Study of Serum Soluble Cell Adhesion Molecules Relation with Severity of Multiple Sclerosis Different Groups

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Abstract

Background: Multiple sclerosis (MS) is a chronic and autoimmune disease of the central nervous system (CNS), The McDonald diagnostic criteria allow an earlier and often more accurate diagnosis of MS to be made by utilizing MRI.

Aim: The purpose of this study was to find correlation between serum level of soluble cell adhesion molecules and the clinical severity assessment using Expanded Disability status Scale and Magnetic Resonance Imaging findings in patients with Multiple Sclerosis disease.

Subjects and Methods: : Our study included 32 patients with clinically definite multiple sclerosis patients and consisted of (18 patients with Relapsing Remittent MS (3 males &15 females), 4 males with Primary Progressive MS and 10 females with secondary progressive MS) who met the criteria of clinically definite MS according to revised McDonald criteria 2017, selected from Neurology Department, Zagazig University Hospitals and Outpatient Clinic. Also 32 age and sex matched healthy volunteers as control group were included in this study. History taking, clinical evaluation of disease severity by the Expanded Disability Status Scale (EDSS), as well as adhesion molecules which was measured in serum, were done to all subjects.

Results: Regarding differences between Multiple Sclerosis patients' subgroups, it was found that, sNCAM level was statistically significant increase in PPMS and SPMS groups compared to RRMS group while in sVCAM there was a statistical significance increase in PPMS and SPMS groups compared to RRMS group and also in SPAM compared to PPSM group. Finally, in sICAM, there was astatistical significant increase in SPMS groups compared to RRMS and PPMS groups.

Conclusion: we can assess serum level of soluble adhesion molecules to find the association between their serum levels & clinical assessment and Magnetic Resonance Imaging findings of disease severity in Multiple Sclerosis patients.

Keywords: Soluble Cell Adhesion Molecules, Multiple Sclerosis, Disease Activity, Magnetic Resonance Imaging

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1. Introduction:

Multiple sclerosis (MS) is a chronic and autoimmune disease of the central nervous system (CNS), mainly characterized by inflammatory demyelination, which manifests as relapses and diffuse damage and brain volume loss, both accounting for neurodegeneration , and therefore, physical disability **(1).**

Multiple sclerosis is the most common demyelinating disease with the highest levels seen in North America and Europe (>100/100,000 inhabitants)and the lowest levels in Eastern Asia and sub-Saharan Africa (2/100,000) **(2).**

Vascular cell adhesion molecule-1 (VCAM-1), a member of the immunoglobulin supergene family, is preferentially involved in T-cell binding to the endothelium but is also involved in monocyte-Endothelial cell interactions. Intracellular adhesion molecule- 1 (ICAM-1, CD54), also a member of the immunoglobulin supergene family, is thought to be constitutively expressed on ECs, and is involved in adhesion of neutrophils, lymphocytes, and other cells bearing the Late function Associated Antigen-1(LFA-1) integrin receptor .The Neural Cell Adhesion Molecule-1 (NCAM-1), also known CD56, is one of immunoglobulin superfamily which is involved in cell migration, axonal growth , organization and modulation of synapses. As cerebral endothelial cells are the major constituents of the blood brain barrier (BBB), morphological and biochemical alterations of these cells may ultimately lead to increased permeability of the BBB, these lesions represent blood-brain barrier damage and correlate with clinical and pathological disease activity **(4).**

In numerous studies, increased serum levels of sICAM-1, sNCAM-1 and sVCAM-1 had been reported to correlate with the clinical course of MS disease severity and MRI activity in MS patients, In this study, subjects underwent neurological and MRI examinations and provided blood samples. The collected data included demographic and clinical information. The Expanded Disability Status Scale (EDSS) was assessed in MS patients **(5).**

Neuroimaging investigation of MS disease severity received considerable attension over the year, mainly evaluating the presence / absence of brain lesions, or T2 lesion volumes by Magnetic Resonance Imaging (MRI) is important to find the correlation between serum level of soluble cell adhesion molecules and MRI characteristics of MS disease severity, The whole brain volume (BV), the cortical volume (CV), lateral ventricular volume (LVV), reflect regional axonal loss as well as demyelination in white and gray matter tissue structures**(6).**

The purpose of this study was to find correlation between serum level of soluble cell adhesion molecules and the clinical severity assessment using Expanded Disability status Scale and Magnetic Resonance Imaging findings in patients with Multiple Sclerosis disease.

2. Subjects and Methods:

This study was carried out on 32 patients with clinically definite multiple sclerosis) who met the criteria of clinically definite MS according to revised McDonald criteria 2017 **(5)** selected from Neurology Department, Zagazig University Hospitals and Outpatient Clinic.

Also 32 age and sex matched healthy volunteers as control group were included in this study. The study was approved by the Ethical Committee of our Faculty and informed written consent was obtained from patients and controls. **ZU-IRB Approval (#5380-21-5-2019).**

Inclusion Criteria

The studied subjects were divided into two groups, each group consisted of 32 subjects.

