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An investigation into the relationship between IL-22, MBP, and MS in Iraq

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Abstract

Multiple sclerosis (MS) is a chronic, inflammatory, and predominantly chronic central nervous system disease with no recognized cause. It is more prevalent in women and also characteristic of autoimmune diseases in general. Since the mid-20th century, the female-to-male ratio has increased in the female-to-male ratio, from an estimated 1.4 in 1955 to 2.3 in 2000. MS is experienced more often between birthdays 15 and over 45 years. The insulating sheaths of nerve cells in the brain and spinal cord include myelin basic protein (MBP), which is important to note. It interacts with lipid membranes to produce compression of the myelin sheath in the central nervous system, which is impaired in telepathic diseases. The lipid composition of the myelin leaflet has a significant impact on the interaction between the membrane and the MBP. Interleukin-22 (IL-22) was initially identified as a member of the IL-10 cytokine family in 2000. Mucosal barrier protection, tissue healing, and epithelial cell proliferation have been shown to be significantly affected by IL-22, according to recent studies. Furthermore, mounting evidence has identified protective effects of IL-22 in a variety of diseases, such as autoimmune disease, infection, and cancer.

Introduction

Multiple sclerosis (MS), a chronic immune-mediated disease, affects the central nervous system. Over time, there has been evidence of a higher incidence of MS in certain regions of the world. MS can have a significant impact on affected individuals, their families, and society because it usually manifests itself around the time people begin their careers and families. An increasing choice of disease-modifying drugs offers the potential to reduce frailty and extend survival for people with the condition, although there is no recognized cure for MS and the etiology of the disorder remains unclear.. Goodin DS, (2012)

Inflammatory lesions, demyelinating plaques, and permanent axonal damage are hallmarks of multiple sclerosis (MS). It is an autoimmune neurodegenerative disease with demyelination and axonal degeneration, according to Dobson (2019). One major hypothesis about the cause of MS One major hypothesis about MBP proposes that MBP may act as an autoantigen by activating reactive T lymphocytes

in those who are genetically sensitive to foreign antigens. MBP may or may not play a direct role as an important antigen in the development of MS in humans, but MS is undoubtedly associated with its involvement in the production and long-term maintenance of MBP and myelin. 2022) Martinsen, F.

Myelin in the central nervous system (CNS) contains a lot of a protein known as myelin basic protein (MBP). Multiple sclerosis (MS), an autoimmune neurodegenerative disease, has long been researched in relation to MBP. Myelin in both the central nervous system and the peripheral nervous system has a similar general profile despite the molecular differences and the fact that it is produced by oligodendrocytes in the central nervous system and Schwann cells in the peripheral nervous system. Several myelin proteins, particularly MBP, help maintain the repeating layers of densely packed lipid bilayers that together form myelin. The fact that myelin proteins are among the most durable proteins in the body underscores how important the stability of this macroscopic supramolecular structure is to the normal functioning of the nervous system. (Toyama et al. 2013;) There is no known molecular basis in the genesis of chronic MS. One of the most widely accepted theories today proposes that people who are sensitive to T-cell reactive immunity do so because of exposure to foreign antigens, as well as environmental and genetic factors. This cross-reactive immune response may target MBP and peptides made from it as self-antigens, causing demyelination and disease onset. A better understanding of the etiology of the disease and the identification of reliable biomarkers will greatly influence the treatment and prevention of multiple sclerosis for people at high risk of developing MS or who already have MS.But in fact more study will be needed to achieve this goal. Martinsen, V., 2022

One of the proinflammatory cytokines, IL-22, is likely to be critical to the pathophysiology of a number of autoimmune diseases, including multiple sclerosis. In 2000, an interleukin-9-stimulated mouse T cell line produced the cytokine interleukin 22 (IL-22), a member of the IL-10 family. Human chromosome 12q15 contains the IL-22 gene, which consists of 146 amino acids arranged into six alpha helices. Structural changes of IL-22 between mice and humans account for more than 80% of the variance. Tahmasebinia F, 2019

IL-22, is essential in the pathogenesis of a number of autoimmune diseases, including multiple sclerosis. Interleukin 22 (IL-22), a cytokine associated with the adaptation of stem/progenitor cell activity for tissue homeostasis and repair, has gained recognition over the past 10 years… Valerie Coronas, 2023

