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Detection of EBV and CMV coinfection among patients under hemodialysis

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***Abstract*---**Background: CMV and EBV infections are a common cause of complications in patients with a variety of chronic diseases, and they are one of the most significant factors preventing patients from completing their treatment successfully. Aim of the study: The study's goal was to determine the frequency of EBV and CMV infections in patients receiving hemodialysis and how that frequency correlated with serum IL-6 levels. Patients and Methods: A cross sectional study was carried out in Kirkuk city from 15th of January 2021 to 15th of November 2021. A total of 87 hemodialysis patients and 33 healthy control group whose ages were between 30-75 years old. These patients admitted to Kirkuk General Hospital. An interview was carried out with these patients using questionnaire form designed by the investigator. Four ml of blood was collected from each person enrolled in this study for detection of specific EBV, and CMV IgM antibodies and Interleukin-6 by using ELISA technique.Results: The study showed that the highest rate of EBV-IgM Abs was occurred in hemodialysis patients (43.68%) comparing with the control group(9.09%), P<0.01. CMV –IgM was found 47.13% of HD patients and 21.21% of the control group, P<0.01. The study demonstrated that 40.23% of all HD who enrolled in the study were suffered from CMV and EBV infection followed by a rate of 11.49% which represent the infection with EBV alone, and 13.49% for CMV alone. In the present study, males were more recorded with hemodialysis (60%) comparing with 30% females. The highest mean of IL-6 level (49.45)

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was detected in HD patients plus EBV infection followed by mean of 34.36 in HD patients without EBV infection, and the highest mean of IL-6 level (39.46) was occurred in HD patients with CMV infection followed by HD patients who were infected without CMV (31.23), while the lowest mean was recorded in the control group (6.45), P<0.01. Conclusions**:** It was concluded that there was a highly significant relation of CMV and EBV IgM Abs with hemodialysis and high level of IL-6 was recorded in infected HD patients

***Keywords*---**EBV, CMV, coinfection, hemodialysis.

Introduction

Patients with a wide range of illnesses, including hematological malignancies, breast cancer, and a host of chronic conditions, are at risk of developing CMV and EBV infections, which are among the most significant obstacles to completing treatment (1,2). Contact with saliva is the most common method of spreading EBV. However, sexual contact, blood transfusions, and organ transplants can all spread the virus (3, 4). End-stage kidney failure patients may need to undergo hemodialysis (HD) in order to remove waste products from their bloodstreams. Renal transplantation is considered the best option for these patients because of its high success rate (5). Due to severe impairments in cell-mediated immunity, patients with end-stage renal failure have an increased lifetime risk of contracting opportunistic viral infections such as EBV infection (6). When the immune system is compromised due to illness or medication, EBV is more likely to cause problems (7). Consequently, patients on dialysis or undergoing renal transplantation who are immunocompromised are more susceptible to EBV infection. A virus known as cytomegalovirus (CMV) infects people all over the world, resulting in illness and death (8). An infection can be spread through close contact with an infected person. Swellings in the saliva, blood, sperm, and breast milk are all examples of bodily fluids where CMV has been found. Blood transfusions and organ transplants are two other ways in which CMV can spread (9,10). Researchers wanted to see how often EBV and CMV infections occurred in people on hemodialysis and if there was a link between those infections and elevated levels of the cytokine IL-6.

Patients and Methods

It was conducted in Kirkuk city from the 15th of January 2021 to the 15th of November 2021, and it included 87 hemodialysis patients and 33 healthy control group participants ranging in age from 30 to 75 years. The patients in this group were admitted to Kirkuk General Hospital. An interview with these patients was conducted using a questionnaire form that had been developed by the investigators. The control group, which was made up of 33 unaffected individuals whose ages ranged from 30 to 75 years, was matched to the patients who were being studied. Each patient who participated in this study had four milliliters of blood drawn through a vein puncture and placed in Vacutainer tubes. Following collection of blood samples in plane tubes for 30 minutes at 37 degrees Celsius, centrifugation at 3000 rpm for 15 minutes, removal of the clot and re-

centrifugation at 3000 rpm for 10 minutes, and aspiration of the obtained sera into clean test tubes for serological testing were carried out using an automatic micropipette. Each test tube was labeled and then placed in a deep freezer at -20°C for serological testing to detect specific EBV and CMV IgM antibodies as well as Interleukin-6 using the ELISA technique. The results of the serological testing were then analyzed.

Results

In relation of EBV-IgM Abs with hemodialysis patients , Table 1 shows that the highest rate of EBV-IgM Abs was occurred in hemodialysis patients (43.68%) comparing with the control group (9.09%). The result was highly significant.

Table 4.2: Frequency of EBV-IgM antibodies in HD patients and control group

EBV IgM	hemodialysis patients		Control	
	No.	%	No.	%
Positive	38	43.68	3	9.09
Negative	49	56.32	30	90.91
Total	87	100	33	100

P < 0.01

Table 2 shows that CMV –IgM was found 47.13% of HD patients and 21.21% of the control group, with a significant relation between the two groups.

Table 2: Frequency of CMV-IgM antibodies in HD patients and the control group

CMV IgM	HD patients		Control	
	No.	%	No.	%
Positive	41	47.13	7	21.21
Negative	46	52.87	26	78.79
Total	87	100	33	100

P < 0.01

In Table 3, 40.23% of all HD who enrolled in the study were suffered from CMV and EBV infection followed by a rate of 11.49% which represent the infection with EBV alone, and 13.49% for CMV alone.

Table 3: Frequency of coinfection with EBV and CMV among HD patients

Infection	No.	%
EBV	10	11.49
CMV	12	13.79
EBV+CMV	35	40.23
No infection	30	34.48
Total	87	100

In the present study, males were more recorded with hemodialysis (60%) comparing with 30% females, Figure 1.