The patients group:

This group included 32 Patients with Multiple Sclerosis (18 patients with Relapsing Remittent MS (3 males &15 females), 4 males with Primary Progressive MS and 10 females with secondary progressive MS) selected according to revised **McDonald criteria (5).**

The control group:

This group included age and sex matched 32 healthy individuals with normal clinical evaluation and radiological scan.

- The included subjects were older than 18 years and their physical and neurological examination were done within 30 days from the standardized Magnetic Resonance Imaging study protocol.

Exclusion criteria:

- Presence of relapse and steroid treatment within 30 days preceding the study.

Pre-existing medical conditions known to be associated in brain pathology (e.g, neurodegenerative disorders, cerebrovascular diseases.) and pregnant females.

All patients were subjected to the following:

(1) History and examination:

- Detailed history taking about age of onset, duration of disease, number of relapse and current treatment(disease modifying therapy).
- The duration of the disease (i.e., the interval between the date of first symptom and the date of examination (measured in years).
- Patient's age at first symptoms.
- Thorough General and Neurological examinations.
- Assessment of disease severity by the Expanded **Disability Status Scale (EDSS)**: The Expanded Disability Status Scale (EDSS) is a method of quantifying disability in multiple sclerosis and monitoring changes in the level of disability over time. It is widely used advance from his previous 10 step Disability Status Scale (DSS) in clinical trials and in the assessment of people with MS. **(6)**

The Expanded Diability Status Scale (EDSS) ranges from 0 to 10 in 0.5 unit increments that represent higher levels of disability. Scoring is based on an examination by a neurologist.

(2) Routine laboratory investigations:

Complete blood count, liver and kidney function tests, erythrocyte sedimentation rate , C-Reactive Protein, fasting and random blood sugar, serum-electrolytes .

(3) Specific laboratory test:

Adhesion molecules will be measured in serum samples, obtained only once at the time of the Neurologic and Radiological examinations, serum levels of soluble cell adhesion molecules will be measured using Luminex magnetic kits by ELIZA Procedure **(8).**

(4) Radiological evaluation: was performed in Zagazig University Radiology MRI Unit MR images were acquired using a 1.5T Philips (Achieva, class IIa) using a standard quadrature head coil. Philips Achevia 1.5T MRI machine is a fast and easy to use machine. It is available in 8,16and 32 channels. All lesions volumes were obtained by LesionQuant(LQ) software. We evaluated the Lateral Ventricular Volume (TLV& T2V) and Normalized Brain Volume (NBV) to find the correlation between seum soluble cell adhesion molecules levels and disease severity.

Statistical analysis of the data:

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) Qualitative data were described using number and percent. The Shapiro-Wilk test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). Significance of the obtained results was judged at the 5% level.

1. Results

Table (1): Clinical Types of MS among the patients group:

Variable		MS (n=32)	
		No	%
Type:	RRMS	18	56.3
	PPMS	4	12.5
	SPMS	10	31.2

Variable	All MS (n=32)	RRMS (n=18)	PPMS (n=4)	SPMS (n=10)	KW/ F	P	Post hoc
Age of onset mean±SD (years)	33.28±8.21 17-50	30.83±8.15 17-47	43.5±4.36 41-50	33.6±6.45 28-48	**4.89**	**0.02***	**0.01*[1]** 0.61 NS[2] 0.08 NS[3]
Disease duration: mean±SD Median Range (years)	4.91±2.665 1-10	3.22±1.663.5 1-5	4.75±0.96 4.5 4-6	8±1.568 5-10	**20.11**	**<0.001****	0.12 NS[1] **<0.001**[2]** **0.004*[3]**
EDSS: mean±SD Range	4.13±1.37 1.5-6.5	3.33±1.15 1.5-5.5	4.63±1.03 3.5-6	5.35±0.78 4.5-6.5	**18.09**	**<0.001****	0.08 NS[1] **<0.001**[2]** 0.47 NS[3]

Variable	N	%	N	%	N	%	N	%	χ^2	P	Within groups
DMT:											
No	3	9.4	3	16.	0	0	0	0			<0.001** [1]
Interferone	17	53.	11	7	0	0	6	60	21.49	<0.001	
B	5	1	4	61.	0	0	1	10		**	0.054 NS[2]
Fingolimod	7	15.	0	1	4	10	3	30			
e		6		22.		0					0.06 NS[3]
Rituximab		21.		2							
		9		0							

RRMS : Relapsing Remittent Multiple Sclerosis SPMS: Secondary Progressive Multiple Sclerosis
PPMS: Primary Progressive MS

Table (2): Clinical data among the studied patients group:

SD: Standard deviation F One way ANOVA KW: Kruskal Wallis test χ2: Chi square test RRMS; Relapsing Remittent Multiple Sclerosis
PPMS: Primary Progressive MS SPMS : Secondary Progressive MS DMT : Disease Mdifying Therapy
P1: RRMS versus PPMS P2: RRMSI versus SPMS P3: PPMS versus SPMS
NS: Non significant (P>0.05) *: Significant (P<0.05) **: Highly significant (P<0.001)

