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Relationship between Helicobacter pylori infection and multiple sclerosis

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Abstract

Background: The relationship between Helicobacter pylori (H. pylori) infection and multiple sclerosis (MS) is unclear, with theories varying from protective immunomodulation to harmful effects through molecular mimicry. This study sought to ascertain the incidence of H. pylori infection in Egyptian MS patients and evaluate its clinical implications. **Methods:** A case-control study at Minia University Hospital, included 71 multiple sclerosis patients and 80 age- and sex-matched controls. The diagnosis of multiple sclerosis was established according to the 2017 McDonald criteria. Serum anti-H. pylori IgG concentrations were measured using ELISA. Statistical analyses comprised chi-square tests, Mann-Whitney U tests, and multivariable linear regression. P-values less than 0.05 were deemed significant. **Results:** The prevalence of H. pylori infection was markedly elevated in multiple sclerosis patients (46.5%) relative to controls (28.7%) ($p = 0.024$). IgG titers were substantially higher in the MS group (mean ± SD: 1.26 ± 0.92 RU/mL) compared to controls (0.99 ± 0.98 RU/mL, $p = 0.009$). No substantial variations were seen in BMI, age, gender, or smoking status across the groups. **Conclusion:** Our results demonstrate an elevated prevalence and antibody titer of H. pylori in MS patients, implying a possible pathogenic correlation. These findings underscore the necessity for additional research on the immunological mechanisms connecting H. pylori with MS, especially in endemic areas.

Keywords: MS, Helicobacter pylori, Seropositivity

Introduction

Multiple sclerosis (MS) is an autoimmune central nervous system (CNS) disorder characterized by inflammatory demyelination of the white matter of the CNS, axonal destruction and neurodegeneration, all of which representing the pathological hallmark of MS (1). MS is typically diagnosed in adults aged 20 to 30 years and often affects physical functioning, cognition, quality of life, and employment (1). Without treatment many patients with MS will enter in irreversible neurological damage stage. The cause of MS is still unclear, but many genetic and complex

environmental causes have been linked to the development of MS. Many pathogens have been linked to development of MS and strong correlation with Epstein-Barr virus infection had been reported before. Usually, presentation of MS come in attacks called relapse of different symptomatology including unilateral optic neuritis, weakness, ataxia of the extremities, sensory disturbance (limb paresthesias) and brainstem syndromes (intranuclear ophthalmoplegia). A clinical attack or relapse in MS is defined as a single clinical episode with symptoms and objective findings reflecting a focal or multifocal inflammatory demyelinating event in the CNS (1). Although genetic and environmental factors influence pathogenesis, the significance of illnesses such as Helicobacter pylori remains contentious. Helicobacter pylori, a bacterium with worldwide distribution, demonstrates immunomodulatory characteristics via methods including molecular mimicry (e.g., heat shock protein 60 HSP60) and modulation of the gut-brain axis (2-4)

Previous research presents contradictory associations: some indicate that H. pylori seropositivity confers protection through the induction of regulatory T-cells (4,5) whilst others associate acute infection with neuroinflammation. And still Geographic diversity in strains and host immunity may elucidate disparities (6,7). This study sought to elucidate the relationship and prevalence between H. pylori and MS patients.

Patients and Methods

Study Design and Population

This observational case-control study included 71 multiple sclerosis patients and 80 controls from Minia University Hospital. Multiple sclerosis diagnosis adhered to the 2017 McDonald criteria. Controls consisted of age- and sex-matched people devoid of neurological or immunological disorders. Demographic and clinical characteristics encompassed of age, sex, body mass index (BMI), and duration of sickness.

Inclusion/Exclusion Standards

Inclusion criteria: Age ≥ 18 years, verified diagnosis of multiple sclerosis (MS). Exclusions: Pregnancy or lactation, previous H. pylori eradication, gastrointestinal symptoms, or concurrent other inflammatory central nervous system illnesses.

Serological and Clinical Evaluations

Serum anti-H. pylori IgG was measured by ELISA (Elabscience Biotechnology; positive threshold ≥ 1.1 RU/mL).

Ethical Approval: Granted approval by the Institutional Review Board of Minia University. Informed consent was acquired in accordance with the Declaration of Helsinki.

