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Original Article

Prevalence of Epstein-Barr Virus Infections among Inflammatory Bowel Disease patients in Kirkuk City/Iraq

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ABSTRACT

Children and adults worldwide are significantly impacted by Epstein-Barr virus infection. The illness typically stays dormant and is well-managed in people with robust immune systems. However, the virus can cause life-threatening infections in those with weakened immune systems, such as those with inflammatory bowel disease (ulcerative colitis and Crohn's disease,). This study aims to evaluate the presence of VCA IgM, IgG, and EBNA-1 antibodies against the Epstein-Barr virus in inflammatory bowel disease patients and explore potential connections between the prevalence of these antibodies, age, and sex. The research carried out in Kirkuk City included 100 individuals (56 patients with ulcerative colitis and 44 with Crohn's disease) and a control group of 100 individuals. Blood samples were collected from all participants in this study and subjected to analysis using the ELISA technique. EBV seropositivity was significantly higher in IBD patients (UC 76.7%, p-value <0.001, and CD 70.4% p-value 0.002) than in controls (6%) (p-value= 1.0). The highest seroprevalence occurred in the 31–40 age group (UC: 30.2%, CD: 38.7%) with a p-value <0.005. Males showed higher EBV positivity than females in Both UC 69.7%, p-value 0.008, and CD: 58.1% with a p-value < 0.002.

Keywords: Virus Infection Inflammatory, Bowel Disease, Epstien-Barr Virus

Introduction

The origin of inflammatory bowel disease (IBD), a chronic inflammatory gastrointestinal disorder that is complex and multifactorial, remains unknown. IBD can manifest as either a progressive inflammatory disease or a relapsing-remitting disorder, and viral infections may influence its progression [1]. Since its discovery by Grotsky et al. in 1971, the Epstein-Barr virus (EBV) has been linked increasingly to IBD. Numerous studies have suggested a potential link between EBV and Crohn's disease (CD) as well as ulcerative colitis (UC) [2]. M.A. Epstein, Y.M. Barr, and B.G. Achong of the United Kingdom discovered the Epstein-Barr virus, or EBV. In cells taken from recently reported lymphoma tissues, these researchers discovered particles that resembled viruses [3]. The EBV genome encodes about 85 genes and is composed of linear, double-stranded DNA. It is relatively large, measuring about 172 kilobase pairs (kbp). Several glycoprotein spikes are inserted into the viral envelope, a viral tegument containing a protein that plugs the gap between the nucleocapsid and the outer envelope, and a toroid-shaped protein core enclosed in an icosahedral capsid with 162 capsomers makes up this structure [4]. EBV seroprevalence increases with age and is generally higher in women, people of color, and people from poorer

socioeconomic backgrounds [5]. T and B lymphocytes are susceptible to EBV infection. They are the stratified squamous epithelial cells of the nasopharynx and oropharynx, as well as cells in the stomach and salivary glands, thyroid gland epithelia, smooth muscle, and follicular dendritic cells. It appears that the stratified squamous epithelium of the oropharynx is the first site of EBV infection and replication. The virus then targets latent B cells [6].I It probable that EBVs can enter any area of the human body because they have been found in both normal and pathological physiological fluids, including blood, urine, saliva, amniotic fluid, cerebrospinal fluid, breast milk, bronchial alveolar lavage, and ascites [7]. Currently, the clinical assessment of EBV infections linked to malignancies uses molecular characterization of viral DNA, RNA, and EBV viral load [8]. Three criteria—anti-VCA IgM, anti-VCA IgG, and anti-EBNA IgG antibodies—can be used to diagnose EBV infection [9]. The presence of IgM antibodies against the viral capsid antigen (VCA) is particularly useful for detecting primary EBV infection because these antibodies are usually detectable mostly in the first few months after symptom onset [10]. Laboratory work will frequently show lymphocytosis, frequently with a lymphocyte differential more than 50%. Under a microscope, a blood sample may exhibit an uncommon lymphocytosis of more than 10% [11].

Material and Methods

This study was conducted between September and November 2024 on 100 patients diagnosed with inflammatory bowel disease (IBD) treated at Azadi Teaching Hospital and a control group of 100 healthy individuals. Data, including age and sex, were collected through interviews using a questionnaire. Each participant provided 5 ml of blood. The blood samples were then centrifuged to separate the serum, which was subsequently tested using the ELISA technique for the presence of Epstein-Barr virus (EBV) VCA IgM, VCA IgG, and EBNA-1 IgG [12].

