

Journal of Ideas in Health



Journal homepage: www.jidhealth.com

Open Access

Review Article

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 predefined 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.

*Correspondence: shahadkhudaier@gmail.com

¹Department of medical microbiology, College of Medicine, University of Diyala, Diyala, Iraq

A full list of authors information is available at the end of the article.

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 middleincome 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

© The Author(s). 2022 Open Access This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author (s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (https://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article unless otherwise stated

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 flulike 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 prepublished 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. As

sessment bias has decreased due to group discussions that led to decisions. In other situations, a second party's opinion was required.



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 IG 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 Suliamania province, 201 women from Zakho city, 150 women from Akra city, and 160 samples from Amedi city, respectively. Another study by Yasir 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 CMVspecific 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 serums, 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-Sammaraee 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 pregnantly 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 -Sammaraee 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 IgG 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 the prevalence of the 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.

Table1: The scrobositive and fictor v 120 AND 121vi among madi women	Table1:	The seropositive	anti-HCMV IgC	HAND IgM	among Iraqi women
---	---------	------------------	---------------	----------	-------------------

HCMV	Rate of	Rate of	Governorate	No. of Cases in the	Study design	References
Prevalence	positive	positive	of Study	Study		
Groups	IgG	IgM				
Low prevalence	0%	0%	Diyala	92 pregnant women	Cross-sectional Study	AL-Jurani 2014 [31]
group (IgM)						
(0%-11%)						
	37%	1%	Kirkuk	100 women	Descriptive correlational study	Ghailan and Mohammed
		2.27%	Kurdistan	1275 women (575	Cross-sectional Study	2020 [32]
	-	212770	(Duhok,	from Duhok, 189	cross sectional stady	Hussein and Balatay
			Suliamania,	from Suliamania, 201		2019 [33]
			Zakho, Akra,	from Zakho, 150 from		
			and Amedi)	Akra, and 160 from		
				Amedi)		
	60.63%	1.25%	Al- Najaf	160 women	Case-control Study	Yasir et al.2020 [34]
	-	6.10%	Al-Anbar	230 women	Cross-sectional Study	Al-Mishhadani andAl-
						Janabi 2008 [35]
	-	6.92%	Diyala	180 women	Cross-sectional Study	Khudhair et al. 2017 [36]
	-	8%	Erbil	75 women	Case-control Study	Ali 2020 [37]
		8.30%	Kirkuk	245 women	Descriptive Case-	Aljumaili et al. 2014 [38]
	26.00/	0.00%	Deebded	152	Cross sectional Study	A1 array 2012 [20]
	30.0% 85%	9.90%	Baghdad	152 women	Cross-sectional Study	Al-azzawi 2012 [39]
	8370	10.0%	Bagiluau	152 women	cross-sectional study	[40]
Moderate	-	16.40%	Salah Al-deen	128 women	Cross-sectional Study	Al-dorri 2018 [41]
Prevalence						
Group (IgM)						
(12%-30%)						
	-	18.8%	Al-Hilla	120 women	Case-control Study	Al-Saeed et al. 2008 [42]
		19.3%	Baghdad	420 women	Comparative Study	Ali et al. 2019 [43]
	40%	25%	Baghdad	100 women	Case-control Study	Jihad 2015 [44]
	100 %	26.7%	Basrah	160 women	Cross-sectional Study	Raisan and Al-Amara
	22 780/	14 704	Paghdad	122 woman	Case control Study	2020 [45] Khudhair and Al Azzawi
	52.78%	14.770	Dagildad	122 women	Case-control Study	2018 [46]
High Prevalence	-	30.8%	Basrah	120 women	Case-control Study	Naame et al. 2021 [47]
Group (IgM)						
31%-100%						
	28.50%	33.3%	Ramadi	87 women	Cross-sectional Study	AL-Ouqaili, and AL-
						Karboli 2010 [48]
	-	35.38%	Kerbala	130 women	Case-control Study	Saad et al. 2013 [49]
	-	36%	Diyala	50 women	Cross-sectional Study	Hussein et al. 2017 [50]
	-	43.9%	Wasit	750 women	Cross-sectional Study	Al-shammary 2014 [51]
		53%	Baghdad	300 women	Cross-sectional Study	Saeed et al. 2022 [52]
	89%	93%	Babylon	90 women	Comparative Study	Al-Mousawi, and AL-
	05.0001	00/	41 37 1 0	204		Hajjar 2020 [53]
	95.09%	0%	Al-Najaf	204 women	Case-control study	Hamoud et al. 2021 [54]

