



SEROPREVALENCE OF CYTOMEGALOVIRUS INFECTION IN PRE-MARITAL WOMEN IN SOME BAGHDAD HOSPITALS

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Abstract

One hundred and sixty one serum samples collected from pre-marital women in Baghdad province, without any clinical evidence of cytomegalovirus (CMV) infection, were screened for the presence of IgG and IgM antibodies against CMV by ELISA test. The IgG antibodies were detected in 58 which gave prevalence rate of 36%, while the IgM antibodies were detected in 16 (9.9%). The number of both IgG and IgM sero positive was 50 (31.1%) and the number of both IgG and IgM sero negative (control) was 37 (23%). rising in seropositivity was observed with young women, reaching to maximum of 46.6% in age group 15-19 years. While the lower percentage 9(5.6%) showed in the age group of (30-35) years. Seroprevalence rate was also found to be more in women from urban area than those from rural area, and the difference was statistically highly significant (p > 0.01).

الانتشار المصلى لفايروس التضخم الخلوي في النساء ما قبل الزواج في بعض مستشفيات بغداد

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الخلاصة

تم جمع ١٦١ (مئة وواحد وستون) عينة مصل من النساء المقبلات على الزواج في محافظة بغداد، واللاتي لا يبدين أي علامات سريرية على أصابتهن بفايروس التضخم الخلوي (Cytomegalovirus) قد تم الكشف عن وجود أضداد IgG و IgG في أمصال هؤلاء النساء ضد فايروس التضخم الخلوي بأستخدام تقنية الاليزا. أظهرت النتائج بأن ٥٨ (ثمانية وخمسون) أمرأة قد سجلت وجود أضداد IgG بنسبة ٣٦%، في حين ان أضداد IgM قد وجدت في ١٦ أمرأة (٩.٩%) . ٥٠ أمرأة أظهرت وجود أضداد IgG و Mgl معا وينسبة ٢١.1% و ٣٧ أمرأة (٣٢%) لم يظهرن وجود أي نوع من أنواع الاضداد وأستخدمن كسيطرة. كما وأظهرت النتائج بأن أعلى نسبة أصابة كانت بين النساء الصغيرات في العمر ووصلت أعلاها (٣.٦%) في وأظهرت النتائج بأن أعلى نسبة أصابة كانت بين النساء الصغيرات في العمر ووصلت أعلاها (٣.٦%) في الفئة العمرية مابين ١٥ – ١٩ سنة. في حين أقل نسبة قد ظهرت في الفئة العمرية بين ٣٠ –٣٥ سنة. كذلك بينت النتائج بأن النساء في المناطق المدنية هي أكثر أصابة من المناطق الريفية والفروقات كانت معنوية بينت النتائج بأن النساء في المناطق المدنية هي أكثر أصابة من المناطق الريفية والفروقات كانت معنوية عالية.

Introduction:

Human Cytomegalovirus (HCMV) is a member of the beta-herpes virinae, a subfamily of the herpesviridae which also includes Herpes simplex virus type 1 and 2 (HSV1) and (HSV2), Varicella-Zoster virus (VZV), Epstein barr virus (EBV) human herpes viruses 6 and 7 (HHV6) and (HHV7), and Kaposi's sarcoma associated herpes virus [1,2]. The beta herpes viruses tend to have a relatively restricted host range, long growth cycle, and slow spread in cell culture. HCMV infected cells may become enlarged (cytomegalial), showing intranuclear or intracytoplasmic inclusion bodies, the former often referred to as the "owl eye" [3]. HCMV is a common congenital viral infection in humans

due to the high prevalence of the virus in the general population. Infected infants may be asymptomatic at birth, but can develop neurological problems later in life [4].CMV is an important cause of abortion and stillbirth after primary infection in pregnant woman. Also Cytomegalovirus, an ubiquitous agent, is one of the important causes of intrauterine infections. The infection is usually asymptomatic in adults but its significance is many times increased when it occurs during pregnancy [5]. It is endemic throughout the world affecting most of the population where the seroprevalence of CMV IgG antibodies varies greatly with a variety of epidemiological factors such as age, geographical distribution, socioeconomic status, marital status and parity.[6,7,8,9,10].

The aim of this study:

The present study was therefore undertaken to determine the prevalence of CMV IgG and IgM antibodies and the various factors affecting it in the premarital women in Baghdad province.

Methodology:

Subjects:

From the January 2009 to August 2009, 161 blood samples were collected from apparently healthy non- married women (Pre-marital women), with age from (15) to (35) years. The samples were collected from different hospitals in Baghdad, Al-Yarmouk Teaching hospital, Al-Nuaman hospital, and Teaching Laboratories of Medical City. Before blood sampling, some information from all females were collected according to a questionnaire sheet prepared previously.

