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## Prevalence of Epstein-Barr virus among hemodialysis patients in Kirkuk city

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### Article Informations

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### ABSTRACT

Epstein-Barr virus infection has a significant global impact on adults. In individuals with a strong immune system, the infection usually remains inactive and is effectively controlled. However, for those with compromised immune systems like hemodialysis patients, the virus can lead to severe illnesses that endanger lives.

This study aims to evaluate the presence of IgM and IgG antibodies against the Epstein-Barr virus in hemodialysis patients and explore potential connections between the prevalence of these antibodies, the duration of dialysis (whether exceeding or less than one year), and the frequency of weekly dialysis sessions. The research carried out in Kirkuk city encompassed 91 individuals undergoing hemodialysis and a control group of 50 individuals. Blood serum samples were collected from all participants in the study and subjected to analysis using the ELISA technique. The recent findings revealed that among hemodialysis patients, the prevalence of EBV IgM/IgG antibodies was 7.6% and 42.8% respectively, while in the control group, these values were 0% and 8%. The presence of EBV IgM and IgG antibodies showed a notable correlation with the younger age group. No statistically significant differences were noted concerning the patients' gender. Notably, EBV IgM levels were elevated in patients undergoing dialysis for over a year (71.4%), displaying significant divergence with a p-value of 0.015. The prevalence of Epstein Barr virus was higher in hemodialysis patients compared to the control group. Additionally, the occurrence of acute EBV infection showed a strong association with the duration of dialysis and the frequency of weekly dialysis sessions.



## **Introduction**

Epstein-Barr virus significantly affects the majority of adults worldwide, frequently staying asymptomatic and managed by a strong immune reaction in individuals with good health. Nonetheless, people with weakened immune systems, like those undergoing hemodialysis, could encounter the virus going dormant and subsequently reactivating within the host, resulting in serious and potentially life-threatening diseases [1]. Patients with end-stage renal disease exhibit notable changes in their cell-mediated immunity, rendering them more susceptible to opportunistic viral infections like EBV. When EBV infects hemodialysis patients or organ transplant recipients, their health can deteriorate significantly. One of the most perilous consequences of EBV is post-transplant lymphoproliferative disorder (PTLD), a significant concern that can arise after solid organ transplantation [2]. The Epstein-Barr virus, also known as EBV, was discovered by M.A. Epstein, Y.M. Barr, and B.G. Achong of the United Kingdom. These scientists identified virus-like particles in cells derived from newly described lymphoma tissues [3]. The EBV genome is made of a linear, double-stranded DNA with a relatively large genome size of ~ 172 kilo base pairs (kbp) that encodes for more than 85 genes. It consists of a toroid-shaped protein core encased in an icosahedral capsid containing 162 capsomers, a viral tegument containing a protein that lines the space between the nucleocapsid and the outer envelope, and numerous glycoprotein spikes that are inserted into the viral envelope [4]. EBV seroprevalence rises with age and is typically higher in women, non-Caucasian ethnic groups, and those with lower socioeconomic status [5]. T and B lymphocytes, in addition to the stratified squamous epithelial cells found in the nasopharynx and oropharynx, as well as cells within salivary and stomach glands, thyroid gland epithelia, smooth muscle, and follicular dendritic cells, are vulnerable to EBV infection. The initial location for EBV infection and replication seems to be the layered squamous epithelium of the oropharynx. Following this, the virus turns its attention to latent B lymphocytes. [6]. Since EBVs have been detected in both normal and abnormal bodily fluids, such as blood, urine, saliva, amniotic fluid, cerebrospinal fluid, breast milk, bronchial alveolar lavage, and ascites, it is possible that these viruses can access any part of the human body [7]. Molecular analysis of viral DNA, RNA, and EBV viral load is currently employed in the clinical evaluation of EBV infections associated with tumors [8]. EBV infection can be diagnosed using three parameters: anti-VCA IgM, anti-VCA IgG, and anti-EBNA IgG antibodies [9]. IgM antibodies targeting the viral capsid antigen (VCA) are typically visible mainly during the initial months following symptom onset, rendering their existence especially valuable for identifying primary EBV infection [10]. In many cases, a laboratory analysis will reveal lymphocytosis, often with a lymphocyte differential exceeding 50%. In a blood sample under microscopic examination, an unusual lymphocytosis surpassing 10% can be observed [11].