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

The 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 factormediated trophoblast apoptosis, HCMV-induced cytokine changes in the placenta, and inhibition of indoleamine 2,3dioxygenase [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 teenager 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

Acknowledgment None.

Funding

The author received no financial support for this article's research, authorship, and/or publication.

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.

Open Access

This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author (s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article unless otherwise stated.

Author Details

¹Department of medical microbiology, College of Medicine, University of Diyala, Diyala, Iraq

Article Info

Received: 09 August 2022 Accepted: 02 September 2022 Published: 08 September 2022

References

- Al Mana H, Yassine HM, Younes NN, Al-Mohannadi A, Al-Sadeq DW, Alhababi D, et al. The Current Status of Cytomegalovirus (CMV) Prevalence in the MENA region: a systematic review. Pathogens. 2019;8 (4):213-236. https://doi.org/10.3390/pathogens8040213
- Cannon MJ, Schmid DS, Hyde TB. Review of Cytomegalovirus Seroprevalence and Demographic Characteristics Associated with Infection. Rev Med Virol. 2010;20(4):202–213. https://doi.org/10.1002/rmv.655
- Lachmann R, Loenenbach A, Waterboer T, Brenner N, Pawlita M, Michel A. Cytomegalovirus (CMV) Seroprevalence in the Adult Population of Germany. PLoS One. 2018;13 (7):e0200267. https://doi.org/10.1371/journal.pone.0200267
- Crough T, Khanna R. Immunobiology of Human Cytomegalovirus: from bench to bedside. Clin Microbiol Rev. 2009;22(1):76–98. DOI: https://doi.org/10.1128/CMR.00034-08
- Buxmann H, Hamprecht K, Meyer-Wittkopf M, Friese K. Primary Human Cytomegalovirus (HCMV) infection in pregnancy. Dtsch Arztebl Int. 2017;114(4):45-52. doi: 10.3238/arztebl.2017.0045.
- Manicklal S, Emery VC, Lazzarotto T, Boppana SB, Gupta RK. The "Silent" global burden of congenital cytomegalovirus. Clin Microbiol Rev. 2013;26: 86–102. DOI: 10.1128/CMR.00062-12 [PMC free article] [PubMed] [Google Scholar]
- Prendergast AJ, Goga AE, Waitt C, Gessain A, Taylor GP, Rollins N. Transmission of CMV, HTLV-1, and HIV through breastmilk. Lancet Child Adolesc Heal. 2019;3(4):264–273. https://doi.org/10.1016/S2352-4642(19)30024-0
- R Schleiss M. Congenital cytomegalovirus infection: molecular mechanisms mediating viral pathogenesis. Infect Disord Targets (Formerly Curr Drug Targets-Infectious Disord. 2011;11(5):449– 465. DOI: https://doi.org/10.2174/187152611797636721
- Boppana SB, Ross SA, Fowler KB. Congenital cytomegalovirus infection: clinical outcome. Clin Infect Dis. 2013;57(suppl_4): S178–181. https://doi.org/10.1093/cid/cit629