The important signaling molecule IL-22 is involved in many critical physiological processes, from innate immune responses to tissue regeneration. Lanfranca MP, 2016

Recent studies have shown that IL-22 is essential for tissue repair, mucosal barrier protection, epithelial cell survival, and proliferation. According to mounting evidence, IL-22 has both protective and deleterious effects in a number of diseases, including cancer, infection, and autoimmune diseases. . (Perusina Lanfranca, M. , 2016)

Serum assortment

Blood samples were prepared and collected in a consistent manner: a serum separator tube was used to collect 25 mL of peripheral whole blood. Samples were left to clot at room temperature for 10–20 minutes. The serum was then collected, aliquoted, and kept in tubes at −20 °C after centrifuging the tubes at 1,500 g for 10 minutes. Agliardi, C., 2023

METHODS

For Interleukin 22 we use a kit that is an enzyme-linked immunosorbent assay (ELISA) based on the instructions of the BIOASSAY TECNOLOGY LABROTY

FOR THE BASIC MEYLEIN PROTEIN WE USE THE KIT IS AN ENZYME LINKED IMMUNIDE ASSISTANCE (ELISA) BASED ON THE INSTRUCTIONS OF THE BIOASSAY TECNOLOGY LABORATORY

RESUALT AND DISCUTION

1- Characteristics of demographic variables in multiple sclerosis patients and control groups.

The basic characteristics of multiple sclerosis patients and control groups are summarized in Table (1). The study included 64 patients with MS with age (mean ± SE) 37.59 ± 1.38, years consisting of 25 healthy control groups 38.96 ± 1.94, which was not statistically significant (p = 0.588) between age groups.

Table 1: Comparison of parameters characteristics in MS patients with the controls group

Variables	Categories	Groups		P-value
		Patients n=64	Control n=25	
Gender	Male	22	14	X^2 =3.490 0.061
		34.4%	56.0%	
	Female	42	11	
		65.6%	44.0%	
Age (year)	mean±SE	37.59±1.38	38.96±1.94	0.588 #
Age groups	16-25 year	9	3	X^2 =0.737 0.865
		14.1%	12.0%	
	26-35 year	18	6	
		28.1%	24.0%	
	36-45 year	24	9	
		37.5%	36.0%	
	≥ 46 years	13	7	
		20.3%	28.0%	

** Significant differences at p-value <0.05. X^2: Chi-Square. #: Independent T-test. Data expressed as Mean±SE, and frequencies (%).*

Results in Figure (1) showed a significant difference (p<0.05) increased in number and percentage in younger MS patients of age groups (26-35) about 18(28.1%) and

(36-45) year was 24(37.5%) as compared with 9(14.1%) and (13(20.3%) in age group 16-25 and older patients ≥ 46 years, (0.049), respectively.

