

Study of Prevalence and Some Immunological Characteristics of Cytomegalovirus Infections among Pregnant Women

Rashaa Hadi Saleh¹, Eman Fadhel Abd Al-Hussien²
and Zaytoon Abulrdia Ighawish³

¹College of Pharmacy, University of Babylon, Iraq.

²College of Biotechnology, Al-Qasim Green University, Iraq.

³College of Medicine Babylon, University of Babylon, Iraq.

<http://dx.doi.org/10.22207/JPAM.12.3.52>

(Received: 25 May 2018; accepted: 20 July 2018)

Cytomegalovirus (CMV) is one of the essential causes of intrauterine infections. The contagion is commonly asymptomatic in immunocompetent adults, but its import in various times elevated when it happens throughout pregnancy. Pregnant women with CMV infection can be responsible for abortion or congenital malformation. This subject was aimed to estimate the prevalence of cytomegalovirus virus amid pregnant women in Babylon province and evaluation of some haematological and immunological parameters in women infected with CMV. The study was conducted on (145) pregnant women referred to the Babylon Teaching Hospital for Maternity and Children to investigate the prevalence of Cytomegalovirus in Babylon province. Overall of (145) pregnant women was contained in this study, CMV specific IgM and IgG antibody were detected by minividas-test. Blood hemoglobin (Hb) concentration, neutrophil and lymphocyte accounts were determinate. Single radial immune diffusion plates were used for assessment of C3 and C4 level in infected women. Among 145 pregnant women were evaluated for CMV, (95.1%) were positive toward I IgG and (4.1%) were positive toward I IgM. Most of CMV infections among women with age ranging between 20-29 years. It was found that there was an increase in the lymphocyte count and complement components C3 and decrease in the C4 level among CMV patients compared to control group, while haemoglobin and neutrophile level appeared normal. This study summarized that there are increasing seropositivity rate for human cytomegalovirus amid pregnant women. The prevalence of CMV was relatively high in our locality.

Keywords: CMV, IgM, IgG. Pregnant women, Babylon.

Pregnancy leads to temporary immune inhibition, that may be causing increase exposure of pregnant women to infection¹. Several viral infections are correlated with essential maternal and fetal sequels if get throughout pregnancy and causes abortion, the most commonly encountered infections is Cytomegalovirus (CMV) infections². CMV is endemic all over the world. It's part of Herpesviridae family that infects human. It is also called as human herpesvirus 5 (HHV5). It can be

transfer via saliva, breast milk, placenta, breast feeding, sexual contact blood transfer and organ transplantation^{3,4,5}.

HCMV infection may be a symptomatic, or may include mononucleosis like symptoms with prolonged fever and mild hepatitis¹. CMV is the most frequent cause of congenital infection. A primitive infection happens in 0.15 to 2.0% of whole pregnancies and causing many risks to the fetuses of pregnant women¹. The transfer of CMV can happen throughout primary maternal infection or during non-primary infection (revive and reinfection) of seropositive mothers, but the transfer rate to the fetus is a lot higher for non-

* To whom all correspondence should be addressed.
E-mail: rashahadi11@yahoo.com

immune mothers (up to 40%) than for immune mothers (0 to 1%)⁶. Monocyte/macrophages and endothelial cells are considered places of CMV survival, latency and reproduction and its important in maintaining life-long infection⁷. CMV (infection in non)-immunocompromised individuals can -shift of immune-response during pregnancy from Th2 to-Th1 and apoptosis which can be seen clinically as an abortion developed⁹.

CMV /infection of immunocompetent persons induce a humoral immune response and the consequent production of stable-levels of anti-CMV IgG antibodies¹⁰. A preceding researches have proved that the cellular immune response to CMV is of essential interest in eradicating the virus from the host in a murine model. CD8⁺ T lymphocytes are considered to be a vital host defense against-viruses¹¹.

