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Gingival and Salivary Changes in Correlation with Multiple Sclerosis

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Abstract

Multiple sclerosis: chronic degenerative autoimmune disease of the central nervous system marked by patchy destruction of the myelin sheath that surrounds the nerve fibers. The gingival or oral changes that associated with multiple sclerosis might be related to disease itself or as sequel of medications that used for treatment. Aims;-to determine the gingival index and assess the SIgA, SFR and PH in MS patients in compare to control group as well as analyses theses parameters according to age group, gender and type of MS. 36 patients with proven diagnosis of MS were selected randomly between 1st Nov.2016-1st nov.2017 from MS center. Medical city .Baghdad. Iraq. Oral examination was done to measure the gingival index as well as saliva was taken to assess the salivary IgA level, salivary flow rate and PH of saliva, in addition 20 subjects who are free of MS or any others autoimmune disease were selected as control group. The GI of patients group was significantly higher than control group(3.4 ,1.4) respectively while the SIgA ,SFR and PH of saliva was significantly lower with patients group in compare to control group510,0.56,6.6 for patients group) 941.8,1.7,7.1 for control group

Key word: *Multiple sclerosis, salivary immunoglobulin A, gingival index, saliva flow rate*

Introduction

Multiple sclerosis (MS) is a progressive, neurodegenerative disorder of the myelin sheath, in which plaques created on the central nervous system (CNS) alter nerve function. (1) Although the exact cause of MS is unknown, a combination of genetic susceptibility, environmental factors, immune system response and systemic inflammation is suspected. Progression of MS and new plaque formations cause CNS changes in motor, sensory and cognitive functions, leading each individual to experience symptoms that vary in degree and severity.(2) The prevalence of MS varies considerably, from high levels in North America and Europe (>100/100,000 inhabitants) to low rates in Eastern Asia and sub-Saharan Africa (2/100,000 population). Concerning mortality, in a large French cohort of 27,603 patients, there was no difference between MS patients and controls in the first 20 years of the disease, although life expectancy was reduced by 6–7 years in MS patients ·MS starts attacks people from age 20–50 years old and the records investigated that females' attacks double than males' attacks (3) There are 4 types of MS. They're named according to the way the disease acts on the body over time. Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system (CNS), usually characterized by a relapsing-remitting (RR) course, or by disability accrual over an extreme variability of time. At diagnosis, about 75% of persons with MS suffer from RRMS, while about 25% of such persons will convert to secondary progressive MS (SPMS) within two to three decades from the onset. About 10% of patients with MS manifest primary progressive MS (PPMS) at diagnosis, and they show gradual worsening of neurological disability from symptom onset (4) . With the term progressive MS (PMS), we usually refer to the combined population of secondary progressive MS (SPMS) and primary progressive MS (PPMS) that still remains a distinct phenotype in the 2013 revision of clinical course in MS (5)

THE 4 TYPES OF MS

Relapsing-Remitting MS (RRMS). This is the most common form of multiple sclerosis. About 85% of people with MS are initially diagnosed with RRMS. People with RRMS have temporary periods called relapses, flare-ups or exacerbations, when new symptoms appear (6)

 Secondary-Progressive MS (SPMS). In SPMS, symptoms worsen more steadily over time, with or without the occurrence of relapses and remissions. Most people who are diagnosed with RRMS will transition to SPMS at some point [7]

 Primary-Progressive MS (PPMS). This type of MS is not very common, occurring in about 10% of people with MS. PPMS is characterized by slowly worsening symptoms from the beginning, with no relapses or remissions2

 Progressive-Relapsing MS (PRMS). A rare form of MS (5%), PRMS is characterized by a steadily worsening disease state from the beginning, with acute relapses but no remissions, with or without recovery2 [6]

The hypothesis states that the pathophysiology of MS is related to myelin antigen-specific CD4+ T cells which become activated. The exact trigger for the activation of the T cells is still unknown. One theory suggests that T cells might become activated by cross-reacting with a particular antigen, such as a microbial agent, known as "molecular mimicry". This theory explains why some viruses have been studied as a possible trigger for the disease. These cells then cross the blood-brain barrier, recognize myelin basic protein, attack the neuronal myelin sheaths, and trigger the onset of muscular symptoms and can lead to cognitive decline. These areas of axonal damage are known as lesions. The actual mediator of myelin and axonal destruction has not been established, but it may reflect a combination of macrophages, antibodies, cytokines, and reactive oxygen intermediates.[8] To our knowledge this is the first study in our country studying the changes in salivary IgA, SFR, PH of saliva in MS patients in compare to control health group as well as assessment the changes according to type of MS.