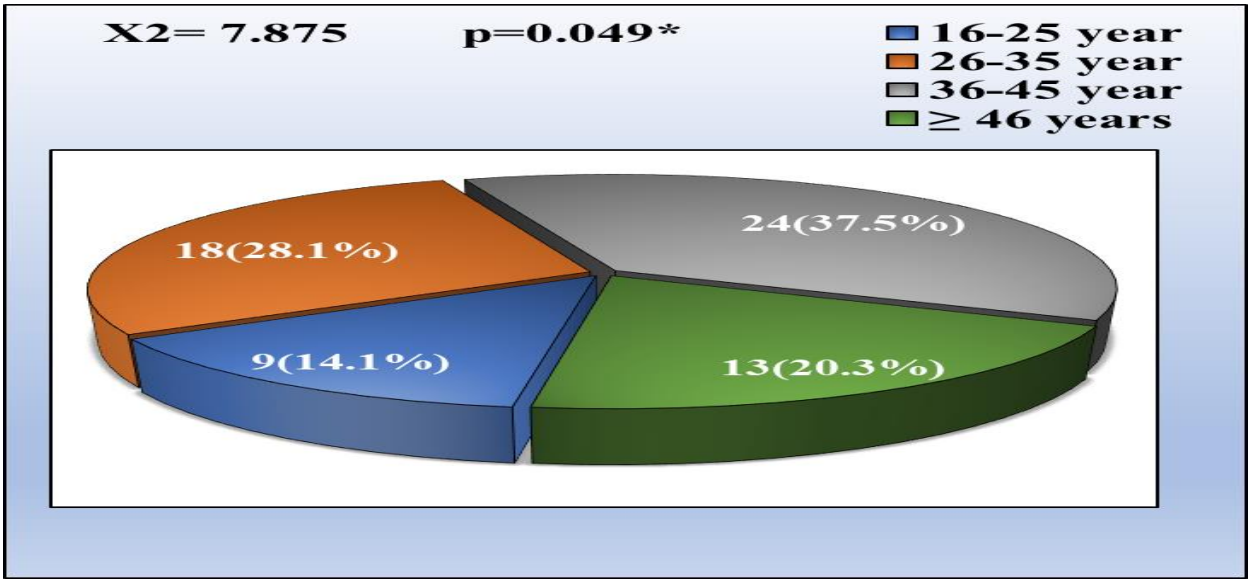

Figure (1) Distribution of MS patients according Age

**** Significant differences at p-value <0.05. X2: Chi-Square test. Data expressed as N(%).***

Hassoun, H. K., 2022 report The mean age in Iraqi MS patients was 32.3 ± 9.8 this nearly to recent study On the other hand Al-Araji A report the mean age of onset being 29.2+/-7.8 years Hassoun, H. K., 2022 Al-Araji A, 2005

2- Prevalence of MS patients according Gender

The prevalence of MS patients according to gender was showed in Figure (2)which indicated to a significant ($p<0.05$) increase in the number and percentage of MS female patients 42(66%), more than of percentage infected male with MS 22 (34%), ($p=0.012$).

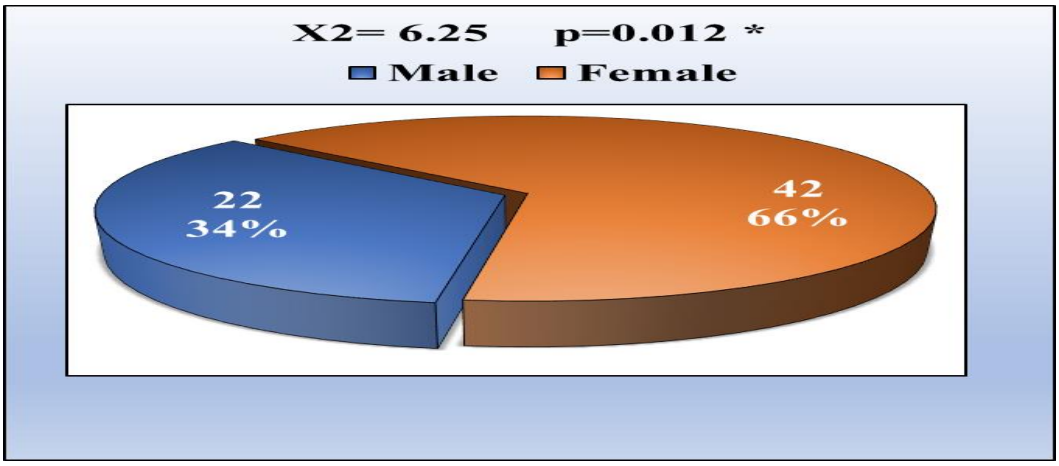

Figure (2) Distribution of multiple sclerosis patients by gender

** Significant differences at p-value <0.05.* X^2: Chi-Square *test. Data expressed as N(%).*

It has been found that women are more likely than men to develop this condition and that the trend may escalate when these findings are compared with those of other researchers. (2017) Huang et al. In addition, Abdel-Fattah, Mohamed N. (2018) reported that the female-to-male ratio was calculated to be (1.8:1), a statistic roughly equivalent to the World Health Organization's Atlas of Multiple Sclerosis, which was (2:1). In addition, we can compare the latest results with those of neighboring countries such as Kuwait (1.7:1), Jordan (1.9:1), and Saudi Arabia (1.34:1). (Mohammed et al., 2018) According to a large Iranian study, the incidence of the disease in women increased from 2:1 to more than 3:1 between 2002 and 2008. 2010 Sahraian MA . Often, women are affected by the majority of autoimmune diseases more often than men. More than 80% of those with autoimmune diseases are women, according to conservative estimates Chan, V.K.Y., 2023

3- Assessment OF (MBP) levels

Serum MBP levels exhibited a significant ($p<0.05$) decrease in MS patients at about (373.5±21.14) ng/L, when compared with the healthy control group (784.08±44.21) ng/L, p=0.0001. Figure (3).