MATERIAL AND METHODS

Samples collection

This study was done on pregnant women aged between (10-50) years who attending to the Babylon Teaching Hospital for-Maternity and Children in Babylon province during the period of one year (2017). Five ml of blood samples were collected from pregnant women and immunocompetent nonpregnant women as control and then divided into two tubes, 3ml of blood put in plain tubes for separation of serum and the remain 2ml of blood put in EDTA tube for hematological test. Sera was used for the detection of antibodies (IgG and IgM) specific to CMV using a minividas test (kits/ BioCheck-USA).

For hematological test, anticoagulated blood samples in EDTA tube) were used to determine concentration of blood hemoglobin (Hb), and percentage of neutrophil and lymphocyte^{12,13}.

Complement components C3 and C4 level were determined in patients and control group by using single radial immune diffusion. Five µl of serum sample or control were applied. The lid was closed firmly, incubated at room temperature 25 °C and the diameter was measured accurately¹⁴.

Statistical analysis

Data have been analyzed statistically using SPSS program version 11. Analysis of quantitative data was done using t-test

RESULTS AND DISCUSSION

Seroprevalence of CMV

This study was carried out on pregnant women to examine the seropositivity rates of IgG-and IgM1 specific to CMV. The results of this study showed that among 140 tested pregnant women, (4.1%) were positive for IgM antibodies, (95.1%) were positive for IgG and (2%) were positive for both IgM-and IgG (Table 1). The results of current study was close to other studies like^{9,3} who found that IgG was detected in (90.2%) and (97.5%) and IgM in (9.18 %) and (6.0%) of pregnant women respectively.

Variable IgM-positivity were recorded worldwide, only 1% in Turkey¹, 2.5% in Iran, 2.5 in Western Sudan and 1.7% in Korea³. Positive IgM results to Cytomegalovirus (CMV) are indicated of a primitive or repeated infection. IgM (antibodies to CMV can continue for (2 to 9) months after the initial infection. Not all patients with reactivated CMV infection will) have noticeable levels of IgM antibodies¹⁵.

The seroprevalence of-CMV IgG detected in this study was similar-to the findings-reported by^{16,17}. The higher percentage of CMV-IgG seropositivity are indicative of past (CMV) infection, specifically when they were IgM-negative, these women as mentioned can assumed immune and their primary infection with CMV was) consider to have been happen before the present pregnancy and they were mostly asymptomatic personnel^{15,18}.

In this study CMV is endemic in our population. The high prevalence proved that CMV is simply transmitted than a some other infections like as measles. Specific care and appropriate vaccination program are needed to prevent the transmission of CMV¹⁹.

The results of the present study showed that highest seropositivity rate of CMV (55.5%) was seen among age group 20-30 years, while others age groups showed percentage of 3(33.3%) for age group 10-20 and (11.1%) for age group 30-40 years (Table 2). These results were confirmed by (20, 21, 19) who stated that most CMV infections seen among age group 20-30- years. Age group 20-30 was determined as the major age group for

the occurrence of CMV primary infections and this may be due to that most marriages in our population occurred among the this age group.

In Iraq, Our study has shown that the common of women of gestation age are seropositive for CMV and that they deal with the infection either through prenatal or postnatal transmission or during early childhood.

Estimation of Immunological and hematological parameters

Concerning the serum complement components level in CMV patients . It was found that there are increase in the levels of C3 (204.40 ±20.33) in patient group compared to control group (105.03 ±10.84) and decrease in the level of C4 (10.52± 3.47) among patients group compared to control group (35.92 ±6.77) as shown in (Table 3,4).

The complement system is increasingly observed as a mediator-of defense or i pathology in a numerous of viral) infections. The antiviral

mechanism for complement is frequently illustrated by that the antibodies detecting viral antigens) on the infected cell surface or virion -envelope, and this would in return promote complement activation in cascades which accumulate the complement complex) leading to membrane distraction, known as (CDC) or virolysis. In addition, complement-improve neutralization without virolysis has been designated, and one suggested mechanism for this is that the gathering of complement on viral envelop would prevent viral interplay with its cellular receptor needed for viral passage²².

