aborted women than in the normal control group (82.7% and 3.6%), respectively. Moreover, the authors reported that the prevalence rate of CMV infection increased with the increasing age of aborted women and the number of abortions. Khudhair et al. [36] found that the anti-HCMV IgM antibody seroprevalence was 6.92% among 180 aborted women who attended Al-Battol Teaching hospital for Maternity and Children, the outpatient clinic in Baquba Teaching Hospital. Ali KS [37] conducted a case-control study of women with abnormal pregnancies who attended the emergency unit of maternity teaching in Erbil city. The author found that the seroprevalence of HCMV- IgM, and IgG was 8.0% and 100%, respectively. The author also detected an association between the history of abortion and CMV-specific IgM seroprevalence. Aljumaili et al. [38] conducted an interesting case-control study among women with bad obstetric history (BOH) and their counterparts. The authors reported that pregnancy and sociodemographic factors (age, residence, and education) were significantly associated with acute CMV infection. The authors found that women with a bad obstetric history presented 8.3% for HCMV IgM and 98.3% for HCMV IgG. Al-Azzawi [39] screened pre-marital women for the presence of IgG and IgM antibodies against CMV by ELISA test. Among one hundred and sixty-one examined sera, the IgG and IgM antibodies were identified at 36% and 9.9%, respectively. The author also found that young women (30-35 years) and urban residents were statistically associated with a rising in seropositivity of HCMV. Al-Baiati et al. [40] examined 152 aborted women to discover the prevalence of HCMV infection at the Kamal Al-Samarrae Hospital and Al-Yarmouk Teaching Hospital for infertility. The authors found that the percentages of IgG and IgM were 85%, and 10%, respectively. Al-Dorri [41] examined 128 aborted women who attended Tikrit Teaching Hospital in Salah Al-Deen province. The author found that 21 out of 128 (16.40%) aborted women presented with seropositive HCMV. Furthermore, among the 21 seropositive cases, 15(71.42%) for IgG Ab and 6 (28.57%) for IgM Ab 6 (28.57%). Al-Saeed et al. [42] examined 44 sera of females who attended the Hospital of Children and Maternity and General Teaching Hospital in Al-Hilla city from November 2006 until April 2007. The authors found that 35(79.5%) and 8(18.8%) were positive for anti-CMV IgG and IgM antibodies, respectively. Ali et al. [43] screened pregnant and miscarriage women for HSV and CMV in Baghdad. The authors found that among the 420 examined sera of pregnant women, 81(19.3%) were positive for HCMV. Jihad and Rehab [44] reported in their case-control study among fifty sera women who had repeated miscarriages due to HCMV at the infertility clinic of Kamal Al-Samarrae hospital, Baghdad. The authors found higher seropositive anti-HCMV IgG and IgM in 40% and 25% of miscarriage women than in the control group of infertile women, where the seropositive anti-HCMV IgG and IgM were 20%, and 15%, respectively. Raisin and Al-Amara [45] conducted an interesting study to detect the relationship between heat shock protein 70 (HSP70) concentration and CMV infection in a sample of 160 aborted women suffering from repeated embryo predictions in Basrah province, south of Iraq. The authors found that the level of anti-HCMV IgM antibody was statistically higher among