

Research Article

Epstein Barr Virus Infection as A Trigger For Multiple Sclerosis: Unravelling Viral-Immune Interactions In Najaf City

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Abstract

Background: Among the most pressing public health issues today are neuroinflammatory disorders that impact the central nervous system, including MS, Alzheimer's, and Parkinson's. Besides infectious mononucleosis, the Epstein-Barr virus (EBV) can cause many disorders and consequences. An EBV infection may affect an individual's nerves, spinal cord, and brain. The symptoms of an EBV infection may be more severe in people with compromised immune systems.

Aim of study: Study of the effect of Epstein-Barr virus infection on the immune response and its relationship to neuroinflammatory diseases.

Methods: The investigation included 120 patients diagnosed with neuroinflammatory disease by neurologists. The total number of patients was 120, with an average age of 45 years for males and 75 years for females. The investigation was conducted from November 2023 to May 2024. An enzyme-linked immunosorbent assay (ELISA) was implemented to evaluate EBV IgM and IgG levels.

Results: The Anti-EBV IgM Antibodies tested positive in 32% of the cases, while the remaining 68% of the cases tested negative. The Anti-EBV IgG Antibodies tested positive in 71% of the cases, while the remaining 29% of the cases tested negative.

Conclusion: Since many people's IgG and IgM levels rise simultaneously, EBV virus infection may cause neuroinflammatory illnesses or worsen pre-existing conditions. A large number of neuroinflammatory illness patients have EBV infection. Positive IgG levels in a tiny percentage of negative results may suggest an infection.

1. Introduction

In the past, the ability of B lymphocytes to develop into plasma cells and create autoantibodies was the main emphasis when discussing their role as autoimmune enhancers. The idea that B cells are only involved in producing autoantibodies has been questioned in recent decades, and the antibody-independent effector roles of B cells have been widely recognized and valued [1–3]. Emerging evidence from both animal studies and human clinical trials points to a tight cooperation between B cells and T cells in the initiation and regulation of T cell-dependent responses throughout the onset of various autoimmune disorders [4–6]. As a negative sensor of autoimmunity, B cells regulate immunological processes by limiting the proliferation of T cells, secreting cytokines that reduce inflammation [7, 8] and regulating the activity of monocytes [9–11].

There has long been investigation into a possible link between Epstein-Barr virus infection and multiple sclerosis brain, and among infectious variables, EBV exhibits the most robust epidemiological and serological correlation with MS [12]. A number of studies have focused on EBV's capacity to infect and promote immortalization of antibody secreting B cell clones [13]. Some have proposed that the

