

Factors Affecting Compliance of Therapeutic Regimen among Patients with Multiple Sclerosis

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Abstract

Background: Multiple sclerosis is a chronic, autoimmune, demyelinating disease of the central nervous system. Multiple sclerosis is an incurable disease. The goal of disease-modifying therapies is to slow the progression of the disease, prevent relapses and increase the patient's overall quality of life. **Aim of the study** was to assess factors affecting compliance regarding therapeutic regimen among patients with multiple sclerosis. **Subjects and Method: Research design:** A descriptive design was utilized. **Setting:** This study was conducted in outpatient neurology clinics (MS unit) at Zagazig University Hospitals, Egypt. **Subjects:** A purposive sample of (105) patients with MS. **Tools of data collection:** Two tools were used for data collection. Tool (I) an Interview questionnaire to assess demographic characteristics of studied patients. Tool (II) a Questionnaire to assess factors affecting patients' compliance regarding therapeutic regimen. **Results:** Current study revealed that the mean age of all patients was 32.5 ±6, (63.8%) were females, and mean of disease duration per years was 4.7±2.6. (30.5%) of studied patients affected by physical factors, (64.8 %) affected by socioeconomic factors, (76.2%) affected by health care team and system related factors (83.8%) affected by psychological factors, (84.8%) affected by therapy related factors, (85.7%) affected by factors related to patient's belief. In multiple linear regressions, belief score was positive predictor of total therapeutic compliance score with p. value was 0.013. While psychological factor and therapy related factor were negative predictors of total therapeutic compliance score with p. value was (0.014 and 0.0001 respectively). **Conclusion:** The study finding concluded that several factors affected on therapeutic compliance as physical factors, socioeconomic factors, psychological factors, patients' belief related factors, therapy related factors, and healthcare team and system related factors. **Recommendations:** Further studies to assess factors affecting compliance with therapeutic regimen among patients with multiple sclerosis.

Keywords: Factors, Multiple sclerosis, Therapeutic Regimen, Compliance.

Introduction:

Multiple sclerosis (MS) is a chronic demyelinating autoimmune disorder affecting the central nervous system and targets the myelin sheaths around nerves, leading to inflammation, myelin loss, and axonal destruction. It is the most common cause of neurological disability among people aged between 20 and 50 years.¹ MS affects about 2.8 million people worldwide.²

Patients are grouped into four major categories based on the course of disease: relapsing remitting MS (RRMS), primary progressive MS (PPMS), secondary progressive MS (SPMS) and progressive relapsing MS (PRMS).³

The estimated prevalence of MS in Egypt was about 25/100.000 in different centers, it attacks women more than men with prevalence ratio reaches 3.2:1.⁴ The main cause of MS clinical symptoms are the plaques which develops in the white matter of the CNS due to inflammation which deter transmission of regular electrical impulses, lead to one or more of the following symptoms; blurred vision, blindness, loss of balance, poor coordination, slurred speech, tremors, numbness, extreme fatigue, problems with memory or concentration, paralysis, loss of cognitive functioning, and psychological disturbances most often characterized by depression lead to temporally or terminal problems.⁵

Early detection of MS is important because it gives us the opportunity to seek treatment and plan for the future. An exact diagnosis of MS is based on medical history and neurological examination using imaging techniques such as magnetic resonance imaging (MRI), lumbar punctures (LP) for cerebrospinal fluid (CSF) analysis, evoked potentials, and blood samples analysis.⁶

Therapy can be divided into three main groups: abortive therapies, preventive therapies and the use of symptomatic drugs. In acute exacerbations, intravenous methylprednisolone in doses of 1000 mg for three to five days is recommended as an abortive therapy. Symptomatic therapies eliminate or reduce the symptoms such as fatigue, cognitive impairment, depression and sphincter dysfunction, which impair the quality the life in patients with MS. Preventive treatment uses disease- modifying drugs (DMDs), whose goal is to decelerate the progression of the disease.⁷

Compliance is not simply a matter of patient choice or will, but is affected by the interplay of multiple determinants of compliance that the World Health Organization (WHO) has classified into five different dimensions—condition-related factors, therapy-related factors, patient-related factors, socio-economic factors and healthcare team and system-related factors.⁸

Compliance has been defined by the World Health Organization "WHO" as the extent to which a person's behavior taking medication, following a diet, and/or executing lifestyle changes corresponds with agreed recommendations from a healthcare provider⁹. For MS patients taking disease-modifying therapies "DMTs", compliance to treatment is a key component of achieving beneficial outcomes, such as delayed disease progression and the reduction and prevention of symptoms and relapses.¹⁰

Means to measure medication adherence include questionnaires, pill counts, electronic monitoring and monitoring drug levels in blood or urine.