the age group (26-30 years) than other age groups at a rate of 26.7%. In contrast, the level of anti-HCMV IgG was higher among the age group (31-35 years) and (36-40 years) at a rate of 100 % using the ELISA test. A case control conducted by Khudhair and Al-azzawi [46] reported a 32.8% prevalence rate of anti-HCMV IgM among 122 pregnant women admitted to Al-Elwiya Maternity Hospital in Baghdad; however, the prevalence of anti-HCMV IgM was 14.7%. Recently, Naame et al. [47] conducted a case-control study among 120 aborted women attending the Public Health Center in Ibn -Ghazwan and Basra hospital in Basra city. The authors reported a 30.8% prevalence rate of anti-HCMV IgG and 2.5% of anti-HCMV IgM, respectively. A cross-sectional study conducted by AL-Ouqaili and AL-Karboli [48] to identify the possible role of anti-cytomegalovirus IgM and IgG antibodies in diagnosing CMV infection in women with recurrent fetal loss in Ramadi City, West of Iraq. The authors found that during the first trimester, the seropositive anti-HCMV IgM and IgG antibodies were 33.3%, and 28.5% among 87 asymptomatic pregnant women, respectively. The authors also concluded the increased liability of HCMV transmission of infection in the uterus to the fetus. Saad et al. [49] reported that the seropositive anti-HCMV IgM was 35.38 among 130 women with Bad obstetric history (BOH) included in the case-control study conducted in Kerbala province. In Diyala province, Baquba city, Hussein et al. [50] collected conceptus tissues of 50 pregnant females with spontaneous abortion admitted to Al-Batool Teaching Hospital for Maternity and Children. The author found that the prevalence of HCMV rate was 36.0%, and the highest rate was among the age group 26-35 years. A study conducted at Al-Karama Hospital and Al-Zahra Hospital of Wasit province reported 43.9% of HCMV IgM among 750 aborted and pregnant women [50]. Al-shammary [51] examined the sera of 750 pregnant women in Al-Karama hospital and Al-Zahra hospital of Wasit province to identify the congenital anomalies in embryos among aborted and pregnant women. The author found that the seropositive anti-HCMV IgM was 43.9%. Moreover, the author reported that the prevalence of HCMV infection significantly increased with the age of pregnant women and embryos at (22-26) weeks of pregnancy. Recently, Saeed et al. [52] collected sera of one hundred and fifty
pregnant women knowing with bad obstetric history (Group I) and Group II including one hundred and fifty primigravida pregnant women knowing with a history of aborted during (first, second, and third trimesters of pregnancy). The authors found that the seropositive anti-HCMV IgM was (53.0% in group I compared to 32.6% in group II. At the same time, the seropositive anti-HCMV IgG was 74% in group I compared to 61.3% in group II. Al-Mousawi and AL-Hajjar [53] reported that among seventy aborted women included in the study at a consultant clinic for infertile women in Babylon province, the seropositive anti-HCMV IgG was 93.0%, compared to 0.07% for the seropositive anti-HCMV IgM. In Al-Najaf city, Hamoud et al. [54] compared one hundred samples of recurrent pregnancy loss (RPL) with one hundred samples having no history of miscarriage. The findings showed no significant difference between the two groups; the seropositive anti-HCMV IgG was 98.0% among the RPL and 96.0% among the other group.

