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Frequency of CMV- Infection among Hemodialysis Patients in Tikrit City

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Abstract

It has been well documented that hemodialysis patients have impaired immune response, which may result in higher prevalence rates of viral infections, including CMV. Infections in these patients may be due to primary infection or, more commonly, by reactivation of latent virus or re-infection with exogenous virus, which may be introduced by blood transfusion. The aim of this study was to evaluate the frequency of CMV-IgG and IgM antibodies among hemodialysis patients. The current research included 116 hemodialysis patients (69 male and 47 female) who attended to Tikrit Teaching Hospital for the period from beginning of October/2013 to the end of April/2014. CMV-IgG was found in 102 out of 116 (87.9%), while CMV- IgM was detected in 10 out of 116 (8.6%) of hemodialysis patients. CMV-IgG was found in a higher rate in females than that in males (91.5% and 85.5% respectively), while CMV-IgM was detected in a higher rate in males than that in females (10.1% and 6.4% respectively). However, there was non-significant difference ($p > 0.05$) between sex and seropositivity. Also, non-significant relation was found between age and seropositivity for both CMV-IgG and CMV-IgM antibodies ($p > 0.05$). Since patients receiving hemodialysis treatment are immunocompromised and can be at risk of primary infection or reactivation of latent infection of CMV, its necessary to identify these patients with anti-CMV IgG and IgM specific serological tests for appropriate management.

Keywords: CMV, hemodialysis patients, ELISA.

تكرار الخمج بالفيروس المضخم للخلايا(CMV) بين مرضى الديلزة الدموية في مدينة تكريت

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الخلاصة

من المعروف جيدا" أن مناعة مرضى الديلزة الدموية تكون ضعيفة والذي ينتج عنه انتشارا" عاليا" للأخماج الفيروسية بينهم والتي من بينها CMV. ان الأخماج بين هؤلاء المرضى قد تكون بسبب إصابة أولية، أو الأكثر شيوعا"، اعادة تنشيط فيروس كامن أو اعادة الإصابة بفيروس جديد، والذي يمكن أن يحدث عن طريق نقل الدم. كان الهدف من هذه الدراسة تقييم تكرار CMV–IgG و CMV–IgM في مرضى الديلزة الدموية. شمل البحث الحالي 116من مرضى الديلزة الدموية (69ذكر و47 أنثى) المراجعين لمستشفى تكريت التعليمي للفترة منذ بداية تشرين الأول/2013 ولغاية نهاية نيسان/2014 . وجدت الأجسام المضادة CMV–IgG في 102 من مجموع 116 (87,9٪)، بينما الأجسام المضادة CMV–IgM كانت موجودة في 10 من مجموع 116 (8,6٪) من مرضى الديلزة الدموية. كان CMV–IgG موجودا" بمعدل أعلى في الاناث عما هو عليه في الذكور(91,5٪ و 85,5٪ على التوالي)، بينما تم الكشف عن CMV–IgM بمعدل أعلى في الذكور عما هو عليه في الاناث (10,1٪ و 6,4٪ على التوالي). على الرغم من ذلك، لم تلاحظ فروقا"

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معنوية ($p<0.05$) بين الجنس والايجابية المصلية. كذلك لم تلاحظ فروقا" معنوية بين العمر والايجابية المصلية لكل من CMV– IgG و CMV–IgM ($p<0.05$). بسبب أن مرضى الديلزة الدموية لديهم مناعة ضعيفة وممكن أن يكونوا تحت خطر الخمج الأولي بالـ CMV أو إعادة تنشيط الخمج الكامن به، فإنه من الضروري معرفة هؤلاء المرضى بالفحوصات المصلية المتخصصة لكل من الـ CMV–IgG وCMV–IgM لغرض المعاملة المناسبة معهم.

Introduction

The human cytomegalovirus (HCMV) is a member of the family Herpesviridae. The virus contains a core with double-stranded DNA, an icosahedral capsid, and a phospholipid-rich envelope. Although most HCMV infections are asymptomatic, certain patients groups are at risk to develop serious illness and long-term effects from an HCMV infection. The HCMV can infect any cell of the body [1]. Cytomegalovirus may be transmitted from person-to-person in several different ways, all requiring close contact with virus-bearing material. There is a 4- to 8-week incubation period in normal older children and adults after viral exposure. The virus causes a systemic infection; it has been isolated from lung, liver, esophagus, colon, kidneys, monocytes, and T and B lymphocytes. Like all herpesviruses, cytomegalovirus establishes lifelong latent infections. Virus can be shed intermittently from the pharynx and in the urine for months to years after primary infection. Prolonged cytomegalovirus infection of the kidney does not seem to be deleterious in normal persons [2].

