



## The Study of the Correlation between Constipation and Fatigue in Patients with Multiple Sclerosis

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### Abstract

Fatigue and constipation are among the most common factors in multiple sclerosis patients. From the perspective of Persian Medicine, constipated patients are prone to fatigue and we suspected that this problem in patients with multiple sclerosis becomes more severe. The Rome III questionnaire is a valid instrument that measures the existence and severity of constipation and FSS is a scale to assess the scale of fatigue. The objective was to assess if there is an association between constipation and fatigue symptoms in patients with multiple sclerosis. Hence, 355 patients with multiple sclerosis participated in this study. Patients were divided into a constipated or non-constipated group and compared to determine the association between constipation and fatigue scores. It was seen that the level of fatigue and depression in the constipated group was significantly higher than those without constipation (P value < 0.001). According to the observed association between constipation and fatigue, and traditional Persian Medicine theories, constipation can lead to fatigue; patients with constipation had worse scores on the FSS questionnaires and future studies should assess if the treatment of constipation with suitable laxative drugs in multiple sclerosis patients leads to a reduction of fatigue.

**Keywords:** Fatigue, Constipation, Multiple Sclerosis, Traditional Medicine, Quality of life, Questionnaires

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## Introduction

Multiple sclerosis (MS) is the most common and disabling neurological disease of the central nervous system affecting young adults. On the other hand, MS is an autoimmune disorder stimulated by environmental factors acting in persons who have susceptible factors genetically [1, 2].

Fatigue is one of the most frequent and disabling symptoms of multiple sclerosis, reducing the quality of life [3-6]. The prevalence of fatigue is reported in 75% of patients according to different studies [4] and 55% of all of patients with MS believe it to be one of their worst symptoms [7]. The level of MS-related fatigue is not fully known [8]. Mill and Young defined fatigue in MS as “a reversible, motor and cognitive impairment with reduced motivation and desire to rest either appearing spontaneously or brought on by mental or physical activity humidity acute infection and food ingestion. It can occur at any time but is usually worse in the afternoon. MS-related fatigue is usually daily, patients suffer from it for years and it has a greater severity than any premorbid fatigue” [9, 10]. The fatigue in MS is different from the fatigue or tiredness in healthy individuals or other diseases and usually worsens with heat and humidity. Compared to relapsing, the remitting of the fatigue is more common in the primary and secondary stages of the disease [10]. Fatigue is the main reason for unemployment in patients with multiple sclerosis [11]. According to the frequency, severity and impact of fatigue, unemployment especially due to exhaustion, the identification and treatment of fatigue should be considered seriously [12, 13].

Bowel dysfunction is common in all stages of the disease. Constipation and or faecal incontinence are more frequent in MS, about two thirds of patients suffer from them. The prevalence of constipation is estimated as being between

43% and 73% [14-16]. Investigations showed that constipation as an effective factor in the community/mental disabling of multiple sclerosis patients and its treatment can be effective in improving quality of life [17, 18]. Based on theories in Traditional Persian Medicine (TPM) and the views of Avicenna, constipation has an important role in the normal physiological functioning of the human body. In PM, constipation is one of the main parts of many diseases and is known as the “mother of some diseases” and in all patients, gastrointestinal (GI) functions have been checked [19, 20]. Anecdotal evidence in our integrative neurology clinic guided us to study constipation in multiple sclerosis patients more and as different studies showed fatigue as the most common and disabling symptoms, we were encouraged to investigate the association between constipation and fatigue in patients with multiple sclerosis. In other words, the relationship between constipation and increased fatigue was investigated and vice versa.

## Methods

### *Patient sample*

Three hundred and fifty five patients with multiple sclerosis participated in this cross-sectional study at the multiple sclerosis research centre in Sina Hospital, Tehran, Iran. We asked patients to fill in the fatigue, depression and constipation questionnaires. The FSS and Beck questionnaires are used to measure fatigue and depression respectively, while the Rome III questionnaire is used to assess constipation.

