Detection of Alpha-1 Antitrypsin, Alpha-2 Macroglobulin and Some Serum Immunoglobulins Levels in a Group of Multiple Sclerosis Patients

Wifaq M Ali Al-Wattar* FICMS

ABSTRACT

Background: Immunological disturbance in multiple sclerosis is one of the pathophysiological processes taking place during disease process.

Objectives: To evaluate the role of some serum antibodies in the pathogenesis of multiple sclerosis in group of multiple sclerosis patients.

Methods: The study was designed to perform (ELISA) testing to estimate the following parameters as α-1antitrypsin,α-2 macroglobulin, IgM, IgG, IgA levels in fifty multiple sclerosis patients as compared to thirty five apparently healthy controls.

Results: The level of α1-macroglobuline was low in 72% of multiple sclerosis patients and only normal in 28% of the cases while the healthy control groups showed normal value in 83% and a high level in 17% of rest of the group, regarding the level of α1-antitrypsin it was low in 54% and normal in 41%, as for the control group it was normal in 88.5% and low in 11.5%, as for the level of IgM was normal in 52% but high in 44% as for the control group the normal value was noticed in 91% and high in the rest 9% of the controls, IgG level was normal in 58% and high only in 36% but low in 6%, most of the control were normal 97% and high in 3%, for the last parameter IgA was normal in 70% of patients and high in 26% of cases, while in the control samples 91% were normal and only 6% showed a high results.

Conclusion: The detection of serum level of those parameters as α-1 antitrypsin, α-2 macroglobuline, IgM, IgG, IgA could be a good indicator for the early detection of multiple sclerosis and to evaluate the severity of the disease, which is linked to the reduction of their values in the serum as multiple sclerosis get worse.

Keywords: Multiple sclerosis, Alpha 1 antitrypsin, Alpha 2 macroglobulin.

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Multiple sclerosis (MS) is a chronic inflammatory autoimmune disease of the central nervous system (CNS), affecting the myelin sheath of CNS, its etiology still unknown and presented with a variable clinical symptoms and courses[1].

The disease onset usually occurs at the young age groups, specially in females more than males in a ratio of 2:1[2,3], which is one of the most common diseases of the central nervous system (brain and spinal cord) that has spiked significantly in the last few years.

The prevalence of MS ranges between

*Unit of Clinical and Communicable Diseases, College of Medicine, Baghdad University.

2 to 150 per 100,000 people. About 87% of MS patients exhibit a relapsing remitting course of disease[2,4]. Much has been done to understand the its etiology, and researchers believed that a combination of several factors may be involved in the pathophysiology, which could be one of the following process alone or combined as: immunological, viral like Human herpes viruses (HPV), Epstein-Barr virus(EBV) or others; like Measles, Mumps and Rubella, other infectious agents like yeasts and its mycotoxines secreted by some candida species as gliotoxines but also some environmental factors and genetic factors could be greatly blamed in some cases[5-7]. The major alpha 1-globulin is alpha 1-antitrypsin, produced by the lungs and liver. Alpha 2-globulins include a group of serum markers like haptoglobin, alpha 2-macroglobulin, and ceruloplasmin. Alpha 2-macroglobulin accounts for about one third of the alpha 2-globulin fractions[8]. An elevated levels of IgG index indicates increased production of IgG within CNS as noticed in some inflammatory conditions affecting it as it was found in about 90% of MS cases[9,10].

However, some researchers believed that an antibody-dependent immune reactions were mostly involved in the formation of MS lesions[11-14]. Recent studies uniformly showed state of clonal expansion of antibody-secreting B-lymphocytes in the CNS and cerebrospinal fluid (CSF) of patients with MS[15-19]. Recent studies have suggested that the innate immune system also plays an important role both in the initiation and progression of MS by influencing the effector function of T and B cells and in turn, cytokines production and activation of markers that further activate the innate immune cells[8,11] that travel to CNS, leading to demyelination of axonal fatty sheaths and resulting in neurological disability[10].

In this study, we will discuss the potential role of serum immunoglobulin IgA, IgM, IgG in the MS patients and the role of α1-antitrypsin and α1-macroglobulin levels in those patients.

Methods

Seventy patients were chosen from the attendant of MS center in Baghdad Teaching hospital in the period between January 2011 and June 2012, to be compared with thirty five healthy Iraqi individuals taken as a control. Five ml of venous blood was aspirated to be stored at -18º C, and used later for enzyme linked immunosorbent assay (ELISA) testing to estimate the following parameters as α1-macroglobulin, α1-antitrypsin and the level of IgM, IgG, IgA.

Results

The α 2-macroglobuline level was low in 72% of MS patients and normal in 28% of the cases while the healthy control groups showed normal level in 83% of them while the rest 17% showed high levels. Regarding the level of α1-antitrypsin it was low in 54% and normal in 41%, whereas the majority of the control group showed a normal level 88,5% and low in 11.5%, (Table1), considering IgM level of MS patients, it was normal in 52% but high in 44% as for the control group the normal value was noticed in 91% and high in the rest 9% of the controls, the IgG level was

normal in 58% and high only 36% IgG level and low in 6% of patients, moreover, it was normal in 97% and high in 3% of the control group. With regard to IgA level of MS patients, it was normal in 70% high in 26% of cases, whereas in the control group 91% showed normal level and only 6% showed high levels, (Table 2).