Table (3): MRI characteristics among the studied MS patients group:

Variable	All MS (n=32)	RRMS (n=18)	PPMS (n=4)	SPMS (n=10)	F	P	Post hoc
T2LV:(ml) Mean±SD Range	17.36±3.48 11.5-22.5	14.6±1.5 11.5-18.5	21.73±0.29 21.5-22.1	20.57±1.52 18.5-22.5	77.11	<0.001**	<0.001** [1] <0.001** [2] 0.37 NS[3]
T1LV: (ml) Mean±SD Range	4.32±1.46 2-7.1	3.21±0.77 2-4.6	5.43±0.65 5.1-6.4	5.87±0.64 4.8-7.1	49.76	<0.001**	<0.001** [1] <0.001** [2] 0.55 NS[3]
NBV: (ml) Mean±SD Range	1428.06±78.94 1321-1599	1480.06±64.56 1325-1599	1370.25±29.64 1345-1402	1357.6±29.79 1321-1402	19.87	<0.001**	0.002*[1] <0.001** [2] 0.91 NS[3]

SD: Standard deviation F One way ANOVA
P1: RRMS versus PPMS P2: RRMSI versus SPMS P3: PPMS versus SPMS

NS: Non significant (P>0.05) *: Significant (P<0.05) **: Highly significant (P<0.001)
NBV: Normalized Brain Volume. LV : Lateral Venticle RRMS: Relapsing Remittent MS PPMS: Primary Progressive MS
SPMS: Secondary Progressive MS

Table (4): Serum Cell Adhesion Molecules Levels groups among the studied patients subgroups and healthy control:

Variable	RRMS (n=18)	PPMS (n=4)	SPMS (n=10)	Group II (Control) (n=32)	KW	P	Post hoc
sNCAM: (ng/ml)	63.92±14.560 47.42-97.98	168±41.8183 107.68-201.52	194.72±17.52 199.26 154-215	21.52±11.20 23.92 3.19-36.05	53.16	<0.001**	0.002*[1] <0.001**[2] 0.20 NS[3] <0.001**[a] <0.001**[b] <0.001**[c]
sVCAM: (ng/ml)	2120.22±995 1968.98 639.41-3677.85	4403.94±1110.6 4378.19 3357.37-5502.02	6622.33±1355 6246.23 4251.52-8547.52	189.41±148.40 167.79 10.82-500.94	53.17	<0.001**	0.005*[1] <0.001**[2] 0.02*[3] <0.001*[a] <0.001**[b] <0.001**[c]
sICAM: (ng/ml)	156.94±40.14 145.55 124.22-298.25	192.10±40.99 191.87 142.52-242.52	287.65±51.44 301.89 201.24-358.25	43.86±26.74 45.74 4.29-96.66	52.08	<0.001**	0.15 NS[1] <0.001**[2] 0.01*[3] <0.001**[a] <0.001**[b] <0.001**[c]

SD: Standard deviation KW: Kruskal Wallis test
sNCAM; serum Neural Cell Adhesion Molecule sVCAM: serum Vascularl Cell Adhesion Molecule
sICAM: serum intercellular Cell Adhesion Molecule RRMS: Relapsing Remittent MS
PPMS; Primary Progressive MS SPMS: Secondary Progressive MS
P1: RRMS versus PPMS P2: RRMSI versus SPMS P3: PPMS versus SPMS
Pa: RRMS versus Control Pb: PPMS versus Control PC: SPMS versus Control

NS: Non significant (P>0.05) *: Significant (P<0.05) **: Highly significant (P<0.001)

