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PREVALENC OF CYTOMEGALOVIRUS INFECTION AMONG BLOOD DONORS AND OUT-PATIENTS ATTENDING ZELITEN TEACHING HOSPITAL, ZELITEN, LIBYA

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الخلاصة:

الفيروس المضخم للخلايا البشرية (HCMV) من الفيروسات الممرضة الانتهازية المرتبطة بنسب ومستويات حاده للمرضية والاماتة عند المرضى المعرضين لخطر المرض بسبب اعتلال في الجهاز المناعى خاصة عند مرضى زراعة الاعضاء وكذلك عند النساء الحوامل. أجريت هذه الدراسة لتحديد مدى تفشى وانتشار الفيروس المضخم للخلايا البشرية (HCMV) بين متبرعى الدم والمرضى المترددين على العيادات الخارجية وكذلك الاشخاص الاصحاء ظاهريا في مدينة زليتن – ليبيا. تم جمع عينات الدم المحيطى من الاشخاص الذين شملتهم الدراسة في مدينة زليتن – ليبيا. ثم الكشف عن مستوى الاجسام المضادة نوع الغلوبولين المناعى (IgM) ونوع الغلوبولين المناعى (IgG) عن طريق استخدام تقنية معروفة ب (ELISA) وفقا للإرشادات والخطوات المتبعة والموضوعة من الشركة المصنعة لمحاليل وكواشف الاختبارات. خلصت نتائج هذه الدراسة الى ان نسبة تفشى وانتشار الفيروس المضخم للخلايا البشرية كانت عالية بين الحالات التي تمت دراستها.

ABSTRACT

Human cytomegalovirus (HCMV) is an opportunistic pathogen associated with severe morbidity and mortality is patients at risk for disease because of immune system disabilities; in particular, recipients of blood, solid organ transplants and pregnant women. The aim of this study was to assess the incidence and risk of HCMV infection among blood donors, cases attending outpatient's clinics and apparently healthy control persons in Zeliten city, Libya. Peripheral blood samples were collected from individuals included in the study, Zeliten City, Libya. Detection of HCMV (IgM and IgG antibodies) was carried out using ELISA technique in accordance with kits instructions. The findings of this study indicated that high percentage of HCMV among the studied cases.

KEY WORDS: Cytomegalovirus, IgM, IgG, Blood Donors and Zeliten.

INTRODUCTION

Human Cytomegalovirus (HCMV) is a ubiquitous virus infection with worldwide distribution. The seroprevalence of CMV in adults ranges from 55% in developed countries to as high as over 90% in developing countries (Cannon et al., 2010), leading to severe diseases in newborns and immunocompromised adults (Tirosh et al., 2015). Human cytomegalovirus (HCMV) is the most common source of congenital malformation resulting from viral intrauterine infection in developed countries (Jahromi et al., 2010). Symptoms in these individuals typically consist of spiking fever, leucopenia (decrease in white blood cells), malaise, hepatitis, pneumonia, gastrointestinal disease and/or retinitis (inflammation of the retina) (Soderberg-Naucler, 2006). HCMV is an important viral cause of fetal infection which may lead to severe clinical complications in the newborn child, such as encephalitis, chorioretinitis, pneumonia, microcephaly and hearing loss, as well as impaired cognitive development (Britt, 2008).

Immunity against the virus controls replication, although intermitent viral shedding can still take place in the seropositive immunocompetent person. Replication of cytomegalovirus in the absence of an effective immune response is central to the pathogenesis of disease. Therefore, complications are primarily seen in individuals whose immune system are immature, or are suppressed by drug treatment or co-infection with other pathogens (Gandhi and Kanna, 2004). There are three antiviral agents (Ganciclovir, Cidofovir, and Foscarnet) are used to treat the HCMV. Recently in 2014, many vaccines are developed with recombinant protein, live attenuated, DNA and other vaccines (Heungan and Mark, 2010). The aim of this study was to assess the incidence and risk of HCMV infection among blood donors, cases attending outpatient's clinics and apparently healthy control persons in Zeliten city, Libya.

MATERIALS AND METHODS

A sero-survey of HCMV IgG and IgM-antibody in 250 cases of voluntary blood donors, attendants of Out-patients Clinics and apparently healthy individuals in Zeliten city population at Zeliten Teaching Hospital, Libya during October 2015 to March 2016. Participants in this study were categorized into:

Group-I Blood donors: One hundred (50 males and 50 females) blood donors at blood bank of Zeliten Teaching Hospital.

