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# Epstein – Barr Virus Serology Among Iraqi Patients with Multiple Sclerosis: A Case-Control Study

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**Abstract**

**Introduction.** Multiple sclerosis (MS) is a chronic immune-mediated inflammatory and neurodegenerative disease of the central nervous system. Epstein – Barr virus (EBV) is highly prevalent worldwide and has been epidemiologically associated with MS.
**Purpose.** To evaluate the association between EBV serology and MS among a sample of Iraqi MS patients.
**Materials and methods.** A case-control study was conducted on fifty MS patients and 50 healthy age- and sex-matched controls were enrolled. EBV viral capsid antigen (VCA) IgG was quantified by ELISA (Alegria system).
**Results.** There were no significant association between-group differences in age, sex, or smoking status. None of the participants had undergone previous EBV testing. EBV VCA IgG positivity was higher in MS patients than controls (98.0% vs 84.0%; p=0.038), and EBV antibody titers were higher in the MS group (p=0.035). EBV VCA IgG seropositivity and antibody titers were significantly higher among MS patients than controls.
**Conclusion.** EBV VCA IgG seropositivity and EBV antibody titers are greater among MS patients, supporting an association between EBV serology and MS.
**Keywords:** multiple sclerosis, Epstein – Barr virus, EBV VCA IgG, ELISA, non-traumatic disabling neurological disease

## ■ INTRODUCTION

Multiple sclerosis (MS) is a chronic, immune-mediated, inflammatory, and neurodegenerative disorder of the central nervous system and is a leading non-traumatic disabling neurological disease affecting young adults [1–3].

Global MS incidence and prevalence are increasing, emphasizing the growing public health burden of the disease [4].

In Iraq, MS is increasingly recognized; a retrospective review (2000–2018) across authorized MS clinics reported a prevalence of 11.73 per 100,000 (higher among females) and rising incidence over time [5].

MS is typically diagnosed between 20 and 40 years of age and shows a clear female predominance [6, 7].

MS is believed to result from an interaction between genetic susceptibility and environmental exposures, with evidence from epidemiology and genetic studies supporting multifactorial causation [8].

Environmental factors implicated in MS include latitude, vitamin D deficiency/sunlight exposure, smoking, obesity, and infections – among which Epstein – Barr virus (EBV) is frequently considered a major risk factor [9, 10].

Pathologically, MS features inflammatory demyelination with gliosis and neurodegeneration, affecting white matter and potentially deep and cortical gray matter, driven by complex peripheral and CNS immune interactions [11].

Epstein – Barr virus is ubiquitous; most individuals acquire infection early in life and remain lifelong carriers through latency with periodic reactivation [12].

EBV has been linked to autoimmune diseases including MS, and several candidate mechanisms have been proposed; clarification of causality and mechanisms remains an ongoing research priority [13].

## ■ PURPOSE OF THE STUDY

To evaluate the association between EBV serology and MS among a sample of Iraqi MS patients.

## ■ MATERIALS AND METHODS

### Study Design and Setting

A case-control study was conducted at the Middle Euphrates Neurosciences Center in Annajaf Al-Ashraf Governorate, Iraq, from 1 June 2024 to 1 January 2025.

### Ethical Approval and Consent

The study procedures were approved by the appropriate institutional scientific and ethical committees, of Faculty of Medicine – University of Kufa; Middle Euphrates Neurosciences Center (no. 9601 in 22/12/2023) and verbal consent was obtained from all participants prior to enrollment.

### Participants, Sampling, and Eligibility

A convenience sample of 100 participants aged 18–65 years was enrolled and categorized into 50 MS patients and 50 healthy controls matched by age and gender. MS diagnosis was established according to contemporary diagnostic criteria. Participants were excluded if they had any recent vaccination or recent infection.

### Data Collection

Data were collected using a structured questionnaire capturing demographic variables and MS clinical characteristics (duration, subtype, clinical presentation), plus EBV testing history and current serology results.

### EBV Serology (VCA IgG)

Anti-EBV viral capsid antigen (VCA) IgG was quantified using an ELISA-based platform (Alegria system) with manufacturer cutoffs defining negative (<20 U/ml), borderline (20–25 U/ml), and positive (>25 U/ml) results.

### Statistical Analysis

Categorical variables were compared using chi-square testing and continuous variables using t-tests, with statistical significance set at $p<0.05$.

## ■ RESULTS

A total of 100 participants were enrolled (50 MS; 50 controls). There were no statistically significant differences between groups regarding age, gender, or smoking status (Table 1).