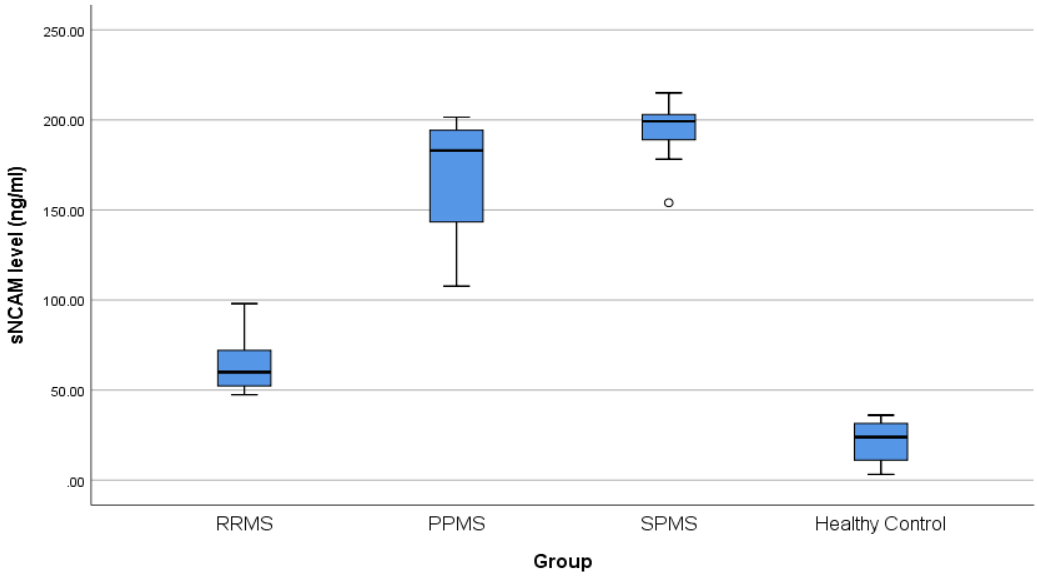

Figure (1): Serum Cell Adhesion Molecules Levels (sNCAM) among the studied patients subgroups and healthy control.

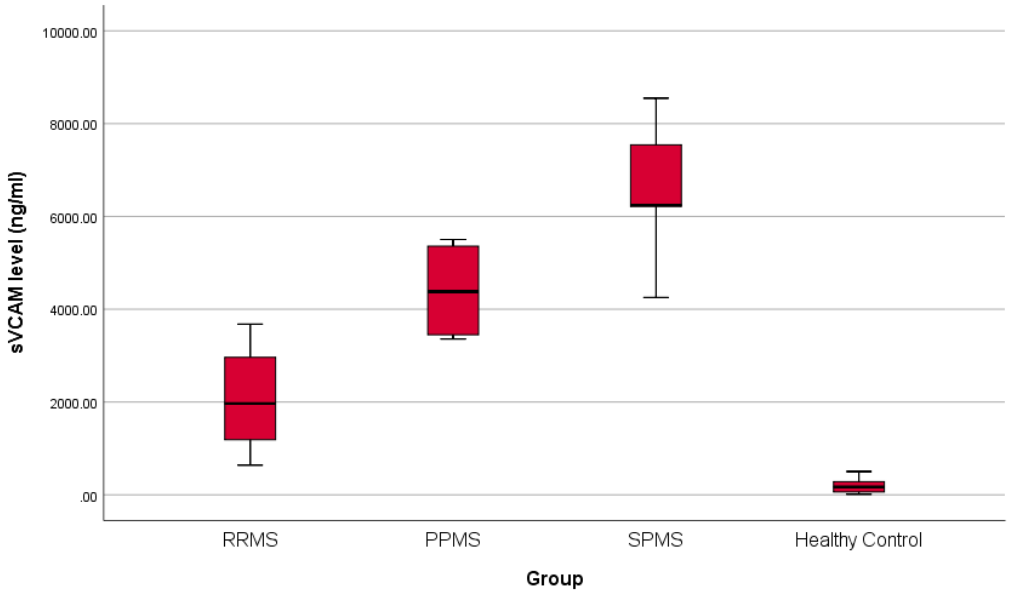

Figure (2): Serum Cell Adhesion Molecules Levels (sVCAM) among the studied MS patients subgroups and healthy control.