The hematological parameters showed that hemoglobin(Hb) concentration and neutrophil count in CMV patients were (13.0233) and (75.2300) in comparison with control group (12.8733) and (74.2800) respectively with no differences between them (Table 5). Similar findings recorded by (9) who found that CMV s seropositivity have no significant effect on some blood parameters included Hb concentration,

Table 1. The seroprevalence rate of anti-CMV IgM) and IgG antibodies among pregnant women

No. of tested women	CMV IgG		CMV IgM		CMV IgM and IgG	
	No. of +ve	% of +ve	No. of +ve	% of +ve	No. of +ve	% of +ve
145	6	4.1%	138	95.1%	3	2%

Table 2. Distribution of infected women with CMV according to age

Age group/ Year	No. of +ve patients with CMV	% of +ve patients with CMV
10-20	1	11.1%
20-30	5	55.5%
30-40	3	33.3%
40-50	0	0

Table 3. Mean concentration of C3 in patients and control sera (mg/dl)

Group	No.	CMV + C3		
		Means	std	Std. error
Patients	30	204.4000	20.33000	3.71173
Control	15	105.0333	10.84341	2.79976

While²³ reported significant decrease for hemoglobin Hb and neutrophil count among CMV patients. CMV is intracellular virus could be localized in leukocytes and is concentrated in neutrophil fraction of the buffy coat²⁴.

The results of present study revealed increase in the levels of lymphocyte in CMV patients (41.9967) in comparison to control group (22.6867). Our results were in-parallel with others

Table 4. Mean concentration of C4 in patients and control sera (mg/dl)

Group	No.	CMV + C3		
		Means	std	Std. error
Patients	30	10.5200	3.47150	.63381
Control	15	35.9267	6.77184	1.74848

Table 5. Haematological parameters in CMV patients

Group	S No.	Hematological parameters								
		Hemoglobin(g/dl)			neutrophil (%)			lymphocyte (%)		
		Meann	Std.	Std. error	Mean	Std	Std. error	Mean	Std	Std. error
Patients	30	13.0233	1.20650	.22028	75.2300	3.08032	.56239	41.9967	6.65290	1.21465
Control	15	12.8733	1.23315	.31840	74.2800	2.88499	.74490	22.6867	1.49564	.38617

observations recorded by others researchers, who noticed elevated level of lymphocyte in CMV patients^{23,25}. In Contrast, The authors⁹ stated that patients with CMV has normal level of lymphocyte.

Primary HCMV infection is characterized by an intense viral replication and a profound T-cell response that may last for several months, with both CD8+ cytotoxic and CD4+ helper T-cells playing central roles in the resolution of acute primary infection and the maintenance of long-term memory during viral persistence. HCMV-specific cytotoxicity is predominantly performed by (CD8+ T-)cells, although HCMV-specific

CD4+ (Ti-cells) also have the ability to lyse infected target cell²⁶, as well as maintain the upkeep of the CD8+ T-cell population. The virus is also capable of periodic reactivation causing large-scale expansions of cytotoxic T-cells that seem to linger long after the infection has been curtailed. Consequently, people with a latent HCMV infection have substantially increased numbers and proportions of CD8+ (and to some extent CD4+) T-cells²⁷.

CONCLUSION

This study concluded that CMV infection is common among pregnant women in our local population and this high seroprevalence reflect the low hygienic standards and low community education . Also the many ways of viral transmission have the role in spreading the viral infection, Missing of effective viral treatment play an major role in the transference of the virus from mother t to fetus and cause either abortion or congenital malformations. Hence periodically screening of women of child bearing i age for CMV -infection is wanted in order to decrease the fatal consequence of the pregnancy appearing due to the CMVi infection

ACKNOWLEDGMENTS

The authors acknowledge the members and staff of Babylon Teaching Hospital for Maternity and Children in In Babylon province for helping in collecting the samples, data and their excellent technical assistance. Authors also thank all patients who participated in this study

