

## RESEARCH ARTICLE

## SEROPREVALENCE OF CYTOMEGALOVIRUS AMONG PREGNANT WOMEN IN AD-DHALE'E CITY - YEMEN

Adel Jumaan Awadh Binsaad<sup>1,\*</sup> and Arafat Abdo Taleb<sup>2</sup><sup>1</sup> Dept. of Microbiology and Parasitology, Faculty of Medicine and Health Sciences, University of Aden, Yemen<sup>2</sup> Dept. of Microbiology and Parasitology, Faculty of Dentistry, University of Aden, Yemen

\*Corresponding author: Adel Jumaan Awadh Binsaad; E-mail: adeljumaan61@gmail.com; Mobile: +967 772434577

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## Abstract

This study aimed to determine the seroprevalence of Cytomegalovirus virus (CMV) infection among pregnant women in Ad Dhale'e city, Yemen. A cross-sectional study was conducted among 130 pregnant women attended for routine antenatal care in Al-Nasser hospital in Ad-Dhale'e city. Serum was obtained and tested for seropositivity of CMV IgG and IgM using electro-chemiluminescence immunoassays (ECLIA) test. Of 130 blood sample, 122 (93.8 %) and 5 (3.8%) were identified with CMV IgG and CMV IgM seropositive respectively. While, 8 (6.2%) were seronegative (susceptible) to CMV infection. Statistically significant association ( $P < 0.05$ ) was found between CMV IgG seropositivity and age. This study concluded that there was high seroprevalence of cytomegalovirus infections among pregnant women in Ad-Dhale'e city. Routine antenatal screening of pregnant women for CMV infection should be considered. Further studies with more sample size using advanced methods is recommended.

**Keywords:** Cytomegalovirus, Seroprevalence, Congenital infection, Ad Dhale'e City.

## Introduction

Cytomegalovirus (CMV) is a member of Betaherpesvirinae, a subfamily of the Herpesviridae family. Infected cells typically are greatly enlarged and multinucleated (hence, "cytomegalo-"). CMV is a ubiquitous virus which is infect humans of all ages. CMV infection usually symptomless and commonly occurs during childhood. CMV is the most common cause of intrauterine infections and congenital abnormalities. It also represents a serious threat to immunodeficient and immunosuppressed patients [1-3].

Close contact with material containing the virus is very important in transmission of CMV. CMV may transmitted in many different ways as the virus is shed nearly in all body fluids, including tears, urine, saliva, semen, breast milk, and vaginal and cervical secretions. Thus, infection in the newborn can be acquired through close contact with body secretions, perinatally through contact with infected genital tract secretions, vertically through transplacental transmission and postnatally through breast-feeding. In addition, blood transfusion may lead to infection. Furthermore, in adults, CMV can be transmitted sexually or via artificial insemination,

through transfusion of whole blood and organ transplantation [1, 2].

Transplacental transmission and CMV intrauterine fetal infection is very serious and may result in death of the fetus in utero and congenital disease in newborns. Depending on whether the mother is experiencing a primary or recurrent infection, there is a great difference in incidence of fetal infection and severity of outcome. It was estimated that 35% to 50% of maternal primary infection during pregnancy may result in utero transmission and congenital fetal infection [4, 5].

In congenitally-infected children, CMV infections can manifest as *cytomegalic inclusion disease (CID)*, whose symptoms at birth may include intrauterine growth retardation, jaundice, hepatosplenomegaly, thrombocytopenia, microcephaly, and retinitis, with mortality rate of about 20%. However, majority of survivors develop severe hearing loss, ocular abnormalities, and mental retardation within 2 years [6].

However, recurrent CMV infection due to reactivation of the latent virus or re-infection with new virus strain may also result in intrauterine infection, but this is rarely

results in fetal disease because maternal antibody protects more against development of serious disease in the infant than viral transmission [2, 3].

The prevalence of CMV is varies and depends upon the socioeconomic status, living conditions, and hygienic practices. In developing countries, the prevalence rate is higher than 90% in children and adults as well as in low socioeconomic groups in developed countries. In developed countries the rate is from 40% to 70% in adults in high socioeconomic groups [1, 2, 7].

In Ad-Dhale'e city there is no available data about the seroprevalence of CMV among pregnant women, and the few studies from Ibb, Hodeidah, Taiz and Sana'a city, showed a seroprevalence rates ranged from 68%-100% [8-11]. The basic data concerned CMV infections during pregnancy is of significant importance for health planners and care providers. Therefore, the aim of this study was to determine the seroprevalence of CMV infection in pregnant women in Ad-Dhale'e city. In addition, the effects of sociodemographic characteristics on the seroprevalence of the CMV were also investigated.