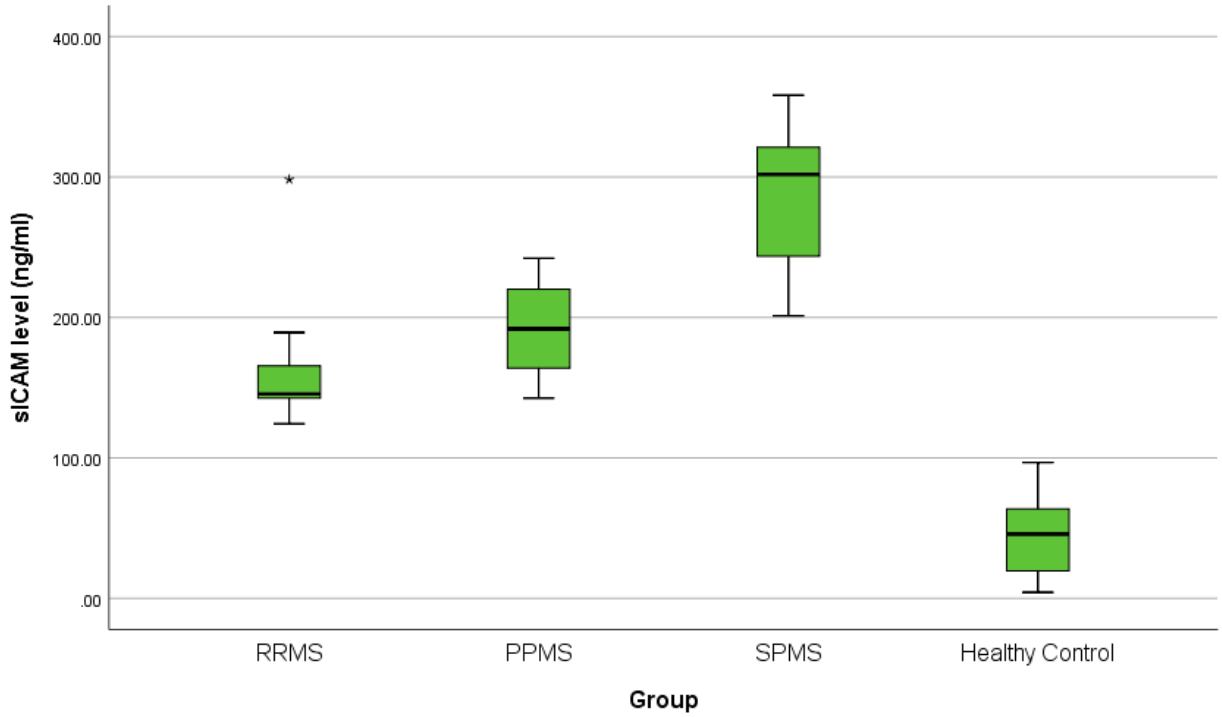

Figure (3): Serum Cell Adhesion Molecules Levels (sICAM) among the studied MS patients subgroups and healthy control.

Table (5): Correlation between clinical data and Serum Cell Adhesion Molecules Levels among Group I:

Variable	sNCAM (*n*=32)		cVCAM (n=32)		sICAM (n=32)	
	r	P	r	P	r	P
Age of onset: (years)	0.41	0.02*	0.20	0.28 NS	0.27	0.13 NS
Disease duration: (years)	0.64	<0.001**	0.68	<0.001**	0.71	<0.001**
EDSS:	0.69	<0.001**	0.69	<0.001**	0.73	<0.001**

sNCAM; serum Neural Cell Adhesion Molecule sVCAM: serum Vascularl Cell Adhesion Molecule
sICAM: serum intercellular Cell Adhesion Molecule r: Spearman's correlation coefficient NS: non significant (P>0.05)
*: Significant (P<0.05) **: Highly significant (P<0.001) EDSS: Expanded Disability Status Scale

Table (6): Correlation between MRI characters and Serum Cell Adhesion Molecules Levels among patients group:

Variable	sNCAM (*n*=32)		cVCAM (n=32)		sICAM (n=32)	
	r	P	R	P	r	P
T2LV/ (ml)	0.67	<0.001**	0.71	<0.001**	0.58	0.001*
T1LV/ (ml)	0.66	<0.001**	0.73	<0.001**	0.67	<0.001**
NBV/ (ml)	-0.64	<0.001**	-0.61	<0.001**	-0.46	0.008*

r: Spearman's correlation coefficient *: Significant (P<0.05) **: Highly significant (P<0.001) LV : Lateral Ventricle NBV: Normalized Brain Volume

Table (7): Correlation between Serum Cell Adhesion Molecules Levels among patients group:

Variable	sNCAM (n=32)		cVCAM (n=32)	
	r	P	r	P
sVCAM	0.75	<0.001**		
sICAM	0.64	<0.001**	0.70	<0.001**

r: Spearman's correlation coefficient **: Highly significant (P<0.001) sNCAM; serum Neural Cell Adhesion Molecule sVCAM: serum Vascularl Cell Adhesion Molecule
sICAM: serum intercellular Cell Adhesion Molecule

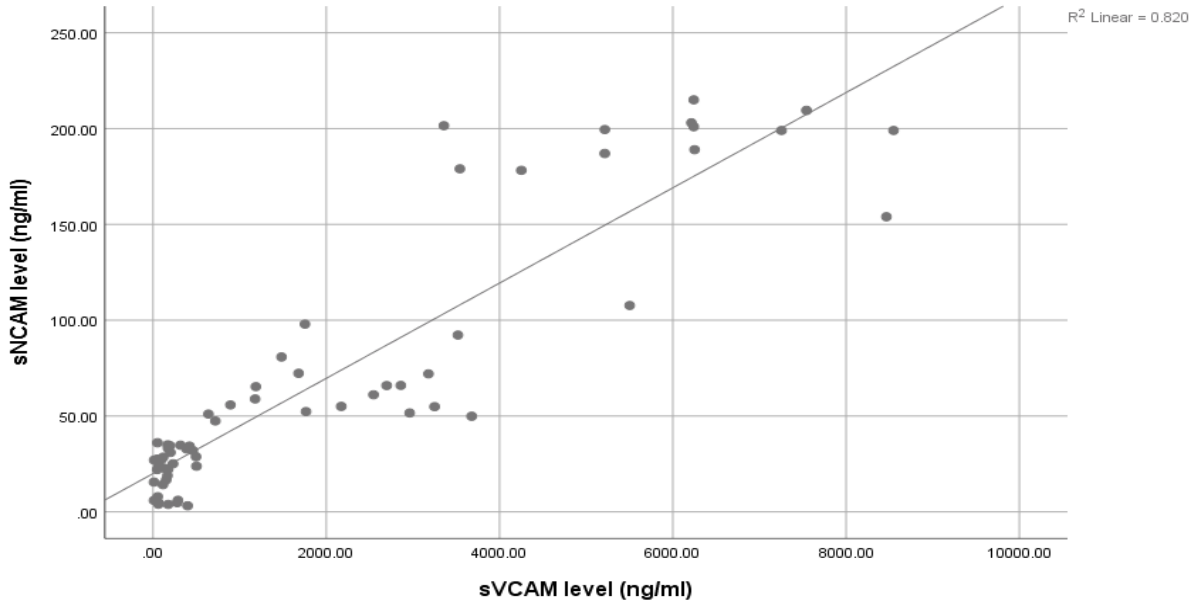

Figure (4): Correlation between sVCAM and sNCAM among Group I.

