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Chlamydia Pneumoniae: The Potential Cause of Multiple Sclerosis

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Abstract

Background Multiple sclerosis is an autoimmune disease, its etiology until know is unknown. Many studies suggested that the environmental risk factors one of them is *chlamydia Pneumonia*e may play a role in the initiation of the disease.

Objectives To investigate the relationship between previously *Chlamydia Pneumoniae* infection and multiple sclerosis disease initiation

Methods Sixty patients with multiple sclerosis (30 newly and 30 previously diagnosed), their ages ranged from 13 to 58 years were enrolled in the present study. They attended seeking for treatment or for the diagnoses of multiple sclerosis in outpatient clinic at the Medical City, Baghdad Teaching Hospital, Baghdad in the period from December 2014 till March 2015. In addition, thirty healthy volunteers their gender and ages were matched with patients group were participated as a control. We measured the anti *chlamydia Pneumonia*e IgG by ELISA technique**.**

Results The *chlamydia Pneumonia*e positivity in the multiple sclerosis patients was considerably higher than the control group but the variation was not significant ($p > 0.05$) and there was no difference between the previously and newly diagnosed multiple sclerosis patients.

Conclusion There is no statistically significant relationship between previously *chlamydia Pneumonia*e infection and MS disease.

Keywords Multiple sclerosis, *chlamydia Pneumonia*e

List of abbreviation: MS = multiple sclerosis, Cpn = Chlamydia Pneumoniae, CNS = central nervous system, Ig = mmunoglobulin, RRMS = relapsing remitting multiple sclerosis, SPMS = secondary progressive multiple sclerosis, PPMS = primary progressive multiple Sclerosis.

Introduction

Multiple sclerosis (MS) is a chronic autoimmune inflammatory disease of the central nervous system characterized by demyelination and axonal loss [(1,2)].

MS is a multifactorial disease, which results from complex interactions between susceptibility genes and environmental factors [(3)]. In the MS pathogenesis, *Chlamydia pneumonia* (Cpn) has been getting increased attention as a possible cause of MS [(4)].

Cpn is found to be common in a variety of neurological disorders and not only in MS. It is possible that MS patients might be less able to clear the organism from the CNS [(5)].

The ability of the Cpn to persist in monocytes and macrophages in tissues for long periods, circumvents the mechanisms of bactericidal and oxidative stress, activate the endothelial cells with production of adhesion molecules and cytokine overproduction has suggested that it may participate in the development or progression of certain acute and chronic inflammatory diseases of the CNS [(6)].

The role of Chlamydia in the pathogenesis of neurobehavioral disorders or mental is

uncertain and will require further confirmation [7].

The objective of this study is to investigate the relationship between previously Chlamydia Pneumoniae infection and multiple sclerosis disease initiation.

Methods

Case control study was done which involved; sixty patients with MS their ages were range from 13 to 58 years. They were attended for seeking treatment or attended for new diagnoses in the MS outpatient clinic at Baghdad teaching medical city in the period which extended from December 2014 to March 2015.

The diagnosis of each case was established according to MC Donald criteria (2010) done by a neurologist and confirmed by MRI. Patients were subjected to questionnaire about name, age, gender, smoking, family history, medication and clinical signs.

Patients were divided into two groups, group I on treatment and group II as newly diagnosed patients. This study was approved by the Ethical Committee of College of Medicine/Al-Nahrain University and all samples were obtained with informed consent in accordance with the teaching hospital of medical city declaration.

Three ml of blood was collected from each patient and control included in this study then centrifuged and the serum was separated and stored at 2-8^{o}C until used. Human immunoglobulin G (IgG) anti-Cpn was measured with an enzyme-linked immunosorbant assay (ELISA) (Nova Tec – Germany).

Statistical analysis

Analysis of data was carried out using the available statistical package of SPSS-22 (Statistical Packages for Social Sciences- version 22). Data were presented in simple measures of frequency, percentage, mean, standard deviation, and range (minimum-maximum values). Statistical significance was considered whenever the P value was equal or less than 0.05.

Results

Table 1 distributes MS and control subjects according to their age and gender and table 2 distributes them according their family history of MS and smoking habits. The MS patients were distributed on three subgroups according to type of the disease, 55 (91.6%) of patients were with relapsing remitting MS (RRMS) RRMS type and 3 (5%) of patients were with secondary progressive MS (SPMS) type while 2 (3.3%) of patients with primary progressive MS (PPMS) type. Moreover, there were no significant differences between treated and newly diagnosed MS patients regarding to the presence of the respiratory signs (Table 3).

