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RESEARCH ARTICLE

GENDER IMPACT ON INSULIN LIKE GROWTH FACTOR 1(IGF-1) AND SELECTED BIOCHEMICAL MARKERS IN IRAQI PATIENTS WITH MULTIPLE SCLEROSIS

***,[1]Fadwa Ghassan, [2]Dr. Sarwer Jamal Al-Bajalan and [1]Dr.Thamer Mutlag Jasim**

[1]Al-Mustansiriyah University, College of Pharmacy, Department of Clinical Laboratory Science.
[2]Sulaimai University, School of Medicine

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ABSTRACT

Objective: To investigate the gender impact on serum IGF-1, Vit. D and other clinical parameters in multiple sclerosis (MS) patients and compare between the studied parameters before and after treatment.
Design: 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. Serum IGF-1, Vit.D, S.GOT, S.GPT, Total Cholestrol and Uric acid were measured.
Results: In MS patients, The serum IGF-1 demonstrated a lowest level in the female subjects of control [9.50 ng/dl], while it showed an increased level in male [10.22 ng/dl] , but with similar levels ($p > 0.05$), The mean of IGF-1 also shown no significant difference between female and male MS patients in pre or post-treatment groups [33.7o vs. 37.46 , 19.22 vs. 21.50 respectively].Similar Vitamin D serum levels(7.59 and 7.39 ng/ml, respectively) in the two groups of pre-treatment patients (Male and Female), and therefore, no significant difference. In contrast, the controls demonstrated a gradual increase of Vit D. serum level (27.83 and 30.77ng/ml, respectively) in the male and female groups, Such difference was not significant ($P \geq 0.05$). In the post-treatment patients also, was no significant difference between male and female patients (11.27 vs. 10.99 ng/ml).Neither SGOT nor SGPT showed a significant variation between the two groups of pre-treatment MS patients for male and for female, although a similar level of SGPT was observed in the control groups for male and female respectively, and the post treatment group of MS patients also not observed and difference between male and female (29.92 vs. 30.17, respectively). No significant difference in uric acid serum level ($p \geq 0.05$) between male and female groups in pre-treatment patients (4.3 and 4.42 mg/dl, respectively). As well as, in post-treatment MS patient, no significant difference was observed between male and female groups (4.92 and 4.72 mg/dl, respectively). The healthy control group show that the uric acid serum level in male (4.41 md/dl) and in female (4.47 mg/dl) and there was no significant difference between them. There was no significant difference in total cholestrol serum level ($p \geq 0.05$) between male and female groups in pre-treatment patients (175.38 and 181.94 mg/dl, respectively). As well as, in post-treatment MS patients there was no significant difference was observed between male and female groups (170.92 and 170.0 mg/dl, respectively).The control group show that the total cholesterol serum level in male (160.5 md/dl) and in female (177.14 mg/dl) and there was no significant difference between them.
Conclusions: The observed increase in IGF-I in patients treated with IFN-beta being of most significance as a potential therapeutic biomarker.MS, occur more frequently in women. Emerging technologies might provide novel methods with the potential to further dissect the genetic *and immunological mechanisms causing the observed differences between women and men with MS.*

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INTRODUCTION

Multiple sclerosis (MS) is a de-myelinating disease in which the insulating covers of nerve cells in the brain and spinal cord are damaged (National Institute of Neurological Disorders and Stroke, 2015). This damage disrupts the ability of parts of the nervous system to communicate, resulting in a range of signs and symptoms, including physical, mental, and sometimes psychiatric problems (Coles *et al*., 2008; Murray *et al*., 2012; Reingold, 1996). Specific symptoms can include double vision, blindness in one eye, muscle weakness, trouble with sensation, or trouble with coordination.[1] MS takes several forms, with new symptoms either occurring in isolated attacks (relapsing forms) or building up over time (progressive forms).[5]Between attacks, symptoms may disappear completely; however, permanent neurological problems often remain, especially as the disease advances (Nakahara *et al*., 2012). IGF-1is an important factor for preventing the depletion of mature oligodendrocy and invrease the rate of early recovery from demyelination (Mason, 2000).

****Corresponding author: Fadwa Ghassan,***
Al-Mustansiriyah University, College of Pharmacy, Department of Clinical Laboratory Science.

