TORCH infections susceptibility in Iraqi Patients with Multiple Sclerosis

Fadwa Ghassan, Wassan Abdul Kareem and Thamer Mutlag Jasim

Al-Mustansiriyah University, College of Pharmacy, Department of Clinical Laboratory Science.

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ABSTRACT

Multiple sclerosis (MS) is a chronic inflammatory disorder of the central nervous system. Several disease-modifying therapies have been shown to ameliorate the disease course; however, the individual treatment response and the occurrence of adverse events remain highly unpredictable. In the last 2 decades, a multitude of studies have aimed to identify biomarkers that enable treatment allocation in the individual patient or subgroup of patients with regard to treatment efficacy and safety profile. To investigate the TORCH infection susceptibility and tin patients with multiple sclerosis. Thirty Iraqi newly diagnosed patients with MS and follow them after one month of treatment (Beta interferon inj. I inj./ week) and compare the results with 20 healthy control. . Females patients(pre treatment group) showed was a highly significant difference(p<0.0001) when compared to control,while in male patients, no significant difference was noticed when compared to control(p>0.05). Rubella percent of infection, the female patients(pre-treatment group) was highly significant difference(p<0.0001) when compared to control as well as, in male patients ,a significant difference was noticed when compared to control(p<0.0001).CMV infection, the female patients(pre-treatment group) was highly significant difference(p<0.0001) when compared to control, table(3) also, in male patients, a significant difference was noticed when compared to control(p<0.0001). The resule of the study showed a possible association between CMV infection and MS. Further experimental and epidemiological studies using case-control approaches are needed to confirm this association.Various additional observations also indicate a protective effect of CMV on autoimmune diseases. CMV immune evasion may mitigate the autoimmune reactions and proinflammatory milieu that contribute to MS.

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INTRODUCTION

Multiple sclerosis (MS) is a chronic demyelinating disease of the central nervous system with an unpredictable time course. Among the plethora of factors affecting the clinical heterogeneity of MS, autoreparative mechanisms are of particular importance. Remyelination is largely known to occur in MS [1], but it is still unclear why its adequacy differs so largely among patients. Many factors have been proposed to influence remyelination, including several neuroendocrine factors [2,3].

Microbial infections have been done in initiating and enhancing severity of autoimmune diseases including the demyelinating disease multiple sclerosis (MS).[79]

MS majority patients usually acquired two upper-respiratory infections per year and this type of infection doubles the risk for MS relapse (potential demonstrating factor).[81]

Hepatitis C virus (HCV) infection has been used in acute disseminated encephalomyelitis but not with tumefactive MS. CNS myelin is a potential target of the immune response to HCV 2a/2c infection, the *HCV 2a/2c* virus could be involved in triggering autoimmune tumefactive brain lesions, and interferon beta-1a is effective against *HCV* geno *type 2a/2c* infection.[86]

TORCH infections classically comprise Toxoplasmosis, *Treponema pallidum*, *Rubella*, *Cytomegalovirus*, *Herpesvirus*, *Hepatitis viruses*, *Human immune Deficiency virus*, and other infections, such as *Varicella*, *Parvovirus B19*, and *Entero viruses*.Epidemiology *TORCH* infections are commonly related to prenatal, and postnatal morbidity and mortality.[91]

A lateral flow immune chromatographic assay (LFIA) system for the detection of immunoglobulin M (IgM) antibodies, related to TORCH[(T)oxoplasmosis, (O)ther agents, (R)ubella (also known as German Measles), (C)ytomegalovirus, and (H)erpes simplex virus infections] has been used in the identification of TORCH IgM-specific antibodies and can potentially be developed for use in the diagnosis of other acute or recently identified autoimmune diseases.[92]

MATERIAL AND METHODS

The study was done in (SHAR 400 BED Hospital) between(July 2015- May 2016). Thirty Iraqi MS patients; aged (20 -50) years. The medical history was taken. All patients had been already diagnosed and the diagnosis had been confirmed according to The 2010 McDonald Criteria for Diagnosis of MS. For comparison with twenty apparently healthy subjects with No inflammation, No infection, Non diabetic, Non hypertensive, No chronic diseases, Non smokers, Non drinking with normal healthy subjects. Patients samples were taken before treatment and after one months of treatment (Beta-interferon injection one per week).

Statistical Analysis:

Data were analyzed using General Linear Model (GLM) in SAS program (2010) to investigate the effect of treatments (pretreatment, post treatment and control),Microsoft Office Excel (Microsoft Office Excel for windows; 2010) were also used to conduct the figures. Means were compared by using least significant difference (LSD) while Fisher exact test was used to compare the differences among proportions because when 25% of the cells have expected counts less than 5. Chi-Square may not be a valid test and the alternative test is Fisher exact test. As such case was found in the present data, hence this test was used to compare the difference between proportions for all cases. Pearson Correlation Coefficients were estimated for all groups. P< 0.05 considered statistically significant.

RESULTS

For the pre-treatment group, females patients showed was a highly significant difference(p<0.0001) when compared to control, table(1) while in male patients, no significant difference was noticed when compared to control(p>0.05).