The FSS (Fatigue Severity Scale) is a self-reporting questionnaire to measure fatigue in all individuals. It contains nine questions, measured by a seven-point Likert scale ranging from strongly disagrees to strongly agree. Lower scores indicate less fatigue in everyday life. The FSS was originally designed to assess fatigue in individuals with multiple sclerosis [21, 22].

The Beck Depression Inventory (BDI) is a 21-item, self-reporting questionnaire that measures symptoms of depression [23].

Rome III consists of 18 items. According to the Rome III criteria for constipation, a patient must have experienced at least two of the following symptoms over the preceding three months:

- Fewer than three bowel movements per week
- Straining
- Lumpy or hard stools
- Sensation of anorectal obstruction
- Sensation of incomplete defecation
- Manual manoeuvring required when defecating [24].

Of 355 patients, 17 patients were excluded due to the incomplete filling in of the questionnaire and 27 patients dropped out because of major depression, so 311 patients remained in this study.

Patients using tricyclic antidepressants for depression and patients who use amantadine for fatigue were not allowed to enter the study because these patients may face to fatigue or constipation due to the use of these drugs, respectively.

It should be noted that patients with severe depression are usually bring out because their answers about the severity of fatigue are not reliable. For this reason, it is necessary to measure the extent and severity of depression

### Statistical analysis

Descriptive statistics and differences for variables such as gender, type of MS, previous use of antidepressants, current use of antidepressants, depression, fatigue and the association of these with constipation were assessed using chi-square and t-student tests. A Pearson correlation coefficient was used to determine the association between depression and fatigue scores.

## Result

Of the 311 patients in the study, 82.8% were female, 86.4% had a RR (relapsing-remitting) type of MS, 26.4% of the participants had used antidepressant drugs previously, 41.9% used selective serotonin reuptake inhibitors (SSRIs) now (Table 1).

**Table 1:** Comparison between constipated and non-constipated patients

Variables	All patients (N = 311)	Patients with constipation (N = 170)	Patients without constipation (N = 141)	P-Value
Gender: female	256(82.8%)	147(87%)	109(77.9%)	0.034
Type of MS: (RR)	248(86.4)	129(81.6)	119(92.2)	0.009
Previous use of antidepressant	82(26.4)	50(29.4)	32(22.7)	0.181
Current use of antidepressant	111(35.7)	81(47.6)	30(21.3)	< 0.001
Pre-drug constipation	96(41.9)	76(61.3)	20(19.0)	< 0.001
Use of Amantadine	70(23.5)	44(27.2)	26(19.1)	0.103
Use of Levothyroxin	32(11.4)	22(14.1)	10(8.0)	0.110
Depression (no)	203(67.5)	95(65.5)	108(74.5)	0.001
Depression (mild)	45(14.5)	30(17.6)	15(10.6)	0.001
Depression (moderate)	45(14.5)	33(19.4)	12(8.5)	0.001
Fatigue Severity Scale (cut off point upper than 36)	125(40.2)	91(53.5)	34(24.1)	< 0.001
Fatigue Severity Scale (cut off point upper than 45)	60(19.3)	43(25.3)	17(12.1)	0.003

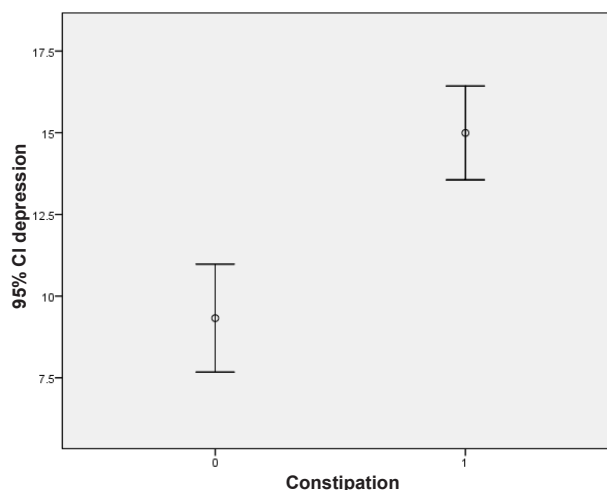
The Rome III, FSS and Beck questionnaires were used to assess constipation, fatigue and depression, respectively (Table 1).