Group-II Out-patients Clinics: One hundred (50 males and 50 females) attending different out-patient clinics in Zeliten city.

Group-III Control: Fifty apparently healthy individuals.

5 ml of Blood was collected from the each cases and prepared serum at 2000 rpm using refrigerated Centrifuge. Seropositivity test of IgM and IgG were tested using the standard ELISA kit (BioChek, Inc. 323Vintage Park Drive, Foster City, CA94404. USA).

RESULTS AND DISCUSSIONS

The most frequently used methods for detecting immunoglobulin M and immunoglobulin G antibodies is the enzymatic immunoassay (ELISA). The presence of a specific immunoglobulin M antibody suggests active infection. The serological tests using the IgG reagent were helpful in determining HCMV seroprevalence and antecedents of previous infections.

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Table 1 showed HCMV IgM prevalence among blood donors, the prevalence of HCMV IgM was found to be 3.0% positive. HCMV IgM was observed among males and in age range 21-40 years old. No positive cases were detected among females. On contrast seropositivty to HCMV IgG was very high (95%) (47% and 48% in males and female cases respectively) and observed among all ages as shown in table. This might reflect an alarming picture of the disease in the population and indicates that seroconversion is an ongoing process. Similarly, Kothari *et al*., reported 95% seroprevalence in voluntary blood donors of Delhi. However, they did not find any IgM positive case amongst donors which was 0% [(66)]. High HCMV seroprevalence ranging from 90-100% in blood donors was also reported from Malaysia and Mauritius (Gargouri et al., 2000 and Pultoo et al, 2001) and Tunisia (Abusetta et al., 2013).

Table (1): Seropositivity to HCMV IgM & IgG among the blood donors according to age and gender

S. No.	Variable	HCMV IgM				HCMV IgG			
		Positive		Negative				Positive	
		Number	%		Number	%		Number	%
1	Gender								
		3.0	3.0	47.0	47.0	47.0	47.0	3.0	3.0
	Male	0.0	0.0	50.0	50.0	48.0	48.0	2.0	2.0
	Female	3.0	3.0	97.0	97.0	95.0	95.0	5.0	5.0
	Total								
2	Age								
	≤ 20	0.0	0.0	15.0	15.0	15.0	15.0	0.0	0.0
	21-40	3.0	3.0	65.0	65.0	63.0	63.0	5.0	5.0
	≥ 41	0.0	0.0	17.0	17.0	17.0	17.0	0.0	0.0
		3.0	3.0	97.0	97.0	95.0	95.0	5.0	5.0
	Total								

Table (2): Seropositivity to HCMV IgM & IgG in attending outpatient's clinics according to age and gender

S. No.	Variable	HCMV IgM				HCMV IgG			
		Positive		Negative				Positive	
		Number	%		Number	%		Number	%
1	Gender								
		2.0	2.0	48.0	48.0	47.0	47.0	3.0	3.0
	Male	3.0	3.0	47.0	47.0	48.0	48.0	2.0	2.0
	Female	5.0	5.0	95.0	95.0	95.0	95.0	5.0	5.0
	Total								
2	Age								
	≤ 20	2.0	2.0	17.0	17.0	17.0	17.0	2.0	2.0
	21-40	3.0	3.0	50.0	50.0	52.0	52.0	1.0	1.0
	≥ 41	0.0	0.0	28.0	28.0	24.0	24.0	4.0	4.0
		5.0	5.0	95.0	95.0	93.0	93.0	7.0	7.0
	Total								

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Table (3): Seropositivity to HCMV IgM & IgG among the control persons according to age and gender

S. No.		HCMV IgM				HCMV IgG			
		Positive		Negative				Positive	
		Number	%		Number	%		Number	%
1	Gender								
	Male	0.0	0.0	25.0	50.0	23.0	46.0	2.0	4.0
	FemalVariablee	1.0	2.0	24.0	48.0	24.0	48.0	1.0	2.0
	Total	1.0	2.0	49.0	98.0	47.0	94.0	3.0	6.0
2	Age								
	≤ 20	0.0	0.0	14.0	28.0	14.0	28.0	0.0	0.0
	21-40	1.0	2.0	19.0	38.0	17.0	34.0	3.0	6.0
	≥ 41	0.0	0.0	16.0	32.0	16.0	32.0	0.0	0.0
	Total	1.0	2.0	49.0	98.0	47.0	94.0	3.0	6.0

Table (4): Seropositivity to HCMV IgM & IgG among the blood donors according to educational level.