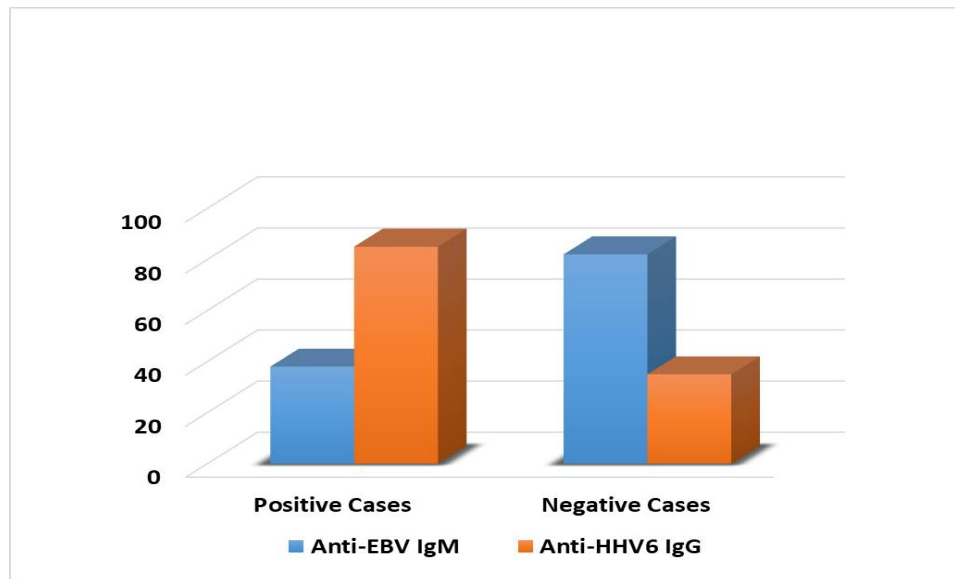


Figure 1: Anti-EBV IgM and IgG seropositivity

virus could facilitate the disruption of immune tolerance to CNS myelin antigens via molecular mimicry [14]. Another theory is that the virus, in conjunction with the existence of OCBs that endure for a long time, can serve as an antigenic stimulus that triggers an immune response in the central nervous system [15].

Infecting, activating, and latently persisting in B cells for the lifetime of the infected individual is possible with EBV, a ubiquitous B-lymphotropic virus [16]. It is also known that EBV can activate dormant B cells into B cell blasts, which then transform into memory B cells that can move in the blood. Some have hypothesized that EBV-infected B lymphocytes in the periphery significantly contribute to the spread of CNS-compartmentalized neuroinflammation when they move into the CNS [17, 18]. The possibility that EBV-infected B cells can stimulate T cells in the periphery is an appealing notion, as the prevailing belief is that T- and B cell interactions are crucial to the development of MS pathogenesis.

2. Methods and Materials

Patients: The investigation included 120 patients who had been clinically diagnosed with neuroinflammatory disease by neurologists. The age of the 2120 patients ranged from 26 to 78, with an average of 75 females and 45 men. The investigation will be conducted from November 2023 to May 2024. Each patient was questioned regarding their medical conditions, and laboratory examination (WBC, PLT, Lymphocytes).

Material: The following apparatus was employed in our study: an ELISA automated washer, an ELISA kit (Anti-EBV IgG, Anti-EBV IgM) from Sunlong, an ELISA printer, and an ELISA reader.

Methods: "Blood samples were obtained only after participants provided written and verbal consent." The research proposal was approved by the ethics board of the Kufa College of Medicine, 5 ml of vein blood was also included. The area was cleansed with 70% strength alcohol prior to the collection of blood samples. The serum was divided into new plain containers for immunological assays (EBV IgG and EBV IgM), centrifuged at 3000 rpm for 15 minutes, and subsequently stored at -20 °C until analysis.

Ethical Approval: Blood samples were collected after the participants provided verbal and written consent. The ethics council of the Kufa College of Medicine has approved the research plan.

Statistical Analysis: The data was entered, managed, and analyzed using Version 24 of the social sciences software. The variables were displayed as percentages, means, standard deviations, frequencies and. The Chi-square test is one method for evaluating the significance of a relationship between two category variables. The significance level for all statistical tests was established at 5%.

3. Results

Serological testing was performed on two distinct viral antibodies, namely Epstein-Barr Virus IgM and IgG. The results of the studies are shown here. In the case of the EBV IgM antibody test, the following results were obtained: As a whole, there were 120 samples, 38 positive cases, 82 negative cases, and a positive percentage of 32%. And negative of 68%. It is common for a positive EBV IgM result to show that the infection is either recent or acute. It appears that the majority of the people in this sample do not have an active EBV infection, as indicated by the comparatively low positive rate of 32%.

With regard to the HHV6 IgG antibody test: There were a total of 120 samples to choose from, 85 positive cases, 35 negative cases, and a positive percentage of 71%. Percentage of Negative Values: 29%. A significant proportion of the individuals in this sample have generated antibodies against EBV as a result of previous exposure to the virus, as indicated by the high percentage of positive EBV IgG (71%) in this sample. Antibodies of the IgG type often indicate a history of infection or immunity. Considerations Regarding the Interpretation EBV IgM antibodies are often present between one and six weeks following the onset of sickness and diminish between three and six months later. A previous exposure to EBV is represented by a level of 5 EBV IgG, which does not necessarily indicate an active infection.

