НИРКИ KIDNEYS

DOI:10.65327/kidneys.v14i4.559

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Seroprevalence of Epstein-Barr virus among hemodialysis patients: post-exposure analysis

Abstract. ***Background.*** *Epstein-Barr virus (EBV) is a ubiquitous member of the γ-herpesvirus subfamily within the Herpesviridae family and is known to cause infectious mononucleosis. EBV may contribute to morbidity and mortality in hemodialysis patients. Hemodialysis is a procedure used in individuals with end-stage renal failure to remove waste products, salts, and excess fluids from the bloodstream. The aim of this study was to assess EBV IgG antibody infection in patients undergoing hemodialysis.* ***Materials and methods.*** *EBV IgG antibodies were evaluated in 88 blood samples collected from hospitalized hemodialysis patients using enzyme-linked immunosorbent assay.* ***Results.*** *The study included 51 males and 37 females, with an age range from ≤ 15 to ≥ 75 years, divided into four categories. The mean age was 52.00 ± 16.46 years. EBV seropositivity was found in 36.36 % of patients (23.86 % in males and 12.50 % in females), while 63.64 % tested negative. No statistically significant differences were observed between gender and age groups (P = 0.5). Among seropositive cases, 12.5 % showed co-infection with hepatitis C virus. The correlation was significant at the 0.01 level.* ***Conclusions.*** *A notable prevalence of EBV IgG antibodies was observed among hemodialysis patients. Seropositivity reached 36.36 %, while 63.64 % of cases were negative. The highest proportion of seropositive individuals was found among elderly patients aged ≥ 75 years, accounting for 31.6 %.*

Keywords: *Epstein-Barr virus; infectious mononucleosis; hemodialysis; seroprevalence; enzyme-linked immunosorbent assay*

Introduction

Epstein-Barr virus (EBV), or human herpes virus-4, from the γ-herpesvirus, *Herpesviridae* family, which causes infectious mononucleosis (IM) [1]. Herpesviruses can establish a persistent latent infection after their initial infection that contributes to the development of numerous diseases. EBV develops a latent infection within B lymphocytes in patients with compromised immune systems and reactivation, which helps escape the host's immune response [2–4]. The most common transmission mode for EBV infection is via blood transfusions, organ transplantations, sexual contact, and contact with saliva [5]. EBV infections are able to produce a variety of diseases, especially the most serious ones, such as tumors and malignancies, particularly chronic illnesses and immunosuppressed patients, which can postpone their healing and medical care and lead to life-threatening infection [6, 7]. Many cancers and immunosuppressive disorders, such as infectious mononucleosis, Hodgkin's lymphoma, nasopharyngeal carcinomas (NPC), African Burkitt's lymphoma (BL), and B-cell of immunocompromised, have been implicated in the Epstein-Barr virus [8]. Over 90 % of adults globally are infected with EBV. In healthy people, EBV infection is asymptomatic. On the other hand, it causes severe diseases in those with compromised immune systems, such as those receiving hemodialysis (HD) or receiving a transplant. One of the major severe complications associated with EBV is transplant lymphoproliferative disease (PTLD). It is a leading life-threatening among patients with immunosuppressive drugs and occurs after the organ transplant process which leads to the rejection of an organ [9, 10]. Acute kidney injury (AKI) and nephrotic syndrome (NS) are uncommon manifestations of EBV mononucleosis. EBV can cause morbidity and mortality in hemodialysis patients. Hemodialysis, or HD, is a procedure performed on patients with end-stage renal failure, where the patient's blood is purified of toxins due to abnormal kidney function, therefore renal transplantation is the best treatment for these patients [11]. EBV is a major factor in the morbidity and death of hemodialysis patients [12]. Hemodialysis patients with end-stage renal failure (HD) are more vulnerable to opportunistic infections, particularly viral infections like EBV infection [13]. So, when these patients receive hemodi-

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alysis or organ transplantation, they are more vulnerable to contracting EBV because of the changes in cellular immunity and its role in suppressing increases the immune system which increases the risk of infection [14–16].

The study was conducted on a convenience sample of 88 hospitalized patients undergoing maintenance hemodialysis.

The purpose was to assess the prevalence of EBV IgG antibodies in a clinically relevant and accessible patient population, as individuals receiving long-term hemodialysis may be at increased risk for latent viral infections due to underlying comorbidities and immune dysfunction.