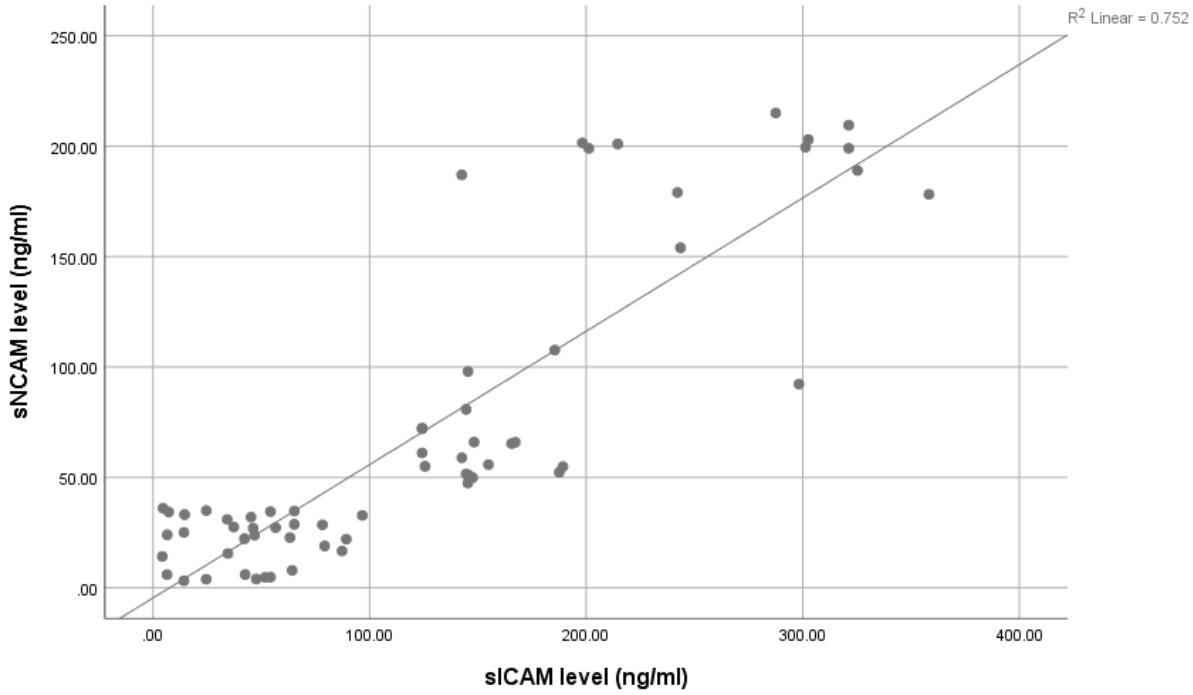

Figure (5): Correlation between sICAM and sNCAM among Group I.

4.Discussion

Multiple sclerosis (MS) is a chronic complex neurodegenerative disease, targeting the central nervous system (CNS) and widely believed to be autoimmune in nature. it is mediated by auto reactive lymphocytes that cross the blood-brain barrier (BBB) and enter the CNS where they cause local inflammation that results in demyelination, gliotic scarring, and axonal loss **(19).**

The members of the immunoglobulin superfamily, intercellular adhesion molecule-1 (ICAM-1) and vascular adhesion molecule-1 (VCAM-1), through binding to integrins LFA-1 and VLA-4 respectively, are critical in leucocyte-endothelia interaction, promoting the immuno inflammatory response in MS **(20).**

In our study, we aimed to find correlation between serum level of soluble cell adhesion molecules and the clinical severity assessment using Expanded Disability Status Scale and Magnetic Resonance Imaging findings in patients with Multiple Sclerosis disease.

Our study was carried out on 32 patients with clinically definite multiple sclerosis (18 patients with Relapsing Remittent MS (3 males &15 females), 4 males with Primary Progressive MS and 10 females with secondary progressive MS) who met the criteria of clinically definite MS according to Revised McDonald Crieteria 2017, also 32 age and sex matched healthy volunteers as control group were be included in this study.

Regarding sex disrtriution, in our study, Female patients formed 78.1% of patients , while males patients formed 21.9 % of the patients in group as a ratio of females : males equals to 3.6:1.