The report provides a thorough examination of Epstein-Barr Virus antibody findings and related hematological parameters. Let us analyze the principal observations: Antibody Status and Leukocyte Counts, Elevated WBC Count: 52% of patients tested positive for

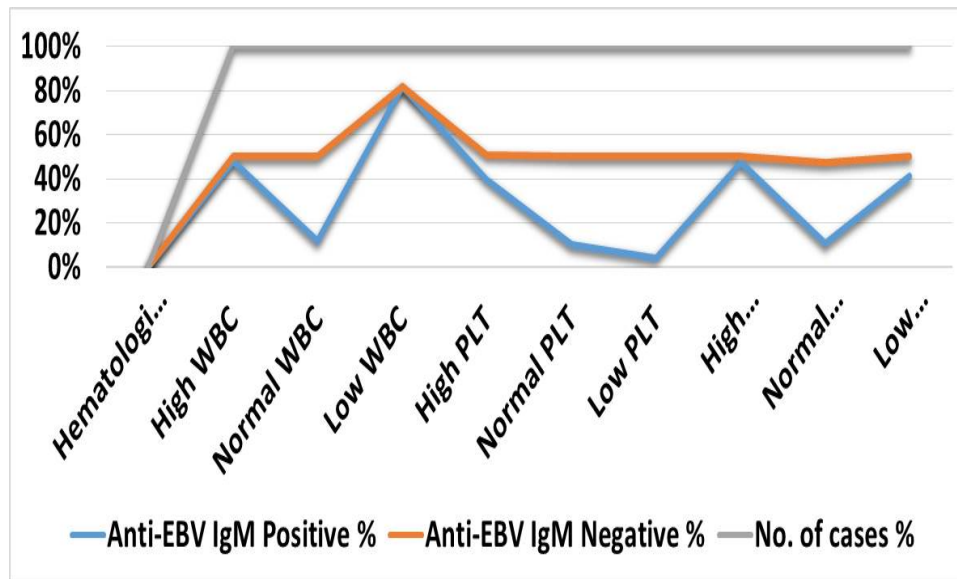


Figure 2: Levels of white blood cells, platelets, and lymphocytes according to anti-EBV IgM seropositivity

Anti-EBV IgG. 2% tested negative for Anti-EBV IgG. Percentage of elevated WBC cases: 54%.

Normal WBC Count: 14% tested positive for Anti-virus IgG. 46% tested negative for Anti-EBV IgG. Percentage of normal WBC cases: 60%, Low WBC Count: 27% tested positive for Anti-virus IgG. 6% were negative for Anti-EBV IgG. Proportion of low WBC cases: 33% Platelet levels, High Platelet Count: 39% tested positive for Anti-virus IgG. 11% were negative for Anti-virus IgG, Proportion of high PLT cases: 48%. Normal Platelet Count: 12% tested positive for Anti-EBV IgG. Also, 48% tested negative for Anti-EBV IgG. Percentage of typical PLT cases: 60%, Low Platelet Count: 1% tested positive for Anti-EBV IgG. 11% tested negative for Anti-EBV IgG. Proportion of low PLT cases: 12% Lymphocyte Levels, Elevated Lymphocyte Count: 57% tested positive for Anti-EBV IgG. 3% tested negative for Anti-EBV IgG.

Total cases of elevated lymphocyte levels: 60% Normal lymphocyte count: 2% tested positive for Anti-EBV IgG, 7% were negative for Anti-EBV IgG. Proportion of normal lymphocyte cases: 10%, Low Lymphocyte Count: 41% had positive Anti-EBV IgG tests. Anti-EBV IgG results were negative in 9%. 50% of cases have low lymphocyte counts. Predominant findings indicate that elevated levels of white blood cells, platelets, and lymphocytes were correlated with positive Anti-EBV IgG results. Normal white blood cell and platelet counts exhibited a greater proportion of negative Anti-EBV IgG findings. Reduced lymphocyte counts were primarily observed in subjects positive for Anti-EBV IgG. The data indicate a possible association between EBV infection and alterations in hematological parameters, specifically in white blood cell and lymphocyte counts.