Materials and methods

Study design and serological testing

The cross-sectional study was carried out from January to March 2023. All blood samples were collected from the dialysis unit at Basrah Teaching Hospital. The 88 hemodialysis patients included 51 males and 37 females, aged of ≤ 15 to ≥ 75 years. In-person interviews and the examination of medical records were used to gather the patient data. All patients gave their informed consent, and documented ethical approval and a questionnaire were received. Each patient participant in the study had a venipuncture to draw five milliliters of blood, which were then separated using centrifugation at 1000 rpm for ten minutes in gel tubes. The samples were kept at –20 °C in a deep freezer. Following the manufacturer's instructions, a commercial kit for enzyme-linked immunosorbent assay (ELISA) (SunLong Biotech Co., LTD) was used to perform serological testing for the presence of EBV IgG. The results were expressed as optical density units.

In this investigation, EBV reactivation was not specifically assessed, as the primary objective was to evaluate EBV IgG seroprevalence among hemodialysis patients. We used an enzyme-linked immunosorbent assay (ELISA) to detect EBV-specific IgG antibodies, which serve as markers of past exposure or latent infection, rather than active or reactivated infection.

No EBV IgM testing or molecular diagnostics such as EBV DNA PCR were employed in this study. Therefore, we did not distinguish between latent, reactivated, or primary infection states.

Exclusion criteria

We did not apply stringent exclusion criteria beyond the requirement that patients were receiving regular hemodialysis and provided informed consent. Patients with acute infections, known malignancies, or those unwilling to participate were excluded. However, no exclusions were made based on prior EBV status, immunosuppressive therapy, or co-infections at the time of enrollment.

Consideration of confounding factors

We acknowledge that potential confounders — such as immunosuppressive therapy, comorbid conditions (e.g., diabetes, HIV), or prior organ transplantation — could influence EBV serostatus. However, due to limitations in sample size and retrospective data collection, these variables were not stratified or controlled for in the current analysis.

Follow-up

In the present study, no follow-up period was included, and clinical outcomes related to EBV reactivation were not assessed. Our investigation was designed as a cross-sectional, seroprevalence study, focusing solely on the detection of EBV IgG antibodies in a cohort of hospitalized hemodialysis patients. Since EBV IgG positivity reflects past exposure or latent infection, and not necessarily active reactivation, we did not track patients longitudinally to observe outcomes such as symptomatic EBV disease, reactivation events, or complications.

Ethical approval

The Medical Ethical Committee of The Department of Microbiology, College of Medicine, University of Basrah approved this study (no. 4495 on 12/02/2023). Participant consent was waived by the committee since only patient files were reviewed.

Statistical analyses

The information collected from the survey was saved in Microsoft Excel 2013. Data were examined through the Statistical Package Version 26 for Social Sciences (SPSS Inc.) software used to assess the seropositive EBV IgG antibodies using the t-test and ANOVA test to investigate P-value. Statistical significance was considered at $P < 0.05$.

Results

To evaluate the seropositive EBV IgG antibodies, we examined EBV IgG antibodies in 88 hemodialysis patients alongside all chronic associated diseases, including HCV, HBV infections, blood glucose levels, hypertension, liver,

Table 1. Demographic characteristics of the individuals who participated in this study, %

Age group (years)	Gender		Total
	Male	Female	
≤ 15–30	7.1	3.1	10.2
31–45	8.2	11.2	19.4
46–60	14.3	13.3	27.6
61 — ≥ 75	21.4	10.2	31.6
Total	51	37.8	88.8
Seropositive EBV IgG antibodies	23.86	12.50	36.36
Mean ± standard deviation	52.00 ± 16.46		

thyroid, and cardiovascular disorders, to evaluate the association among these variables. Table 1 offers a comprehensive overview of the study participants' demographics, categorized by gender and age group. The study involved 51 (51 %) males and 37 (37.8 %) females, and the average age ranged from ≤ 15 to ≥ 75 years was divided into four categories with a mean age of 52.00 ± 16.46 years. There were no significant differences (P = 0.5) among the individuals concerning gender. However, the total positive EBV IgG antibodies using ELISA were 36.36 % (23.86 % in males, 12.50 % in females), and 63.64 % were negative cases (Fig. 1).

Moreover, Fig. 2 demonstrates the prevalence of chronic associated diseases and co-infections among hemodialysis patients, including HCV infection (27.3 %), HBV infection (1.1 %), blood sugar (23.9 %), hypertension (38.6 %), liver diseases (2.3 %), thyroid disease (1.1 %), and heart disease (2.3 %). Also, most positive cases exhibit co-infections between EBV IgG and HCV (12.5 %). Correlation is significant at the 0.01 level (2-tailed).