Table 1: The seropositive anti-HCMV IgG AND IgM among Iraqi women

<table>
<thead>
<tr>
<th>HCMV Prevalence Groups</th>
<th>Rate of positive IgG</th>
<th>Rate of positive IgM</th>
<th>Governorate of Study</th>
<th>No. of Cases in the Study</th>
<th>Study design</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low prevalence group IgM (0%-11%)</td>
<td>0%</td>
<td>0%</td>
<td>DIYALA</td>
<td>92 pregnant women</td>
<td>Cross-sectional Study</td>
<td>AL-Jurani 2014 [31]</td>
</tr>
<tr>
<td></td>
<td>37%</td>
<td>1%</td>
<td>Kirkuk</td>
<td>100 women</td>
<td>Descriptive study</td>
<td>Ghailan and Mohammed 2020 [32]</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>2.27%</td>
<td>Kurdistan (Duhok, Sulamania, Zakho, Akra, and Amedi)</td>
<td>1275 women (575 from Duhok, 189 from Sulamania, 201 from Zakho, 150 from Akra, and 160 from Amedi)</td>
<td>Cross-sectional study</td>
<td>Hussein and Balatay 2019 [33]</td>
</tr>
<tr>
<td></td>
<td>60.63%</td>
<td>1.25%</td>
<td>Al-Najaf</td>
<td>160 women</td>
<td>Case-control study</td>
<td>Yasir et al. 2020 [34]</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>6.10%</td>
<td>Al-Anbar</td>
<td>230 women</td>
<td>Cross-sectional study</td>
<td>Al-Mishhadani and Al-Janabi 2008 [35]</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>6.92%</td>
<td>Diyala</td>
<td>180 women</td>
<td>Cross-sectional study</td>
<td>Khudhair et al. 2017 [36]</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>8%</td>
<td>Erbil</td>
<td>75 women</td>
<td>Case-control study</td>
<td>Ali 2020 [37]</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>8.30%</td>
<td>Kirkuk</td>
<td>245 women</td>
<td>Descriptive study</td>
<td>Aljumaili et al. 2014 [38]</td>
</tr>
<tr>
<td></td>
<td>36.0%</td>
<td>9.90%</td>
<td>Baghdad</td>
<td>152 women</td>
<td>Cross-sectional study</td>
<td>Al-azzawi 2012 [39]</td>
</tr>
<tr>
<td></td>
<td>85%</td>
<td>10.0%</td>
<td>Baghdad</td>
<td>152 women</td>
<td>Cross-sectional study</td>
<td>Al-Batati et al. 2014 [40]</td>
</tr>
<tr>
<td>Moderate Prevalence Group IgM (12%-30%)</td>
<td>-</td>
<td>16.40%</td>
<td>Salah Al-deen</td>
<td>128 women</td>
<td>Cross-sectional study</td>
<td>Al-dorri 2018 [41]</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>18.8%</td>
<td>Al-Hilla</td>
<td>120 women</td>
<td>Case-control study</td>
<td>Al-Saheed et al. 2008 [42]</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>19.3%</td>
<td>Baghdad</td>
<td>420 women</td>
<td>Comparative study</td>
<td>Ali et al. 2019 [43]</td>
</tr>
<tr>
<td></td>
<td>40%</td>
<td>25%</td>
<td>Baghdad</td>
<td>100 women</td>
<td>Case-control study</td>
<td>Jihad 2015 [44]</td>
</tr>
<tr>
<td></td>
<td>100%</td>
<td>26.7%</td>
<td>Basrah</td>
<td>160 women</td>
<td>Cross-sectional study</td>
<td>Raisan and Al-Amara 2020 [45]</td>
</tr>
<tr>
<td></td>
<td>32.78%</td>
<td>14.7%</td>
<td>Baghdad</td>
<td>122 women</td>
<td>Case-control study</td>
<td>Khudhair and Al-Azzawi 2018 [46]</td>
</tr>
<tr>
<td>High Prevalence Group IgM 31%-100%</td>
<td>-</td>
<td>30.8%</td>
<td>Basrah</td>
<td>120 women</td>
<td>Case-control study</td>
<td>Naame et al. 2021 [47]</td>
</tr>
<tr>
<td></td>
<td>28.50%</td>
<td>33.3%</td>
<td>Ramadi</td>
<td>87 women</td>
<td>Cross-sectional study</td>
<td>AL-Ouquaili, and AL-Karbol 2010 [48]</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>35.38%</td>
<td>Kerbala</td>
<td>130 women</td>
<td>Case-control study</td>
<td>Saad et al. 2013 [49]</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>36%</td>
<td>Diyala</td>
<td>50 women</td>
<td>Cross-sectional study</td>
<td>Hussein et al. 2017 [50]</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>43.9%</td>
<td>Wasit</td>
<td>750 women</td>
<td>Cross-sectional study</td>
<td>Al-shammary 2014 [51]</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>53%</td>
<td>Baghdad</td>
<td>300 women</td>
<td>Cross-sectional study</td>
<td>Saeed et al. 2022 [52]</td>
</tr>
<tr>
<td></td>
<td>89%</td>
<td>93%</td>
<td>Babylon</td>
<td>90 women</td>
<td>Comparative study</td>
<td>Al-Mousawi, and AL-Hajjar 2020 [53]</td>
</tr>
<tr>
<td></td>
<td>95.09%</td>
<td>0%</td>
<td>Al-Najaf</td>
<td>204 women</td>
<td>Case-control study</td>
<td>Hamoud et al. 2021 [54]</td>
</tr>
</tbody>
</table>
Discussion