According to the search results and the supplied data, this is an analysis of the Epstein-Barr Virus antibody findings and hematological parameters.

Relationship Between Antibodies and White Blood Cells The data elucidates intriguing patterns in EBV infection and hematological alterations: White Blood Cell Levels 52% of patients with elevated WBC were Anti-EBV positive. Positive for IgG.

Merely 2% of elevated WBC patients were IgG negative. 14% of cases with normal white blood cell counts tested positive for IgG. 46% of normal white blood cell instances were negative for IgG. 23 Lymphocyte Observations The lymphocyte data corresponds with established research on EBV infections: In 57% of instances with elevated lymphocyte levels, patients tested positive for IgG. Merely 3% of individuals with elevated lymphocyte levels were IgG negative. 41% of patients exhibited reduced lymphocyte levels and positive IgG findings Platelet Assessments: 39% of individuals with elevated platelet counts tested positive for IgG. 11% of individuals with elevated platelet levels were IgG negative. Merely 1% of instances of decreased platelet counts tested positive for IgG 23, Clinical Analysis: The data indicates a robust connection between EBV infection and hematological alterations. EBV infection correlates with modifications in leukocyte numbers. A significant elevation of lymphocytes is observed in EBV-positive patients. The presence of IgG antibodies signifies a past or ongoing EBV infection 27. Essential Diagnostic Insights: Positive VCA IgG findings indicate a past or present infection. The fluctuations in WBC, lymphocyte, and platelet counts may signify the stages of EBV infection.

4. Discussion

Even though there has been proof of a link between EBV and these types of diseases for more than 30 years [19]. This research demonstrates that the meninges and perivascular compartment of white matter lesions are frequently associated with the accumulation of EBV-infected B cells and plasma cells, a characteristic of multiple sclerosis by looking at brain tissue from MS patients who had different disease courses after they died. The amount of brain inflammation is related to the number of cells that carry EBV. The research also revealed that EBV is primarily lodged in aberrant B cell follicles that develop in the meninges of MS patients who have secondary progressive disease. Also can now say for sure that there is a link between EBV infection and B cell problems in MS. Two earlier studies [20] that tried to find EBV in MS brains using in situ hybridization for EBER and immunohistochemistry for virus proteins were not successful.

Based on how the viral proteins were expressed in the brains of most of the MS cases we studied, it looks like the EBV infection has two programs, one for growth (EBNA2) and one for default (LMP1). The fact that cells expressing EBNA2 and LMP1 are rarely found in the blood shows that EBV control is completely thrown off [21]. This could be because of a problem with the immune system or because T cells can't get rid of infected cells that are dormant in places like the central nervous system that aren't easily watched by the immune system. The