There was not any significant relationship between constipation and previous use of antidepressants but there is a significant relationship between constipation and current use of antidepressants (Table 2).

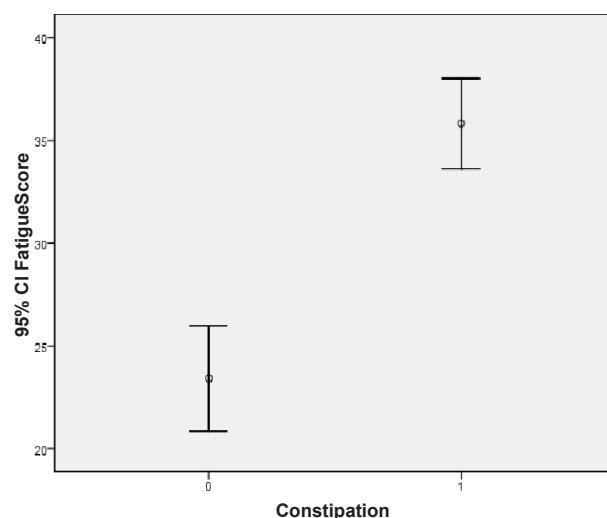
**Table 2:** comparison of fatigue and depression scores in constipated and non-constipated patients

	Constipation	N	Mean	Std. Deviation	P value
Age	No	139	33.58	9.402	0.208
	Yes	167	34.92	9.123	
Duration	No	133	5.4990	5.55978	0.118
	Yes	167	6.4714	5.15314	
Fatigue Score	No	141	23.42	15.360	<0.001
	Yes	170	35.82	14.525	
Depression Score	No	141	9.33	9.922	<0.001
	Yes	170	14.99	9.475	

Among patients with MS, constipation in females is considerably more than in males (P value: 0.034). Constipation in the RR type of MS is more than those with the Non-RR of MS too (P value: 0.009). (Table1).



**Chart 1:** Comparison of the mean of depression scores in constipated and non-constipated group



**Chart 2:** Comparison of the mean of fatigue scores in constipated and non-constipated groups

It was seen that fatigue and depression scores in patients with and without constipation are both significantly correlated ( $P$  value  $< 0.001$ ), (correlation coefficient: 0.368 & 0.406 respectively).

## Discussion

In our study for the investigation of the correlation between constipation and fatigue, patients with severe depression were excluded because their answers about the severity of fatigue are not reliable. Our research shows a significant association between constipation and fatigue symptoms. Patients with constipation had worse scores on the FSS questionnaires. Furthermore, constipation is severe in moderately depressed patients compared with non-depressed patients or those with mild depression.

Most patients with multiple sclerosis complain of constipation or faecal incontinence and these bowel symptoms have a major impact on their life. In Persian Medicine and Avicenna point of views, physicians believed there is a relationship between constipation and many diseases, especially the nervous system, so we seek to prove this correlation between constipation and fatigue, because fatigue is one of the most common and disabling symptoms of MS.

## Conclusion

Our study included a large number of patients with MS at Sina Hospital, Tehran, Iran, and this was the first investigation to assess the correlation of constipation and fatigue symptoms in patients with MS.

Our investigation showed that constipation and its severity may cause patients with MS to feel fatigue symptoms more than other patients without constipation. Constipation and fatigue are very common in MS, and future studies should assess if the treatment of constipation with lax-

ative drugs leads to a reduction of fatigue and depression.

In fact, we demonstrate that constipation in patients with MS is significantly associated with symptoms of fatigue and future studies will investigate if the treatment of constipation can improve fatigue symptoms in patients with MS.

## Conflict of Interests

None.

## Acknowledgments

None.