## **Material and method**

Study was done on 91 hemodialysis patients who underwent to the unit of dialysis in Kirkuk teaching hospital and on 50 individual as control group from the November 2022 to March 2023, the following variables were covered in an interview with these patients via a questionnaire form created by the researcher. Age, place of residence, sex, length of dialysis (more than a year or less). A total of 5 ml of blood was collected from each person who took part in this study then the sample centrifuged for the separation of serum and then the serum sample was tested for the presence of Epstein Barr virus IgM and IgG antibody by using (ELISA) technique.

## **Statistical analysis**

The data was analyzed by using T-test and Chi-square test to obtain p.value of each group sample in this research, p.value significant > 0.05.

## **Result and discussion:**

There was a significant difference between the two groups, as indicated by a p-value of 0.044, which reveals that the EBV IgM was found in (7.6%) HD patients, while the rest patients were negative for EBV IgM (92.3%). While the EBV IgG was discovered in 39 HD patients (42.8%), while the remainder of the patients were negative for EBV IgG (57.1%) with (p-value 0.001) as shown in table [1].

**Table 1.** Prevalence of EBV IgM/IgG Ab among hemodialysis patient and control group

Anti-EBV Ab (ELISA)	HD patients		Control group		P. value
	N = 91	%	N = 50	%	
IgM +	7	7.6%	0	0%	0.044
IgM -	84	92.3%	50	100%	
IgG +	39	42.8%	4	8%	0.001
IgG -	52	57.1%	46	92%	

Highest incidence of EBV IgM was found in HD patients between the ages of 20 and 35 (57.1%), followed by those between the ages of 36 and 50 (28.6%), and those between 51 and 65 (14.3%). There was no IgM found in any of the age groups represented by the control group as shown in table [2].

**Table 2.** Relation of EBVIgM/IgG Ab with age of patients and control

Groups	AGE	EBV IgM				EBV IgG				Total
		+VE	%	-VE	%	+VE	%	-VE	%	
Patient	20 - 35	4	57.1	18	13.4	13	30.2	9	9.2	22
	36 - 50	2	28.6	27	20.1	11	25.6	18	18.3	29
	51 - 65	1	14.3	39	29.2	15	35	25	25.5	40
Control	20 - 35	0	0.0	21	15.7	2	4.6	19	19.4	21
	36 - 50	0	0.0	16	11.9	2	4.6	14	14.3	16
	51 - 65	0	0.0	13	9.7	0	0.0	13	13.3	13
Total		7	100%	134	100%	43	100%	98	100%	141
		*				**				
		P-Value = 0.049				P-Value = 0.008				

The females (57.1%) had the greatest prevalence of EBV IgM infection compared to males (42.9%). In contrast, the present study's control group yielded no positive results between genders. No significant relation was found (p.value = 0.193).On the other hand, females had higher levels of EBV IgG (48.8%) than males (41.9%).In contrast, females and males made up (4.6%) of the control group. Significant relationship was identified between the two groups (p.value = 0.001) as it shown in table [3].

**Table 3.** Relation of EBV IgM Ab with sex of patients with hemodialysis vs control

Groups	Sex	EBV IgM				EBV IgG				Total
		+VE	%	-VE	%	+VE	%	-VE	%	
Patients	Male	3	42.9	47	35.1	18	41.9	32	32.7	50
	Female	4	57.1	37	27.6	21	48.8	20	20.4	41
Control	Male	0	0.0	27	20.1	2	4.6	25	25.5	27
	Female	0	0.0	23	17.2	2	4.6	21	21.4	23
Total		7	100%	134	100%	43	100%	98	100%	141
		ns				**				
		P-Value = 0.193				P-Value = 0.001				

According to the findings presented in table [4], the greatest rate of EBV IgM infection was discovered in patients who had been undergoing dialysis for more than one year (71.4%) and the rate of EBV infection rose with increasing time of undergoing dialysis treatment, the finding had a p-value that was highly significant (0.015). While patients who had been receiving dialysis for more than a year had a rate of EBV IgG of 53.8%, whereas those who had been receiving it for less than a year had a rate of 46.2%. According to statistical analysis, the result had a p-value of 0.715, which was not statistically significant.