## Patients and Methods

This is a descriptive cross-sectional study conducted among healthy pregnant women attended for routine antenatal care at Al-Nasser hospital in Ad-Dhale'e city over a period of four months (September –Decembers 2021). Dhale is one of the Yemeni governorates. The population of the province accounts for 2% of the total population of the republic. The city of Ad-Dhale'e is the administrative centre of the province holding a population of around 80,213 [12].

The sample size for this study was based on the previous study (98.7%) conducted in the country in Hodeidah city [9]. Sample size was calculated by Epi-Info ver. 3.5.1. A total sample size of 20 women was calculated, however, for the purpose of strengthening the power it has agreed to increase the sample size to include up to a total of 130 pregnant women. Randomisation process was applied to recruit the participant pregnant women.

A questionnaire was used to collect information on the participants' sociodemographic data.

Five millilitres of venous blood sample was drawn from each participant, centrifuged at 2000 rpm for 5 minutes; serum was separated, and then tested for CMV specific Immunoglobulin IgG and IgM by electro-chemiluminescence immunoassays (ECLIA) test (Roche) in accordance with the manufacturer's instructions.

Permission to perform the study was granted by the administration of Al-Nasser hospital and oral consent

was obtained from all participants after the explanation of the purpose of the study.

The Statistical Package for Social Sciences (SPSS) software version of 20 was used to enter, clean and analyse the data. Chi-square test was used to determine associations between seroprevalence and the sociodemographic variables. P-Values < 0.05 were considered statistically significant.

## Result

In this study, more than half (73; 56.2%) of the pregnant women were between 25 and 34 years of age, 29 (22.3 %) of pregnant women were between 16-24 years of age, and 28 (21.5%) were between 35-44 years of age. On the other hand, 51 (39.2%) of pregnant women were completed the elementary level of education, and 54 (41.5%) were completed the secondary education, while 25 (19.3%) were completed university education. The majority of pregnant women (49; 37.7%) were in their third trimester, and 42 (32.3 %) were in their first trimester of pregnancy, while 39 (30%) were in their second trimester. Moreover, 74 (56.9 %) of the pregnant women were carrying their first pregnancy (primigravida) and 56 (43.1 %) had more than one child (multiparous) (Table 1).

**Table (1):** Socio-demographic characteristics of pregnant women (n=130).

Characteristics	Participated pregnant women	
	No	%
<b>Age groups (years)</b>		
16-24	29	22.3
25-34	73	56.2
35-44	28	21.5
<b>Educational level</b>		
Elementary	51	39.2
Secondary	54	41.5
University	25	19.3
<b>Gestational age</b>		
1st Trimester	42	32.3
2nd Trimester	39	30.0
3rd Trimester	49	37.7
<b>Parity</b>		
Primigravida	74	56.9
Multiparous	56	43.1

Table 2 shows the association between sociodemographic characteristics of the pregnant women and CMV-IgG seroprevalence.

Out of 130 pregnant women participated in this study, 122 (93.8%) were seropositive for CMV-IgG antibodies, whereas 5 (3.8%) were seropositive for CMV-IgM

antibodies and 8 (6.2%) were seronegative (susceptible) to CMV infection.

In the current study, the highest (97.3%) CMV IgG seroprevalence rate was in pregnant women between 25-34 years of age, followed by seroprevalence rate of 96.6% in pregnant women between 16-24 years of age and the lowest rate of 82.1% was in pregnant women between 35-44 years. The results showed that there was statistically significant association between the age and CMV-IgG seropositivity ( $P= 0.014$ ).

Of all the infected pregnant women, the elementary group represented a high seroprevalence rate of 96.1%, the secondary group 94.4 %, and the university group

88%. Although, high seroprevalence rate (96.1%) of infection was found in pregnant women with elementary levels of education there was no statistical significant association between the low level of education and CMV seropositivity ( $P= > 0.05$ ).

In addition, high CMV IgG seroprevalence rates of 95.9% and 94.6% were found in women in their third trimester and those with parity of more than one child respectively. However, there were no statistically significant ( $P= > 0.05$ ) association between the gestational age and parity of the pregnant women and the CMV IgG seroprevalence (Table 2).

**Table (2):** Seroprevalence of CMV IgG among pregnant women according to their sociodemographic characteristics(n=130).