Subjects and methods

Between 1st Nov.2016-1st Nov.2017 and after approval was obtained from concerned authouritis,36 patients with proven diagnosis of MS who are attending the MS center of medical city. Baghdad.Iraq were selected randomly and oral examination was doing to measure the Gingival Index as well as saliva was taken to assess the salivary IgA level, Salivary Flow Rate and PH of saliva, in addition 20 subjects who are free of MS or any others autoimmune disease were selected as control group.

Saliva sample:

Un stimulated whole saliva (2 ml) were collected from patient group and control by expectoration into sterilized vials then saliva sample were centrifuged at 12000 rpm for 10 minutes and the supernatants were stored at -20˚C until use .

Estimation of SIgA by ELISA procedure of the test: -

1- Standard was constituted to 1000 pg/ ml with standard dilution buffer. a serial diluents of the standard were prepared from original standard.

2- One hundred ml of standard or sample was added per well, then 100 ml of diluent were added for each well. The plate was incubated for 4 hours.

3- The contents of well were discarded and washed by washing solution.

4- Two hundred ml of conjugate reconstituted was added into each well and incubated at 25 C° and then washed three times.

5- Two hundred ml of substrate was added into each well, followed by incubation for 15 minutes at 25 C° with continuous shaking in the dark.

6- Fifty ml of stopping solution H_2SO_4 was added into each well and mixed gently.

7- Absorbance was measured by spectrophotometer at 450 nm within two hours.

The flow rate of saliva (SFR) ml/min was estimated by dividing the total collected saliva volume (ml)by collecting time (min) that was measured by sample collection:

SFR ml/min = saliva sample volume (ml)/ collection time (min). Salivary pH was measured with a digital pH-meter (Hanna Instruments, USA) 30 to 60 minutes after saliva samples were collected, and pH was considered as a quantative variable. The BMI for a person is defined as their body mass divided by the square of their height with the value universally being given in units of Kg/m^2.

Statistical Design

SPSS version 23 was used for data entry and analysis, mean and standard deviation was used to represent the continuous data. ANOVA and student t test were used

to confirm significance. P-value≤0.05 was considered significant.

Results and Discusion

The findings indicated that the mean age of patients group was 37.2±4.3, 47.2% belong to age group of 20-40 years,75% was females and 72.2% of RRD type. With regards to control group; the results revealed that the mean age was 38.7±6.8 years, 45.5% was fall to age group of 20-40 years and 63.6% was females as seen in table.1.

Table.1. descriptive characteristics of studied groups

		Groups			
	Patients(n=36) Mean age=37.2±4.3years		Control(n=22) Mean age=38.7±6.8 years		
	No.	%	No.	%	
Age groups	<20	8	22.2%	6	27.3%
	20-40	17	47.2%	10	45.5%
	>40	11	30.6%	6	27.3%
Gender	Female	27	75.0%	14	63.6%
	Male	9	25.0%	8	36.4%
Type	RRD	26	72.2	-	-
	SPD	3	8.3	-	-
	PPD	4	11.1	-	-
	PRD	3	8.3	-	-

The results demonstrated that the mean value of GI, SIgA, SFR and PH of patients group were significantly higher than that of control group (p≤0.05 for all) as displaced in table.2.

Table.2. Mean of GI, SIgA, SFR and PH of patients and control group.

	Groups				
	Patients group		**Control group**		
	Mean	**Std. Deviation**	**Mean**	**Std. Deviation**	**p-value**
GI	3.4	0.6	1.4	0.5	0.01
SIgA	510.8	59.7	941.8	63.8	0.01
SFR	0.56	0.1	1.7	0.2	0.01
PH	6.6	0.2	7.1	0.1	0.01

Our data showed that the mean value of GI was significantly increased with aging while the mean value of SIgA, SFR and PH were decreased as the patient get elderly but the significant difference was reported with SIgA and SFR only as illustrated in table.3.

Table.3. Mean of GI, SIgA, SFR and PH of patients according to age groups

		N	Mean	Std. Deviation	p-value
GI	<20	8	2.8	0.3	0.01
	20-40	17	3.1	0.2	
	>40	11	3.4	0.12	
SIgA	<20	8	561.0	58.8	0.02
	20-40	17	512.0	62.3	
	>40	11	415.3	66.1	
SFR	<20	8	0.6	0.05	0.03
	20-40	17	0.4	0.1	
	>40	11	0.3	0.08	
PH	<20	8	6.5	0.05	0.09
	20-40	17	6.4	0.23	
	>40	11	6.1	0.18	

The results showed there was no significant difference ($p \geq 0.05$ for all) regarding the mean value of GI, SIgA, SFR and PH when compared according to the type of multiple sclerosis, however the patients who had remission relapsing type showed higher value for all these studied parameters but the difference did not reach the significant level as displaced in table 4.