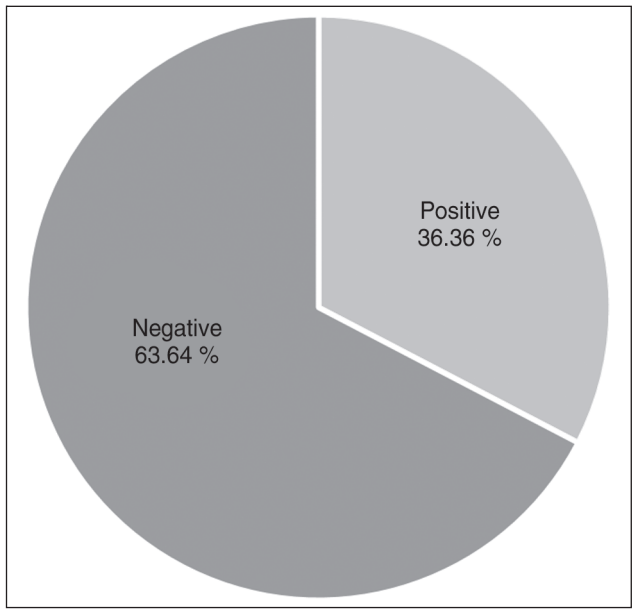

Figure 1. Seroprevalence of Epstein-Barr virus among hemodialysis patients

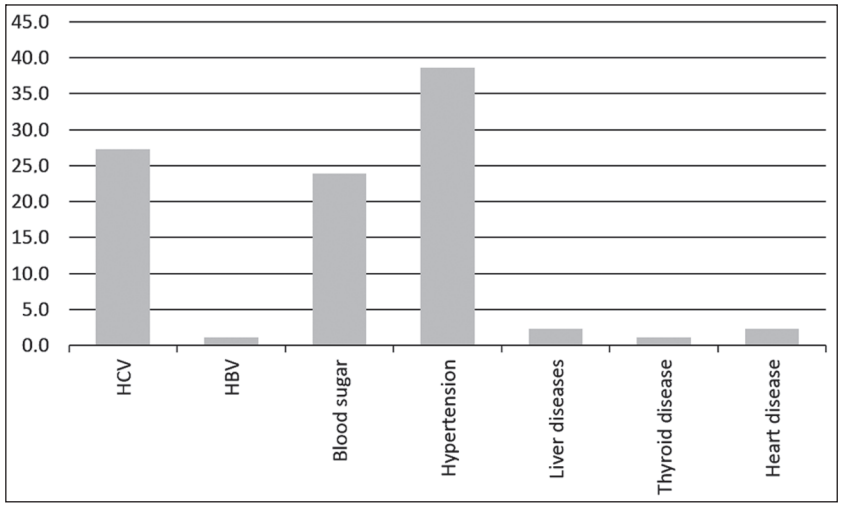

Figure 2. Frequency of co-infection with EBV among hemodialysis patients

Discussion

Epstein-Barr virus (EBV) is one of the most common opportunistic viral pathogens in immunocompromised patients, including those on hemodialysis, these patients suffer from a weakened immune response to viral infection, which can result in complications of persistent infection, so, the presence of IgG antibodies is an indicator of chronic viral infection in hemodialysis patients [17, 18]. According to several studies conducted done globally, EBV infection is highly risk rates in hemodialysis patients [19–21].

The current study shows that the seroprevalence of EBV IgG in patients who underwent hemodialysis was 36.36 % (23.86 % in males, 12.50 % in females), and 63.64 % were negative. The category of older participants was highest among elderly patients, specifically those aged ≥ 75 years, at 31.6 %. The results of the current study findings that the elderly especially susceptible to the viral infection. This may be due to the continuous hemodialysis sessions, weakened immune systems, immunosuppressive therapies, underlying disease, deteriorating health status, and aging, which makes them increases their susceptible to viral activity. The main risk factor for Epstein-Barr virus infection in patients is advanced age due to inadequate to establish a successful immune defense response against EBV [22].

Research validates the risk of opportunistic EBV among patients with end-stage renal failure with a significant increase in infection rates due to it being one of the most contagious viruses. The results of an earlier study conducted in Iraq by Al-Azzawy et al. indicated that the seropositivity of EBV IgG antibodies in hemodialysis was 43.68 % [23]. However, various results from previous studies have shown that the prevalence of EBV infection varies across countries and that its prevalence in many hemodialysis patients was high, as evidenced by a study conducted in Croatia 98 % [24], in Cyprus 94 % [25], While a study on potential adult donors and recipients by Saghafi et al. found that the prevalence of Epstein-Barr virus IgG antibodies was 100 % ages and sexes [26]. A study in Iran by Samiei et al. revealed a high prevalence of the positivity rate of Epstein-Barr virus IgG antibodies among hemodialysis patients 96.42 %. The findings of previous studies demonstrated that the prevalence rate of EBV infection varies in many countries are varied, including [23, 24, 26].