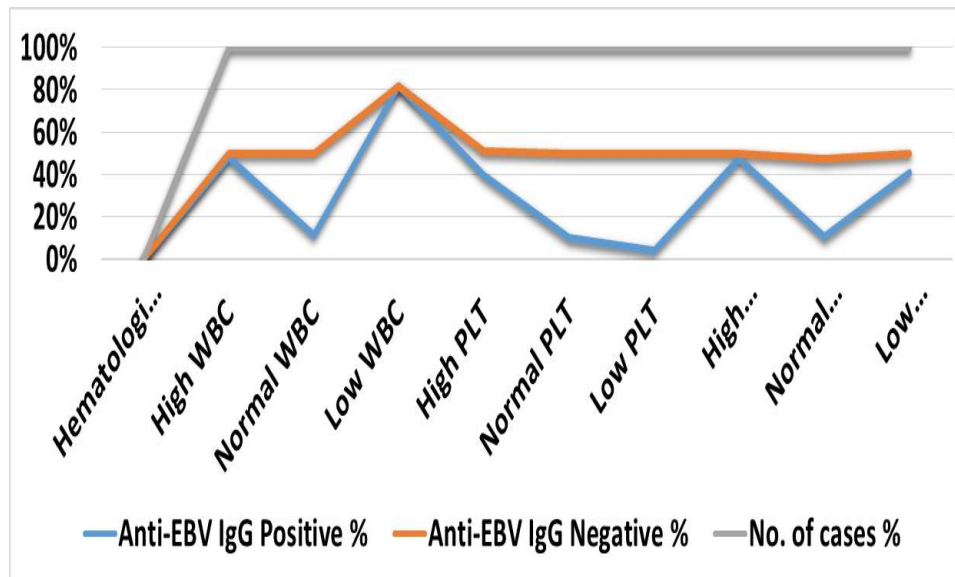


Figure 3: Levels of white blood cells, platelets, and lymphocytes according to anti-EBV IgG seropositivity

MS CSF sometimes had low amounts of EBV DNA and a robust, oligoclonal humoral immune response, both of which indicate that the infection is currently mostly quiescent [22].

Evidence of EBV trying to join the replicative cycle has been found in cases of acute, fatal MS and severely infiltrated brains in patients with secondary progressive MS. This is based on the early replicative cycle-associated BFRF1 protein. It is thought that the inflammatory activity in the brain tissue of MS patients, which can be seen on gadolinium-enhanced magnetic resonance imaging may be linked to EBV activation every so often. A study found that people with relapsing-remitting multiple sclerosis who had stable levels of serum IgG specific for EBV early antigens, which are signs of EBV reactivation, had more gadolinium-enhanced lesions than people who did not have this antibody [23].

There are numerous factors that could maintain the intracerebral pool of virus-carrying B cells in MS patients, including the movement of infected B cells from the bloodstream, the growth of virus-driven B cells, and potentially the local shedding of small numbers of viral particles as a result of viral replication [24]. B cells usually don't get into the central nervous system, and they only make up a small part of the lymphocytes in the cerebrospinal fluid. Still, B cells that have been activated by antigens (memory B cells) or that have become activated in the wrong way (malignant B cells, EBV-infected B cells, etc.) may be able to attach to the central nervous system [25]. This is likely because of chemokines like CXCL12 and CXCL13 that attract B cells. The fact that there are areas in the MS brain where B cells are multiplying and the presence of the latency proteins LMP1 and EBNA2, which tell B cells to multiply and survive, supports the idea that EBV causes B cells to get bigger. Later on, in the course of secondary progressive multiple sclerosis, activated B cells that are infected with the Epstein-Barr virus may be encouraged to form B cell follicles. This lets the virus stay active by taking advantage of the development process that happens inside [26]. CD40 receptor and the B cell receptor are activated. There is a good chance that virus reactivation happens when B cells change into plasma cells that make Ig. This process is mostly connected to B cell follicles that are not where they should be and new MS plaques. This may be helped by the way viral factors and inflammatory cytokines interact with each other. B cell-activating factor, a member of the tumor necrosis factor family, collaborates with LMP1 to induce Ig heavy chain class switching that is independent of T cells [27].

Studies that look at antibodies and population trends are the strongest proof that EBV is a major cause of multiple sclerosis. This is because blood antibody levels to EBV antigens rise significantly years before MS symptoms show up [28]. This suggests that EBV is involved in the early stages of MS pathogenesis. Antibodies against EBV may be linked to this process because it spreads to the central nervous system long before MS symptoms show up. Infectious mononucleosis is also linked to a higher chance of developing multiple sclerosis [29]. This finding makes it more likely that having more infected B cells in the blood can cause virus entry to the brain and/or cause the immune system to respond too strongly to EBV, which then causes an immunopathologic response. The notion that EBV infection contributes to the development of multiple sclerosis is substantiated by the numerous epidemiological similarities between infectious mononucleosis and multiple sclerosis [30].

5. Conclusion

Given that the IgG and IgM levels of numerous individuals increased concurrently, it is possible that the activation of EBV viral infection is the cause of neuroinflammatory disorders or the aggravation of a pre-existing condition. A substantial number of individuals with neuroinflammatory diseases are infected with the EBV virus. A small proportion of individuals who have negative results still have positive IgG levels, which may indicate a previous infection.

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