Statistical analysis

Statistical analysis was performed using SPSS software, version 18 (Statistical Package for the Social Sciences). Data was coded and entered the software for analysis. Descriptive statistics were used to summarize the data, and the Chi-square test was applied to assess associations between categorical variables. A p-value of less than 0.05 was considered statistically significant [13].

Results and Discussion

Table (1) shows a significantly higher prevalence of EBV seropositivity among patients with ulcerative colitis (76.7%, $p < 0.001$) and Crohn's disease (70.4%, $p = 0.002$) compared to the control group (6%, $p = 1.0$). This indicates a strong association between EBV infection and inflammatory bowel disease (IBD).

These findings are consistent with previous studies demonstrating that chronic immunological activation in immunosuppressive patients facilitates EBV persistence and reactivation [14]. For example, a study on hemodialysis patients in Kirkuk City also reported a higher prevalence of EBV compared to controls [15].

Furthermore, EBV seroprevalence varies by demographic and geographic factors. Our results aligned with Ghazi et al. [16], who found that 96.67% of UC and CD patients were IgG positive. Differences in immune response pathways may explain variations in EBV positivity among patient groups, where UC is associated with a Th2 response and CD with a Th1/Th17 response, the latter providing stronger antiviral control [17–19]. Our results are also consistent with those of Baran et al. [20], who found that 74% of pediatric IBD patients had EBNA-1 IgG positive and 67% had VCA IgG positivity, showing that EBV exposure is common in IBD patients. The higher seropositivity rates in both trials support the link between persistent EBV infection and IBD etiology.

Table 1. Distribution of EBV infection among ulcerative colitis, Crohn's disease patients, and control group

Results	EBV+ve	EBV-ve	Total of patients	P-value
UC patients	43(76.7%)	13(23.2%)	56(100%)	< 0.001
CD patients	31(70.4%)	13(29.5%)	44(100%)	0.002
Control	6(6%)	94(94%)	100(100%)	1.0

p-value < 0.005 is considered significant

Tables (2 and 3) demonstrate that male patients with both Crohn's disease (CD) and ulcerative colitis (UC)had significantly higher EBV seropositivity rates compared to females. In UC patients, 69.7% of males tested positive for EBV antibodies compared to 30.2% of

females (p = 0.008). Similarly, in CD patients, 58.1% of males were EBV positive versus 41.9% of females, with a significant difference in males (p = 0.002) but not in females (p = 0.73).

Table 2. Correlation between EBV serology result and sex among Ulcerative colitis Patients

Sex	Anti-EBV Ab +VE			Total of EBV		Total of patients	P-value
	VCA IgM	VCA IgG	EBNA-1+VCA IgG	+VE	-VE		
Male	1(2.3%)	4(9.3%)	25(58.1%)	30(69.7%)	10(76.9%)	40(71.4%)	0.008
Female	2(4.6%)	3(6.9%)	8(18.6%)	13(30.2%)	3(23.0%)	16(28.5%)	0.03
Total	3(7.0%)	7(16.3%)	33(76.7%)	43(100%)	13(100%)	56(100%)	-

Table 3. Correlation between EBV serology result and sex in Crohn's disease Patients

Sex	Anti-EBV Ab +VE			Total of EBV		Total of patients	P-value
	VCA IgM	VCA IgG	EBNA-1 + VCA IgG	+VE	_VE		
Male	0(0%)	2(6.4%)	16(51.6%)	18(58.1%)	2(15.3%)	20(45.4%)	0.002
Female	1(3.2%)	1(3.2%)	11(35.4%)	13(41.9%)	11(84.6%)	24(54.5%)	0.73
Total	1(3.2%)	3(9.6%)	27(87.1%)	31(100%)	13(100%)	44(100%)	-

Beyond IgM, we also examined IgG seropositivity by distinguishing between the presence of EBNA-1 + VCA IgG positivity and VCA IgG positivity alone. According to Ekşi et al. [21], EBNA-1 + VCA IgG positivity indicates past infection and long-term immune memory, whereas VCA IgG positivity alone may indicate either acute or past infection. Male patients exhibited higher overall EBV seropositivity rates in both UC (69.7%) and CD (58.1%) compared to females (30.2% in UC and 41.9% in CD), with statistically significant differences (p = 0.008 and 0.002, respectively). These gender-based variations align with findings by Teshome et al. [22], who reported higher EBV seropositivity in males. Possible explanations include demographic factors, hormonal influences—where estrogen may enhance immune control over EBV, while testosterone may suppress viral clearance [23] and differences in immunological regulation.