This was in agreement with Egyptian registry on MS patients with ratio was 2.14:1.0 **Hamdy et al., (21)** and an Egyptian multicenter registry study of clinical characteristics of

patients with multiple sclerosis that enrolled 950 Egyptian patients reported female dominance in MS patients with female to male ratio was 2.57:1 **(22)**

In our study, we reported that the most frequent MS subtype among the studied cases was RRMS 56.3% followed by SPMS 31.2% while PPMS found only in 12.5% of the selected cases.

Our Results were in accordance to **Kheradmand et al., (23)** who showed that RRMS was the most common subtype of MS among selected population , SPMS and PPMS, respectively, were the next most common subtypes. The clinical course of MS is very heterogeneous.

Regarding age distribution , our study reported that , in all MS patients groups ,Mean age of onset of first symptom was 33.28±8.21 with range 17-50 .,divided into 30.83±8.21 in RRMS patients , 43.5±4.36 in PPMS patients and 33.6±6.45 in SPMS ,these findings revealed that there was a statistical significance increase in mean age of onset among PPMS cases compared to RRMS cases.

This was in agreement with the reported large Egyptian epidemiological MS study conducted by **Zakaria and colleagues (22)** found that the mean age of onset was 36.17 ± 7.6 years, **Sidhom et al., (24)** found that Mean age of onset of MS among Tunisian population was 35.3 ± 9.5 years and 30.2±10.2 years in Lebanon .

As regards disease duration among all MS patients , the mean of disease duration was 4.91±2.66 , in RRMS patients 3.22±1.66, PPMS patients 4.75±0.96 and in SPMS 8±1.56 , there was a statistically significant increase in mean disease duration among SPMS cases compared to other types.

This was in accordance with other studies **of Abd El-Rahman et al., (25); Zakaria et al., (22)**who revealed increasing in the disease duration in SPMS 9±1.45 compared to PPMS 6.54 ±1.24 and RRMS 4.4±0.24.

In contrast, a study done by **Llufriu et al. (26),** who reported a higher disease duration that was 10.3± 9.7 years among RRMS than progressive types of MS patient, these differences between studies originated from diverse inclusion criteria, distinctive ethnic and geographical variations.

On Doing Expanded Disability Status Scale (EDSS) in different MS groups ,we found that high grades of disability among progressive MS patients more than that of RRMS subtypes.

There was a statistically significant increase in mean EDSS among SPMS cases compared to RRMS cases.

These Findings were in agreement with previous puplished studies of **Bacioglu et al, (27)** and the study of **Kavaliunas et al, (28)** that found EDSS score in SPMS 3.6-6.5, PPMS 2.5-8 and RRMS 1.5-6 with the higher grades of EDSS among progressive rather than relapsing subtypes of MS.

On the other hand, **Reich et al, (29)** reported that in relapsing-remitting multiple sclerosis patients (RRMS) disability progressively accumulates over time and their studies contained large numbers of RRMS patients with high opportunity of longer duration of disease disability accumulation, so their studies revealed higher EDSS score among RRMS and SPMSS subtypes patients compared to PPMS subtype patients.

The results of the current study reported that there was a statistically significant increase in T2-LV, T1-LV and decrease in Normalized Brain Volume NBV among PPMS and SPMS cases compared to RRMS cases. No difference was found between PPMS &SPMS patients in all MRI characters.

Our findings that were supported by studies of **Ortiz, et al (4) and Iwanowski,et al (5)** that found that statistical paramerters of T2V and T1V MRI lesions increased in progressive types of MS compared to RRMS subtypes while there was decrease in NBV parameters among progressive rather than RRMS subtye.

The members of immunoglobulin superfamily, ICAM-1, VCAM-1 and NCAM through binding to integrins are critical in leucocyte-endothelia interaction, promoting the immune-inflammatory response in Multiple Sclerosis and to be considered as markers of blood-brain barrier disruption and might regulate functions of the corresponding cell-bound forms **(30).**

These Cell Adhesion molecules are attractive targets for directed immunomodulatory therapies for several reasons. First, such therapies are not dependent on antigen specificity. Secondly, selective regulation of different adhesion molecules allows the possibility of differentiated treatment strategies in different autoimmune conditions **(31).**

In our study findings ,There was was a statistically significant increase in all Serum Cell Adhesion Molecules Levels among MS patients group compared to control group. In MS patients ,sNCAM level (ngm/ml) was 117.9±65.6 , sVCAM level (ng/ml) was 3812.59±2334.71 and sICAM level (ng/ml) was 202.18±73.30, with highest serum levels of sVCAM followed by serum levels of sICAM and the least levels of sNCAM among MS patients compared to control group .

our study was in agreement with other previous studies of **Niezgoda,et al , (32) and Khan, et al , (6)** and the study of **Ziliotto,et al (31)** which found that higher serum levels of adhesion molecules in MS patients compared to control group and no significant differences in sICAM-1 plasma levels were observed between the study groups.