Statistical Analysis

Data were analyzed utilizing SPSS version 26. Normality was assessed using the Shapiro-Wilk and Kolmogorov tests. Non-parametric variables were analyzed using the Mann-Whitney U test, while categorical variables were assessed with chi-square or Fisher's exact tests. Correlations utilized Pearson and Spearman coefficients. Linear regression determined the determinants of H. pylori titers. The significance level was established at $p<0.05$.

Results

The prevalence of H. pylori infection was significantly higher in MS patients (46.5%) compared to controls (28.7%) ($p = 0.024$). H. pylori antibody titers were also significantly elevated in MS patients (mean ± SD: 1.26 ± 0.92) relative to controls (0.99 ± 0.98) ($p = 0.009$). No significant differences were observed in sociodemographic variables (age, gender, residence) or BMI ($p > 0.05$). (Table 1).

Fig 1 and 2 showed higher H. pylori titers and infection rates in MS cases. Figure 3 shows: The distribution of MS types in our cases is similar to world prevalence, where RRMS is predominant. So, no significant relationship between MS type and H. pylori infection was observed.

Table (1): Comparison between Cases & Controls as regarding sociodemographic, clinical and laboratory characteristics

Socio-demographic characteristics	Cases N=71	Controls N=80	$\chi 2$	P-value
Age (Years) Mean ± SD Median (IQR) Range	 34.99±8.14 34(29-42) (20-56)	 35.04±12.65 32(26-41) (17-65)	 M= 2623.5	 0.419
Gender® Male Female	 25(35.2%) 46(64.8%)	 38(47.5%) 42(52.5%)	 2.336	 0.126
Residence® Rural Urban	 47(66.2%) 24(33.8%)	 41(51.2%) 39(48.8%)	 3.456	 0.063

Body Mass Index Mean ± SD Median (IQR) Range	 25.2 ±4.61 24.44(23.23-26.3) (17.63-43.25)	 24.81 ±3.79 24.2(21.94-26.7) (18.37-36.75)	 M= 2753.5	 0.747
BMI Categories Underweight Normal Overweight Obese	 2(2.9%) 43(61.4%) 18(25.7%) 7(10%)	 1(1.35) 44(55%) 28(35%) 7(8.8%)	 1.966	 0.617
Smoking No Yes	 55(77.5%) 16(22.5%)	 52(65%) 28(35%)	 2.830	 0.092
H.Pylori antibody titer (IgG) Mean ± SD Median (IQR) Range	 1.26 ±0.92 0.9(0.43-1.99) (0.15-3.6)	 0.99±0.98 1.45(0.3-1.6) (0.1-3.7)	 M= 2142	 **0.009***
H.pyloric infection® Negative Positive	 38(53.5%) 33(46.5%)	 57(71.3%) 23(28.7%)	 5.067	 **0.024***

*p value is considered statistically significant at <0.05. χ^2Chi Square test was used, (M) Mann Whitney statistics was used