**Table 1**
**Distribution of Sociodemographic according to the study groups (n=100)**

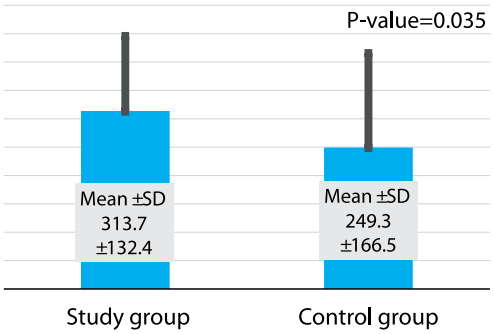
| Sociodemographic characteristics | | Study group N (%), n=50 | Control group N (%), n=50 | P-value |
|---|---|---|---|---|
| Age (years) | <30 | 25 (25.0) | 15 (15.0) | 0.195 |
| | 30–39 | 18 (18.0) | 22 (22.0) | |
| | 40–49 | 6 (6.0) | 11 (11.0) | |
| | ≥50 | 1 (1.0) | 2 (2.0) | |
| Gender | Female | 29 (29.0) | 32 (32.0) | 0.376 |
| | Male | 21 (21.0) | 18 (18.0) | |
| Smoking state | Smokers | 5 (5.0) | 12 (12.0) | 0.062 |
| | Non-smokers | 45 (45.0) | 38 (38.0) | |

Among MS patients, nearly half had duration <5 years, and relapsing-remitting MS was the predominant subtype; optic neuritis and sensory symptoms were the most frequent presentations (Table 2).

**Table 2**
**Characteristics of MS (n=50)**

| Patients' characteristics | | N (%) |
|---|---|---|
| Duration of MS | <5 years | 23 (46.0) |
| | 5–10 years | 19 (38.0) |
| | >10 years | 8 (16.0) |
| Types of MS | RRMS | 46 (92.0) |
| | SPMS | 2 (4.0) |
| | PPMS | 2 (4.0) |
| Clinical presentation | Optic neuritis | 17 (34.0) |
| | Sensory symptoms | 17 (34.0) |
| | Motor symptoms | 15 (30.0) |
| | Brainstem syndromes | 8 (16.0) |
| | Sphincter uncontrol | 1 (2.0) |

None of the participants had undergone EBV testing previously. EBV VCA IgG positivity was significantly higher among MS patients than controls (98.0% vs 84.0%; p=0.038), and EBV antibody titers were significantly higher in the MS group (p=0.035) (Table 3; Figure).




**Difference between the study groups regarding the EBV test titer**

**Table 3**
**Difference between the study groups regarding the previous EBV test and current EBV test**

| EBV characteristics | | Study group N (%) | Control group N (%) | P-value |
|---|---|---|---|---|
| Previous EBV test | Yes | 0 | 0 | n/a |
| | No | 50 (50.0) | 50 (50.0) | |
| Current EBV test | Negative | 0 | 5 (5.0) | 0.038 |
| | Equivocal | 1 (1.0) | 3 (3.0) | |
| | Positive | 49 (49.0) | 42 (42.0) | |

A high mean titers recorded for MS group (313.7) compared to control arm (249.3) with significant difference (p=0.035).

## ■ DISCUSSION

The observed demographic pattern (female predominance and young adult distribution) is consistent with established MS epidemiology and with regional cohorts, and plausible biological explanations include hormonal, genetic, and immune-microbiome differences [14–16].

Smoking patterns vary between populations, and prior work suggests smoking contributes to MS risk; differences in smoking prevalence across studies may reflect sociocultural and regional factors [17, 18].

Relapsing-remitting MS predominance and the frequency of optic neuritis/sensory/motor presentations in this cohort align with typical clinical phenotypes reported in regional registries and observational studies [14, 15, 19].

MS is driven by complex immune-mediated mechanisms and may be influenced by infectious exposures; EBV has repeatedly emerged as a prominent candidate environmental risk factor, although heterogeneity exists across studies [20].

In this Iraqi case-control study, MS patients demonstrated significantly higher EBV VCA IgG seropositivity and higher titers compared with matched healthy controls, supporting an epidemiologic association between EBV serology and MS in this population [20, 21].

Our EBV findings are consistent with Iraqi data reporting higher EBV-related antibody positivity/levels in MS than controls, and with studies suggesting EBV may contribute to MS susceptibility or disease biology [20, 21].



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Mechanistically, EBV-MS links have been discussed in terms of molecular mimicry, altered antiviral immunity, impaired immune surveillance, and pathogenic roles of infected B cells, but further work is needed to clarify causal pathways and clinically actionable implications [12, 22, 23].

## ■ CONCLUSIONS

EBV VCA IgG seropositivity and EBV antibody titers were statistically significant higher among MS patients compared with healthy controls, supporting an association between EBV serology and MS in this Iraqi sample. Future studies should be carried out to explore facilitator factors that could increase the number of people being tested. Public health stakeholders should enhance awareness about EBV, screening importance, and complications through educational initiatives and media campaigns.

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