- Ho M. Cytomegalovirus: biology and infection. Springer Science & Business Media; 2013.
- Zuhair M, Smit GSA, Wallis G, Jabbar F, Smith C, Devleesschauwer B. Estimation of the worldwide seroprevalence of cytomegalovirus: A systematic review and meta-analysis. Rev Med Virol. 2019;29(3):e2034. https://doi.org/10.1002/rmv.2034
- Kagan KO, Hamprecht K. Cytomegalovirus infection in pregnancy. Arch Gynecol Obstet. 2017;296(1):15–26. https://doi.org/10.1002/bdra.23601
- Atik RB, Hepworth-Jones BE DP. Early pregnancy, chapter2, Risk factors for miscarriage. Cambridge university press,2010: 9-18.
- Chow SSW, Craig ME, Jacques CFH, Hall B, Catteau J, Munro SC. Correlates of placental infection with cytomegalovirus, parvovirus B19 or human herpesvirus 7. J Med Virol. 2006;78(6):747–756. https://doi.org/10.1002/jmv.20618
- Kim ID, Chang HS, Hwang KJ. Herpes simplex virus 2 infection rate and necessity of screening during pregnancy: a clinical and seroepidemiologic study. Yonsei Med J. 2012;53(2):401–407. DOI: https://doi.org/10.3349/ymj.2012.53.2.401
- Zhou Y, Bian G, Zhou Q, Gao Z, Liao P, Liu Y. Detection of Cytomegalovirus, human parvovirus B19, and herpes simplex virus-1/2 in women with first-trimester spontaneous abortions. J Med Virol. 2015;87(10):1749–1753. https://doi.org/10.1002/jmv.24218
- Fowler KB, Pass RF. Sexually transmitted diseases in mothers of neonates with congenital cytomegalovirus infection. J Infect Dis. 1991;164(2):259–264. https://doi.org/10.1093/infdis/164.2.259
- Kawasaki H, Kosugi I, Meguro S, Iwashita T. Pathogenesis of developmental anomalies of the central nervous system induced by congenital cytomegalovirus infection. Pathol Int. 2017;67(2):72–82. https://doi.org/10.1111/pin.12502
- Papazian L, Hraiech S, Lehingue S, Roch A, Chiche L, Wiramus S. Cytomegalovirus reactivation in ICU patients. Intensive Care Med. 2016;42(1):28–37. https://doi.org/10.1007/s00134-015-40669.
- Nigro G, Anceschi MM, Cosmi E V, Group TCCDC. Clinical manifestations and abnormal laboratory findings in pregnant women with primary cytomegalovirus infection. BJOG An Int J Obstet Gynaecol. 2003;110(6):572–577. https://doi.org/10.1016/S1470-0328(03)01902-5
- Collinet P, Subtil D, Houfflin-Debarge V, Kacet N, Dewilde A, Puech F. Routine CMV screening during pregnancy. Eur J Obstet Gynecol Reprod Biol. 2004;114(1):3–11. https://doi.org/10.1016/j.ejogrb.2003.09.016
- Zaker Bostanabad S, Rahimi MK, Mahdavi Z, Pourazar SH. Evaluation of Cytomegalovirus (CMV) in Abortion Compared with Embryos Vaginal Delivery by Using PCR. Sarem J Reprod Med. 2017;2(1):43–48. http://saremjrm.com/article-1-28-en.html
- Dollard SC, Grosse SD, Ross DS. New estimates of the prevalence of neurological and sensory sequelae and mortality associated with congenital cytomegalovirus infection. Rev Med Virol. 2007;17(5):355–363. https://doi.org/10.1002/rmv.544
- Dahl H-HM, Ching TYC, Hutchison W, Hou S, Seeto M, Sjahalam-King J. Etiology and audiological outcomes at 3 years for 364 children in Australia. PLoS One. 2013;8(3):e59624. https://doi.org/10.1371/journal.pone.0059624
- Ross S, Novak Z, Pati S, Boppana S. Overview of the diagnosis of cytomegalovirus infection. Infect Disord Targets (Formerly Curr Drug Targets-Infectious Disord. 2011;11(5):466–474. DOI: https://doi.org/10.2174/187152611797636703
- Tan BH. Cytomegalovirus treatment. Curr Treat Options Infect Dis. 2014;6(3):256–270. DOI 10.1007/s40506-014-0021-5
- 27. Lischka P, Zimmermann H. Antiviral strategies to combat cytomegalovirus infections in transplant recipients. Curr Opin