Cytomegalovirus causes infection in immunocompromised, transplant recipients and those patients who are in need of frequent blood transfusion. Risk factors for primary CMV infection include blood transfusion (treatment for clotting factors, and etcetera), infected transplants, hemodialysis, and the frequency of dialysis in a week [3]. CMV seroprevalence has been shown to be highest in South America, Africa, and Asia, while it is lowest in Western European countries and the United States[4]. In developed countries, about 70% of adults have asymptomatic latent CMV infection. It can be reactivated if individual becomes immunosuppressed. CMV is the most common viral infection after kidney transplantation [5]. Depending on the socioeconomic status, seropositivity for adult population over forty years ranges from 60 to 100% possibly as a result of transmission through intrauterine (or at parturition), breastfeeding, blood transfusion, sexual contact and spread from children. It tends to be lower in the developed countries than the developing countries [6, 7]. The aim of this study was to evaluate the frequency of CMV-IgG and IgM antibodies among hemodialysis patients in Tikrit City.

Materials and Methods

The current research included 116 hemodialysis patients (69 male and 47 female) who attended to Tikrit Teaching Hospital for the period from beginning of October/2013 to the end of April/2014. Five ml of blood was collected from each patient by vein puncture using disposable syringes. The blood was placed in plastic disposable tubes; it was left to stand at room temperature (20- 25°C) to allow it to clot, then the sera was separated by centrifugation 10000 rpm for 5 minutes and stored at -20°C until the time of test.

Serological investigation included detection of CMV-IgG antibodies and CMV-IgM antibodies by using enzyme-linked immunosorbent assay (ELISA) (Abbott kits, Abbott Laboratories, USA). The procedure was carried out according to the manufacturer's instructions.

Statistical Analysis

The statistical analysis was performed using chi-square test. P values less than 0.05 were considered statistically significant.

Results and Discussion

Cytomegaloviruses are ubiquitous herpesviruses that are common causes of human disease. It is present throughout the year, with no seasonal variation seen in infection rates [2]. Most people become infected with this virus at some time during their life; in the United States, as many as 80% of individuals older than 35 years have been exposed to this virus and carry a lifelong infection [1]. Cytomegalovirus is endemic in most areas of the world. The seroprevalence of CMV varies in different geographical areas and it ranges from 30-100% [8]. Cavlek *et al* [9] confirmed that hemodialysis and older age are significant predictors for CMV seropositivity.

The laboratory diagnosis which was done in the current research revealed that CMV-IgG was found in 102 out of 116 (87.9%), while CMV- IgM was detected in 10 out of 116 (8.6%) of hemodialysis patients. No one of patients had CMV-IgG with IgM at the same time Table-1.

Table 1-Frequency of CMV-IgG and IaM Antibodies in Hemodialysis Patients.

No. of patients	CMV- IgG		CMV-IgM	
	No.	%	No.	%
116	102	87.9	10	8.6

Abou- El-Yazed *et al* [10] has found that seroprevalance of CMV infection among hemodialysis patients (HD) was 98% using CMV ELISA IgG and 11% using CMV/IgM. A study was carried out in Antakya, Turkey to determine the seroprevalence of CMV infections. Positivity for anti-CMV IgG was found in 99.6% of the HD patients. Anti-CMV IgM antibody was noted in 0.4% of the HD patients [11]. Furthermore, Cavlek *et al* [9] reported a significantly higher CMV seropositivity among hemodialysis patients(91%). The overall seroprevalence of CMV in hematologic disorders in Brazil was 89.4% [12].

The high CMV prevalence in hemodialysis patients could be explained by the acquisition of CMV through repeated blood transfusions or exposure to CMV during hemodialysis procedures.

However, other studies were done regarding CMV in individuals other than hemodialysis patients.

A study was done in Mosul city to evaluate the percentage of infections that could occur due to blood transfusion reported that CMV- IgM was found in 10% of blood donors [13]. In Baghdad city, a serological diagnosis of anti- Cytomegalovirus (IgM and IgG) in women specimens 178 (72 pregnant and 106 non pregnant) using enzyme linked fluorescent assay (ELFA) revealed that only 2.8% positive for anti cytomegalovirus IgM antibodies and 13.4% positive for anticytomegolovirus IgG antibodies [14].

A research concerning patients were attending King Abdulaziz University Hospital at different departments (Gynecology and Obstetrics, Blood bank, Nephrology and Dialysis centers) showed that antibodies for cytomegalovirus was mostly prevalent among blood donors (82.9%) [15].