Neurohormones such as GH and IGF-I are involved in the neuroreparative processes in multiple sclerosis (MS). Low level of GH was noticed in MS patients with severe attacks, age is the main factor driving IGF-I levels (MS prognosis) (Gironi, 2013). Vitamin D affecting both the incidence and the severity of MS. High levels of vitamin D shows a protective effect against Ms development (Gironi, 2013). Vitamin D has beneficial effects in experimental autoimmune encephalomyelitis and a therapeutic potential for MS. Genes associated with vitamin D are critical susceptible genes for MS (Rotstein *et al*., 2015). Oxidative and nitrosative stress (O&NS) considered as the causative agents in the pathogenesis of Alzheimer's and Parkinson's disease, multiple sclerosis, chronic fatigue syndrome, schizophrenia and depression. O&NS, cause proteins, lipids and DNA damage. Chronic O&NS effects include inhibits palmitoylation resulting in composition changes of the lipid membrane, high membrane permeability and reduced fluidity, leads to alteration intracellular signal transduction, receptor dysfunction and high neurotoxicity level (Garvin, 2015).

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). Serum insulin like growth factor-1, Vit D, Liver function test, total cholesterol and uric acid were measured.

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), the effect of sex and age within treatment on cholesterol, SGOT, SGPT, Uric acid, IGF-1 and Vit. D. SPSS-21 (Statistical Packages for Social Sciences- version 21) and 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 (SAS, 2010 and Costello *et al*., 2011) ROC curves have been widely accepted as the standard method for describing and comparing the accuracy of radiologic imaging and other medical diagnostic tests (Metz *et al*., 1986; Zhou, 2002).

RESULTS

The serum IGF-1 demonstrated a lowest level in the female subjects of control [9.50 ng/dl], while it showed an increased level in male [10.22 ng/dl] , but with similar levels (p> 0.05),as shown in Table (1). The mean of IGF-1 also shown no significant difference between female and male MS patients in pre or post-treatment groups [33.7o vs. 37.46, 19.22 vs. 21.50 respectively], Figure (1) Table (1). The MS patients showed similar Vitamin D serum levels (7.59 and 7.39 ng/ml, respectively) in the two groups of pre-treatment patients (Male and Female), and therefore, no significant difference.

Table 1. Comparison among means of IGF-1 according to sex in different groups

Subjects	Gender	IGF-1		
		Control	Pre-treatment	Post-treatment
	Male	10.22±1.83	33.70±5.81	19.22±2.15
	Female	9.50±0.93	37.46±4.51	21.50±2.66
	P-value	0.49	0.38	0.43
	ANOVA Probability > 0.05 (not significant)			