Tables (4 and 5) show that EBV seropositivity varies with age among UC and CD patients. In UC patients, the highest EBV IgM positivity (4.6%) was in the 21–30 years group, with EBNA-1 + VCA IgG positivity peaking at 30.2% in the 31–40 years group. Overall EBV positivity was the highest (34.8%) in the 21–30 years group. In CD patients, EBV IgM was highest (3.2%) and EBNA-1 + VCA IgG positivity (29.0%) in the 31–40 years group. Overall seropositivity peaked at 38.7% in this group.

Table 4. Correlation between EBV serology result and age in Ulcerative Colitis Patients

Age Range	Anti-EBV Ab +ve			Total of EBV		Total of patients	P-value
	VCA IgM	VCA IgG	EBNA-1+VCA IgG	EBV +VE	EBV –VE		
<10-20 years	0(0%)	2(4.6%)	4(9.3%)	6(13.9%)	4(30.7)	10(17.8%)	0.605
21-30 years	2(4.6%)	2(4.6%)	11(25.5%)	15(34.8%)	5(25%)	20(35.7%)	0.064
31-40 years	0(0%)	0(0%)	13(30.2)	13(30.2%)	1(38.4%)	14(25%)	0.006
41-50 years	0(0%)	1(2.3%)	3(6.9%)	4(9.3%)	1(38.4%)	5(8.9%)	0.264
>51 years	1(2.3%)	2(4.6%)	2(4.6%)	5(11.6%)	2(15.3%)	7(12.4%)	0.350
Total	3(6.9%)	7(16.1%)	33(76.5%)	43(76.7%)	13(100%)	56(100%)	-

Table 5. Correlation between EBV serology result and age in Crohn's disease Patients

Age Range	Anti-EBV Ab +VE			Total of EBV		Total of patients	p-value
	VCA IgM	VCA IgG	EBNA-1 +VCA IgG	+VE	-VE		
<10-20 years	0(0%)	1(3.2%)	1(3.2%)	2(6.4%)	4(30.7%)	6(13.4%)	0.502
21-30 years	0(0%)	0(0%)	10(32.2%)	10(32.2%)	4(30.7%)	14(31.8%)	0.186
31-40 years	1(3.2%)	2(6.4%)	9(29.0%)	12(38.7%)	1(7.4%)	13(29.5%)	0.009

41-50 years	0(0%)	0(0%)	4(12.9%)	4(12.9%)	4(30.7%)	8(18.1%)	1.000
>51 years	0(0%)	0(0%)	3(9.6%)	3(9.6%)	0(0%)	3(6.8%)	0.134
Total	1(3.2%)	3(9.6%)	27(86.9%)	31(100%)	13(100%)	44(100%)	-

The current investigation showed that EBV seropositivity increased with age, with the highest frequency of both UC (30.2%) and CD (38.7%) in the age group of 31 to 40. These results confirm the idea that age has a significant influence in seroconversion, as reported by Al-Bawardy et al. [24], who found that 92.9% of IBD patients over 40 were seropositive for EBV. Similarly, 94.8% of people over 40 tested positive for EBV IgG, according to Sharifipour and Rad [25], demonstrating that exposure to EBV is almost universal in elderly populations. Furthermore, EBV seroprevalence rises significantly with age, from 60.4% in adolescents to 93% in young adults, as shown by Winter et al. [26]. Age-related increases in EBV seropositivity could be brought about by repeated viral reactivations, cumulative exposure, or a decline in immune surveillance, which promotes viral persistence.

Conclusion

This study highlights a significantly higher prevalence of Epstein-Barr virus (EBV) infection among patients with inflammatory bowel disease (IBD) compared to the control group. The seropositivity rates for EBV were notably higher in both ulcerative colitis (UC) and Crohn's disease (CD) patients, indicating a strong association between EBV infection and IBD. The highest EBV prevalence was observed in the 31-40 age groups of patients (UC and CD), indicating a possible role of age in viral infections. Additionally, males showed a higher seropositivity rate than females in both study groups, which may indicate gender-related differences in immune response.

Conflict of Interest

The authors declare no Conflict interests.

References

[1] Irving PM, de Lusignan S, Tang D, Nijher M, Barrett K. (2021). Risk of common infections in people with inflammatory bowel disease in primary care: a population-based cohort study. BMJ open Gastroenterology. 8(1):e000573.