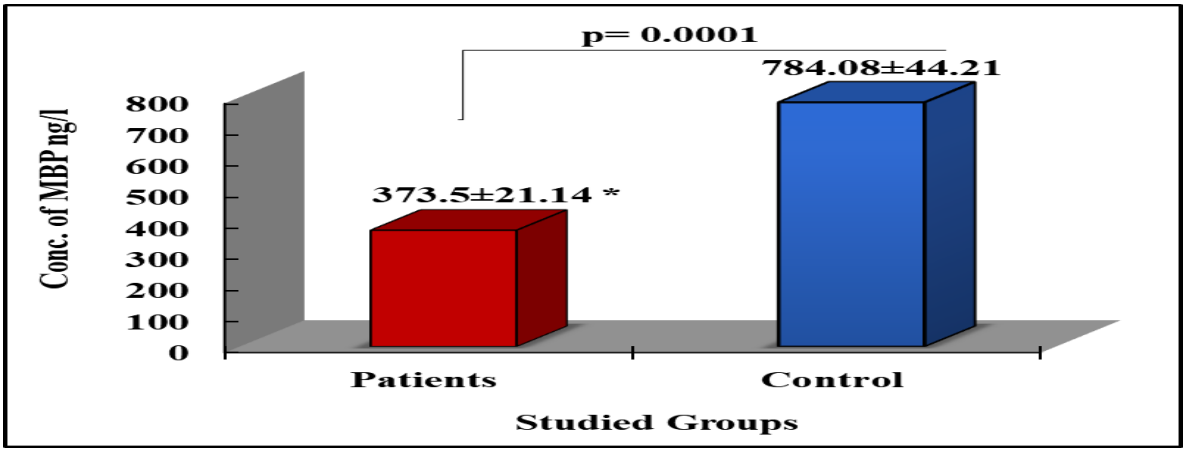

Figure (3): Serum MBP level in MS patients and the controls group.

****Significant differences at p-value <0.05. The values are expressed as mean±SE. patients n=64, control n=25 participants***

The first attack on the AQP4-rich astrocyte terminal spreading to oligodendrocytes is thought to be caused by toxic mediators secreted by astrocytes that elevate Ca2+ oligodendrocytes. As the innermost tongue of the myelin sheath is attached to the oligodendrocyte cell body via small areas rich in cytoplasm, damage to the cell soma results in an excess of intracellular calcium and rapidly diffuses into the myelin sheaths. This rise in Ca2+ may affect the ability of MBP to bind to the lipid bilayer. Thus, increased calcium in myelin may activate the MBP network.(Will, M.T., 2016)

Snidero. N. 2014 indicates that MBP loses contact with the myelin sheath, which ultimately appears to cause myelin vesiculation when the physical fixation of myelin sheets is damaged.

There is no recognized molecular basis for the origin of chronic chronic MS. One of the most widely accepted theories today holds that exposure to foreign antigens, along with environmental and genetic factors, plays a role in an individual's susceptibility to cross-reactivity of T-cell immunity. This cross-reactive immune response may target MBP and peptides made from it as self-antigens, causing demyelination and disease onset. A greater understanding of the etiology of the disease and the identification of reliable biomarkers will have a significant impact on MS treatment and prevention for people at high risk or who already have MS. Martinsen, V., 2022

MBP expression was decreased in the serum of MS patients compared to controls. A significant difference was found between controls and MS patients using serum MBP as a prognostic marker by analyzing receiver operating characteristics. (Mirzai Dazgah, M.H., 2021)

Many of the lesions that arise during demyelinating processes are associated with partial disruption of the tight junctions between the myelin proteins and the lipid bilayer. One of the most common myelin proteins is myelin basic protein (MBP). It is present in oligodendrocytes and Schwann cells, respectively, in the central nervous system and peripheral nervous system, where it is relatively abundant. . (Smirnova, EV, 2021)

The results of Huang, H. T., 2021 MBP suggest that during early development, there may be an association between the immune system and the nervous system. Therefore, these proteins may also have a different, as yet undiscovered, function in development in addition to their known function in myelination. Huang, HT, 2021

A protein known as myelin basic protein (MBP) is found in the insulating membranes that cover nerve cells in the brain and spinal cord. By interacting with lipid membranes, it is responsible for compaction of the myelin sheath of the central nervous system, which is damaged in demyelinating diseases. J. Treasure, 2021

4- Evaluation of Interleukin 22 (IL-22) Levels

Figure 4 shows that the mean IL-22 level was significantly elevated in MS patients for comparison with control groups (54.83 ± 2.32, vs. 37.36 ± 2.04, p = 0.0001) ng/mL, respectively.