S. No.	Educational level	HCMV IgM				HCMV IgG			
		Positive		Negative		Positive		Negative	
		Number	%	Number	%	Number	%	Number	%
1	Illiterate	0.0	0.0	7.0	7.0	7.0	7.0	0.0	0.0
2	High school	2.0	2.0	55.0	55.0	53.0	53.0	4.0	4.0
3	Graduated	1.0	1.0	26.0	26.0	26.0	26.0	1.0	1.0
4	Post graduated	0.0	0.0	9.0	9.0	9.0	9.0	0.0	0.0
	Total	3.0	3.0	97	97	95	95	5.0	5.0

Table (5): Seropositivity to HCMV IgM & IgG among cases attending outpatient's clinics according to educational level

S. No.	Educational level	HCMV IgM				HCMV IgG			
		Positive		Negative		Positive		Negative	
		Number	%	Number	%	Number	%	Number	%
1	Illiterate	2.0	2.0	33.0	33.0	33.0	33.0	2.0	0.0
2	High school	3.0	3.0	45.0	45.0	44.0	44.0	4.0	4.0
3	Graduated	0.0	0.0	16.0	16.0	15.0	15.0	1.0	1.0
4	Post graduated	0.0	0.0	1.0	1.0	1.0	1.0	0.0	0.0
	Total	5.0	5.0	95.0	95.0	93.0	93.0	7.0	7.0

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Table (6): Seropositivity to HCMV IgM & IgG among control persons according to educational level.

S. No.	Educational level	HCMV IgM				HCMV IgG			
		Positive		Negative		Positive		Negative	
		Number	%	Number	%	Number	%	Number	%
	Illiterate	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
1	High school	0.0	0.0	18.0	36.0	17.0	34.0	1.0	1.0
2	Graduated	1.0	2.0	27.0	54.0	26.0	52.0	2.0	2.0
3	Post	0.0	0.0	4.0	8.0	4.0	8.0	0.0	0.0
4	graduated	1.0	2.0	49.0	98.0	47.0	94.0	3.0	6.0
	Total								

Table (7): Seropositivity to HCMV IgM & IgG among the blood donors according to Occupation.

S. No.	Occupation	HCMV IgM				HCMV IgG			
		Positive		Negative		Positive		Negative	
		Number	%	Number	%	Number	%	Number	%
1	Unemployed	0.0	0.0	7.0	7.0	7.0	7.0	0.0	0.0
2	Student	0.0	0.0	32.0	32.0	31.0	31.0	1.0	1.0
3	Administration	3.0	3.0	40.0	40.0	39.0	39.0	4.0	4.0
4	Housewife	0.0	0.0	18.0	18.0	18.0	18.0	0.0	0.0
	Total	3.0	3.0	97.0	97.0	95.0	95.0	5.0	5.0

Table (8): Seropositivity to HCMV IgM & IgG among cases attending outpatient's clinics according to occupation

S. No.	Occupation	HCMV IgM				HCMV IgG			
		Positive		Negative		Positive		Negative	
		Number	%	Number	%	Number	%	Number	%
1	Unemployed	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
2	Student	2.0	2.0	30.0	30.0	30.0	30.0	2.0	2.0
3	Administration	1.0	1.0	31.0	31.0	29.0	29.0	3.0	3.0
4	Housewife	2.0	2.0	34.0	34.0	24.0	24.0	2.0	2.0
	Total	5.0	5.0	95.0	95.0	93.0	93.0	7.0	7.0

Table (9): Seropositivity to HCMV IgM & IgG among the control persons according to occupation.

S. No.	Occupation	HCMV IgM				HCMV IgG			
		Positive		Negative		Positive		Negative	
		Number	%	Number	%	Number	%	Number	%
1	Unemployed	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
2	Student	0.0	0.0	10.0	20.0	10.0	20.0	0.0	0.0
3	Administration	1.0	2.0	32.0	64.0	30.0	60.0	3.0	3.0
4	Housewife	0.0	0.0	7.0	14.0	7.0	14.0	0.0	0.0
	Total	1.0	2.0	49.0	98.0	47.0	94.0	3.0	6.0

The table 2 showed numbers and percentages of seropositive cases for HCMV (IgG) among cases attending outpatient clinics according to their ages. Among the 100 cases attending outpatient clinics were entitled in this study, only five cases (5.0%) tested positive for anti-IgM HCMV. On the other hand, 93% of cases were positive for IgG antibodies, indicating past exposure to the infection (table 2).