## References

- [1] Rejdak K, Jackson S, Giovannoni G. Multiple sclerosis: a practical overview for clinicians. *Br Med Bull* 2010;95:79-104.
- [2] Zahednasab H, Mesbah-Namin SA, Sahraian MA. Relationship between NF\_kB1-94 ins/del ATTG polymorphism and susceptibility of MS in Iranian MS patients. *Neurosci Lett* 2013;545:46-49.
- [3] Krupp LB, Alvarez LA, LaRocca NG, Scheinberg LC. Fatigue in multiple sclerosis. *Arch Neurol* 1988;45:435-437.
- [4] Yusuf A, Koshi L. A qualitative review of the neurological under pinning of fatigue in multiple sclerosis. *J Neurol Sci* 2013;330:4-9.
- [5] Bakalidou D, Giannopoulos S, Stamboulis E. Effect of seasonal fluctuation of ambient temperature on fatigue in multiple sclerosis patients living in attica, Greece. *J Clin Neurosci* 2014;21:1188-1191.
- [6] Thelen J M, Lynch GS, Bruce AS. poly pharmacy in multiple sclerosis: relationship with fatigue, perceived cognition, and objective cognitive performance. *J Psychosom Res* 2014;76: 400-404.
- [7] Andreasen AK, Stenage E, Dalgas U. The effect of exercise therapy on fatigue in multiple sclerosis. *Mult Scler Journal* 2011;17:1041-1054.
- [8] Bol Y, Duits AA, Hupperts RMM. The psychology of fatigue in patients with multiple sclerosis: A review. *J Psychosom Research* 2009;66:3-11.
- [9] Mills RJ, Young CA. A medical definition of fatigue in multiple sclerosis. *QJM* 2008;101:49-60.
- [10] Induruwa I, Constantinescu CS, Gran B. Fatigue in multiple sclerosis. A brief review. *J Neurol Sci* 2012;323:9-15.

- [11] Ziemssen T. Multiple sclerosis beyond EDSS: depression and fatigue. *JNS* 2009;277:37-41.
- [12] Branas P, Jordan R, Fry-Smith A. Treatments for fatigue in multiple sclerosis: a rapid and systematic review. *HTA* 2000;4:1-61.
- [13] Geoffrey L, Sheean NM, Rothwell JC, Miller DH, Alan J. An open-labelled Brain, 1998;121:967-975.
- [14] De Seze J, Stojkovic T, Gauvrit JY. Autonomic dysfunction in multiple sclerosis: cervical spinal cord atrophy correlates. *J Neurol* 2001;248:297-303.
- [15] Hinds JP, Eidelman B, Wald A. Prevalence of bowel dysfunction in multiple sclerosis. *J Gastroenterol* 1990;98:1538-1542.
- [16] Gulick EE. Bowel management related quality of life in people with multiplesclerosis: psychometric evaluation of QOL-BM measure. *IJNS* 2011;48:1066-1070.
- [17] Wiesel PH, Norton C, Roy A. Gut focused behavioural treatment (biofeedback) for constipation and faecal incontinence in multiple sclerosis. *JNNP* 2000;69:240-243.
- [18] Winge K, Rasmussen D, Werdelin LM. Constipation in neurological diseases. *J Neurol Neurosurg Psychiatry* 2003;74:13-19.
- [19] Avicenna H. The Canon in Medicine. Institute of Al-A'lami Li Al-Matboat. Beirut 2005.
- [20] Hamed SH, Jokar A, Abbasian A. Viewpoints of Iranian Traditional Medicine (ITM) about Etiology of Constipation. *J Gastro int Dig Syst* 2012;S8:005.
- [21] Krupp LB, LaRocca NG, Muir-Nash J. The Fatigue Severity Scale: Application to patient with Multiple Sclerosis and Systemic Lupus Erythematosus. *Arch Neurol* 2008;46:1121-1123.
- [22] Ziino C, Ponsford J. Measurement and prediction of subjective fatigue following traumatic brain injury. *JINS* 2005;11:416-425.
- [23] Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry* 1961;4:561-571.
- [24] Longstreth GF, Thompson WG, Chey WD. Functional bowel disorders. *J Gastroenterol* 2006;130:1480-1491.