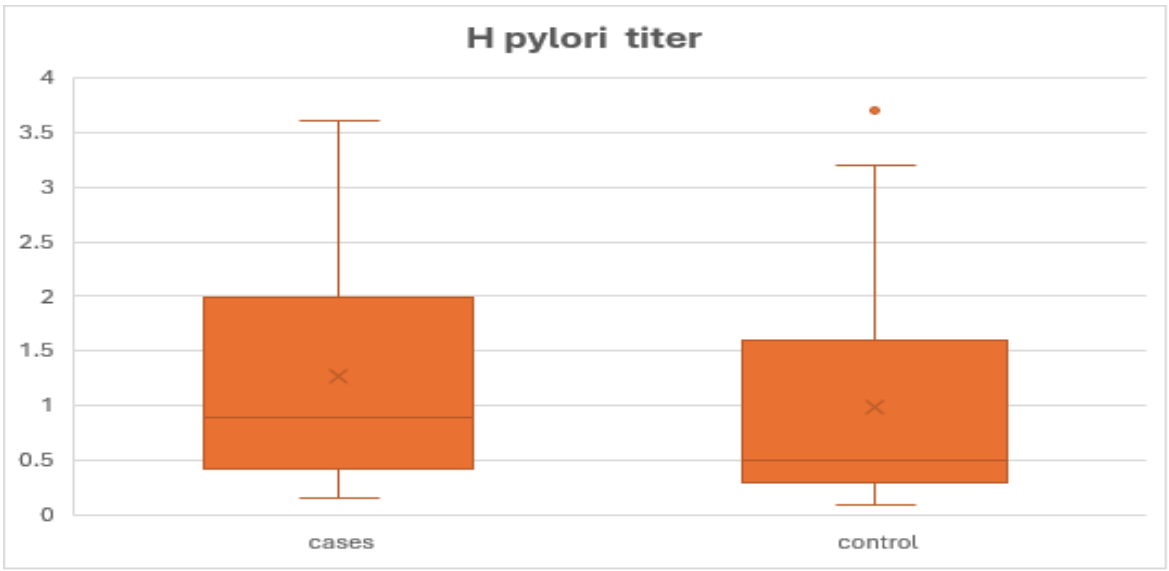

Fig (1): Box Plot showing Comparison between Cases & Controls as regarding H pylori titer

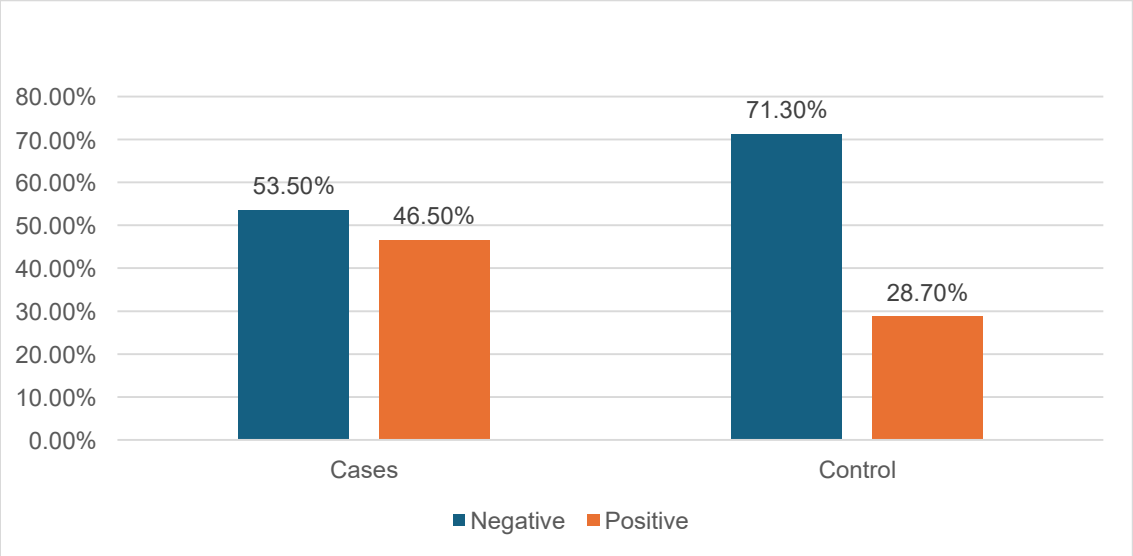

Fig (2): Cluster Bar chart showing Comparison between Cases & Controls as regarding H pylori infection