Characteristic	Positive CMV-IgG		Negative CMV-IgG		Total		p-value
	No	%	No	%	No	%	
<b>Age groups (years)</b>							
16-24	28	96.6	1	3.4	29	22.3	$\chi^2= 8.48$ $P= 0.014$
25-34	71	97.3	2	2.7	73	56.2	
35-44	23	82.1	5	17.9	28	21.5	
<b>Educational level</b>							
Elementary	49	96.1	2	3.9	51	39.2	$\chi^2= 1.95$ $P=0.377$
Secondary	51	94.4	3	5.6	54	41.5	
University	22	88.0	3	12.0	25	19.3	
<b>Gestational stage</b>							
1st Trimester	39	92.9	3	7.1	42	32.3	$\chi^2= 0.595$ $P= 0.743$
2nd Trimester	36	92.3	3	7.7	39	30.0	
3rd Trimester	47	95.9	2	4.1	49	37.7	
<b>Parity</b>							
Primigravida	69	93.2	5	6.8	74	56.9	$\chi^2= 0.108$ $P= 0.742$
Multigravida	53	94.6	3	5.4	56	43.1	

## Discussion

This study showed a high CMV IgG seroprevalence of 93.8%. However, this high seroprevalence rate was similar to that reported in the country; in Ibb, Hodeidah, Taiz and Sana'a city, in which a seroprevalence rates of 68%, 98.7%, 99%, and 100% were reported among pregnant women respectively [8-11]. In accordance with this result, a seroprevalence rate of more than 90% were reported from some Arabic countries such as Palestine [13], Saudi Arabia and Qatar [14], and from other countries such as Nigeria [15], and Turkey [16]. This high seroprevalence may be explained by high endemicity of infection, low socioeconomic status, and higher prevalence of risky behaviors in the population [17]. However, a relatively low seroprevalence rate of 40% up to 60% were reported in developed countries such as Australia, Belgium, France, Germany and USA among high socioeconomic groups [18, 7]. The variations in CMV IgM seroprevalence between countries may be attributed to the endemicity, differences in the living and hygienic standards, differences in environmental conditions, socioeconomic statuses,

social habits, lack of personal and community hygiene, and different in educational levels of the studied populations [19]. In addition, it was reported that variations in CMV seroprevalence among women could be based on ethnical and/or racial groups [7].

In this study, statistically significant association between the CMV IgG seropositivity and socio-demographic characters was found only with age ( $P=< 0.05$ ). This could be due to the high CMV IgG seroprevalence reported in this study and the small sample size that might be was not enough to yield the power of significance. In this study, the CMV seroprevalence was gradually increased in the age groups, 16-24 years and 25-34 years, with values of 96.6% and 97.3%. This finding was in agreement with previous studies in which the seroprevalence was increased with age [9, 19]. The reason for the increase in seroprevalence in these two age groups may be related to the sexual activity in adult age, as sexual contact is significant source of CMV transmission [20, 21]. In addition, child-to-mother transmission during pregnancy is very important as infected children shed virus in their saliva and urine for

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years, providing an opportunity for virus spread to their parents, other family members, and children [22, 23]. On other hand, in this study, the CMV seroprevalence was reduced (82.1%) in women of the age group 35-44 years. This could be attributed to the waning immunity in old age [20].

Regarding the educational status, higher non-significant CMV IgG seroprevalence rate (96.1%) was in women with elementary educational level. This finding was similar with other studies [10, 24, 25]. However, low education level was considered as a risk factor for high CMV seroprevalence, and this finding could be explained by the presence of low socioeconomic status and low personal hygiene in the low educational level populations [26].

The time of maternal infection during pregnancy has influence on the expression of disease in the fetus, and pregnant women who develop CMV infection in the third trimester are more likely to deliver fetuses with congenital abnormalities [24, 27]. Although, our study showed increased seropositivity of CMV IgG in pregnant women within the third trimester (95.9%) of gestation, however, there was no statistically significant association with CMV IgG seroprevalence. This was in agreement with other studies [24, 28].

On the other hand, our result showed a high CMV IgG seropositivity of 94.6% in multiparous women. However, high parity also has been implicated as associated risk factor for CMV infection, and previous studies suggested a positive correlation of congenital CMV with a household size, overcrowding, and low socioeconomic status [23]. This high seroprevalence rate among multiparous women could be related to the unhygienic practices in large sized family and direct contact with infected children [29].

In this study, five (3.8%) of pregnant women were seropositive for CMV IgM which indicate current infection, and 8 (6.2%) were seronegative (susceptible) to CMV infection. Considering the considerable risk for congenital infection caused by maternal primary CMV infection during pregnancy, which may leads to fetal infection in comparison with maternal reactivations or re-infections (recurrent infection) which may rarely or not result in severe disease in the child because maternal antibody protects more against development of serious disease in the infant than viral transmission [2-5, 30]. In addition, for the reason that IgM antibodies can persist for months or even years after primary infection and can be reappeared following reactivation or reinfection in some individuals. Moreover, as a false positive test result can occur [4]. Therefore, routine antenatal screening will offer the opportunity for seropositive for CMV IgM pregnant women, who are at high risk of congenital CMV infection, to distinguish between primary and recurrent CMV infections considering IgM positive results in