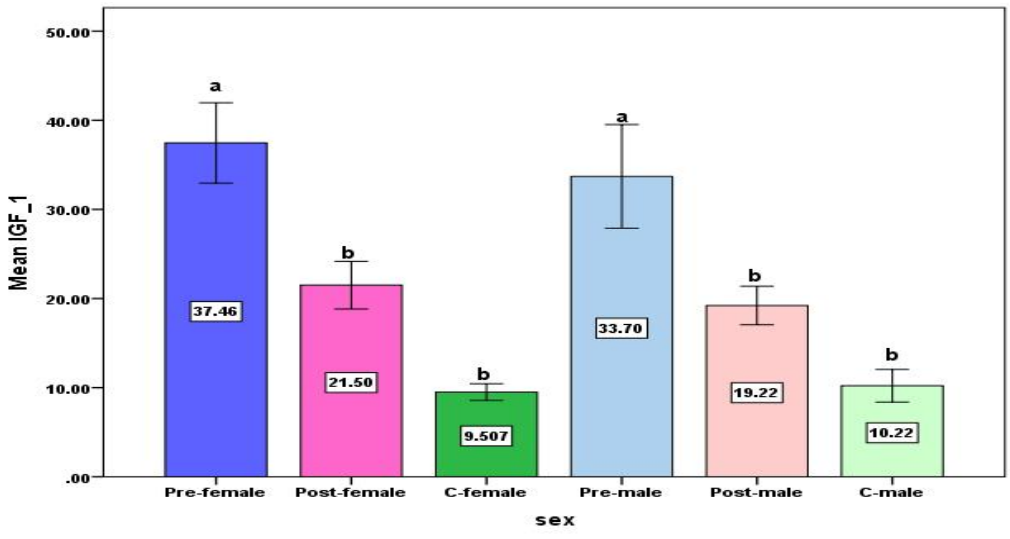

Figure 1. Serum level of IGF-1 in pre and post treatment compare with control

In contrast, the controls demonstrated a gradual increase of Vit D. serum level (27.83 and 30.77ng/ml, respectively) in the male and female groups. Such difference was not significant (P ≥ 0.05), (Table 2) and Figure (2). In the post-treatment patients also, was no significant difference between male and female patients (11.27 vs. 10.99 ng/ml), Table (2) and Figure (2). It was found that, neither SGOT (Table 3) nor SGPT (Table 4) showed a significant variation between the two groups of pre-treatment MS patients (25.33 IU/L) for male and (27.06 IU/L) for female, although a similar level of SGPT was observed in the control groups (26.17 vs. 26.168 IU/L) for male and female respectively, and the post treatment group of MS patients also not observed and difference between male and female (29.92 vs. 30.17, respectively). Table (4) shown, no significant difference (P ≥ 0.05) in SGPT between male (23.0 IU/ L) and female (24.78 IU/L) for pre-treatment MS patients.In post-treatment MS patients also, no significant diffrance between male and female groups (28.0 vs. 29.17 IU/L, respactivly).

Healthy control group behaved in a similar manner in the patients. It showed slightly increased GPT serum level in female compared to male (26.43 and 20.67 IU/L, respectively), (Table 4 & Figure 4). No significant difference in uric acid serum level (p≥ 0.05) between male and female groups in pre-treatment patients (4.3 and 4.42 mg/dl, respectively) as shown in Table (5). As well as, in post-treatment MS patient, no significant difference was observed between male and female groups (4.92 and 4.72 mg/dl, respectively) as shown in Table (5). The healthy control group show that the uric acid serum level in male (4.41 md/dl) and in female (4.47 mg/dl) and there was no significant difference between them as shown in Table (5) & Figure (5). There was no significant difference in total cholestrol serum level (p≥ 0.05) between male and female groups in pre-treatment patients (175.38 and 181.94 mg/dl, respectively). As well as, in post-treatment MS patients there was no significant difference was observed between male and female groups (170.92 and 170.0 mg/dl, respectively) as shown in Table (6).

Table 2. Comparison among means of Vit.D according to sex in pre and post treatment compare to control

Subjects	Gender	Vit. D ng/ml		
		Control	Pre-treatment	Post-treatment
	Male	27.83±1.20	7.59±0.69	11.27±0.79
	Female	30.77±2.72	7.39±0.57	10.99±0.58
	P-value	0.31	0.51	0.66
ANOVA Probability > 0.05 (not significant)				

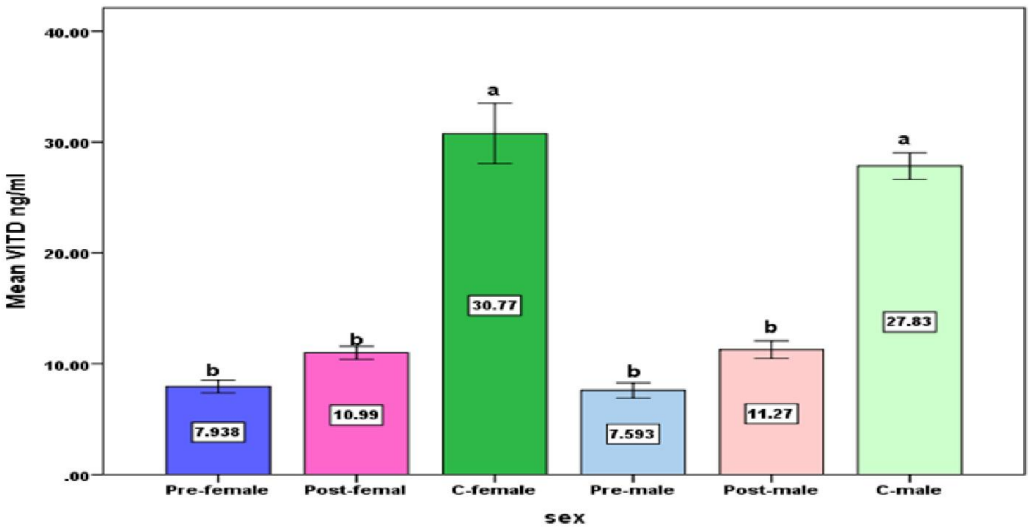

Figure 2. Serum level of Vit.D according to sex in pre and post treatment compare with control