REFERENCES

1. Salman. Y.G. Serological Cross Reaction among Songle Causative Agents Of Women Abortions(Toxoplasma gondii and Cytomegalo Virus AND Rubella Virus) with the Incidence of Hepatitis Virus(B and C). *Tikrit Journal of Pharnnaceutical Sciences*. 2007; **3** (2):102 – 111.
2. Janna, M.A.;Al-shanawee, F.A.; Waheeda,N.E. and Al-Anny, N.G. Evaluation the immunological state of women 's sera infected with Toxoplasmosis. *QMJ*. **5**(8):80-98.
3. Khairi, S.I.; Intisar, K.H.;Enan; K.H.; Ishag, M.Y. Baraa, A.M. and Ali, Y.H. Seroprevalence of cytomegalovirus infection among pregnant women at Omdurman Maternity Hospital, *Sudan Journal of Medical Laboratory and Diagnosis*. 2013; **4**(4):45-49.
4. Al-Hindawi, N.Gh, and Al-Shanawi, F.A. Seroprevalence of Toxoplasma gondii and Cytomegalovirus in Aborto Women in Baghdad-Iraq. *Iraqi Journal of Science*, 2015; **56**(C)649-655.
5. Hussan, B.M. Study the Prevalence of ACL,APL,CMV,HSV, Rubella and Toxoplasma Gondii in Aborted Women in Baghdad Medical *Journal of Babylon*. 2013; **10**(2):455-464.
6. Lagrou, K.; Bodeus, M.; Van Ranst, M. and Goubau, P. Evaluation of the New Architect Cytomegalovirus Immunoglobulin M (IgM), IgG, and IgG Avidity Assays. *Journal of Clinical Microbiology*. 2009; **47**(6):1695–1699.
7. Jianhui, Z.; Shearer, G.M.;Marincola, F.M.; Norman, J.E.; Rott, D.;Zou, J; Epstein, S.E.