Table.4. mean of GI, SIgA, SFR and PH of patients according to MS types

		N	Mean	Std. Deviation	p-value
GI	RRD	26	3.6	0.5	0.06
	SPD	3	3.4	0.3	
	PPD	4	3.5	0.7	
	PRD	3	3.4	0.4	
SIgA	RRD	26	517.4	67.3	0.06
	SPD	3	482.0	69.2	
	PPD	4	502.8	66.4	
	PRD	3	506.7	61.8	
SFR	RRD	26	0.6	0.08	0.07
	SPD	3	0.4	0.05	
	PPD	4	0.5	0.08	
	PRD	3	0.5	0.15	
PH	RRD	26	6.7	0.18	0.09
	SPD	3	6.4	0.25	
	PPD	4	6.4	0.08	
	PRD	3	6.6	0.2	

Cont... **Table (4): Association between (IgG) and (IgM) anti -*T.gondii* seropositivity and risk factors**

The result of current study demonstrated that the mean value of GI, SIgA, SFR and PH of MS patients were higher with females in compare to male patients but the difference not significant statistically (p≥0.05for all) as showed in table 5.

Table.5. mean of GI, SIgA, SFR and PH of patients according to their gender.

	gender				p-value
	Female(N=27)		Male(N.=9)		
	Mean	Std. Deviation	Mean	Std. Deviation	
GI	3.6	0.4	3.4	0.3	0.06
SIgA	562.4	78.8	554.3	81.03	0.07
SFR	0.6	0.1	0.5	0.09	0.7
PH	6.5	0.2	6.6	0.15	0.09

The results showed there was significant direct correlation between duration of disease in years and gingival index while negative correlation was reported between each of SIgA, SFR and PH and duration of disease as displaced in table.6.

Table.6. correlation of age,

		GI	SIgA	SFR	PH
Duration	Pearson Correlation	0.8**	-0.9**	-0.9**	-0.3
	p-value	0.001	0.001	0.001	0.1

Multiple sclerosis (MS) is a chronic inflammatory demyelinating disorder of the central nervous system affecting white and possibly grey matter. MS characterized by multiple focal demyelinating lesions affecting the white matter, which is not infrequently associated with cortical demyelination. The finding of this study indicated that the mean age of patient group was 37.4±6.3 SD (ranged from 20-40) year while the control group was 36.3±4.8 SD years old. The studies showed that the age at MS onset follows a similar pattern across different regions, with incidence low in childhood, rapidly increasing after adolescence, reaching a peak between 25 and 35 years, and then slowly declining [11], this opinion support our work in the term of spread of the MS in this age group. With regard to gender distribution, our data indicated that female was 75% of patient group and 63.6% of control group, this result in consistent with finding of other studies that revealed the women are affected more commonly than men, with the female-to-male ratio varying between 1.5:1 and 2.5:1, with a trend toward higher values in the most recent studies [17,18]. Recent research though anyone can be affected, but MS most frequently occurs in white women ages 20 to 45. [1,2] According to some authors the lifetime risk of developing MS in high-risk populations is approximately 1 in 200 for women which coincide our study, others supposed MS 3 times more common in females than in males. Although controversy surrounding sex factor. several investigators indicated that females had a relatively favorable course [19]. For salivary IgA changes that associated with MS, a studies reported that chronic stress mostly reported with MS patients result in an increased levels of salivary cortisol and decreased level of salivary IgA. [20]. This study revealed effect of

MS on saliva immunoglobulin A comparing with saliva of healthy individuals (control) group which show decreased salivary IgA levels as well as the (SFR) with duration. Increased autoimmunity with age may result from increased numbers of auto aggressive T-cells or reduced immune regulation. Autoimmune diseases with interleukin-17 as an important messenger cytokine may also be relevant in periodontitis [27], T cells protect from autoimmune inflammation despite reduced STAT3 activation and decreased constraint of IL-17 producing T cells. This may be an appropriate explanation for this outcome in this study. However, many other studies correspond our result it is observed Individuals with MS are at increased risk for dental caries, gingivitis and periodontitis due to the physical effects of MS, as well as these patients' reduced immune response [2,10]

Conclusion

The gingival index increased but the S.IgA, SFR, and s.PH in MS patients but we could not prove these changes due to the disease itself where they might be induced by used medications that used for MS treatment

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the College of Dentistry/Al-Mustansiriyah University and all experiments were carried out in accordance with approved guidelines.

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