[2] Marongiu L, Venturelli S, Allgayer H. (2022). Involvement of HHV-4 (Epstein–Barr virus) and HHV-5 (cytomegalovirus) in inflammatory bowel disease and colorectal cancer: a meta-analysis. Cancers. 14(20):5085.

[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., Karsligil, T., Erinmez, M., Pehlivan, 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] Bruu AL, Hjetland R, Holter E, Mortensen L, Natås O, Petterson W, Skar AG, Skarpaas T, Tjade T, Åsjø B. Evaluation of 12 commercial tests for detection of Epstein-Barr virus-specific and heterophile antibodies. Clinical Diagnostic Laboratory Immunology. 2000 May 1;7(3):451-6.

[13] Norman GR, Streiner DL. Biostatistics: the bare essentials. PMPH USA (BC Decker); 2008.

[14] Loosen SH, Kostev K, Schöler D, Orth HM, Freise NF, Jensen BE, May P, Bode JG, Roderburg C, Luedde T. (2023). Infectious mononucleosis is associated with an increased incidence of Crohn's disease: results from a cohort study of 31 862 outpatients in Germany. European Journal of Gastroenterology & Hepatology. 35(3):255-60.

[15] Medhat L, Mohammed W. (2023). Prevalence of Epstein-Barr virus among hemodialysis patients in Kirkuk city. NTU Journal of Pure Sciences. 2(4):17-22.

[16] Ghazi HF, Alubaidi GT, Fahad HM. (2022). Sero-prevalence of epstein-barr virus in iraqi inflammatory bowel disease. Wiad Lek. 75(8):2.

[17] Feng BS, Wu YJ, Zeng XH, Yu D, Liu ZQ, Zhou CJ, Liu ZG, Zheng PY, Yang PC. (2018). Bcl2L12 mediates effects of protease-activated receptor-2 on the pathogenesis of Th2-dominated responses of patients with ulcerative colitis. Archives of biochemistry and biophysics. 657:8-14.

[18] Otake-Kasamoto Y, Kayama H, Kishikawa T, Shinzaki S, Tashiro T, Amano T, Tani M, Yoshihara T, Li B, Tani H, Liu L. (2022). Lysophosphatidylserines derived from microbiota in Crohn's disease elicit pathological Th1 response. Journal of Experimental Medicine. 219(7):e20211291.

[19] Hokello J, Tyagi K, Owor RO, Sharma AL, Bhushan A, Daniel R, Tyagi M. (2024). New insights into HIV life cycle, Th1/Th2 shift during HIV infection and preferential virus infection of Th2 cells: Implications of early HIV treatment initiation and care. Life. 14(1):104

[20] Baran M, Aksoy B, Vardı K, Appak YÇ, Öncel EK, Çiftdoğan DY. (2018). The Frequency and Importance of Cytomegalovirus and Epstein-Barr Virus Infections in Children with Inflammatory Bowel Disease: Single Center Experience. Journal of Pediatric Infection/Cocuk Enfeksiyon Dergisi. 12(4).

[21] Ekşi F, Karslıgil T, Erinmez M, Pehlivan M. (2022). Investigation of Epstein-Barr Virus antibodies by ELISA and IFA methods. Journal of Experimental and Clinical Medicine.;39(1):66-70.

[22] Teshome S, Zealiyas K, Abubeker A, Tadesse F, Balakrishna J, Weigel C, Abebe T, Ahmed EH, Baiocchi RA. (2023). Detection and Quantification of the Epstein-Barr Virus in Lymphoma Patients from Ethiopia: Molecular and Serological Approaches. Microorganisms. 11(10):2606

[23] Ortona E, Pierdominici M, Rider V. (2019). Sex hormones and gender differences in immune responses. Frontiers in immunology. 10:1076.

[24] Al-Bawardy B, Alfadley AF, Almousallam M, AlShathri S, Aboueissa M, Alsulaiman A, Attamimi M, AlMutairdi A. (2024). Epstein-Barr virus seroprevalence among inflammatory bowel disease patients in Saudi Arabia. Saudi Journal of Gastroenterology. 30(3):168-72.

[25] Sharifipour S, Rad KD. (2020). Seroprevalence of Epstein–Barr virus among children and adults in Tehran, Iran. New microbes and new infections. 34:100641.

[26] Winter JR, Taylor GS, Thomas OG, Jackson C, Lewis JE, Stagg HR. (2019). Predictors of Epstein-Barr virus serostatus in young people in England. BMC infectious diseases. 19:1-9.