Table 3. Comparison among means of SGOT according to sex in pre and post treatment compare with control

Subjects	Gender	SGOT(IU/L)		
		Control	Pre-treatment	Post-treatment
	Male	26.17±2.48	25.33±2.09	29.92±2.07
	Female	26.28±1.68	27.06±1.34	30.17±0.89
	P-value	0.55	0.38	0.12
ANOVA Probability > 0.05 (not significant)				

Table 4. Comparison among means of SGPT in pre and post treatment compare with control

Subjects	Gender	SGPT(IU/L)		
		Control	Pre-treatment	Post-treatment
	Male	20.67±2.49	23.00±2.65	28.00±2.47
	Female	26.43±2.41	24.78±1.64	29.17±2.25
	P-value	0.24	0.42	0.62
ANOVA Probability > 0.05 (not significant)				

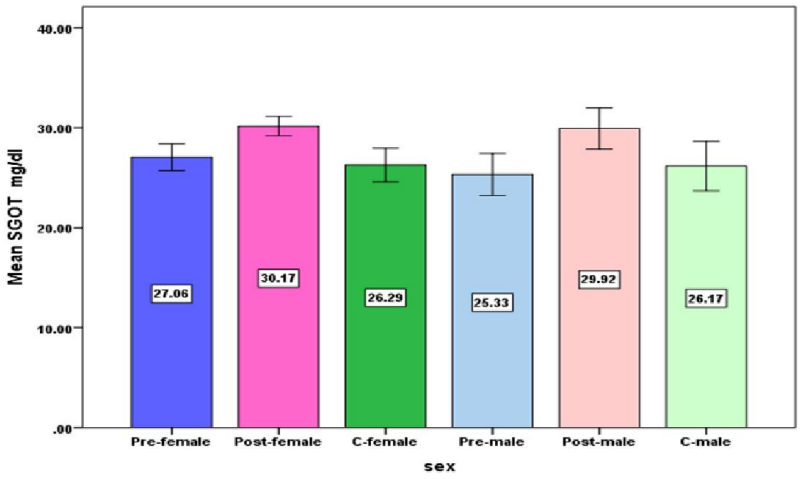

Figure 3. Serum level of SGOT in pre and post treatment compare with control

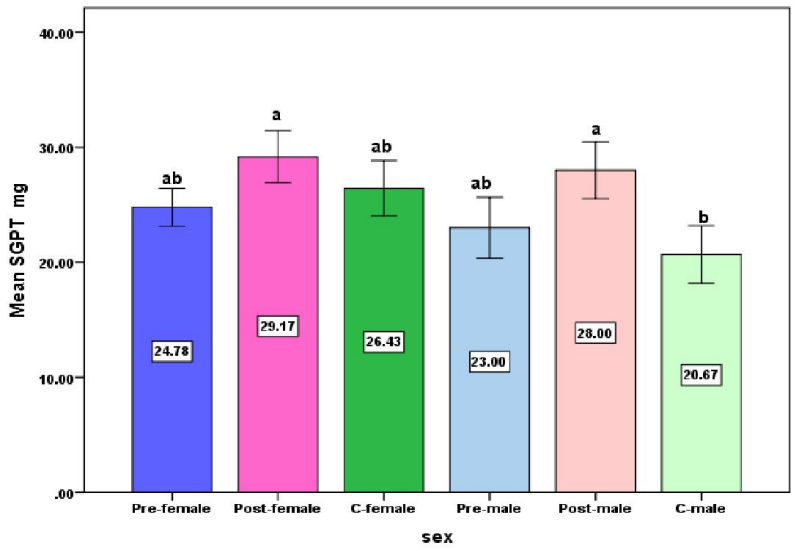

Figure 4. Serum level of SGPT in pre and post treatment compare with control

Table 5. Comparison among means of S.Uric acid according to sex in pre and post treatment compare to control

