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Detection of anti-*Helicobacter pylori* in patients with Multiple Sclerosis

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ABSTRACT

To determine the relationship between *Helicobacter pylori* infection and Multiple Sclerosis (MS) disorder, 20 patients with MS aged (25-60) years have been investigated from the period of 2016/12/1 to 2017/3/1 and compared to 15 apparently healthy individuals. All study groups were carried out to measure anti *H.pylori* IgA and *H.pylori* IgG antibodies by enzyme linked immunosorbent assay (ELISA) technique. There was a significant elevation ($p<0.05$) in the concentration of anti *H.pylori* IgG and IgA antibodies (Abs) compared to control group, and there was no significant difference ($p>0.05$) in the concentration of IgA and IgG (Abs) of *H.pylori* according to gender, and there was no significant difference ($p>0.05$) in the concentration of IgA and IgG (Abs) of *H.pylori* according to gender and age. This result indicates that infection with *H.pylori* may play a role in the pathogenesis of MS.

Keywords: Multiple Sclerosis (MS), *Helicobacter pylori*, IgG, IgA.

1. INTRODUCTION

Helicobacter pylori is a Gram negative bacterium that usually establishes lifelong colonization of the human stomach from early childhood. Approximately 10%-15% of those infected develop symptomatic disease, including gastric or duodenal ulcers and gastric cancer [1].

In the vast majority of cases, however, colonization leads to asymptomatic chronic gastritis, with increased infiltration of neutrophils, dendritic cells (DCs), macrophages, natural killer (NK) cells, and lymphocytes into the gastric mucosa [2]. There is increased abundance of pro inflammatory T helper 1(Th1) and Th17 subsets, as well as anti-inflammatory regulatory T cells (Tregs) [3]. The bacterium enter through oral and oral fecal ways and virulence factors are related to pathogenicity, as well as host factors were defined [4]. *H.pylori* strains that possess cytotoxic-associated gene A (*CagA*), encoding a type IV bacterial protein secretion system is more strongly associated with increased levels of inflammation and disease, as are those producing an active form of VacA, a pore forming toxin that induces cytoplasmic vacuolation *in vitro* [5,6].

The topic of the extra gastric manifestation of *H.pylori* infection continues to capture the attention of many researchers all over the world. The humble gastric pathogen has been linked to multiple conditions, including cardiovascular disease, lung disease, hematologic disease, eye and skin disease, hepatobiliary disease, diabetes mellitus, neurological disorders and arthritis [7, 8].

It is proposed that *H.pylori* may cause some of its pathogenic effects via direct gastric mucosal damage and some others, via the immunological response evoked by the host. The role of *H.pylori* in neurological disease has been a hot topic in the scientific literature over the last number of years [9].

Multiple sclerosis (MS) is a demyelinating disease of the central nervous system and has a variety of signs and symptoms and many factors affect its development and progression. MS prevalence varies considerably from high levels in North America and Europe to low rates in Eastern Asia and sub-Saharan Africa. In addition, geographical correlation between MS and its prevalence rates have been reported worldwide [10, 11].

The etiology of MS is unknown yet probably a combination of infectious and noninfectious environmental factors triggers the pathogenesis process in each individual. High *H.pylori* frequency has been reported in various disorders of both CNS and MS. another study indicated the presence of immunomodulation properties of *H.pylori* administration in an experimental model of MS, suggesting the possible role of *H.pylori* infection in the pathophysiology of MS disease [12], *H.pylori* infections has been linked to MS and demyelinating peripheral neuropathies, as it may trigger cellular and humoral immunity due to the sharing of similar epitopes present in the nervous tissue. These antibodies cross-react with different components of central and peripheral nerves resulting in their damage studied the prevalence of *H.pylori* infection in different MS subtypes including classic (CMS) and optic spinal MS (OSMS) in the Japanese population and demonstrated a difference in *H.pylori* seropositivity between Japanese patients with OSMS and those with CMS. *H.pylori* infection was significantly lower in patients with CMS [13,14].

The aim of this study was to determine the association between *H.pylori* infection and Multiple Sclerosis.

2. MATERIALS AND METHODS

2.1 Patient samples

The study was carried out on 20 patients suffering from multiple sclerosis who intended neurological science hospital, during period from 2016/11/1 to 2017/1/1. The ages of the patients were ranged from (25-60) years. The interviews were performed for each patient.

2.2 Control samples

Fifteen samples of apparently healthy individuals were studied as control groups of different age and gender. All samples were marked by the number of sample, name of patient and day of sample collection.

2.3 Blood samples collection

Blood samples (5 ml) were collected by disposable syringe into gel tubes and stand at room temperature until it clots. Then the samples were centrifuged at 3000 rpm for 5 min. and stored at (-20Ċ) until carried out to detect anti *Helicobacter pylori* IgA and IgG according to the leaflet of the kit [15].

2.4 Statistical Analysis

The Statistical Analysis System –SAS [16] program was used to study different factors in study parameters. T-test was used to compare between means and Chi-square test was used to compare between percentage in this study whether it is significant or not.