Collection of blood samples:

Five (5) ml of venous blood was drawn from each woman aseptically. The sera were collected and dispensed in to Eppendrof- tubes and stored at -20° C till analysis.

Cytomegalovirus (CMV) detection:

IgG- anti CMV and IgM anti- CMV in sera were detected, and they were measured by means of enzyme linked immunosorbant assay by using (ELISA) kit (Bioactive Diagnostica) as recommended by the manufacture. The results were interpreted as seropositive if the antibody titer was more than 11NTU and seronegative if less than 9 NTU. Samples with titer between 9-11 NTU were considered as equivocal and should be retested after 2-weeks.

Statistical analysis:

The Chi-square (x^2) test for significance was adopted for the comparison and calculation of association in quantitative data according to contingency tables method within the SAS (2001) program[11].

Results and Discussion:

The blood samples were collected from apparently healthy pre-marital females referred to the laboratory units of Al-Yarmouk Teaching hospital, Al-Nuaman hospital, and Teaching Laboratories of Medical City for marriage testing profile, also these Hospitals are considered as a reference hospital for distance areas of rural and urban quarters. The total number of apparently healthy females included in this study was161. The number of IgG seropositive with CMV was 58(36%) in Baghdad province, while the number of IgM sero positive was 16 samples (9.9%). The number of both IgG and IgM sero positive was 50 (31.1%) and the number of both IgG and IgM sero negative (control) was 37 (23%) (Table 1). The statistical analysis showed that there was a significance differences (p>0.05) (in Laboratories Teaching of Medical City and A- Yarmouk Teaching hospital) between the controls and the positive results of CMV infection in pre-marital females in Baghdad. However, no significant differences in Al-Numan hospital; there was a highly significant difference between the controls and the positive sera in total in Baghdad. We try to make these serological tests (IgM, IgG) mandatory in priminarly test before marriage. Other local studies on pregnant women showed that the percentage of IgM only was (7.7%) and the IgG percentage was (71.8%). In negative result of both IgG and IgM the percentage was (20.5%) [12]. Other studies showed that the percentage of CMV IgG seropositive in

unmarried women was (86.7%) and the marital status did not show much difference from that of married women (87.4%) [10]. The study of Fowler *et al.*, 2006[13] showed that the percentage of unmarried women was 130(86.7%) out of 150.

Other universal result of the CMV-IgM antibody assay for detection of primary infection, sera from 300 women known to be seropositive for at least 1 year were tested. IgM antibody to CMV was found in 2/300 (1.5%). Among 43 women who seroconverted from CMV-IgG negative to positive, 36 (83.7%) had CMV-IgM in their first positive serum. The mean interval between the last CMVIgG negative serum and the first positive serum was 30 weeks. When the interval between negative and positive sera was <15 weeks, 12/13 (92.3%) of sera were CMV-IgM positive [14].

Age is one of the factors affecting the prevalence of CMV seropositive in a community. In this study stepwise rise in seropositivity was observed with young women, reaching to maximum of 46.6% in age group 15-19 years. The percentage distribution of CMV in

females according to the age groups by ELISA was showed in (Table 2). While the lower percentage 9(5.6%) showed in the age group of (30-35) years, and the results showed that there were a highly significant differences (p<0.01) between each age groups.

Table	1:The	percentage	distribution	of apparently	healthy	females	in Baghdad	province	by ELISA	test
				(FI	IS A)					

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Test							
Result		IgG +ve IgM -ve	IgG +ve IgM +ve	IgG -ve IgM +ve	IgG –ve IgM-ve (control)	Total	X ² Value
Teaching Laboratories	No	22	24	7	12	65	4.003*
of Medical City	%	37.9	48	43.75	32.5	40.4	-
Al-Yarmouk Teaching	No	24	14	5	15	58	3.604*
hospital	%	41.4	28	31.25	40.5	36	
Al-Nuaman	No	12	12	4	10	38	1.545ns
nospitai,	%	20.7	24	25	27	23.6	
Total in Baghdad	No	58	50	16	37	161	6.816**
	%	36	31.1	9.9	23	100	
	*	(P< 0.05)	** (P	< 0.01)	ns: non- sig	nificant	

Table 2: The percentage distribution of CM	V in females according to the age groups in Baghdad provin	ice
1	by ELISA.	