Monitoring drug levels is the most reliable method if the half-life of the drug is proper but it is costly and invasive. Contrary of those questionnaires often do not provide accurate and reliable assessments¹¹.

Strategies to improve medication adherence in older adults include appropriate formats for medication information, feedback about medication-taking patterns, inpatient self-medication programs, and external organizers. Educational and clinical expertise in the geriatric population is an asset in this area, so nurses should develop and implement patient-centered educational efforts. Information sharing and educational initiatives were measured and can improve adherence but alternative interventions should also be explored¹².

Significance of the study:

According to WHO in Multiple Sclerosis Atlas (2020) reported that an estimated 2.8 million people worldwide have MS and the MS prevalence is at least from 2 to 3 times affects women rather than men, (ratio 1:2).¹³. In 2009, the WHO found that only 50% of patients with chronic disease were adherent to their medications. A 50% level of adherence means that every second patient is not being treated properly. The treatment of chronic disease is quite a challenge and depends on various elements. A high level of compliance and adherence to therapeutic recommendations in chronic disease is connected with a better quality of life and lower rates of hospital visits.⁷

Aim of the study:

The aim of this study was:

To assess factors affecting compliance level regarding therapeutic regimen among patients with multiple Sclerosis.

Research Question:

1. What are the factors affecting compliance regarding the therapeutic regimen among patients with multiple sclerosis?

Subjects and Methods:

Research design:

A descriptive research design was used in this study. Descriptive research is usually defined as a type of quantitative research, though qualitative research can also be used for descriptive purposes.

Study Setting:

The study was conducted in neurology outpatient clinics (MS unit) at Zagazig University hospitals. Neurology clinic is located in the first floor and consisted of neurology clinic and MS unit and waiting area.

Study Subjects:

A purposive sample of (105) patients with MS. **Inclusion criteria;** agree to participate in the study, age between 20 and 40 years old, both sex, at least had average education, diagnosed with MS for at least one year, had no co-morbid serious chronic illnesses.

Tools of data collection:

In order to fulfill the objectives of the study two tools were used to collect necessary data:

Tool I: An interview questionnaire: It was developed by the researcher after reviewing of related literature in a simple Arabic language to avoid misunderstanding, and adapted from Taha et al.,¹⁴ & Gendy et al.⁽¹⁵⁾. It used to assess patient's demographics, past, present medical history and family history of the studied patient and composed of two parts:

Part one: Tool 1: Demographic characteristics of the studied patients. Which were composed of ten closed ended questions including patient's age, gender, marital status, job, type of work, level of education, residence, income, method of transportation.

Part two: Tool 1: Medical history of the studied patients. It concerned with assessment of past, present medical history and family history of the patients. Covered the following items: Past medical history which was consisted of (2 items): disease history, types

of diseases. Present medical history which was consisted of (9 items): Current diagnosis, disease onset, current treatment, duration of treatment, date of last attack, action during attack, frequency of attacks, type of investigations, preference route of drug administration. Gendy et al.¹⁵ Family history which was consisted of 2 questions: family history to multiple sclerosis, degree of relevance.

Tool II; Factors affecting patient compliance regarding therapeutic regimen among patients with multiple sclerosis which adapted from Abo Seliman et al¹⁶, & Abd Allah⁽¹⁷⁾ and modified by researchers to suite aim of the study. It was translated into Arabic language and included six items: physical factors included 9 points, psychological factors included 5 points, Socioeconomic factors included 7 points, therapy related factors included 8 points, factors related to patient beliefs included 4 points and factors related to health care team and system included 15 points.