Table 1: The level α1-antitrypsin and of α 2-macroglobulin in multiple sclerosis patients and control group.

Parameter	Normal	%	High	%	Low	%	Total	%
α 2-macroglobulin								
MS	14	28	0	0	36	72	50	100
Control	29	83	6	17	0	0	35	100
Total	43	51	6	7	36	42	85	100
α1-antitrypsin								
MS	21	42	2	4	27	54	50	100
Control	31	88.5	0	0	4	11.5	35	100
Total	52	61	2	2.3	31	36.7	85	100

*The data presented as No (%), MS: multiple sclerosis, using SPSS program for statistical analysis version 19.

Table 2: The level of IgM, IgG and IgA in the MS patients and control group.

Study groups	Normal		High		Low		Total	
IgM Level	No.	%	No.	%	No.	%	No.	
MS	26	52	22	44	2	4	50	100
Control	32	91	3	9	0	0	35	100
Total	58	68	25	29.4	2	2.6	85	100
IgG Level								
MS	29	58	18	36	3	6	50	100
Control	34	97	1	3	0	0	35	100
Total	63	74	19	22	3	4	85	100
IgA Level								
MS	35	70	13	26	2	4	50	100
Control	32	91	3	6	0	0	35	100
Total	67	78	16	18.8	3	3.2	85	100

Discussion

MS is an autoimmune neuro-degenerative disease leading to destruction of the myelin sheath that ultimately affects the ability of nerves to conduct electrical impulses[20,21]. Auto antibody mediate destruction of tissues is among the main features of organ-specific autoimmunity but still with a poor understanding of the etiology of MS has delayed the development of effective therapeutics[13]. The search for biomarkers in bodily fluids such as CSF and serum in MS patients had been the focus of many

studies abroad[22,23]. Numerous studies have reported the recognition of a high levels of CNS antimyelin autoantigens as autoantibodies present in CSF and the serum of MS patients, but also in patients with other inflammatory neurological degenerative diseases[24,25]. Until now, the information on the involvement of specific antigens in MS was still limited. More recently, other CNS antigens have been identified as a potential bio-markers in MS[26,27].

Despite strong evidence for the role of T-cell responses to manifestations of autoimmunity in (CNS) of patients with MS[3,4], recent findings encouraged investigators to search also for B cell-mediated contributions to the MS pathogenesis. It was in favor to our results as the level of IgG, IgM and IgA was variably increased in MS patients as compared to the control groups who were mostly normal or low and as the disease process started the B- cell over activity will be expressed in forms of a higher level of serum Ig and subsequently CSF levels of IgG and (IgG) Index. Increased levels of CSF IgG can be due to excess production of IgG within the CNS, which is seen in MS and several other diseases. It can also be due to leakage of plasma proteins into the CSF, as it might occur with inflammation or trauma[17], therefore, detection of oligoclonal antibodies in CSF of MS patients was an important diagnostic marker in MS[20,21]. Thus, the level of catalytic antibodies in serum may provide a clinically important marker for disease progression, and may provide an approach for developing an effective treatment of MS[17].

The result of this study showed low serum level of both alpha 2-macroglobulin and alpha 1-antitrypsin as it was reduced as compared to healthy individuals that could be due to the consumption of the on going autoimmune process occurring in those patients with active disease process as it was stated that the proteases enzymatic activity was increased in patients with autoimmune neurological diseases leading to this low serum levels than that seen in healthy individuals[26]. A significant decrease in both alpha 1 antitrypsin due to protease enzyme activity in MS patients and reduction in the level of the alpha 1 macroglobulin was reported in a the Spanish research in 2013 which noticed a dramatic decrease and explained it as one of the early diagnostic parameters in MS[27].

It was also reported that the level of ᾱ- 2 macroglobulin is greatly disturbed in the patients with severe degenerative neurological diseases[18,19] and because of its immunoregulatory activity and immunosuppression the low level might refer to poor physiological role of α1molecule as it has only recently been clarified as immunoregulatory, and mainly suppressive leading to more tissue damage[30]. As the level of Alpha 1-antitrypsin in CSF of patients with neurologic diseases was extensively studied. However, its activity in patients with inflammatory diseases tend to be decreased relatively to normal immunochemical level, suggesting inactivation of alpha antitrypsin in these disorders as part of increased protease activity in active MS disease process[29,30] leading to poor immunosuppression and aggravation of destructive immune

response to the axonal myelin sheath ending in MS sign and symptoms.

From all we concluded that the detection of serum level of those parameters as α-1 antitrypsin, α-2 macroglobulin, IgM, IgG and IgA could be a good indicators for the early detection of MS and evaluation of the severity of the disease as the reduction of α1 molecule values in the serum might be linked to relapsed multiple sclerosis cases.

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