Serum level of IgG anti *Chlamydia Pneumonae* antibodies

The results of ELISA concerned with the IgG positivity against Chlamydia for studied groups are described in table 4. This study revealed no significant difference in the percentage of IgG positivity between patients group and healthy control group ($p > 0.05$), out of 60 patient, 19 were positive (31.7 %) for IgG anti- Chlamydia, while out of 30 healthy control, 4 were positive (13.3 %). Furthermore, there were no significant differences ($p > 0.05$) in the percentage of IgG positivity between two patients groups (Fig. 1).

Table 1. Distribution of multiple sclerosis patients and healthy controls according their age and gender

Age (years)	Multiple sclerosis N = 60	Control group N = 30
<30	21 (35%)	11 (36.7%)
30-39	20 (33.3%)	8 (26.7%)
40-49	13 (21.7%)	9 (30.0%)
>50 years	6 (10.0%)	2 (6.7%)
Mean±SD	34.5±10.6	34.7±10.1
(Range)	(13-58)	(18-53)
Males	25 (41.7%)	8 (26.7%)
Females	35 (58.3%)	22 (73.3%)

Table 2. Distribution of multiple sclerosis patients according to family history and smoking habitat

Parameter		Multiple sclerosis		
		New cases	Treated cases	Total
Family history	Positive	3 (10%)	3 (10%)	6 (10%)
	Negative	27 (90%)	27 (90%)	54 (90%)
Smoking	Yes	3 (10%)	5 (16.7%)	8 (13.3%)
	No	27 (90%)	25 (83.3%)	52 (86.6%)

Table 3. Distribution of multiple sclerosis patients according to clinical features

Parameter		Multiple sclerosis		
		New cases	Treated cases	Total
Multiple sclerosis Type	RRMS	28 (93.3%)	27 (90.0%)	55 (91.6%)
	PPMS	1 (3.3%)	1 (3.3%)	2 (3.3%)
	SPMS	1 (3.3%)	2 (6.7%)	3 (5.0%)
Medications type	IFN -b1		25 (83.3%)	
	Rebif		3 (10.0%)	
	Avonex		2 (6.7%)	
Respiratory signs	Yes	10 (33.3%)	13 (43.3%)	23 (38.4%)
	No	20 (66.7%)	17 (56.7%)	37 (61.1%)

RRMS = relapsing remitting multiple sclerosis, SPMS = secondary progressive multiple sclerosis, PPMS = primary progressive multiple sclerosis.

Table 4. The positivity of studied groups for anti *Chlamydia Pneumonae* IgG antibodies

IgG anti-Chlamydia pneumoniae Abs	Multiple sclerosis N = 60	Control group N = 30
Positive (> 11.0)	19 (31.7)	4 (13.3)
Negative (< 11.0)	41 (68.3)	26 (86.7)

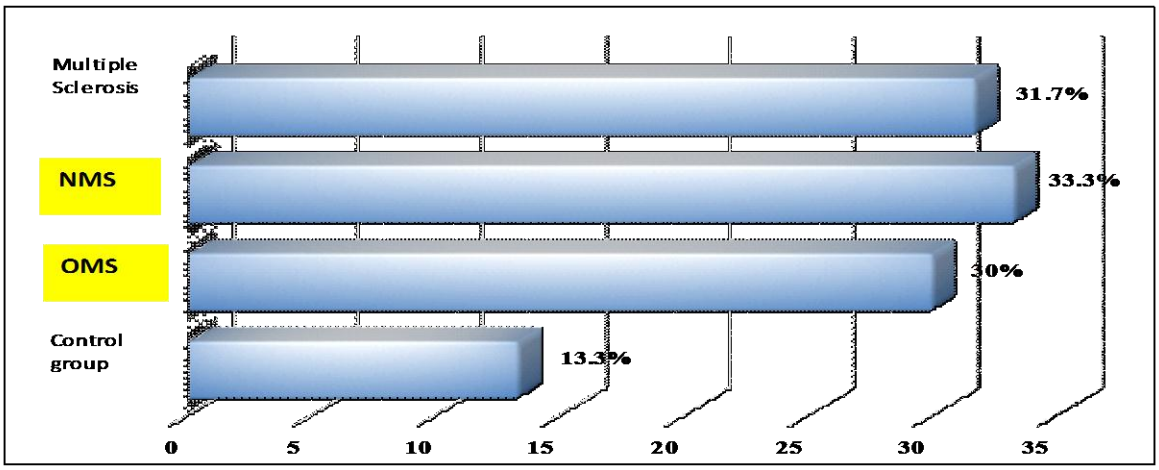

Fig. 1. Chlamydia Pneumoniae positivity in studied groups

Table 5. The relation between IgG anti *Chlamydia Pneumonae* antibodies positivity with demographic and clinical factors in the studied groups