1- Physical Factors of patient:

Includes four items: having physical problems, type of physical problem, having hearing problem, having visual problem.

2- Psychological Factors:

Includes five items: your psychological condition affected negatively with your disease, feeling that your disease has serious consequences on your health, having troubles at sleeping, feeling of depression and anxiety, feeling of low self-esteem.

3- Socioeconomic Factors:

Includes seven items: problems preventing follow up, type of problem, treatment cost, family go with patient for follow up, family encourage for compliance, family neglect the patient, disease causes problems in home and family.

4- Therapy related factors:

Includes eight items: taking many drugs several times a day, problems with medication times, duration of treatment, continuing treatment make you upset, side effects of treatment, effectiveness of medications, cost and availability of medications.

5- Factors related to patient beliefs:

Includes four items: compliance with treatment makes you feel constrained, compliance changes your lifestyle, compliance lead to dependence on others, effectiveness of treatment will decrease with time.

6- Factors related to health care team and system:

Includes fifteen items: doctor language, doctor care about your talk , answer all your questions, describe how to take treatment, maintain privacy, Provide health advice, education about disease, truthfulness and efficiency of the information about treatment, Far distances, Inconvenient opening time, doctor/nurse - patient relationship, effect of physician-patient relationship on compliance, waiting time, Routine procedures.

Scoring system:

Scoring system for factor items: Total score for whole factors assessment tool was calculated for every patient and the mean of total score was calculated. These scores were converted into percent scores. Patient compliance was affected with this factors when the total score equal or above 50% and not affected when the total score below 50% based on statistical analysis. The responds to these statements were on two scales as follows: Scored one grade for affected and zero for not affected.

Content validity and Reliability:

Content validity for Tool (I) and (II) were revised by a panel of five experts from different specialties including medical and nursing faculty staff, which included four assistant professors and one lecturer who reviewed the tool's content for clarity, relevance, comprehensiveness, understanding, and ease for implementation. All recommended modifications were done. Cronbach's alpha that used to measure the internal consistency (reliability of used tool) was reliable at 0.69 for total factors.

Filed Work:

The data collection phase lasted for 6 months during the period from the

beginning of January 2022 to the beginning of June 2022. The data were collected one day a week (Monday) from 9:00 am to 12:00 pm, the time used for finishing the self- administered questionnaire ranged between 15-20 minutes for each patient according to patients' physical and mental readiness. The first phase of the work is the preparatory phase that done by meeting with nurses the mentioned siting after obtaining the official permissions, to know the average number of patients coming to outpatient clinics and working days and clarify the objective of the study and applied methodology to ensure their cooperation. The second phase that done by meeting the patients, each patient was met individually, got a full explanation about the aim of the study and was invited to participate. The patient who gave his/her verbal informed consent to participate was handed the self-administered questionnaire and was instructed during the filling.

Pilot study:

A pilot study was conducted on 10 patients (10%) in the setting. The goal was to check the clarity, applicability, relevance and feasibility of the tools. And to identify the difficulties may be faced during the application. It also helped to estimate the time needed to fill in the sheets. Since no modifications were done.

Administration and ethical considerations:

An official permission for data collection in Zagazig University Hospitals was obtained from the hospital administrative personnel by the submission of a formal letter from the dean of the faculty of nursing Zagazig University explaining the aim of the study in order to obtain permission and help. Each subject (patient) was informed about the purpose, benefits of the study, and they were informed that their participation is voluntary, and they have right to withdraw from the study at any time without given any reason. In addition, confidentiality, and anonymity of the subjects were assured through coding of all data. The researcher assured that the data collected will be confidential and would be used only to assess compliance

level regarding therapeutic regimen among patients with multiple sclerosis.

Statistical analysis:

All data were collected, tabulated and statistically analyzed using IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp. Quantitative data were expressed as the mean \pm SD & median (range), Qualitative data were expressed as number & (percentage). Chi square test was used to compare between categorical variables. Spearman 'correlation coefficient was calculated to assess relationship between various study variables, (+) sign indicate direct correlation & (-) sign indicate inverse correlation, also values near to 1 indicate strong correlation & values near 0 indicate weak correlation. Multiple linear regression is a predictive analysis. Multiple linear regression is used to describe data and to explain the relationship between one dependent continues variable and one or more independent variables .All tests were two sided. p-value < 0.05 was considered statistically significant, p-value \geq 0.05 was considered statistically insignificant.