Pharmacol.2008;8(5):541–548. https://doi.org/10.1016/j.coph.2008.07.002

- Ligat G, Cazal R, Hantz S, Alain S. The human cytomegalovirus terminase complex as an antiviral target: a close-up view. FEMS Microbiol Rev. 2018;42(2):137–145. https://doi.org/10.1093/femsre/fuy004
- Biron KK, Harvey RJ, Chamberlain SC, Good SS, Smith III AA, Davis MG. Potent and selective inhibition of human cytomegalovirus replication by 1263W94, a benzimidazole Lriboside with a unique mode of action. Antimicrob Agents Chemother. 2002;46(8):2365–2372. DOI: https://doi.org/10.1128/AAC.46.8.2365-2372.2002
- Goldberg MD, Honigman A, Weinstein J, Chou S, Taraboulos A, Rouvinski A. Human cytomegalovirus UL97 kinase and nonkinase functions mediate viral cytoplasmic secondary envelopment. J Virol. 2011;85(7):3375–3384. DOI: https://doi.org/10.1128/JVI.01952-10
- AL-Jurani AHH. Seroprevalence of Anti-Cytomegalovirus IgM, IgG antibodies among pregnant women in Diyala province. DJPS. 2014;10(2-part 2):116–122. https://www.iasj.net/iasj/download/e3feba324fc007b3
- Ghailan SH, Mohammed SS. Assessing the risk factors for cytomegalovirus and prediction the relationship between abortion and virus in Kirkuk City Hospitals. Mosul J Nurs. 2020;8(2):127– 141. https://mjn.mosuljournals.com/article_166078.html
- Hussein N, Balatay AA. The Seroprevalence of Toxoplasma, Cytomegalovirus and Rubella Infections in Women with Abortion in Kurdistan Region of Iraq: A Brief Report. Int J Infect. 2019;6(1): e86734. Doi: 10.5812/iji.86734.
- Yasir SJ, AL-Khafaji YA-R, Al-Kelaby KKA. Cytomegalovirus UL83 Gene as Diagnostic Marker for Preliminary Infection in Pregnant Women in AL-Najaf City. Syst Rev Pharm. 2020;11(5):123–129. DOI: 10.31838/srp.2020.5.20
- Al-Mishhadani JI, Al-Janabi AU. Toxoplasmosis and cytomegalovirus infection among aborted women in Al-Anbar Governorate. AJVS. 2008;6(1): 88-97 https://www.iasj.net/iasj?aId=15678&func=fulltext
- Khudhair MK, Mohammed MR, Jassim N-AS. The Serologicalrates of Cytomegalovirus Among Women in Diyala Province, With a Study of Some the Immunological Markers. DJPS. 2017;13(3-part 3): 232-241 https://www.iasj.net/iasj/article/128777
- Ali KS. The Sero-Prevalence of Cytomegalovirus Infection among Women with Abortion and Intrauterine Death in Erbil City Kurdistan Region, Iraq. DJM. 2020;18(1):77–90. https://www.djm.uodiyala.edu.iq/index.php/djm/article/view/535
- Aljumaili ZKM, Alsamarai AM, Najem WS. Cytomegalovirus seroprevalence in women with bad obstetric history in Kirkuk, Iraq. J Infect Public Health. 2014;7(4):277–288. https://doi.org/10.1016/j.jiph.2013.08.006
- Al-azzawi RHM. Seroprevalence of cytomegalovirus infection in pre-marital women in some Baghdad hospitals. Iraqi J Sci. 2012; 53:40–45. https://www.iasj.net/iasj/download/b324df73e8ae0f31
- Al-Baiati AMH, Muhsin MA, Jabbar RN. Seroprevalence of human cytomegalovirus (HCMV) in aborted women in Baghdad. International J. Curr. Microb. Appl. Sci.2014;3(2):97-102.
- Al-dorri AZR. Estimation of some immunological biomarkers in aborted women infected with human cytomegalovirus (HCMV) in Salah Al-deen province. MJOTU. 2018;24(2):12–24. DOI: http://dx.doi.org/10.25130/mjotu.24.02.02
- Al-Saeed MS, Muhsin MA, AL-Juburi GJ. Study the role of Toxoplasma gondii, cytomegalovirus, and anti-phospholipids antibodies in cases of abortion among women in Hilla city. QMJ. 2008;4(6):27–34.