Feature		IgG anti *Chlamydia Pneumonae* positivity			
		Multiple sclerosis N = 60		Control group N = 30	
		No	Mean±SD	No	Mean±SD
Age (years)	<30	21	8.09±4.91	11	5.63±4.11
	30-39	20	7.40±5.76	8	5.66±3.23
	40-49	13	9.41±6.26	9	9.30±2.81
	>50	6	10.00±1.90	2	7.20±2.12
Gender	Male	25	9.48±5.78	8	8.01±4.22
	Female	35	7.51±4.83	22	6.42±3.47
MS Type	RRMS	55	8.26±5.37	-	-
	PPMS	2	13.10±2.69	-	-
	SPMS	3	6.50±3.97	-	-
Family history	Positive	6	10.23±3.88	-	-
	Negative	54	8.12±5.41	-	-
Smoking	Yes	8	11.25±7.01	-	-
	No	52	7.88±4.91	-	-
Medications type	IFN -b1	25	8.34±4.84	-	-
	Rebif	3	5.20±6.35	-	-
	Avonex	2	17.30±3.25	-	-
Respiratory signs	Yes	23	7.62±5.57	-	-
	No	37	8.78±5.13	-	-

Discussion

Over the past 10 years, a many of reports have found a possible relationship between Cpn infection and CNS diseases including MS, and other variety of neurobehavioral disorders. Many of researchers whom investigate the relationship between Cpn and MS examined the serum of the patients after disease occurrence and other examined prospectively.

The Results from studies on Cpn in MS patients have led to discordant results due to the lack of an efficient and standardized method for detection of Cpn [8]. In a comparative trial, one research group distinguished Cpn in the majority of MS patients but not in controls whereas three other researchers did not detect Cpn in any sample [9].

In present study, out of sixty MS patients there were nineteen seropositive for IgG anti Cpn and four persons from healthy control out of thirty also was seropositive. The differences were considerably high but not significant the p- value was (0.060) and OR (3.01) (0.92-9.85). The study, which is done on US army personnel and used samples of blood collected prior to the onset of the disease, it found no association between Cpn and the risk of RRMS when compared to healthy controls adjusting for latitude of residence at time of entry into active duty and education level [10].

Also the current study agrees with Villoslada et al [11], but disagree with Sriram et al [12] which was strongly connect between the Cpn and MS. Their study referred to that 97% polymerase chain reaction assays confirmed the presence of Cpn outer membrane protein gene in the CSF versus 18% of other neurological disease controls and 86% of MS patients had increased CSF antibodies to Cpn elementary body antigens by ELISA. This result is never repeated

in subsequent researches, Sriram et al study depended on the detection of Cpn in the CSF of patients by PCR technique and detection of IgG against Cpn by ELISA, which is differ from the current study [12].

In another study, an association between Cpn infection and development of MS was found, this association was mostly attributable to a strong association with risk of progressive MS. Overall, the titer of anti – Cpn IgG in the serum were elevated in women with MS. The titer of Cpn-specific IgG antibody were elevated in women which were suffering from progressive MS as compared with controls, but did not differ between RR MS cases and controls [13]. In the current study, PPMS was 6.6% and SPMS 10% of all patients whom enrolled in this study so if the progressive MS patients were more than this ratio the differences in the anti-Cpn IgG titer between the patients and control may be more than know. This is one of the probabilities.

Finally, some studies suggest a role of Cpn only as a CNS innocent bystander secondary effect, encouraged by excessively active chronic inflammation operating in MS. Others suggest a role of Cpn as a cofactor in development and progression of the disease in a subset of MS patients, the past infection with Cpn may play a role as a cofactor in a part of patients but not in all of them. Although the current results did not show significant deference between the patients and control group, yet, the difference was considerable [14].

In conclusion, our study revealed no statistically significant relationship between previously Cpn infection and MS disease.

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Author contribution

Khaliel collects the patient data and did the laboratory work and Dr. Abbas write the article.

Conflict of interest

No conflict of interest

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