Test	ELISA								
Age group	Teaching Laboratories of Medical City		Al-Yarmo Teaching ho	Al-Nuaman hospital,		Total in Baghdad			
(year)	No	%	No	%	No	%	No	%	
15-19	30	46.1	27	46.6	18	47.4	75	46.6	
20-24	20	30.8	22	37.9	14	36.8	56	34.8	
25-29	10	15.4	7	12.1	4	10.5	21	13	
30-35	5	7.7	2	3.4	2	5.3	9	5.6	
Total	65	100	58	100	38	100	161	100	
X^2 Value	8.637**		8.975**		8.738	**	8.725**		

** (**P** < 0.01)

Previous studies have shown that children who excrete CMV may spread infection to a parent and to other adults in the household [15]. Other studies have demonstrated that having children in child care centers with high rates of CMV infection correlates with an increased risk for CMV infection in the parents of these children [16,13]. Possibly young children in these households were acquiring CMV infection in child care centers, resulting in CMV exposure for other household members.

Although young children and sexual activity are recognized as sources of CMV infection, previous studies did not evaluate whether these exposures both singly and together contribute to increases in maternal infections that then may lead to congenital CMV infections [13].

The present study shows that CMV infection is widespread among the women of child bearing age group of Amritsar. Significant association of the various epidemiological factors (age, socioeconomic status and parity) with CMV suggests also revealed that women of child bearing age are more exposed to this infection. As no effective treatment and vaccine against the CMV is available, more emphasis should be laid upon educating women (to maintain good hygiene, limited contact with infected children and responsible sexual practices) and their prospective screening to reduce the foeti maternal transmission.

This study also found that women aged (15-19) years were more likely to have an infant with congenital CMV infection than women who were older. Young maternal age may be a marker of recent exposure to CMV, although it also may be indicative of a biological effect of age on maternal infection. Possibly the combination of an age-related factor with recent exposure to the virus in young women enhances CMV infection during pregnancy and increases the risk for transmission to the fetus [17]. Other study [10] found that the age group of (36-42) years was the higher incidence group (98%) of infection.

In this study the percentage of women in urban community that were infected with CMV is 107(86.3%), while in the women of rural community the percentage is 17(13.7%) (Table 3). The results showed that there were a highly significant differences (p<0.01) between urban and rural infected women with CMV. Also there was a highly significant (p<0.01) and a significant differences (p<0.05) between the positive results (IgG +ve, IgG+ve and IgM +ve, and IgM +ve).

The study of Mohammed [12] showed that the percentage in urban area was (82.9%). Rates of congenital CMV infection are higher in urban, low-income, predominantly black populations in which the CMV seroprevalence rates among women of childbearing age are high, suggesting that CMV exposures occurred frequently in these populations [13].

The prevalence of CMV antibodies during child bearing age varies greatly in different population groups. Lower prevalence rate of CMV IgG antibodies (40-80%) has been reported from developed countries, and higher rate (90 -100%) from developing countries, depending upon the variability of accessibility of virus and its circulation rate in the community [18].

In our study, statistically significant difference in prevalence rates was observed between the lower and upper socioeconomic classes. IgG antibody levels were also found to be higher in women of urban background as compared to the women residents of rural area. Adverse observations have been reported from other studies. [12,19].

Test	ELISA Test								
	IgG +ve IgM -ve		IgG +ve IgM +ve		IgG -ve IgM +ve		Total in Baghdad		X ² Value
Subject	No	%	No	%	No	%	No	%	
Urban	49	84.5	43	86	15	93.75	107	86.3	9.763**
Rural	9	15.5	7	14	1	6.25	17	13.7	3.613*
Total	58	46.8	50	40.3	16	12.9	124	100	6.743**
X^2 Value	9.862**		10.041**		10.480**		9.894**		

Table 3: The percentage distribution of positive CMV females in Baghdad province according to educational level by ELISA test.

For prevention of congenital CMV infection, young women of childbearing age should be informed about CMV transmission routes [20]. Young women should be instructed to practice good hygiene (ie, hand-washing) when caring for young children. Adolescents and young women should be advised to avoid salivary and genital contact with others

However, changing behaviour through health communication is challenging. A randomized, clinical trial that provided information on CMV and the importance of hand-washing failed to show a decrease in CMV acquisition by women of childbearing age, demonstrating the difficulty in changing behaviours,[21] yet successes have been observed in lowering

the risk for HIV infection in black adolescents through health education interventions [22]. Even if behavioural changes through health communication decreases some congenitalCMV infections, more likely an effective vaccine

that is given to children or young teens and could prevent congenital infection would be more successful in preventing congenital CMV infection in most populations.

The diagnosis test for CMV must be introduced with other tests in the marriage test profile. Also the need for further studies to follow up the infected pre-marital women after the marriage especially in those with IgM +ve and (IgG and IgM) +ve women.