3. RESULTS AND DISCUSSION

The result of the present study showed that there was a significant elevation ($p<0.05$) in the concentration of *H.pylori* IgA Abs 7.15±1.04 (U/ml) compared to control as shown in figure (1).

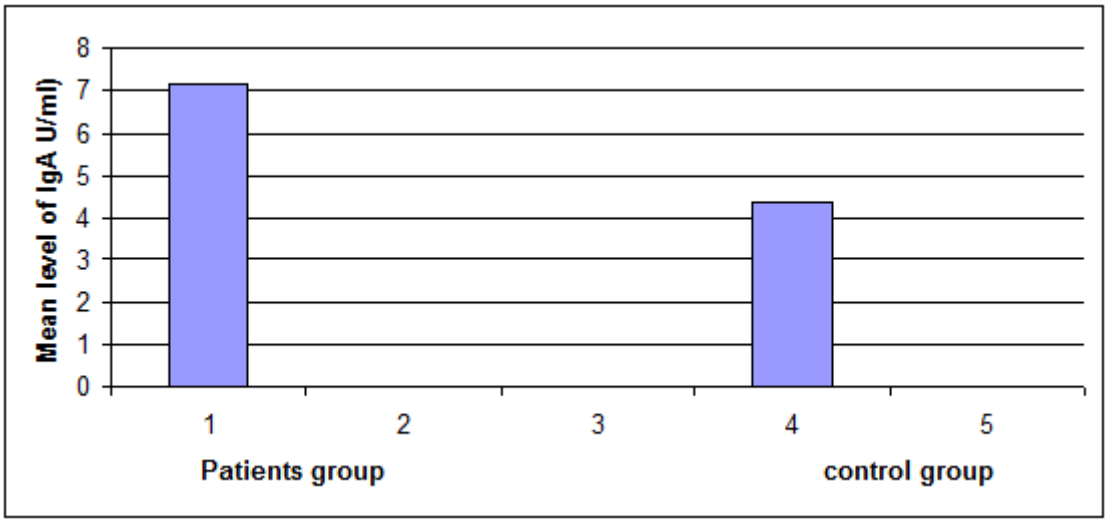

Figure 1: Mean level of anti *H.pylori* IgA Ab (U/ml) in sera of MS patients and control group**.**

Also, there was a significant elevation ($p<0.05$) in the concentration of *H.pylori* IgG Abs 7.81±0.96(U/ml) compare to control group 4.99±0.80(U/ml) as shown in figure (2) .

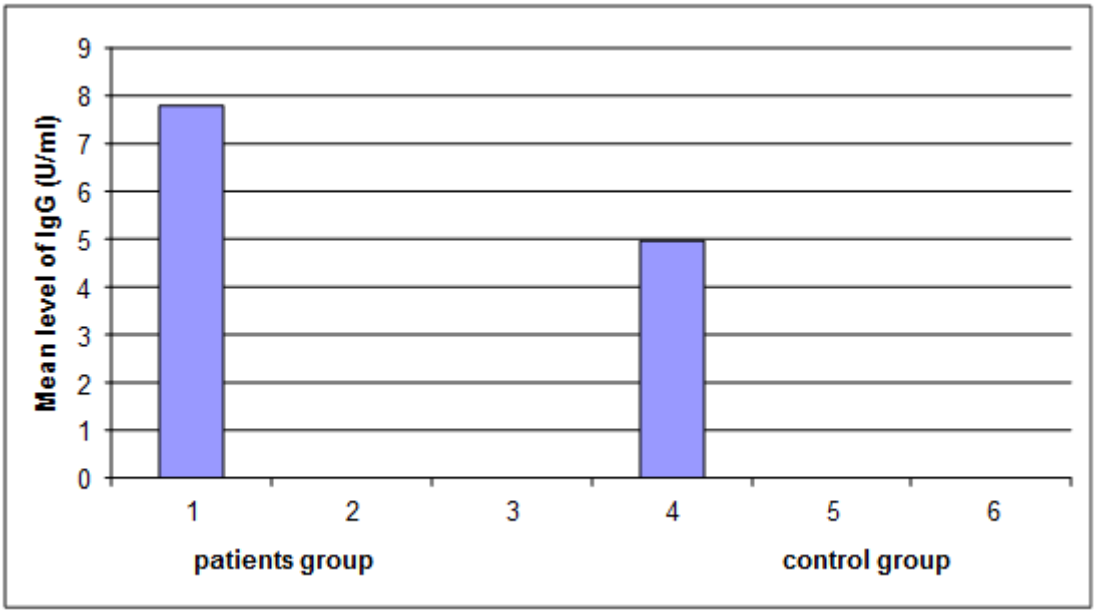

Figure 2: Mean level of anti *H.pylori* IgG Ab(U/ml) in sera of MS patients and control group**.**

While, there was no significant difference (p>0.05) of the concentration of *H.pylori* IgA Ab in male 6.64±1.79 (U/ml) and female 7.50±1.33(U/ml) and there was no significant difference (p>0.05) in the concentration of *H.pylori* IgG Ab in male 6.77±1.52 (U/ml) and female 8.51±1.325(U/ml) as shown in table(1).