Ahmed *et al* [16] recorded that the prevalence of human cytomegalovirus seroposoitivity among blood donors at the unit of blood transfusion medicine in Malaysia was 97.6%.

Cytomegalovirus seroprevalence within the United States has also provided substantial geographic variation, differing by as much as 30 percentage points between states, though differences may be explained by variation in the types of populations sampled [4].

The variation in the presence of anti CMV IgM and IgG positive level in different studies may be related to the number of individuals sera examined, geographical distribution and sensitivity of different immunoassays for defection of level of anti- CMV IgM and IgG antibodies.

The study presented here included 69 male, CMV-IgG was found in 59 (85.5%) of them. Regarding females, CMV-IgG was detected in 43 out of 47 (91.5%). However, the result was non-significant ($p > 0.05$). The laboratory investigation concerning CMV- IgM among hemodialysis patients revealed that 7 out of 69 (10.1%) of males and 3 out of 47 (6.4 %) of females have CMV- IgM antibodies. However, the result was non-significant ($p > 0.05$) Table-2.

Table 2-Distribution of CMV- IgG and IaM Antibodies According to Gender.

Gender of patients	No. of patients	CMV- IgG		CMV-IgM	
		No.	%	No.	%
Male	69	59	85.5	7	10.1
Female	47	43	91.5	3	6.4
Total	116	102	87.9	10	8.6
X^2		0.116		0.49	
P		> 0.05		> 0.05	

In Turkey, gender did not contribute independently to the seroepidemiology of CMV($p > 0.01$) [17]. Also, Cavlek *et al* [9] reported that there was no difference in CMV prevalence between males (87.9%) and females (96.3%). de Matos *et al* [12] showed non- significant relation concerning sex status of the CMV-cases.

On the other hand, a previous studies by Gargouri *et al* [18] in Tunisia and Cannon *et al* [4] in U.S. reported that females had higher seroprevalence than males. de Ory Manchon *et al* [19] found that seroprevalence for anti-CMV IgG in the general population in Madrid was 62.8%, ranging from 58.4% in men to 66.7% in women. It is possible that the gender difference in CMV seroprevalence reflects females' exposure to young children. The relationship of child care to CMV infection has been presumed to be attributable to the presence of CMV at high titers in urine and/or saliva. Nevertheless, a previous study suggested that, similar to females, adolescent males are at an increased risk of CMV infection when exposed to young children in the household [20].

Data obtained by the current work revealed that the highest rate of CMV-IgG antibodies was found in hemodialysis patients within the age group 50-64 yr. followed by those within the age group ≥ 65 yr. (93.2% and 92 % respectively), although the result was non-significant ($p> 0.05$). On the other hand, CMV- IgM was detected at a highest rate in patients within the age group ≤34 yr. followed by those within the age group 35-49 yr. (21.1% and 7.1% respectively). However, the result was non-significant ($p> 0.05$) Table-3. Similar result was obtained by Kothari *et al* [21] who reported no relation between age and seropositivity among voluntary blood donors.

Table 3- Distribution of CMV- IgG and IaM Antibodies According to Age Groups.

Age Group (yr.)	No. of patients	CMV- IgG		CMV-IgM	
		No.	%	No.	%
≤34	19	14	73.7	4	21.1
35-49	28	24	85.7	2	7.1
50-64	44	41	93.2	3	6.8
≥ 65	25	23	92	1	4
Total	116	102	87.9	10	8.6
X^2		0.637		4.336	
P		> 0.05		> 0.05	

A previous study identified an independent correlation between CMV infection and the mutation levels in both IgM and IgG-expressing B cells in individuals regardless of age. This could be a direct effect of some B cells being specific for CMV [22].

An increase in the seroprevalence rates was observed with age ($p < 0.001$) in a research in Turkey [17]. Also, a significant association between increase of the age and increment of the seroprevalence was observed in Madrid [19]. Cavlek *et al* [9] confirmed that according to age, a progressive increase in seropositivity was observed in hemodialysis patients.

Varying methodologies perhaps may have contributed to the disparities observed. Although immunocompromised patients are at risk for morbidity due to wide variety of pathogens, few, if any of these are capable of producing such widspread disease as CMV. CMV-related morbidity follows a progressive, relentless course in the absence of effective therapeutic intervention. Thus, rapid diagnosis of active CMV infection is of great importance to avoid over treatment with immunosuppressive drugs and to guide antiviral therapy. In recent years, treatment of CMV infection in high-risk patients prior to the onset of clinical disease is preferred [23].

Conclusion

Since patients receiving HD treatment are immunocompromised and can be at risk of primary infection or reactivation of latent infection of CMV, its necessary to identify these patients with anti CMV IgG and IgM specific serological tests for appropriate management.

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