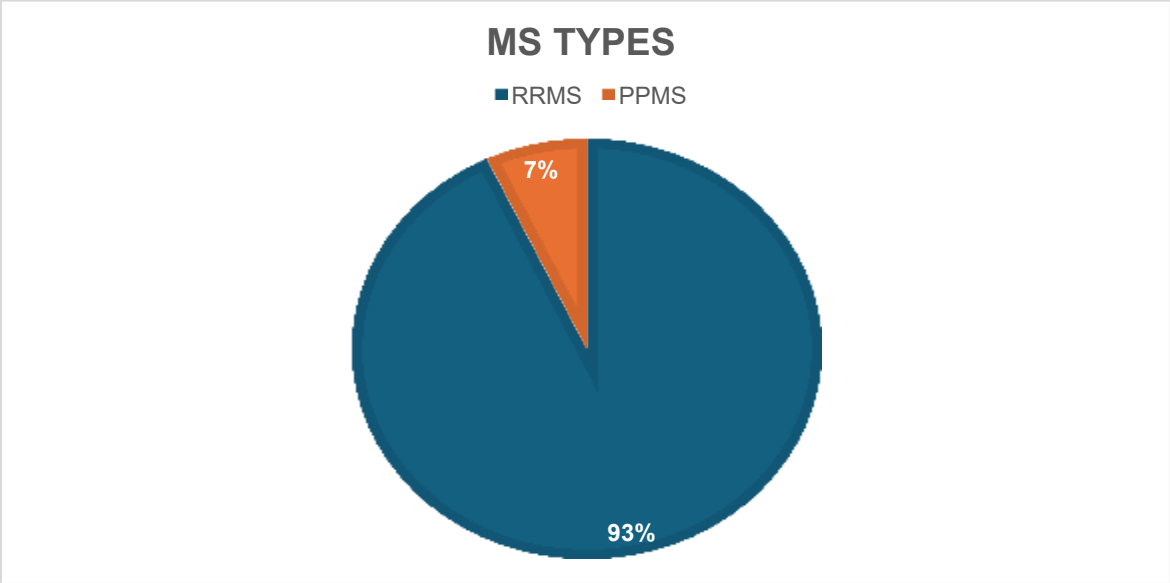

Fig (3): Pie chart showing MS types among the studied cases

Discussion

The results of this study show that MS patients have a much higher frequency and titer of Helicobacter pylori (H. pylori) antibodies, so supporting the mounting data on a complex immunological link between

microbial exposure and autoimmune neuroinflammation.

By encouraging immunological tolerance via the proliferation of regulatory T-cells (Tregs), early exposure to bacteria including gastrointestinal pathogens like H. pylori may confer protection against autoimmune diseases, according to the "hygiene hypothesis". Particularly when colonization occurs in early development, several studies imply that H. pylori may have a protective effect by changing gut brain immunological interactions via Treg induction and lowered pro inflammatory Th17 responses. Reduced seroprevalence of H. pylori found in Japanese MS patients suggested a possible protective immunomodulating mechanism connected to gut-immune axis control (6,7).

Recent studies challenging this theory propose that in the context of an active or chronic H. pylori infection, persistent low-grade inflammation, molecular mimicry, and disturbance of the blood-brain barrier may help multiple sclerosis to establish or progress. Baj et al. underlined how H. pylori cause extragastral symptoms by means of systemic cytokine release and cross-reaction of H. pylori antigens with human myelin proteins (9).

Arjmandi et al.'s meta-analysis highlights how the chosen diagnostic technique affects the apparent correlation. Although ELISA-based serological studies usually indicated a protective effect indicating that may be actual infection, rather than simple seropositivity, may be dangerous (7,8). These results match ours since we noted that MS patients showed noticeably higher IgG titers, presumably due to ongoing antigenic stimulation rather than simple past exposure.

H. pylori can increase intestinal permeability, so allowing the circulation to absorb pro-inflammatory bacterial products (LPS). By means of the gut-brain axis and molecular mimicry this could encourage the pathogenesis of multiple sclerosis (MS) (10) by Cross-reactivity between host CNS antigens and H. Pylori antigens

Recent research suggests that microbial infections, including H. pylori, may cause epigenetic reprogramming in immune cells, so producing a proinflammatory phenotype even after the bacteria have been removed (9).

Furthermore, besides microbial exposure, may be regional differences in the incidence of H. pylori and MS could be ascribed to host

genetics, dietary patterns, and environmental influences.

One also must consider the effect of the MS subtype and disease activity. Research indicates that in some RRMS populations H. pylori seropositivity correlates with lowered EDSS scores and decreased relapse rates; yet, the results are inconsistent and often influenced by therapeutic regimens (6,7).

Also, we don't know the relationship between disease modifying therapy (DMT) of MS and microbes like H. Pylori, further research studying the effect of DMT on gut microbes is needed, we don't know if DMT flares up or decrease gut microbes and consequences of this on treatment for future research.

limitations and advantages of the research:

Comparability is achieved using standardized ELISA techniques, and our study provides important information from a minority population. Nevertheless, ELISA's tests need more confirmation. Future studies should use stomach biopsies, stool antigen tests, or urea breath testing to improve diagnostic accuracy.

Conclusion

There is a possible link between H. pylori seropositivity and multiple sclerosis. The need for additional longitudinal research, ideally with histological confirmation, is supported by the higher prevalence and titers in MS patients. This relationship could provide new understandings of the pathophysiology of MS and have therapeutic implication in the future.

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