Subjects	Gender	S.Uric acid (mg/dl)		
		Control	Pre-treatment	Post-treatment
	Male	4.41±0.14	4.30±0.16	4.92±0.15
	Female	4.47±0.11	4.42±0.06	4.72±0.12
	P-value	0.47	0.41	0.17
	ANOVA Probability > 0.05 (not significant)			

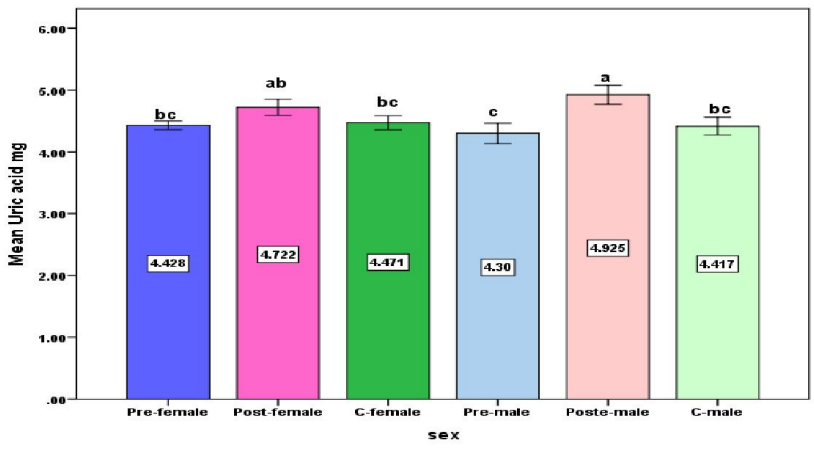

Figure 5. Serum level of Uric acid according to sex in pre and post treatment compare to control

Table 6. Comparison among means of cholesterol according to sex in pre and post treatment compare to control

Subjects	Gender	Total cholesterol (mg/dl)		
		Control	Pre-treatment	Post-treatment
	Male	160.50±7.06	175.83±5.08	170.92±4.14
	Female	177.14±7.86	181.94±6.72	170.00±4.87
	P-value	0.58	0.2	0.88
	ANOVA Probability > 0.05 (not significant)			

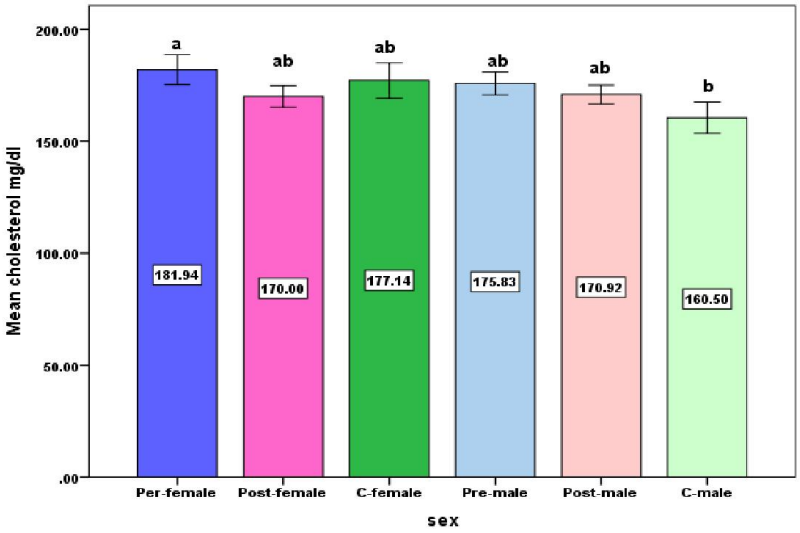

Figure 6. Difference in serum level of Uric acid according to sex in pre and post treatment and control