In fact, the risk of EBV infection transmission and its clinical importance is related to its ability to reactivate with the possibility of serious complications [27]. The present study recommends the need for further research with an increased sample size to explain the clinical role of EBV in hemodialysis patients. Also, it is essential to conduct periodic checkups

of patients to avoid the consequences of infection. Patients with EBV have risk due to its transmission through hemodialysis to seropositive and seronegative cases, Therefore, our study advises that patients get tested for EBV prior to starting dialysis process and that it is best to perform viral screening on a regular basis.

In our study, the primary objective was to assess the seroprevalence of EBV IgG antibodies among hemodialysis patients. While we observed patterns suggestive of a relationship between EBV seropositivity and age, we did not perform a direct or comprehensive statistical correlation between EBV markers and renal function parameters such as estimated glomerular filtration rate (eGFR), serum creatinine, or dialysis duration. The mention of correlation in the discussion referred primarily to descriptive observations rather than a formal statistical association. The only inferential statistical test applied was the Chi-square test to evaluate associations between EBV sero-status and categorical variables, such as age groups, gender, and co-infection status. No multivariate analysis or regression modeling was used to control for potential confounders or to quantify the strength of association between EBV seropositivity and renal function markers. We acknowledge this as a limitation of our study, and we plan to address this in future research by incorporating quantitative renal function data and employing more robust statistical techniques, such as Pearson or Spearman correlation coefficients and multivariate logistic regression, to better define the relationship between EBV infection and renal impairment in this population.

We acknowledge that EBV reactivation is best confirmed through quantitative PCR for EBV DNA in plasma or peripheral blood mononuclear cells, and future studies should include molecular assays to better characterize the dynamics of EBV infection and reactivation in the hemodialysis population. Future research with a larger cohort and detailed clinical stratification — including immunosuppression status and co-infections — will be important to better understand the true impact of these factors on EBV seropositivity and reactivation in the hemodialysis population.

We acknowledge that a prospective follow-up with serial EBV viral load measurements and clinical correlation would be valuable in identifying the impact of EBV reactivation on morbidity and mortality in the hemodialysis population. This represents an important direction for future research.

Conclusions

Our current findings demonstrated, hemodialysis patients had a significant rate of seropositive for EBV IgG antibodies, and that the risk might increase if hemodialysis treatment lasts longer. The prevalence of EBV IgG antibodies was considerably observed among patients. the seropositive EBV IgG antibodies were 36.36, and 63.64 % were negative cases. The category of older age group of participants was highest among elderly patients, specifically those aged ≥ 75 years, at 31.6 %.

Acknowledgments

We thank everyone who contributed to the research and those who offered assistance during the study.

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Received 04.09.2025
Revised 02.10.2025
Accepted 17.10.2025

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Conflicts of interests. Authors declare the absence of any conflicts of interests and own financial interest that might be construed to influence the results or interpretation of the manuscript.

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Серопревалентність вірусу Епштейна — Барр серед пацієнтів на гемодіалізі: постконтактний аналіз

Резюме. Актуальність. Вірус Епштейна — Барр (EBV) є поширеним представником підродини γ-герпесвірусів родини *Herpesviridae* і відомий як збудник інфекційного мононуклеозу. EBV може спричиняти захворюваність і смертність серед пацієнтів, які проходять гемодіаліз. Гемодіаліз — це процедура, що застосовується у хворих із термінальною стадією ниркової недостатності для видалення з крові продуктів обміну, солей і надлишкової рідини. **Мета:** оцінити інфікування антитілами EBV IgG пацієнтів, які проходять гемодіаліз. **Матеріали та методи.** Антитіла EBV IgG були оцінені у 88 зразках крові, отриманих у госпіталізованих пацієнтів на гемодіалізі, за допомогою імуноферментного аналізу. **Результати.** У дослідженні взяли участь 51 чоловік і 37 жінок віком від ≤ 15 до ≥ 75 років, розподілених на чотири вікові категорії. Середній вік дорівнював 52,00 ± 16,46 року. Серопозитивність щодо EBV становила 36,36 % (23,86 % серед чоловіків і 12,50 % серед жінок), тоді як 63,64 % осіб були серонегативними. Статистично значущих відмінностей між статтю та віком не виявлено (P = 0,5). Серед серопозитивних випадків у 12,5 % зафіксовано коінфекцію з вірусом гепатиту С. Кореляція була значущою на рівні 0,01. **Висновки.** У пацієнтів, які проходять гемодіаліз, спостерігалася помітна поширеність антитіл EBV IgG. Серопозитивність становила 36,36 %, а 63,64 % випадків були негативними. Найвищий рівень серопозитивності зафіксовано серед літніх пацієнтів віком ≥ 75 років (31,6 %).

Ключові слова: вірус Епштейна — Барр; інфекційний мононуклеоз; гемодіаліз; серопревалентність; імуноферментний аналіз