Results:

Table (1): Regarding age, the mean age of all patients was 32.5 ± 6 ranged from 21 to 40 years old, females in present study were 63.8 %. Regarding to marital status, 74.3% were married. (67.6 %) of studied patients had secondary education, (66.7%) not work, (66.7%) had insufficient income.

Table (2): Regarding medical history, Mean disease duration was 4.7 ± 2.6 , ranged from 1 to 10 years. Most of patients had relapsing multiple sclerosis (92.4%). Duration of treatment was 27.1 ± 15.6 and ranged from 12 to 108 months. 33.3% of patients had frequency episode of disease which managed at hospital .Regarding comorbidities, it revealed that high blood pressure was present in 6.7%, diabetes mellitus in 5.7%. Regarding family history, it showed that all patients (100%) had no family history of multiple sclerosis.

Table (3): Concerning factors affecting compliance with therapeutic regimen, the

present study revealed that physical factor affected in about one third (30.5%) of studied patients, psychological factor affected in the majority (83.8%) of studied patients, Socioeconomic Factor affected in more than two thirds (64.8%) of studied patients, therapy related factor affected in the majority (84.8%) of studied patients, factors related to patient's belief affected in the majority (85.4%) of studied patients, factors related to health care team and system affected in the majority (76.2%) of studied patients.

Table (4): Regarding Correlation matrix between patients' total compliance with therapeutic regimen and factors affecting their compliance, demographic characteristics and medical history. The current study revealed that there were positive statistical significant difference correlation between patients total compliance score and patients total knowledge score, belief factor score, duration of disease and duration of treatment, with p. value (0.007, 0.0001, 0.005, 0.003 respectively), while there were negative statistical significant difference correlation between patients total compliance score and psychological factor score, therapy related factors score and total factor, with p. value (0.0001, 0.0001, 0.01, respectively).

Table (5): Multiple linear regression model to predict therapeutic compliance score for patients with multiple sclerosis The study revealed that there were positive statistical significant predictors of therapeutic compliance score for patients with multiple sclerosis with belief score with $\beta = 2.36$, p. value was 0.013. While there was negative statistical significant predictors of total therapeutic compliance score with psychological factor score with $\beta = -1.82$, p. value was 0.014 and therapy related factor score with $\beta = -4.06$, p. value was 0.0001.

Discussion:

Demographic Characteristics and Medical History of Studied Patients

Regarding demographic characteristics, the present study revealed

that more than two thirds of studied patients were females, the mean age of all patients was 32.5 ± 6 ranged from 21 to 40 years old. Regarding to marital status, about three-quarters was married. Concerning the educational level, more than two thirds were secondary education; more than two thirds of studied patients were not working and had insufficient income.

This result is supported by Alhazzani, et al⁽⁹⁾ revealed that the mean age of the overall patient population was 32.4 ± 8.4 years. Schriefer, et al⁽¹⁸⁾ revealed that approximately three-quarters were females. Buja, et al⁽¹⁹⁾ revealed that about two thirds of studied patients were married.

Regarding diagnosis of studied patients, the present study revealed that nearly most of studied patients have Relapsing remitting multiple sclerosis. This is in agreement with Saiz, et al⁽²⁰⁾ revealed that most of studied patients experienced relapsing–remitting pattern of MS.

Regarding disease duration, the present study revealed that about two thirds of studied patients have the disease for more than 4 years with mean 4.7 ± 2.6 . This is in harmony with Ibrahim, et al⁽²¹⁾ revealed that majority of studied patients experienced their first complains from 5-10 years, with mean 3.88 ± 3.224 years.

Regarding comorbidities, the majority of studied patients had no chronic disease while about one fifth of the sample had chronic disease (Hypertension & DM, 6.7 % & 5.7% respectively). This is in agreement with Shawli, et al⁽⁵⁾ revealed that the majority of studied patients had no chronic diseases while about one quarter of the sample had chronic disease (DM & Hypertension, more than two thirds & more than one third respectively).