Table 7. Demographic table of ROC analysis

Parameter	Sensitivity	95%CI	Specificity	95%CI	Cut off point
Vit D	100.0	88.4 - 100.0	100.0	83.2 - 100.0	≤13.4
IGF-1	100.0	88.4 - 100.0	100.0	83.2 - 100.0	>15.5
Cholesterol	63.3	43.9 - 80.1	55.0	31.5 - 76.9	>166
SGOT	86.6	69.3 - 96.2	10.0	1.2 - 31.7	≤31
SGPT	86.7	69.3 - 96.2	20.0	5.7 - 43.7	≤32
Uric acid	50.0	31.3 - 68.7	55.0	31.5 - 76.9	≤4.2

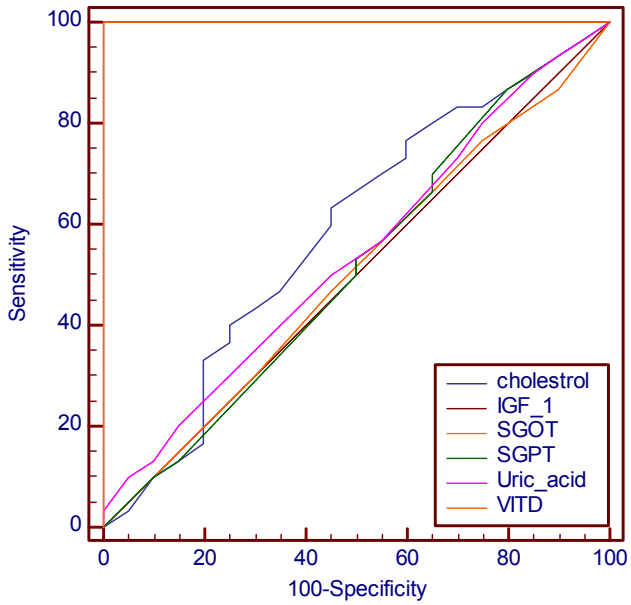

Fig.7. Roc curve Analysis for pre treatment patients and control

The control group show that the total cholesterol serum level in male (160.5 md/dl) and in female (177.14 mg/dl) and there was no significant difference between them as shown in Table (6).

ROC curve result showed that the Vit D and IGF have excellent sensitivity (100%) and specificity (100%). These results are not unexpected because there is no overlap between the values of patients and control for each of Vit.D and IGF-1. In such case, the maximum value of vit D in the patients will represent the cutoff point as shown in demographic Table (7) because the patients showed a deficiency in Vit.D. On the contrary, the elevated level of IGF-1 was shown in the patients so, the maximum values of control represent the cutoff points shown in demographic Table (7). Concerning the other markers the overlap was existed so the ROC curve method is the best method to estimate the cutoff point that can be used for the diagnosis of the patients. As the sensitivity and specificity were excellent for Vit D and IGF-1, these two markers will considered the best for the diagnosis. The comparisons among other markers depend on the area under curve showed there was no significant difference.

DISCUSSION

The present study design to investigate the impact of gender on the investigated parameters (IGF-1, Vit.D, SGOT, SGPT, uric acid, total cholesterol). The present study showed that the mean of serum IGF-1 shown no significant difference between female and male MS patients in pre or post-treatment groups while it was the least among female of the control group in

compare to male. Recent study reports the beneficial effects of a systemic delivery of insulin-like growth factor-1 (IGF-1) in suppressing autoimmune diseases. This new finding suggests a novel approach for toning down the immune system so that in a disease like MS, destruction of myelin can be slowed down or even halted (Zhou, 2002). Insulin-like growth factor-1 (IGF-1) is of considerable interest because it is not only a potent neuroprotective trophic factor but also a survival factor for cells of the oligodendrocyte lineage and possesses a potent myelinogenic capacity (Chesik *et al*., 2007). Similar Vitamin D. serum level in the two groups of pre-treatment patients (Male and Female), and therefore, no significant difference. In contrast, the controls demonstrated a gradual increase of Vit D. serum level in the male and female groups.For post-treatment patients also, was no significant difference between male and female patients. Multiple sclerosis (MS) is universally found to be more prevalent in women than men.