In our study , we reported also that there were statistically differences between MS patients subgroups regarding serum adhesion molecules ,there was a statistically significant increase in sNCAM level in PPMS and SPMS groups compared to RRMS group and there was a statistically significant increase sVCAM level in PPMS and SPMS groups compared to RRMS group and in SPAM compared to PPSM group. Finally, there was a statistically significant increase in sICAM level in SPMS groups compared to RRMS and PPMS groups

Our findings were in agreements with many pevious published studies of **Kappus,N et al , (18), Khan , et al , (6) Lassmann, (19),** and the study of **Ziliotto,et al (31)** that reported

that serum levels of of sVCAM and sNCAM elevated in patients with SPMS and PPMS compared to RRMS serum levels , while there was no difference between seum levels of sICAM in MS subtypes.

Our study also came in agreement with data obtained from previous studies of **Niezgoda,et al , (32) and Khan, et al , (6)** that revealed that the comparison between the levels of soluble cell adhesion molecules in different MS subtypes with higher levels of VCAM -1 in SPMS than RRMS or PPMS and the higher levels of sNCAM in SPMS than both PPMS and RRMS ,but there was no significant differences regarding serum levels of ICAM in different MS subtypes.

Also **Zivadinov et al, (12)**, **Massaro et al (33),** and the study of **Langer-Gould et al, (34)** that **revealed** higher plasma levels of sNCAM in PPMS patients compared to SPMS and RRMS , increased levels of sVCAM were also detected in sera of patients with various types of MS compared to control group but there was no differences of their levels in MS subtypes compared to each other.

Lassman et al , (19) found that the serum levels of all adhesion molecules elevated by different propotions in all MS subtypes throughout the course of the disease ,levels might be elevated in exacerbation , up regutlated levels were also detected in clinically stable phase of SPMS which indicate leucocyte endothelial activation in acute and stable MS, the differences between the chronically progressive types MS and RRMS suggest that the cellular sourse of the adhesion molecules and the kinetics of cleavage of endothelial cell surface molecules to their soluble form may differ in relapsing and chonic progressive disease course.

The present study revealed also that study that there was a statistically significant positive correlation between all Serum levels of Cell Adhesion Molecules and disease duration and but there was a statistically significant positive correlation only between sNCAM and age of first symptom onset ($p<0.001$).

The current study also found that there was positive correlation between serum levels of all cell adhesion moleules and EDSS .

Our findings were in agreement with previous studies of **Streber et al, (35) and van Munster CEP et al, (9) , Niezgoda,et al , (32)** and the study of **Khan, et al , (6)** that found the positive correlation between serum levels of VCAM , ICAM and EDSS but there was negative correlation between EDSS and serum levels of NCAM.

Our study also found that there was a statistically significant increase in sNCAM & sVCAM levels among patients treated with Rituximab compared to patients who received other DMT like Interferone B and Fingolimode or patients who did not receive any DMT , but there was no a statistical significance difference in sICAM levels among patients treated with any DMT or patients who did not receive any DMT.

Our findings agreed with previous studies of **Lassmann, et al (19), De Angelis et al , (36)** and the study of **Ortiz,et al (4)** that found a noticeable correlation between sNCAM and

sVCAM-1 plasma levels observed in patients grouped by Rituximab , but other patients treated by drugs other than Rituximab displayed the lowest levels .

Regarding MRI changes in different MS groups , our study revealed that there was a statistically significant positive correlation between all Serum Cell Adhesion Molecules and T2LV and T1LV and also there was a statistically significant negative correlation between all Serum Cell Adhesion Molecules and NBV.

Our study findings were in agreement with previous studies of **Zivadinov, et al (12) , Reich et al ,(29) ,**and the study of **De Angelis et al ,(36)** that revealed that patients with diagnosis of progressive MS in MRI data presented with higher levels of sVCAM and sNCAM and significant differences in MRI measures of disease severity

While the studies of **Lassmann, et al, (19)** and **Ziliotto,et al (31)** revealed that there was negative correlation between adhesion molecules serum levels and MRI measures of disease severity.

In our present study , we found there was a statistically significan positive correlation between Serum Cell Adhesion Molecules and each other's ($P<0.001$) .

Our study came in agreement with previous studies of **Niezgoda,et al , (32) , and Khan, et al , (6) Lassmann, (19) ,** and the study of **Ziliotto,et al (31)** who revealed anoticeable correlation between sNCAM and sVCAM-1 plasma levels, and no correlation between serum ICAM-1 with other adhesion molecules.

Conclusion:

In conclusion, Multiple Sclerosis is an unpredictable ,often disabling disease of the central nervous system involving an immune mediated process in which an abnormal response of the immune system of the body is directed against the central nervous system, several adhesion molecules are involved in immune-inflammatory proceses promoting progressive neurodegenerative disability of the central nervous system and increasing the brain atrophy, so we can assess serum level of soluble adhesion molecules to find the association between their serum levels & clinical assessment and Magnetic Resonance Imaging findings of disease severity in Multiple Sclerosis patients

Conflict of Interest: None

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