**Table 4.** Relation of EBV IgM/IgG Ab with duration of HD.

Group	Duration of dialysis	EBV IgM				EBV IgG				Total
		+VE	%	-VE	%	+ VE	%	-VE	%	
Patients	More than 1 year	5	71.4	46	54.8	21	53.8	30	57.7	51
	less than 1 year	2	28.6	38	45.2	18	46.2	22	42.3	40
	Total	7	100%	84	100%	39	100%	52	100%	91
		**				ns				
		P-Value = 0.015				P-Value = 0.715				

Patients with dialysis treatment for more than 3 times per week had highest percentage of EBV infection than 1 time per week with a significant differences p.value (0.059) as it shown in table [5].

**Table 5.** Relation of EBV in HD patient with number of dialysis.

Number of dialysis/week	No. of patients	EBV Seroprevalence				P. value
		Positive		Negative		
		No.	%	No.	%	
1 times	3	1	2.2	2	4.4	0.059
2 times	22	6	13.0	16	35.6	
3 times	66	39	84.8	27	60	
Total	91	46	100%	45	100%	

## 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. There are few data available on the kinetics of EBV seroprevalence in HD patients and these study 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 current study [12]. The present study revealed that EBV IgM Antibody was found in only 7.6% of patients with hemodialysis, while in the case of IgG was found in 42.8% of patients. The result of the present study confirmed the data recorded by another study done in Croatia, and this study found that the prevalence of EBV IgM was only 2.6 % of HD patients [13]. In Egypt, Ibrahim et al (2022), illustrated that, among hemodialysis cases (20.7%) were positive for EBV IgM antibodies, (56.3%) were positive for EBV-IgG antibodies (140). While such finding disagree with other study done in Cyprus found that 94 % of HD patients had EBV IgG antibodies [14]. In Iran the finding of Samiei et al (2019), analysis indicate that hemodialysis patient have a high rate of IgG (96%) seropositivity, as consequence given the clinical significance of EBV reactivation and the severe complication it may cause in immunocompromised patients [2].

The majority of children in developing nations become infected with EBV by the age of 6 years and develop stable immunity to the virus since EBV infection occurs at a young age in these countries. In industrialized countries, the onset of the EBV infection is delayed until adolescence in more than fifty percent of instances; roughly fifty percent of adult infections take the form of infectious mononucleosis. This is the case because the virus does not replicate well in adults [15]. finding of this study was agree to Rostgaard et al (2019), who is found that EBV IgM seroprevalence at age 0–29 years (57%) and in female more than male, because of Mechanisms that involve growth and/or sex hormones whose levels change as part of sexual maturation. In this

regard, it is noteworthy that both estrogen and androgens are known to influence immune responses via epigenetic mechanisms [16]. In Japan, Sasaki Y et al (2020), find that acute EBV infection was 45.9% in male and 54.1% in female with median age (22–31.5 years old) these results were agreed with the results of the current study [17]. Kuri et al (2020), suggest that in UK, EBV seroprevalence of IgG was high in older age (95%), and this study agree with present study in that, EBV seroprevalence tends to be higher among females than male [18]. Finally another study in china suggest that EBV most commonly occur in age group (20-40) possibly due to activation of primary EBV infection [19]. Because patients on HD share their dialysis equipment, the risk of viral transmission to these individuals is at an extremely high level. Therefore, in order to make use of these devices in a more cautious manner, it appears important to identify patients on HD who are afflicted with a virus in order to estimate the risk of transmission of these viruses to HD patients who are not affected. In addition, the sterility of HD devices should be tested after each usage for these patients, and this testing should be conducted in accordance with stringent laws [20,21]. Rahbar et al (2017), show that patients had (ESRD) and all had a history of 1-2 years dialysis before their renal transplantation and all of them was positive for EBV IgG antibody [22,23]. Another study was done on patients before renal transplantation with history of more than 16 month of dialysis and this study show that about (357) patient from (388) (92%), were positive for EBV [24,25].