Generally, the differences in the prevalence of HCMV infections in the above studies may be related to the difference in the geographical region, the sample, and the study's design. The age of women included in each study had a possible role in the distribution of infection. Jerman et al. [57] studied the characteristics of abortion women (2008-2014) in the United States of America. The authors reported that the most spontaneous and first abortions occur in women in the age group 20-24 years, and the lowest cases of miscarriage occur in women above 30 years. Cannon [58] reported that the acquisition of HCMV in a population is characterized by an age-dependent rise in seroprevalence, closely related to socioeconomic status and race. Another factor is the type of HCMV infection in another ward; acute infections are more frequently transferred to the fetus and more likely to cause fatal harm than recurrent infections [59]. Due to latency after the first infection and reactivation of viral infection causing recurrent symptoms, HCMV transmission in the womb [60]. Living in developed countries had an influential title role in delivering HCMV rates. Zhang et al. [61] showed that the seropositivity of HCMV in adults varies from 55% in developed countries to more than 90% in developing countries. Regarding financial status, the recurrence of human cytomegalovirus is the most common cause of a severe disease which is higher in the developed countries among lower financial strata [62]. A variety of factors can bring on fetal injury, including a woman's immune system, deficiencies in "trophoblast progenitor stem cell differentiation" and function, extravillous trophoblast invasiveness, dysregulation of "Wnt signaling pathways" in cytotrophoblasts, tumor necrosis factor-mediated trophoblast apoptosis, HCMV-induced cytokine changes in the placenta, and inhibition of indoleamine 2,3-dioxygenase [63,64]. The virus was detected by serological tests, which are very accurate and sensitive, and even though antibodies may decrease with aging and chronic immunosuppressive, IgG seroprevalence is frequently lifelong. The ability to detect the virus is constantly improving, and nucleic acid assays like the polymerase chain reaction are now available at developed centers [65]. The variances in the sensitivity and specificity of the serologic markers utilized in various studies of Iraq could be the cause of these inconsistencies. The high seroprevalence in women between the ages of 26 and 35 years is consistent with earlier research that linked it to these women's exposure to school-age children, particularly as their children started going to school [66], for the need for routine screening in antenatal clinics. Regional differences necessitate local adaptation of national HCMV infection prevention and management policy. Therefore, the widespread practice of breastfeeding throughout infancy in Iraq may also be responsible for the high seroprevalence because breastfeeding is one of the main routes of transmission of infection [67]. On the other hand, the study that reported the low rate of infection due to maternal IgM test findings that are positive is used to confirm the diagnosis of acute HCMV infection in pregnancy [40]. Additionally, samples taken too early during the primary infection may not have detectable levels of IgM, and it may emerge after CMV reactivation. Thus, a negative IgM result does not always rule out the initial infection with CMV [68].

The HSV family of viruses includes HCMV, which has a strong affinity for humans. The first phase of viral replication and shedding with body fluids, such as saliva, breast milk, urine, and vaginal secretions, follows primary infection with the virus. A viremia and, in some instances, an infectious mononucleosis phase follow this. After that, the infection enters a latent phase. While an effective vaccine is being developed, the ongoing relationship between inferior socioeconomic situations, such as overcrowding, breast milk transfer, and high HCMV seroprevalence, presents an opportunity to address this issue [69].

Conclusion

Out of seventy-nine studies published in Iraq between 2008 to 2022, twenty-four articles have undergone systematic review. About 5442 Iraqi women were included in these studies. The reviewed articles covered 15 provinces out of 18 in Iraq, indicating the generalization of the study findings. The prevalence of HCMV IgG and IgM was (0%-100%) and (0%-93%), respectively. Several articles found a significant relationship between the HCMV infection and frequent abortion among Iraq females. Many challenges in our country, such as a lack of management and diagnostic policies on HCMV, contributed to the high prevalence of HCMV infection. Several factors such as lack of optimal/structured antenatal and postnatal care, a lack of adequate equipment and funding for laboratory facilities, socioeconomic factors such as poverty, low awareness, literacy, sexually transmitted diseases, and teenage pregnancies, are intolerably predisposing to unwanted consequences health problems among Iraqi women. Therefore, many countries, including Iraq, demand more knowledge and international recommendations on managing HCMV.

Abbreviation

HCMV: Human cytomegalovirus; CDCs: Centers for Disease Control and Prevention; WHO: World Health Organization; PCR: Polymerase Chain Reaction; ELISA: Enzyme-Linked Immune Sorbent Assay; HSP70: Heat Shock Protein 70; GCV: Ganciclovir; HHV-5: herpesvirus 5

Declaration

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Availability of data and materials

Data will be available by emailing shahadkhudaier@gmail.com.

Authors' contributions

All authors equally participated in conceiving, designing, collecting data, drafting, and writing the manuscript. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

We conducted the research following the Declaration of Helsinki. However, Review Articles need no ethics committee approval.
Consent for publication
Not applicable

Competing interest
The author declares that he has no competing interests.

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Figure 1 PRISMA 2009 diagram

Records identified through database searching (n=97)

Records screened (N=54)

Full-text articles assessed for eligibility (n = 42)

Articles were involved in the study (N=24)

Duplicates and unrelated theme (N=23)

Exclusion due to exclusion criteria (N=18)

Exclusion due to unmatched content (N=12)

Identification

Screening

Eligibility

Included

Additional records identified through other source (n=0)

Studies included in qualitative synthesis (n = 0)