- 43. Ali MK, Shia JS, and Al-marsome HD. Detection of HSV and CMV in Pregnant and Miscarriage women by ELISA and real time PCR Assay. Res J Pharm Technol, 2019. 12(9), 4090-4094. DOI: 10.5958/0974-360X.2019.00704.2
- 44. Jihad SA. Molecular Detection of Cytomegalovirus (CMV) Isolated from Repeated Miscarriage Women and Its Relation to TLR2 and ILT2 Receptors. MS.c Thesis Submitted to the Counsel of College of Science/Al-Nahrain, Supervised by Dr. Rehab Subhi Ramadhan 2015.
- 45. Raisan SJ, Al-Amara SSM. Determine anti-human cytomegalovirus antibodies (IgM, IgG) and heat shock protein 70 in aborted women. Eurasian J Biosci. 2020;14(1):265–268. https://www.proquest.com/openview/d871ae13f38f758cdbd44deb bccbe84c/1?pqorigsite=gschola r&cbl=2042720
- Khudhair SA, Al-Azzawi RH. Estimation of Anti-CMV Antibodies in Iraqi Pregnant Women Infected with Chronic Cytomegalovirus. J Glob Pharma Technol. 2018;10(11):52–56.
- Naame, ZK, Thuwaini, MM, Mahdi, DS. Seroprevalence of Toxoplasma gondii, CMV, Rubella and HSV-1&2) in Aborted Women in Basra, Southern of Iraq, Ann. Trop. Med. Public Health. 2021; 24(5): 295-301. DOI: http://doi.org/10.36295/ASRO.2021.24543
- AL-Ouqaili MT, AL-Karboli AY. Immunological Study of Cytomegalovirus Infection in Women with Recurrent Fetal Loss in Ramadi City, West of Iraq. AMJ. 2010;8(1):74-78
- Saad A, Rahi SJ, Hussein BW. Serological Study for TORCH Infections by ELISA Method in Women with Bad Obstetric History in Kerbala City. KJM. 2013;6(2): 1621-1624
- Hussein AA, Salman ST, Khashman BM. Frequency of Human Cytomegalovirus and Human Herpesvirus-1 Antigens in Product of Conceptus Tissues of Pregnant Women with Spontaneous Abortion. Iraqi J Med Sci. 2017;15(1):94-102
- Al-shammary RN. Prevalence of Cytomegalovirus among pregnant women relation to congenital abnormalities in embryos and children in Wasit province, J KU. 2014;12(1):86-91 https://www.iasj.net/iasj/download/8f1d01530e853d1b
- Saeed NAHAA, Ibraheem LJ, Mahmood SI. Immune Antibodies Diagnosis Of Pregnant Women In Iraq Infected With Herpes Simplex Virus And Human Cytomegalo Virus. WBPH, 2022,12, 35-42.

https://scholarexpress.net/index.php/wbph/article/view/1126

- 53. Al-Mousawi, HT, and AL-Hajjar, QN. Immunogenic Diagnosis of Human Cytomegalovirus Infection in Aborted and Pregnant Women in Babylon Governorate. Journal of the college of basic education, 2020, Proceedings of the Second International Scientific Conference - Academics Syndicate Iraqi:215-227 https://www.iasj.net/iasj/download/0ea7cec68284aa4d
- Hamoud, HR, Al-Kashwan, TAJ, Tarish, HR. Cytomegalovirus seropositivity among Iraqi women suffering from recurrent pregnancy loss. Al-Kufa University Journal for Biology, 2021 13(1):26-34