## Conclusion

Epstein Barr virus prevalence among hemodialysis patients was higher than control group. Infection with Epstein Barr virus is connected to several factors like duration of dialysis and hemodialysis frequency per week and number of blood transfusion.

## References

- [1] Yasir, S. J., Marzoq, H. S. (2022, January). Detection of Epstein-Barr virus in hemodialysis cases in Al-Najaf governorate. In AIP Conference Proceedings, 2386 (1).
- [2] Samiei, R. N., Mahmoudvand, S., Shokri, S., Makvandi, M., Shahbazian, H., Pirmoradi, R., & Nowrozi, S. (2019). The frequency of Epstein-Barr virus among hemodialysis patients, Ahvaz, Iran. *Iranian Journal of Microbiology*, 11(1), 75.
- [3] Britannica, T. (2020). Editors of Encyclopaedia. "Alienation effect", 19(10):2953.
- [4] Smatti, M. K., Al-Sadeq, D. W., Ali, N. H., Pintus, G., Abou-Saleh, H., Nasrallah, G. K. (2018). Epstein-Barr virus epidemiology, serology, and genetic variability of LMP-1 oncogene among healthy population: an update. *Frontiers in oncology*, 8, 211.
- [5] Kuri, A., Jacobs, B. M., Vickaryous, N., Pakpoor, J., Middeldorp, J., Giovannoni, G., & Dobson, R. (2020). Epidemiology of Epstein-Barr virus infection and infectious mononucleosis in the United Kingdom. *BMC Public Health*, 20(1), 1-9.
- [6] Abusalah, M. A. H., Gan, S. H., Al-Hatamleh, M. A., Irekeola, A. A., Shueb, R. H., & Yean Yean, C. (2020). Recent advances in diagnostic approaches for Epstein-Barr virus. *Pathogens*, 9(3), 226.
- [7] Zhao, M., Nanbo, A., Sun, L., Lin, Z. (2019). Extracellular vesicles in Epstein-Barr virus' life cycle and pathogenesis. *Microorganisms*, 7(2), 48.
- [8] Fahriye, E. K. Ş. İ., KARSLIĞİL, T., ERİNMEZ, M., PEHLİVAN, M. (2022). Investigation of Epstein-Barr Virus antibodies by ELISA and IFA methods. *Journal of Experimental and Clinical Medicine*, 39(1), 66-70.
- [9] Crowley, A., Connell, J., Schaffer, K., Hall, W., & Hassan, J. (2012). Is there diagnostic value in detection of immunoglobulin G antibodies to the Epstein-Barr virus early antigen?. *BioResearch Open Access*, 1(6), 291-296.
- [10] Geris, J. M., Stancari, A. L., Meirhaeghe, M. R., Gautam, S., Cayatte, C., Schmeling, D. O., Balfour Jr, H. H. (2022). Rapid antibody responses to Epstein-Barr virus correlate with reduced severity of primary infection. *Journal of Clinical Virology*, 155, 105267.
- [11] Koester, T. M., Meece, J. K., Fritsche, T. R., Frost, H. M. (2018). Infectious Mononucleosis and Lyme Disease as Confounding Diagnoses: A Report of 2 Cases. *Clinical Medicine & Research*, 16 (3-4), 66-68.
- [12] Al-Azzawy, M. A., Tawfiq, S. K., Qader, S. M. Detection of EBV and CMV Coinfection Among Patients Under Hemodialysis. *International Journal of Health Sciences*, (II), 4456-4463.
- [13] Vilibić-Čavlek, T., Kolarić, B., Bogdanić, M., Tabain, I., Beader, N. (2017). Herpes group viruses: a seroprevalence study in hemodialysis patients. *Acta clinica Croatica*, 56(2.), 255-261.
- [14] Ibrahim, M. N., Alhadi, M. S., Elbadawy, W. Y. (2022). Serodetection of Cytomegalovirus and Epstein-Barr virus antibodies among hemodialysis patients. *Biomed Pharmacol J*, 15(1).
- [15] Deeba, E., Koptides, D., Gaglia, E., Constantinou, A., Lambrianides, A., Pantzaris, M., Christodoulou, C. (2019). Evaluation of Epstein-Barr virus-specific antibodies in Cypriot multiple sclerosis patients. *Molecular immunology*, 105, 270-275.