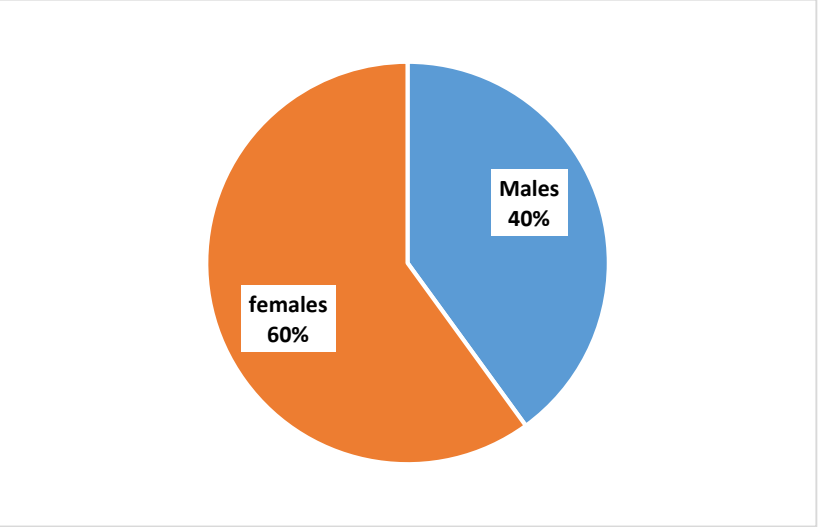

Figure 1: Distribution of HD patients according to sex

As shown in Table 4, the highest mean of IL-6 level (49.45) was detected in HD patients plus EBV infection followed by mean of 34.36 in HD patients without EBV infection, while the lowest mean was recorded in the control group (5.32). The relation was statistically highly significant.

Table 4: Relation of EBV infection with IL-6 among HD patients and the control group

IL-6 level (pg/ml)	HD patients		Control group
	EBV +	EBV-	
Mean	49.45	34.36	5.32
SD	3.65	4.23	1.28

P<0.001

Table 5 shows that the highest mean of IL-6 level (39.46) was occurred in HD patients with CMV infection followed by HD patients who were infected without CMV (31.23), while the lowest mean was recorded in the control group (6.45). The relation was statistically highly significant.

Table 5 : Relation of CMV infection with IL-6 among HD patients and the control group

IL-6 level (pg/ml)	HD patients		Control group
	CMV +	CMV-	
Mean	39.46	31.23	5.32
SD	4.38	4.37	1.28

Discussion

Among immunocompromised individuals, including hemodialysis patients, it is one of the most frequently encountered opportunistic viral pathogens, and it is also one of the most contagious (8,9). When hemodialysis patients were compared to the control group, it was discovered that they had the highest rate of EBV-IgM antibodies (43.68%). Several studies conducted around the world have demonstrated that there is a significant increase in the rates of EBV infection in people who are on dialysis when compared to healthy people, which supports the findings of our study (11,12,13). The fact that viral infections such as EBV infect humans and cause a variety of diseases, including infection with multiple cancers, such as breast cancer and oropharyngeal cancer, is undeniable. This is due to the genetic interference caused by the virus as it weakens within human cells during its weakening within the human body (14). It was the subject of several published articles at the time about the seroprevalence of CMV among hemodialysis patients around the world, including the United States (15,16,17). According to some studies, co-infection with CMV and EBV is possible. But these findings should be interpreted with caution because other factors, such as underlying diseases, the regimen of immunosuppressive therapy, HLA matching, and the source of the donor kidney, may also have an impact on the outcome of CMV infection or reactivation in the recipient. Moreover, the source of the donor kidney may also have an impact on the outcome of CMV infection or reactivation (18,19). According to the findings of various studies, HD patients have a high prevalence of EBV and CMV IgM seropositivity, which is consistent with previously discovered findings. Consequently, given the clinical significance of those viruses reactivation and the serious complications that can result in immunosuppressed patients, it is recommended that additional studies with a larger sample size be conducted to determine the role of those viruses in patients undergoing hemodialysis therapy. It is necessary to conduct additional research in this area because the current study did not assess the status of their latency. The current findings demonstrate that, when compared to the control group, HD had significantly higher serum interleukin-6 (IL-6) concentrations, particularly when CMV and EBV infections were present. IL-6 is an important factor to consider when it comes to the progression of human breast cancer (20,21). The expression of interleukin-6 (IL-6) and/or its receptors has been observed in patients with chronic kidney disease (CKD); endothelial cells, infiltrating neutrophils, and tumor cells, suggesting that IL-6 may play an important regulatory role within the tumor microenvironment in patients with CKD (22). Increased serum levels of pro-inflammatory cytokines, according to previous research, are associated with a significant increase in cardiovascular and total mortality among patients with end-stage renal disease (ESRD), and more specifically among HD patients (23,24). IL-6 levels before dialysis were found to be the most significant predictor of mortality in a prospective study of chronic heart failure patients in both univariate and multivariate analyses, according to the results of the study. As the most significant predictors of mortality, this was followed by age, serum albumin level, and body mass index as the most significant predictors of mortality (25). Recent research compared the prognostic value of interleukin-6 (IL-6) to that of CRP in patients with heart failure, and it was discovered that IL-6 was a more significant predictor of mortality than CRP (26).

Conclusions

There was a highly significant relation of CMV and EBV IgM Abs with hemodialysis and high level of IL-6 was recorded in infected HD patients.

Recommendations

Supporting the serological investigations of EBV and CMV with possible available molecular tests like PCR.

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