Table (1): The percent of *Toxoplasma* infection according to sex

Toxo IgG	Total No	Female	%	Male	%
Control	20	15	0	5	0(0%)
Patient	30	18	11(61.1%)	12	1(8.3%)
			<0.0001		0.70

Table(2) showed the percent of Rubella infection, the female   patients(pre-treatment group) was highly significant difference(p<0.0001) when compared to control as well as, in male patients ,a significant difference was noticed when compared to control(p<0.0001).

Table(2) show the percent of Rubella infection according to sex

RubellaIgG	Total No	Female	%	Male	%
Control	20	15	0(0%b)	5	0(0%)b
Patient	30	18	17(94.4%)a	12	11(94.4%)a
P			<0.0001		<0.0001

Relate to the percent of *CMV* infection, the female patients(pre-treatment group) was highly significant difference(p<0.0001) when compared to control, table(3) also, in male patients, a significant difference was noticed when compared to control(p<0.0001).

Table(3) show the percent of CMV infection according to sex

CMV IgG	Total No	Female	%	Male	%
Control	20	15	0(0%)	5	0(0%)
Patient	30	18	17(94.4%)	12	11(91.6%)
			<0.0001		0.006

Fig.1, demonstrated the proportion variation of the triple infection according to sex, there was a non significant difference among them (p value= 0.036),The infection percentage was the highest in compare to male group (44% vs.8%).
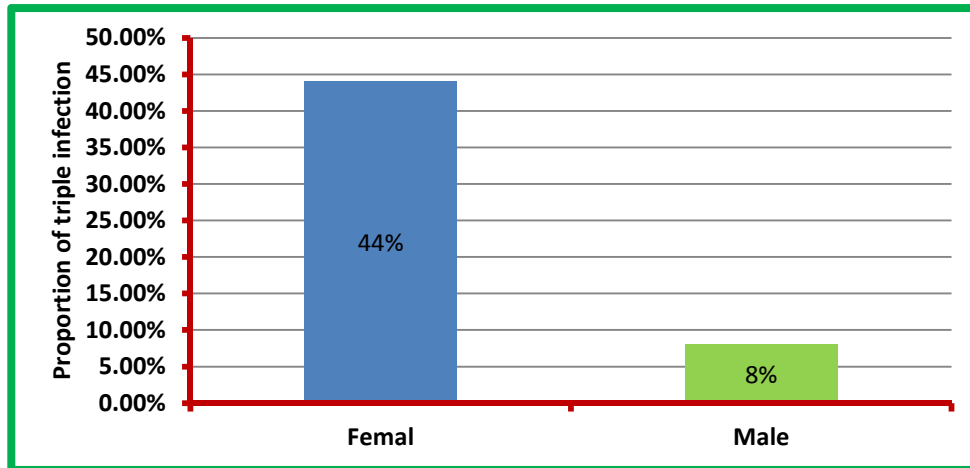
P=0.036

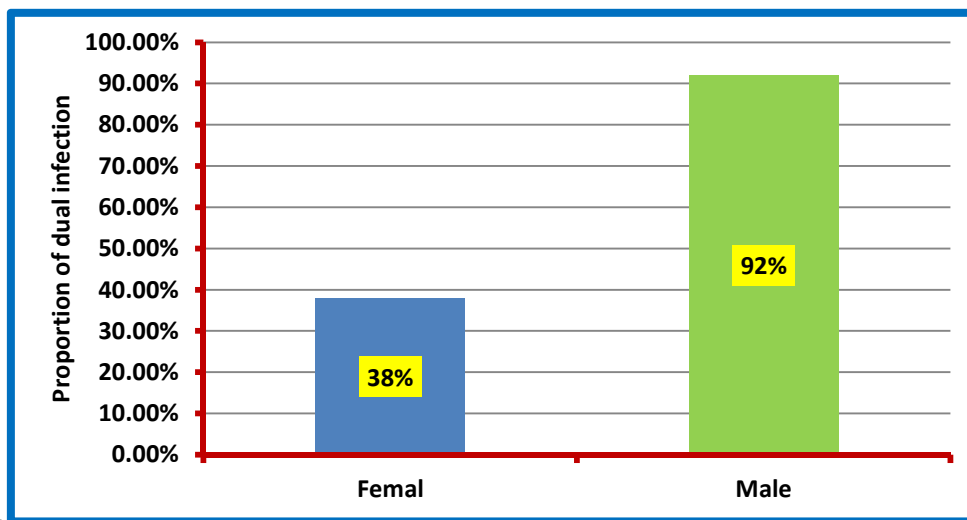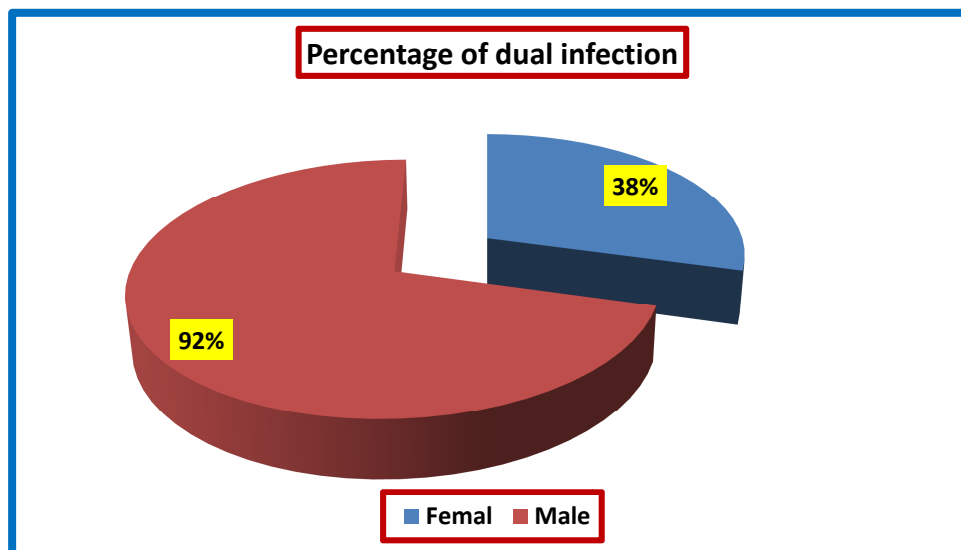**Figure.1 Proportion of triple infection according to sex**