Factors affecting patient's compliance regarding therapeutic regimen:

Regarding physical factors, the present study revealed that the majority of studied patients reported that they suffered from fatigue. This result was in the same line

with Kapucu, et al⁽²²⁾ revealed that most of studied patients experienced fatigue.

Regarding psychological factors: The present study revealed that majority of studied patients had depression and anxiety. This result was in the same line with Karimi, et al⁽²³⁾ revealed that one fourth of studied patients suffered from depression and severe anxiety. In my opinion it is due to sudden occurrence of the disease, onset in the youth period, lack of good prognosis and lack of definitive.

Regarding Socioeconomic Factors, the current study found that most of studied patients reported that their income can't cover the cost of treatment and the majority of studied patients attain their treatment by health insurance organization. This result is supported by Ahmed, et al⁽²⁴⁾ found that more than three quarters of studied patients reported that income was Not enough for treatment regimen.

Regarding family support; the present study found that majority of studied patients reported that they receive support from family. This result is constant with Karataş & Bostanoğlu⁽²⁵⁾ revealed that high level of social support was received from family.

Regarding factors related to patient's belief, the present study revealed that the majority of studied patients need to change their lifestyle to comply with treatment regimen, feel that compliance leads to dependence on others. This result was in the same line with Gendy, et al⁽¹⁵⁾ revealed that the majority of patients mentioned that compliance leads to change of life-style & dependent on others.

Concerning therapy related factors, most of studied patients denied taking medications several times a day, timing of medications is problematic. All of studied patients feel upset from continuing treatment, And about one third of studied patients stop medication due to long duration. This result disagree with Ismail, et al⁽²⁶⁾ revealed that the majority of the studied sample complain of taking medications several times a day and long duration of treatment.

Correlation between Different Variables

The present study revealed that there was a positive statistical significant correlation between patients' compliance score and belief factor score, duration of disease and duration of treatment. Alatawi, et al⁽²⁷⁾ found that there was significant positive correlation between total health belief score and medication adherence. Jin, et al⁽²⁸⁾ reported that longer duration of the disease resulted in good compliance. In my opinion that because patient's attitude of denying the disease is reduced and they accepted treatment after years of suffering from the disease.

The present study revealed that there was negative significant correlation between patients compliance score, with psychological factor score, therapy related factors score. This result was in harmony with Ingersoll & Cohen⁽²⁹⁾ found that compliance was inversely correlated with the number of doses per day, with increasing dosing related to poorer compliance. And Abo Seliman Abdel-Aziz, et al⁽¹⁶⁾ reported that there was statistically significant relation between patient's compliance and having a depression.

Multiple linear regression model to predict treatment compliance score for multiple sclerosis patients. The current study reported that therapy related factor score and psychological factor score were negative predictors, whereas belief factor score was positive predictor of treatment compliance score throughout the study phase. This result was supported by Neter, et al⁽³⁰⁾ revealed that Beliefs about medication were then tested as a predictor of adherence.

Also, Salt & Frazier⁽³¹⁾ reported that the number of medications taken was a predictor of medication compliance, as patients taking more medication were

significantly more likely to have poorer medication compliance.

Conclusion:

On the light of the current study results, it can be concluded that, factors affecting compliance regarding therapeutic regimen were, physical factors, psychological factors, socioeconomic factors, patients' beliefs about disease and medications, therapy related factors and health care team and system related factors, and the majority of studied patients were affected by the total factors. Additionally, There were positive statistical significant difference correlation between patients total compliance score and patients total knowledge score, belief factor score, duration of disease and duration of treatment, while there were negative statistical significant difference correlation between patients total compliance score and psychological factor score, therapy related factors score and total factor. The present study findings answered the research questions.

Recommendation:

Based on the results of the study the following recommendations were suggested:

- Further studies by utilizing a large sample of multiple sclerosis patients should be done to assess the compliance with the therapeutic regimen among those patients in different hospitals.
- More health care policy efforts are needed to increase the availability of subsidized drugs which have better efficacy and low side effects.