References:

- 1. Schmidt,NK.andEmmons,RW.**1989**.Dia gnostic approach for viral, reckettsial and Chlamydial infections .6th ed., American Public Health Association (APHA).;321-378.
- Jawetz, M.,and Adelberg, S. 2001. Herpesviruses. In: Medical microbiology, Twenty-Two Edition, Lange Published, pp.370-390.
- 3. Roizman, B., Carmichael, L.E.,and Deinhard,F..**1981**. Herpesviridae. Definetion, provisional nomenclature and taxonomy. *Intervirology* ; **16**:201-217.
- 4. Yow, M.D. **1989**. Congenital CMV infection, a new problem. *J. Infect. Dis.*; **159**: 163-167.
- Mathur, A., Jindal, I.and Chaturvedi, U.C. A.1981. serological study of Cytomegalovirus infection at Lucknow. *Ind J Med Res.* 73:678-681

- Hizel S, Parker S, and Onde U. 1999. Seroprevalence of Cytomegalovirus infection among children and females of Ankara, *Turkey. Pediatr – Int.* 41(5):506-509.
- Griffiths, P.D., Babboonian C, Ruttea D, and Peckham C. **1991**. Congenital and maternal cytomegalovirus infections in a London population. *Br J Obstet Gynaecol.* **98**:135-140.
- 8. Wen, L., Wu, S., and Lu, S.**1996**. The epidemiological study on human cytomegalovirus infection in pregnant women and maternal foetal transmission in three Chinese metropolis. *Chung Hua Fuchar Ko Tsa Chih.* **31**(12): 714-717
- Gratacap, C.B., Bosson, J.L., Morand, P., Dutertre, N., Chanzy, B., Jouk, P.S., Vandekuckhove, C., Cary, L.P., and Seigneuren, J.M. **1998**. Cytomegalovirus seroprevalence in French pregnant women: Parity and place of birth as major predictive factors. *Eur J Epidemiol.* **14**(2):147-152.
- Jindal,S.N, and Aggarwal, A. 2005. A pilot seroepidemiological study of cytomegalovirus infection in women of child bearing age. *Indian J.Med. Microbiol.*23 (1): 34-36.
- 11. SAS. 2001. SAS/ STAT User s Guide for Personal Computers
- 12. Mohammed, M.K. **2007.** Study of some immunological and cytogenetic aspects in patients infected with Cytomegalovirus. M.Sc. thesis. University of Baghdad.
- 13. Fowler, K.B., and Pass, R.F.**2006.** Risk Factors for Congenital Cytomegalovirus Infection in the Offspring of Young Women: Exposure to Young Children and Recent Onset of Sexual Activity.*Pediatr*.**118** (2): e286e292.
- Pass,K.B., Fowler, S.B.,Boppana, W.J. and Britt, S.S. 2006. Congenital cytomegalovirus infection following first trimester maternal infection: Symptoms at birth and outcome. J. *Clinic. Virol.* 35: 216–220
- 15. Pass, R.F., Hutto, S.C., Ricks, R.,and Cloud, G.A. **1986.** Increased rate of cytomegalovirus infection among parents of children attending day care centers. *N Engl J Med.* **314**:1414–1418.

- Hutto, S.C., Ricks, R.E., Garvie, M., and Pass, R.F. **1985**. Epidemiology of cytomegalovirus infections in young children: day care vs home care. *Pediatr Infect Dis.* **4**:149–152.
- Fowler, K.B., Stagno, S.,and Pass, R.F. 1993. Maternal age and congenital cytomegalovirus infection: screening of two diverse newborn populations 1980– 1990. J Infect Dis. 168:552–6.
- Brooks, G.F., Butel, J.S., and Morse, S.A. 2001. Herpes viruses Cahpter 33 in Jawetz, Melnick and Adelberg's Medical Microbiology 22nd Ed. Lange Medical Books/McGraw-Hill, USA: 385.
- De Jong, M.D., Galasso, G.J., Gazzad, B., Griffith, P.D., Jabs, D.A., Kern, E.R.,and Spector, S.A. **1998**. Summary of the II International symposium on cytomegalovirus. *Antiviral-Res.***39** (3): 141-162.
- 20. Griffiths, P.D. **2002**. Strategies to prevent CMV infection in the neonate. *Semi Neonatol*.**7**:293–299.
- Adler SP, Finney JW, Manganello AM, and Best AM. **1996**. Prevention of child-to-mother transmission of cytomegalovirus by changing behaviors: a randomized controlled trial. *Pediatr Infect Dis J.***15**:240 –246.
- DiClemente RJ,and Wingood GM.
 2003. Human immunodeficiency virus prevention for adolescents: windows of opportunity for optimizing intervention effectiveness. *Arch Pediatr Adolesc Me*.
 157:319-320.