combination with IgG avidity results [31]. As low IgG avidity is indicative of recent primary infection, while high IgG avidity suggests recurrent infection [31, 32]. However, at present, combination of CMV IgM and low avidity CMV IgG along with maternal or fetal symptoms is used for the diagnosis of a primary CMV infection [32]. Also, routine antenatal screening will provide opportunity for seropositive pregnant women identified with primary infection, to perform additional investigations such as ultrasonography, magnetic resonance imaging and amniocentesis to detect prenatal infection and planning for suitable intervention such as use of hyperimmune globulin or termination of pregnancy [33]. On the other hand, pregnant women (8; 6.2%) who are seronegative (susceptible) to CMV infection, also at a significant risk of acquiring a primary infection and congenital CMV infections [4, 5]. Therefore, those women should be educated and counseled about hygiene measures such as hand washing, wearing gloves, avoiding contact, and sharing utensils with children that used to prevent congenital CMV infections [34]. In Yemen, antenatal screening is not recommended, and CMV IgM and IgG antibodies test is performed if it requested by gynecologist or general practitioner. Therefore, routine national screenings of pregnant women for CMV should be considered.

On other hand, this low (3.8%) CMV IgM seroprevalence found in this study may be due to that vast majority of the participated pregnant women have been exposed to CMV infection early in their life, and by the time, they loss IgM when they reached child bearing age [35]. This finding was in agreement with other studies from China (3.8%) and Yemen (2.0%) [36, 10], but it is lower than that reported in Palestine that was 11.5% [37] and in Nigeria that was 28.0% [29]. However, this seroprevalence rate is higher than that reported in Turkey and Iran that showed 1.7% and 1.0% respectively [16], [28]. However, the differences in CMV IgM seroprevalence between countries may be attributed to the differences in environmental conditions, socioeconomic statuses, social habits, lack of personal and community hygiene, and different in educational levels of the studied populations [19].

## Conclusion:

The present study reveals a high CMV IgG seropositivity among pregnant women in Ad-Dhale'e City. There was a high seroprevalence among pregnant women with elementary level of education. This study showed a statistically significant association ( $P < 0.05$ ) between CMV IgG seropositivity and age. Moreover, there were high seroprevalence among participated pregnant women within the third trimester of pregnancy.

## Recommendation:

Pregnancy health care centers should be improved and routine antenatal screening of all pregnant women with advanced methods should be considered. Health educational programs must be improved to facilitate in prevention and control of CMV infections. Further studies with large sample size and advanced techniques are required to validate the results of this study.

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## مقالة بحثية

## الانتشار المصلي لفيروس مضخم الخلايا بين النساء الحوامل في مدينة الضالع - اليمن

عادل جمعان عوض بن سعد<sup>1\*</sup> و عرفات عبده طالب<sup>2</sup><sup>1</sup> قسم الأحياء الدقيقة والطفيليات، كلية الطب والعلوم الصحية، جامعة عدن، اليمن  
<sup>2</sup> قسم الأحياء الدقيقة والطفيليات، كلية طب الأسنان، جامعة عدن، اليمن

\* الباحث الممثل: عادل جمعان عوض بن سعد؛ البريد الإلكتروني: adeljumaan61@gmail.com؛ رقم الهاتف: +967 772434577

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## المُلخَص

هدفت هذه الدراسة الى تحديد الانتشار المصلي للفيروس المضخم للخلايا بين النساء الحوامل في مدينة الضالع، اليمن. تم اجراء مسح مقطعي بين 130 امرأة حامل تمت معاينتهن في عيادة الحوامل في مستشفى النصر في مدينة الضالع. تم فحص مصل الدم للكشف على الأجسام المضادة باستخدام تقنية فحص اللمعان الكهربائي الكيميائي المناعي (ECLIA). وأظهرت النتائج أن من أصل 130 عينة دم 122 (93.8%) و 5 (3.8%) كانت ايجابية للأجسام المضادة IgG و IgM على التوالي للفيروس المضخم للخلايا. بينما 8 (6.2%) كانت سلبية للأجسام المضادة اي انهم معرضون للإصابة. كما أظهرت الدراسة وجود ارتباط ذو دلالة احصائية معيارية بين معدل الإصابة بالمرض والعمر. وخلصت الدراسة إلى أن الانتشار المصلي لعدوى الفيروس المضخم للخلايا لدى النساء الحوامل في مدينة الضالع عالي، وعلى الحاجة الماسة للفحص الروتيني لكل النساء الحوامل. وإجراء مزيد من الدراسات مع عدد كبير من العينات وبأستخدام التقنيات المتقدمة.

الكلمات المفتاحية: الفيروس المضخم للخلايا، الانتشار المصلي، العدوى الخلقية، مدينة الضالع.

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