- Discordant cellular and humoral immune responses to cytomegalovirus infection in healthy blood donors: existence of a T_H1-type dominant response *International Immunology* 2001; **13**(6):785–790.
8. Kadum, S.A. and Abbas, A.F. A study of some immunological features in aborted women infected with *Toxoplasma gondii* and Cytomegalovirus in Hilla city. *AL-Qadisiy a J. Sci.*, 2013; **18**(4): 62-70.
 9. Hama, S.A. and Abdurahman, K.J. Human Cytomegalovirus IgG and IgM Seropositivity among Pregnant Women in Sulaimani City and Their Relations to the Abortion Rates. *Current Research Journal of Biological Sciences*, 2013; **5**(4): 161-167.
 10. Spiller, O.B.; Hanna, M.; Devine, D.V. and Tufaro, F. Neutralization of Cytomegalovirus Virions: The Role of Complement. *The Journal of Infectious Diseases*; 1997; **176**: 339–347.
 11. Simpson, R.J.; Bigley, A.B.; Spielmann, G; LaVoy, E.C.; Kunz, H, and Bollard, C.M. Human cytomegalovirus infection and the immune response to exercise. *Exerc Immunol Rev.*; 2016; **22**:8-27.
 12. Voigt, G. L. Hematology Techniques Concepts for Veterinary Technician, 1st ed., Iowa state university press 2000; pp28-52.
 13. Pilaski, J. (1972). Cited by Sturkie, P. D. & Griminger, P. Blood fluid: In Sturkie, P. D. (ed). Avian physiology .4th ed. Springer- verlog. New york Berlin, Heidelberg.Tokyo, 1982; pp.113-114.
 14. Lewis, S.M.;Bain, B.J. and Bates, I. Dacie and Lewis.Practical Hematology.9thed. Churchills livingstone,London 2001.
 15. Ahmed, Z.K.; Ahmed, Z.K. and Salman, Z.Q. Quantitative Detection of Human Cytomegalovirus (HCMV) Gene in Iraqi Women with Pregnancy Associated Problems. *Iraqi Journal of Biotechnology*, 2014; **13**(1):30-38.
 16. Nahla, K.H.; Ali, Y.H. and Enan, K.H. Studies on congenital infections in Sudan: Seroprevalence of cytomegalovirus. *J. Sci. Tech.* 2011; **12**(4):82-90.
 17. Kafi, S.K.; Eldouma; E.Y.; Saeed, S.B.M. and Musa, H.A. Seroprevalence of Cytomegalovirus among blood donors and antenatal women attending two hospitals in Khartoum State. *Sudan J. Med. Sci.*; 2009; **4**(4):399-401.
 18. Nader, S. and Ayad, M. “Cytomegalovirus Seroprevalence in Iraqi Pregnant Women”. *The Iraqi Postgraduate Medical Journal.* 2012; **11**(3): 304-307.
 19. Shams, S.; Ayaz, S.; SKhan, s.; Khan, S.N.; Gul, I.; Attaullah, S.; Parveez, R.; Farzand, R. and Hussain,M. Prevalence and detection of cytomegalovirus by polymerase chain reaction (PCR) and simple ELISA in pregnant women. *African Journal of Biotechnology.*; 2011; **10**(34); 6616-6619.
 20. Abd-ul-Aziz, S. Sero-prevalence of anti- CMV- IgM and anti -CMV- IgG in Iraqi Aborted Women Infected with Human Cytomegalovirus in Nasiriyah city. *J.Thi- Qar.*; 2015; **10**(4):55-60.
 21. Al-shammary, R.N. Prevalence of Cytomegalovirus among pregnant women relation to congenital abnormalities in embryos and children in Wasit province. *J. Kerb Univ.*; 2014; **12**(1):86-91.
 22. Li, F.; Freed, D.C.; Tang, A.; Rustandi, R.R.; Troutman, M.C; Espeseth, A.S.; Zhang, N.; An, Z.; McVoy, M.; Zhu, H.; Ha, S.; Wang, D.; Adler, S.P. and Fu, T. Complement enhances in vitro neutralizing potency of antibodies to human cytomegalovirus glycoprotein B (gB) and immune sera induced by gB/MF59 vaccination. *npj Vaccines*, 2017; **2**:36:1-8.
 23. Alebady, F.A.M.; Salman, A.N. and Hadi, N.A. Detection of some Immunological parameters Related with *Cytomegalovirus* (CMV) Infections in aborted women at THI-QAR province in south of IRAQ. *Al-Qadisiyah J. Pure Scie.*, 2016; **21**(3):69-77.
 24. Bonnet, F.; Morlat, P.; Neau, D.; Viillard, J.F.; Ragnaud, J.M.; Dupon, M.; Legendre, P.; Imbert, Y.; Lifermann, F.; Le Bras, M.; Beylot,J. and Longy-Boursier, M. Hematologic and immunologic manifestations of primary cytomegalovirus infections in non-immunocompromised hospitalized adults. *Rev Med Interne.*; 2000; **21**(7):586-94.
 25. Michael; O,A.; Theresa, O.A.; Olusayo, A.O. and Nwadioha, S.I. Assessment of Some Key Haematological Parameters on Cytomegalovirus Antibody Positive Pregnant Women in Makurdi Nigeria. *International Blood Research & Reviews* 2017; **7**(3): 1-8.
 26. Simpson, R.J.; Bigley, A.B.; Spielmann, G.; LaVoy, E.C.P.; Kunz, H.; and Bollard, C.M. Human cytomegalovirus infection and the immune response to exercise *Exerc Immunol Rev.*; 2016; **22**:8-27.
 27. Cicin-Sain, L.; Brien, J.D; Uhrlaub, J.L.; Drabig, A.; Marandu, T.F.; and Nikolich-Zugich, J. Cytomegalovirus Infection Impairs Immune Responses and Accentuates T-cell Pool Changes Observed in Mice with Aging. *PLoS Pathog.* 2012; **8**(8):