Table 1: Mean level of anti H.pylori IgA and IgG (U/ml)Ab in sera of MS according to gender.

Gender	No.	Mean ± SE	
		IgA	IgG
Male	8	6.64 ± 1.79	6.77 ± 1.52
Female	12	7.50 ± 1.33	8.51 ± 1.25
T-test	-	4.870 NS	4.072 NS
P-value	-	0.554	0.153

NS: No significance

Also the results of the present study revealed that there was no significant difference (p>0.05) into the concentration of *H.pylori* IgA Ab in people less than 40 years 5.88±1.33 (U/ml) and people more than 40 years 8.22±1.75(U/ml) and there was no significant difference (p>0.05) into the concentration of *H.pylori* IgG Ab in people less than 40 years 7.74±1.51 (U/ml) and patients more than 40 years 7.12±1.13(U/ml) as shown in table(2).

Table 2: Mean level of anti *H.pylori* IgA and IgA(U/ml) Ab in sera of MS patients according to age.

Age group (year)	No.	Mean ± SE	
		IgA	IgG
Less than 40	11	5.88 ± 1.33	7.74 ± 1.51
More than 40	9	8.22 ± 1.75	7.12 ± 1.13
T-test	-	4.704 NS	3.934 NS
P-value	-	0.306	0.743

NS: no- significance.

The results of present study were in agreement with several other studies. Recent studies have demonstrated that at least (38/78) 48.71% of MS patients are positive for *H.pylori* [16]. Other studies show that *H.pylori* sero positivity was significantly lower in patients with CMS (22.6%) compared with HC (42.4%) and patients with OSMS (51.9%) [17]. While another study revealed that 21.1% of MS patients infected with *H.pylori* (15/17) compared with (14/42) 42.9% of the healthy controls, this show that patients with MS were half as likely to have a *H.pylori* infection [18]. In a study in Poland, it was reported that 19% of MS patients have high levels of antibodies against *H.pylori*, which is a lower rate than in the general population [19].

While in 2007 it was announced that the anti *H. pylori* in patients with MS was 23% of cases. In a study in America by Deter and colleagues in 2011, it was found that the level of antibodies against *H. pylori* in patients with MS were more than the general population, In study by Long and colleagues in the united states in 2013, reported that 74% of MS patients have high levels of antibodies against *H.pylori* [20,21]. Additionally, two case control studies found that amongst MS patients, neurological disability was reduced in those with *H. pylori*. In contrast, other studies have failed to find any association between *H.pylori* infection and MS [22].

Multiple sclerosis (MS) is a human demyelinating disease of the central nervous system (CNS) characterized by the presence of lesion mainly in the white matter of the brain and sometimes in the spinal cord. In addition in the latter stages of disease, the chronic demyelination of axons and neuro axonal injury become dominant causing irreversible damage and neurological symptoms. Evidence from animal models of MS, such as experimental autoimmune encephalomyelitis (EAE), as well as post mortem analysis of patients tissues has suggested that MS might be autoimmune mediated, and accordingly, CNS lesions contain many types of activated immune cells and resident CNS cells, such as astrocytes and microglia [23].

In terms of MS pathogenesis, genetic susceptibility is thought to be important for the risk of MS, however, no specific locus has been identified as causative. In addition, many epidemiological studied have been suggested potential roles for pathogens, both bacterial and viral, although no specific pathogen has been identified as a causative agent. Hypothetical mechanism of pathogen-induced CNS demyelinating disease includes molecular mimicry and by stander demyelination. However, these mechanisms have been conclusively shown in human MS [24].

However, it has been suggested that pathogens might play a different role in the pathogenesis of MS. In 1989, starch an proposed “hygiene hypothesis” that described an increased incidence of chronic inflammatory disease in developed countries in the 20th century concomitant with a decrease in infectious diseases, starch an suggested that increased cleanliness and sanitary conditions had diminished the chance of infection in early childhood thus, enhancing the risk of developing allergic diseases, such as asthma[25].

Several mechanism have been proposed for how pathogens might induce activation and critical expansion of auto reactive T cells and start autoimmune disease such as MS. Activation of resting auto reactive T cells may be achieved by viral and bacterial spurt antigens that bind a variety of MHC class II molecules and activate large numbers of T cells, irrespective of their specificity. Pathogen-induced tissue inflammation may result in local activation of APCs and enhanced processing/presentation of self-antigens that causes T cell priming, followed by T cell activation and expansion of additional specificities (epitope spreading). Another mechanism would imply that the inflammatory setting and the paracrine secretion of T cell growth factors induce the expansion of activated auto reactive T cell, whose small number was previously insufficient to drive an autoimmune disease. Such mechanism is referred to as bystander activation. Moreover, a microbial antigen can include an epitope that is structurally similar to an auto antigen epitope, providing the basic element of the mechanism referred to as molecular mimicry [26].

4. CONCLUSION

Helicobacter pylori infection may play a trigger role in the pathogenesis of neurological disorders such as Multiple Sclerosis.

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