This has led to extensive studies of differences in the immune system or nervous system between women and men, which might be caused by the effects of gonadal hormones, genetic differences, and different environmental exposures and modern lifestyle in men and women (Hanne *et al*., 2013). There was no significant difference in total cholestrol serum level between male and female groups in pre-treatment patients. As well as, in post-treatment MS patients there was no significant difference was observed between male and female groups.The control group show that the total cholesterol serum level in male and there was no significant difference between them. Dyslipidemia can potentiate inflammatory processes at the vascular endothelium, lead to the induction of adhesion molecules, and the recruitment of monocytes. Associations between dyslipidemia and increased inflammation are well established in conditions such atherosclerosis, cardiovascular disease, metabolic syndrome and obesity (Pugliatti, 2002).

REFRENCES

Chesik D, Wilczak N, De Keys2007er J The insulin-like growth factor system in multiple sclerosis. *Int Rev Neurobiol*., 79:203-26

Costello M, Sabatini, Yungbluth M. Viral infections. In: McPherson RA, Pincus MR, eds. *Henry's Clinical Diagnosis and Management by Laboratory Methods*. 22nd ed. Philadelphia, *PA: Elsevier Saunders*; 2011:chap 55.

Garvin, R.A. 2015. Elevated Phospholipid Transfer Protein in Subjects with Multiple Sclerosis, *J Lipids.* 2015:518654.

Gironi, M., Solaro, C., Meazza, C., Vaghi, M., Montagna L., Rovaris, M., Batocchi, A.P., Nemni, R., Albertini, R., Zaffaroni, M., Bozzola, M. 2013. Growth hormone and disease severity in early stage of multiple sclerosis, *MultScler Int*., Oct 23.

Ljubisavljevic, S, Stojanovic, I, Vojinovic, S., Milojkovic, M, Dunjic, O, Stojanov, D, Pavlovic, D. 2013. Association of serum bilirubin and uric acid levels changes during neuroinflammation in patients with initial and relapsed demyelination attacks, *Metab Brain Dis*., Dec;28(4):629-38.

Mason, J. L., Ye, P., Suzuki, K., D'Ercole, A. J. and Matsushima, G. K. 2000. Insulin-Like Growth Factor-1 Inhibits Mature Oligodendrocyte Apoptosis during Primary Demyelination, *The Journal of Neuroscience*, 1 August, 20(15).

Metz CE. ROC methodology in radiologic imaging. Invest Radiol, 1986;21:720–33.

Murray, E.D., Buttner, E. A., Price, B.H. 2012. "Depression and Psychosis in Neurological Practice". In Daroff R, Fenichel G, Jankovic J, Mazziotta J. Bradley's neurology in clinical practice. (6th ed.). Philadelphia, PA: Elsevier/ Saunders.

National Institute of Neurological Disorders and Stroke. November 19, 2015. Retrieved 6 March, 2016.

Pugliatti M, Sotgiu S, Rosati G. 2002. The worldwide prevalence of multiple sclerosis. *Clin Neurol Neurosurg*., Jul;104(3):182-91

Rotstein, D.L., Healy, B.C., Malik, M.T., Carruthers, R.L., Musallam, A.J., Kivisakk, P., Weiner, H.L., Glanz, B, Chitnis, T. 2015. Effect of vitamin D onMS activity by disease-modifying therapy class, *Neurol Neuroimmunol Neuroinflamm*., Oct 29;2(6).

Zhou XH, Obuchowski NA, McClish DK. Statistical methods in diagnostic medicine. New York: Wiley & Sons Interscience, 2002: 437pp.

Reingold, S.C. April 1996. "Defining the clinical course of multiple sclerosis: results of an international survey". *Neurology*, 46 (4): 907–11.

Coles, A. October 2008. "Multiple sclerosis". Lancet. 372 (9648): 1502–17. Compston A, Coles A (April 2002). "Multiple sclerosis". Lancet. 359(9313): 1221–31.

Nakahara, J., Maeda, M., Aiso, S., Suzuki, N. February 2012. "Current concepts in multiple sclerosis: autoimmunity versus oligodendrogliopathy". *Clinical Reviews in Allergy & Immunology*, 42 (1): 26–34.

Hanne F. Harbo, Ralf Gold, and Mar Tintoré2013 Jul; Sex and gender issues in multiple sclerosis, *Ther Adv Neurol Disord*., 6(4): 237–248.

SAS.2010.SAS/STAT Users Guide for Personal Computer. Release 9.1. SAS Institute, Inc., Cary, N.C., USA.IBM Corp. Released 2012. IBM. SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.

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