Table (1): Frequency and percentage distribution of demographic characteristics of studied patients with multiple sclerosis.(n=105)

variables	No.	%
Age		
≤30 years	43	41.0
>30 years	62	59.0
Mean ±SD		
Range	32.5 ±6	
	21-40	
Sex		
Males	38	36.2
Females	67	63.8
Marital status		
Married	78	74.3
Single	27	25.7
Job		
Working	35	33.3
not working	70	66.7
Type of Work		
Need physical activity	10	9.5
Education		
secondary education	71	67.6
University education	34	32.4
Residence		
Rural	60	57.1
Urban	45	42.9
Income		
Sufficient income	35	33.3
Insufficient income	70	66.7

Table (2): Frequency and percentage distribution of medical history of multiple sclerosis patients under study (n.105)

	No.	%
Disease duration per years		
< 4years	39	(37.1%)
≥ 4 years	66	(62.9%)
Mean ±SD	4.7±2.6	
Median(Range)	4(1-10)	
Diagnosis		
Relapsing multiple sclerosis	97	92.4
Secondary progressive multiple sclerosis	8	7.6
Onset of treatment		
<24months	32	30.5
≥24 months	73	69.5
Mean ±SD	27.1±15.6	
Range/ month	12-108	
Time lapse of last episode		
<1 months	12	11.4
≥1 months	93	88.6
Mean ±SD	1.5±0.95	
Range/ week	2 weeks-5	

Frequency of episode		
frequent	35	33.3
un frequent	70	66.7
<hr/>		
Action during episode		
Hospitalization	105	100.0
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Type of investigation		
MRI	105	100.0
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Comorbidity *		
Yes	19	18.1
No	86	81.9
<hr/>		
Cardiac	1	0.95
Hypertension	7	6.7
Rheumatic fever	1	0.95
Renal failure	1	0.95
Hepatic disease	1	0.95
Diabetes	6	5.7
Others	2	1.9
<hr/>		
Family history		
No	105	100.0
<hr/>		
Treatment affiliation		
national expense	88	83.8
health insurance	17	16.2
<hr/>		
transportation type		
Taxi	3	2.9
Bus	102	97.1
<hr/>		
Preference method treatment		
oral		
injection	51	48.5
any method	3	3.0
	51	48.5

Table 3: Frequency and percentage distribution of factors affecting patients with multiple sclerosis compliance regarding therapeutic regimen: (n=105)

Factors affecting compliance regarding therapeutic regimen	Affected		Not affected	
	No	%	No	%
Physical factor	32	30.5	73	69.5
Psychological factor	88	83.8	17	16.2
Socioeconomic factor	68	64.8	37	35.2
Factors related to patients' belief	90	85.7	15	14.3
Therapy related factors	89	84.8	16	15.2
Health care team and system related factors	80	76.2	25	23.8
Total factors	93	88.6	12	11.4

Table (4): Correlation matrix between patients' total compliance with therapeutic regimen and factors affecting their compliance, demographic characteristics and medical history.

Different studied variables	Patients' total compliance with therapeutic regimen	
	r	p
Patients knowledge score	.261**	0.007
Physical factor score	0.053	0.59
Psychological factor score	-0.499**	0.0001
Economic social factor score	0.018	0.85
therapy related factors score	-0.699**	0.0001
Belief factor score	0.528**	0.0001
Health care team and system score	0.074	0.45
Total factor score	-0.24	0.01
Patients age	0.055	0.58
Duration of disease	0.272**	0.005
Duration of treatment	0.286**	0.003
Time of previous episode	0.16	0.103

(r) Correlation coefficient *significant p<0.05 **significant p <0.01.

Table (6): Multiple linear regression model to predict treatment compliance score for multiple sclerosis patients (n.105):

Predictors	Regression coefficients					
	β	Std. Error	t	Sig.	r	R ²
(Constant)	38.6					
Psychological factor score	-1.82	.724	2.52	0.014		
therapy related factor score	-4.06	.645	6.29	0.0001	0.78	.604
Belief score	2.36	.932	2.54	0.013		

β = regression coefficients, R square =60.4 % of predictors anova model=21.2, p=0.0001

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