https://www.iasj.net/iasj/download/dbd3e8826ba4edb2

- Lazim HH, Kadhim HS. Review of sero-prevalence of human cytomegalovirus in Iraq. J Microbiol Exp. 2018;6(2):50-55. doi: 10.15406/jmen.2018.06.00188.
- 56. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, et al. (2009) The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions: Explanation and Elaboration. PLoS Med 6(7): e1000100. doi: 10.1371/journal.pmed.1000100.
- 57. Jerman J, Jones RK, Onda T. Characteristics of US abortion patients in 2014 and changes since 2008, a report. 2016:1-26
- Cannon MJ. Congenital cytomegalovirus (CMV) epidemiology and awareness. J Clin Virol. 2009;46:S6–10. https://doi.org/10.1016/j.jcv.2009.09.002

- Fowler KB, Stagno S, Pass RF, Britt WJ, Boll TJ, Alford CA. The outcome of congenital cytomegalovirus infection to maternal antibody status. N Engl J Med. 1992;326(10):663–667. DOI: 10.1056/NEJM199203053261003
- Ahlfors K, Ivarsson S-A, Harris S, Svanberg L, Holmqvist R, Lernmark B. Congenital cytomegalovirus infection and disease in Sweden and the relative importance of primary and secondary maternal infections: preliminary findings from a prospective study. Scand J Infect Dis. 1984;16(2):129–137. https://doi.org/10.3109/00365548409087131
- Zhang S, Zhou Y-H, Li L, Hu Y. Monitoring human cytomegalovirus infection with nested PCR: comparison of positive rates in plasma and leukocytes and with quantitative PCR. Virol J. 2010;7(1):1–7. https://doi.org/10.1186/1743-422X-7-73
- Schoenfisch AL, Dollard SC, Amin M, Gardner LI, Klein RS, Mayer K. Cytomegalovirus (CMV) shedding is highly correlated with markers of immunosuppression in CMV-seropositive women. J Med Microbiol. 2011;60(6):768–774. https://doi.org/10.1099/jmm.0.027771-0
- Tilburgs T, Strominger JL. CD 8+ Effector T Cells at the Fetal– Maternal Interface, Balancing Fetal Tolerance and Antiviral Immunity. Am J Reprod Immunol. 2013;69(4):395–407. https://doi.org/10.1111/aji.12094

- Hamid KM, Onoja AB, Tofa UA, Garba KN. Seroprevalence of cytomegalovirus among pregnant women attending Murtala Mohammed Specialist Hospital Kano, Nigeria. Afr Health Sci. 2014;14(1):125–130. https://DOI: 10.4314/ahs. v14i1.19
- 65. Rawlinson W, Scott G. Cytomegalovirus: a common virus causing serious disease. Aust Fam Physician. 2003;32(10): 789-793
- Hameed MY, Aziz IH. Detection of Cytomegalovirus in Iraqi Recurrent Miscarriage Women. J. Pharm. Pharm. Sci. 2015;5(1):79-89.
- Al-Samarrai MAM, Al-Rawi RA, Yaseen SM, Ali Jadoo SA. Knowledge, attitude, and practice of mothers about complementary feeding for infants aged 6-12 months in Anbar Province, Iraq. Journal of Ideas in Health 2020 May 09;3(1):125-9. doi: 10.47108/jidhealth.vol3.iss1.17.
- Ogbaini-Emovon E, Oduyebo OO, Lofor PV, Onakewhor JU, Elikwu CJ. Seroprevalence and Risk Factors for Cytomegalovirus Infection among Pregnant Women in Southern Nigeria. J. Microb. Infect. Dis.2013 ;3(03):123-127 https://doi.org/10.5799/ahinjs.02.2013.03.0094
- Pembrey L, Raynor P, Griffiths P, Chaytor S, Wright J, Hall AJ. Seroprevalence of cytomegalovirus, Epstein Barr virus and varicella zoster virus among pregnant women in Bradford: a cohort study. PLoS One.2013; 8(11): e81881https://doi.org/10.1371/journal.pone.008188