Figure 2. Proportion of dual infection according to sex

P=0.0068

Figure 3. Percentage of dual infection according to male and female
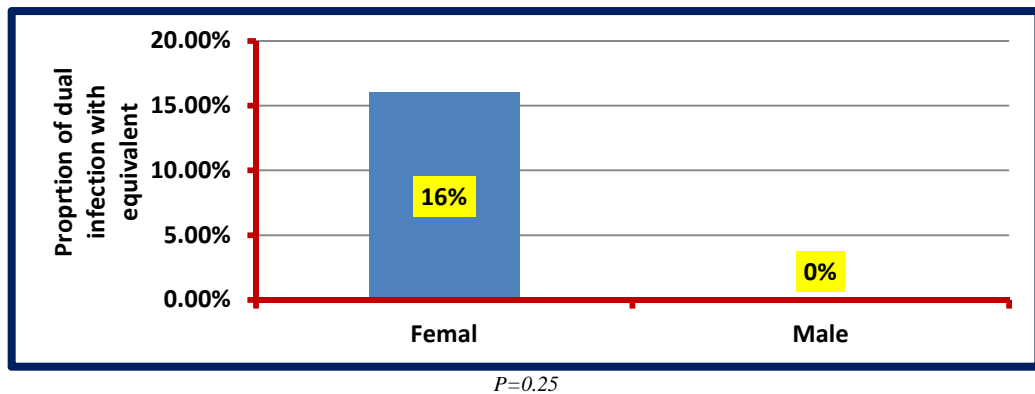
P=0.25

Figure 3.16 Proportion of dual infection with equivalent according to sex

The dual infection percentage according to sex, was varying between male and female groups(92% vs. 38%) the highest percentage were noticed among male group, Non significant difference was noticed between them (Fig.2&3) (p value 0.0068)

DISCUSSION

The current study showed the percent of *Toxoplasma* infection, the female patients(pre-treatment group) was highly significant difference in compared to control, while in male patients there was no significant difference when compared to control and this results were in agreement with [117].

Serdar Oruç found that the level of seropositivity for anti-T.gondii IgG antibodies was highest in patients with MS than in control healthy subjects,which indicates the presence of chronic *Toxoplasma* infection in patients with MS. [118]

Toxoplasma gondii infection is a most common parasitic disease in human. In Turkey, the rate of seropositivity was reported (23.1% to 36%). Because of increased affinity of parasite into Central Nervous System (CNS), chronic *Toxoplasma* infection has been found correlated with many neuropsychiatric disorders, including altered mental status, obsessive-compulsive disorder, cognitive impairment, epilepsy, headache and schizophrenia. [118]

The current study founded that the percentage of *Rubella* infection, among the female patients(pre-treatment group) show highly significant difference in compared to control as well as, in male patients there was a significant difference in compared to control, and results were in agree with [120] who reported that viruses which remained hidden inside the body for years, when encouraging latent immunological changes in the body, will eventually resulting in autoimmune demyelination and the appearance of disease symptoms, that confirms the high titer of antibodies for certain viruses in patients with the MS.First of them are *cytomegalovirus* and *rubella virus.*

The *CMV* infection in the current result show that the female patients(pre-treatment group) show highly significant difference in compared to control as well as, in male patients there was a significant difference in compared to control and this finding was agree with [120,121]

Vanheusden M recorded that a lot of evidences indicated that *CMV* contributed to MS disease by interaction of different mechanisms such as molecular mimicry, bystander activation, and epitope spreading. Activation and expansion of a specific T cell subset, CD4 (+) CD28 (null) T cells, by *CMV* infection was linked to MS pathology. Various additional observations also demonstrated the protective effect of *CMV* on autoimmune diseases.*CMV* immune evasion demonstrated mitigate the autoimmune reactions and pro inflammatory milieu that lead to MS.[122]

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