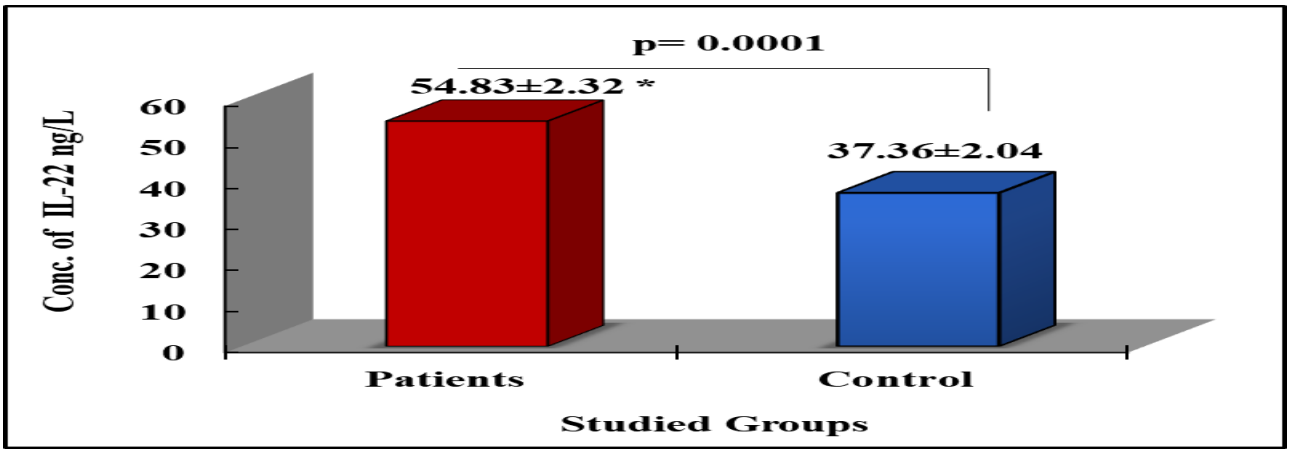

Figure (5): Serum IL-22 Level in Multiple Sclerosis Patients and Control Group *Statistically Significant Differences at p-value <0.05. Values are expressed as mean ± SE. Patients n = 64, control n = 25 participants

The study (Effect of interferon B1b, interferon B1a, and fingolimod treatments on the concentration of serum interleukin-22, in patients with relapsing-remitting multiple sclerosis) was published in the Journal of Neuroimmunology, the result of which showed a concentration higher levels of IL-22 in patients with MS compared to control individuals

Tissue injury triggers the production of IL-22, an inflammatory cytokine. Thus, after a limited inflammatory reaction in the tissues, it is easily detectable in the plasma. Therefore, in inflammatory conditions such as tissue injury or infection, IL-22 levels increase significantly. The timing and location of increased IL-22 expression as well as its shutdown depends on environmental factors such as cytokines, metabolites, and oxygen (which are listed as causes of induction of IL-22 production in the section IL-22 Sources and Targets). . Arshad, T., M 2020 perriad G 2015 According to a study published in Neuroinflammation, the inflammatory cytokine IL-22 is produced as a result of tissue injury. After a concentrated tissue inflammatory reaction, it is rapidly recognized in plasma. In inflammatory conditions such as tissue injury or infection, IL-22 levels increase significantly. Cytokines, which are listed as causes of induction of IL-22 production in the section IL-22 Sources, Targets, Metabolites and Oxygen are all important environmental factors controlling when and where IL-22 expression is increased as well as when it is suppressed.

Interleukin (IL)-22-secreting CD4+ T (Th22) cells are involved in the pathogenesis of autoimmune disorders such as multiple sclerosis. Shaw W,. In addition, CD4+ Th cell subsets, including regulatory, Th1, Th2, and Th17 T cells, control immune responses by promoting (or inhibiting) the proliferation, differentiation, and activation of other immune cells.

Conclusion

Multiple sclerosis is a devastating chronic disease with an unknown pathogenesis mechanism at the molecular level. We show that there is a dysregulation in the expression of IL-22 and a lower level of MBP in MS patients.

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