On comparing seropositivty to HCMV IgG between male and female cases attending outpatient clinics were 46 out of 50 and 47 out of 50 in males and female cases respectively. The results revealed that there was no significance difference between males and females.

Table 3 showed HCMV IgM prevalence among apparently healthy control persons, the prevalence of HCMV IgM was found to be 2.0% positive. HCMV IgM was observed among males and in age range 21-40 years old. No positive cases were detected among females. On contrast seropositivty to HCMV IgG was very high (94%), (46% and 48% in males and female cases respectively). The effect of education state on seronegativity for HCMV among the blood donors were obtained in table 4. The results showed that, the lowest percentage of seronegative cases for HCMV (IgG) in blood donors was 0.0% in both illiterate and postgraduate blood donors respectively and the highest percentage of seronegative cases for HCMV (IgG) in blood donors was 4.0% and 1.0% among high school and graduated blood donors. Also the same results were also observed with HCMV (IgM), where the percentage of seronegative cases was 0% in both illiterate and postgraduate blood donors and the highest percentage of cases 55.0% and 26.0% among high school and graduated blood donors respectively.

The effect of education on seronegativity for HCMV among the outpatient's clinics was obtained in table 5. The results showed that the lowest percentage of seronegative cases for HCMV (IgG) in outpatient's clinics was 0.0% in postgraduate outpatient's clinics and the highest percentage of seronegative cases for HCMV (IgG) in outpatient's clinics was 4.0%, 2.0% and 1.0% among high school illiterate and graduated outpatient's clinics. However, HCMV (IgM), the percentage of seronegative cases was 16% and 1.0% in both graduated and postgraduate outpatient's clinics respectively and the highest percentage of cases 45.0% and 35.0% among high school and illiterate outpatient's clinics respectively. Concerning the apparently healthy control persons, only one case (2.0%) was detected IgM seropositive to HCMV and the other control persons were IgM seronegative. On contrast, only three persons were IgG seronegative (one had high school graduation and two graduated) (table 6).

Concerning the effect of occupation on seropositivity for HCMV among the studied cases were illustrated in tables 7 - 9. The percentages of seropositive cases for HCMV (IgM) in blood donors were high (3.0%) among those possessing administration jobs. Other groups were IgM HCMV seronegative. IgG to HCMV detected in all studied blood donors except in four working in administration position and one student (seronegative). Meanwhile among those attending outpatient clinics IgM seropositivity to HCMV were observed in two students and in one cases had administration job. In respect to IgG all studied cases were IgG seropositive except seven cases were IgG seronegative including two students, two housewife and three with administration jobs. However, only one control person found to be IgM

seropositive and had administration job and all were IgG seropositive except three working in administrative position.

The complexity and uncertainty related to the geographic distribution of HCMV infection, determination of its associated risk factors and evaluation of cofactors that accelerate its progression, underscore the difficulties in global prevention and control of HCMV. Although HCMV is endemic worldwide, there is some degree of geographic variability in its distribution. This could be due to the non-adherence to the strict universal infection control measures and the unavailability of vaccines to prevent HCMV infection.

CONCLUSION

HCMV exists in all geographic locations and socioeconomic groups. HCMV is the virus most frequently transmitted to a developing child before birth. HCMV infection is more widespread in developing countries and in communities with lower socioeconomic status and represents the most significant viral cause of birth defects in industrialized countries. The prevalence of HCMV IgG was found to be 93.0% - 95.0% in healthy blood donors, cases attending outpatient's clinics and even apparently healthy control persons. The results of the current study indicated that there was no difference between different ages, gender, educational levels and different occupations (Socio-economic factors) in the prevalence of HCMV-IgG and IgM antibodies.

PREVENTION

The only measure available to prevent HCMV infection is to avoid exposure. HCMV is not very contagious, and horizontal transmission requires close contact with infected secretions or occasionally fomites. Basic hygiene practices could be recommended to all pregnant women without testing for HCMV antibody status (Adler et al., 1996). Routine HCMV screening of HCMV during pregnancy. Isolation of newborns with generalized cytomegalic inclusion disease from other newborns is advisable. Screening of Blood donors and organ transplant donors and recipients for HCMV prevent some transmissions of primary HCMV.

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