- [16] Sharifipour, S., Rad, K. D. (2020). Seroprevalence of Epstein–Barr virus among children and adults in Tehran, Iran. *New Microbes and New Infections*, 34, 100641.
- [17] Rostgaard, K., Balfour Jr, H. H., Jarrett, R., Erikstrup, C., Pedersen, O., Ullum, H., Hjalgrim, H. (2019). Primary Epstein-Barr virus infection with and without infectious mononucleosis. *PloS one*, 14(12), e0226436.
- [18] Sasaki, Y., Ishii, T., Maeda, T., Mori, T., Shigeta, T., Kashiwagi, K., Urita, Y. (2020). Sex difference in clinical presentation of patients with infectious mononucleosis caused by Epstein-Barr virus. *Journal of Infection and Chemotherapy*, 26(11), 1181-1185.
- [19] Kuri, A., Jacobs, B. M., Vickaryous, N., Pakpoor, J., Middeldorp, J., Giovannoni, G., Dobson, R. (2020). Epidemiology of Epstein-Barr virus infection and infectious mononucleosis in the United Kingdom. *BMC Public Health*, 20(1), 1-9.
- [20] Xiong, G., Zhang, B., Huang, M. Y., Zhou, H., Chen, L. Z., Feng, Q. S., Zeng, Y. X. (2014). Epstein-Barr virus (EBV) infection in Chinese children: a retrospective study of age-specific prevalence. *PLoS One*, 9(6), e99857.
- [21] Ali, H. M., Al-Shuwaikh, A. M., & Manuti, J. K. (2022). DETECTION OF TORQUE TENO VIRUS ANTIGEN AND ASSOCIATED RISK FACTORS AMONG HEMODIALYSIS PATIENTS. *Wiad Lek*, 75(3), 624-628.
- [22] Jasim, M. T ., Y.Noraldeen , M. ., & Al-Kadi, N. A. . (2022). Comparison of Some Biochemical Parameters in Covid-19 Patients and Vaccinated Individuals in Kirkuk/Iraq. *NTU Journal of Pure Sciences*, 1(4), 1–9.
- [23] Rahbar, M., Poormand, G., Mahmoodi, M. K., Jazayeri, A., & Jazayeri, S. M. (2016). Asymptomatic Epstein-Barr Virus Shedding in the Urine of Kidney Transplant Recipients: Case Reports and Review of the Literature. *Infectious disease reports*, 8(4), 6817.
- [24] Breesam , A. A. ., & Nooruldeen , M. Y. . (2022). Evaluation of the Immunochromatography Assay’s Diagnostic Performance for Quickly Detecting the Presence of COVID-19 Antigen in Patients with Positive PCR Results. *NTU Journal of Pure Sciences*, 1(4), 35–43.
- [25] Bamoulid, J., Courivaud, C., Coaquette, A., Chalopin, J. M., Gaiffe, E., Saas, P., & Ducloux, D. (2013). Subclinical Epstein-Barr virus viremia among adult renal transplant recipients: incidence and consequences. *American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons*, 13(3), 656–662..
- [26] Mohammed, S. A. ., Tawfeeq, A. A. ., Noraldin, M. Y. . (2023). Identification and antibiotics Sensitivity of Secondary Bacterial Infection in COVID-19 (SARS-CoV-2) Pneumonia patients in Kirkuk/Iraq. *NTU Journal of Pure Sciences*, 2(1).