



Explaining the Barriers to Adherence to Treatment Regimens in Multiple Sclerosis Patients: A Qualitative Content Analysis

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Abstract

Objectives: Multiple sclerosis (MS) is a chronic and debilitating disease of the central nervous system and the most common cause of neurological deficits in young adults. Long-term adherence to a treatment regimen is an important challenge for MS patients. This study used a qualitative content analysis approach to explain the barriers to adherence to treatment regimens in MS patients.

Materials and Methods: In this qualitative study, we conducted in-depth semi-structured interviews with 12 MS patients, two parents, two spouses, one child, two experienced nurses in neurology wards, two neurologists, one physiotherapist, one pharmacy technician and MS medications supplier, and one director at MS Society. Data were collected from 2017 to 2020 and analyzed with a conventional content analysis approach.

Results: The analyses yielded four main themes and some related subcategories as the barriers to adherence to treatment regimens in MS patients: "discouraging treatment team" (similar symptoms and multiple differential misdiagnoses, delayed diagnosis and loss of treatment time, misinforming the patient, disparaging and mechanical view of the patient, damage to the trust-based relationship and developing defensive medicine, inappropriate interference of other medical team staff in doctors' job, lack of compassion and disregard for the patient's educational and medical needs, lack of effort to gain patient trust, doubts about adherence to the treatment regimen, doctor-patient disagreement about the treatment); "disappointing family" (poor cooperation, negative behaviors, misconduct of the spouse's family, fear and misconceptions); "ignorant society" (hasty judgments, weak culture, economic sanctions); and "personal problems" (devastating unemployment, debilitating economic poverty, disappointment in the future).

Conclusions: Adherence to treatment regimens in Iranian MS patients is associated with individual, family, and social factors and health care providers, such that they can discourage the patients from adhering to their treatment regimens. The focus of the treatment team staff on these factors can help promote adherence to the treatment regimen in MS patients and reduce the recurrence of the disease and readmissions to hospitals.

Keywords: Barriers, Adherence to the treatment regimen, Multiple sclerosis, Qualitative research, Conventional content analysis

Introduction

Multiple sclerosis (MS) is a chronic and debilitating disease of the central nervous system and the most common cause of neurological deficits in young adults (1). It mainly affects the youth, and due to its progressive nature, has profound effects on patients' quality of life in a way that imposes a significant economic burden on them (2,3). Studies show that 2.5 million people have MS across the world (4-6). Preliminary studies in Iran indicate that approximately 50 000 people are affected by this disease, placing Iran among the top 10 countries in the world (7,8). The importance of this disease is its high prevalence over the past years, such that many people around the world are affected by MS, and their number is increasing every day. MS is also the most common cause of disability and non-traumatic disability (9,10). The most important complications of MS include impaired vision, difficulty in walking, sensory impairment, difficulty in concentrating, imbalance, muscle weakness, fatigue, paralysis, and spasm

(11). These complications have devastating effects on patients' roles, job duties, and daily activities in a way that could threaten their independence and abilities to participate effectively in family and community (12, 13).

Currently, there is no definitive cure for MS. However, the existing treatments mainly aim to mitigate the disease severity (reducing the recurrence and progression of the disability). Also, disease-modifying therapies (DMTs) or symptom-reducing therapies (reducing inflammation) aim to improve patients' quality of life. MS treatments impose significant costs on the health care system (14,15). Despite the incurability of MS, studies show that DMTs reduce MS recurrence, myelin sheath lesions, development rate, and disability (16-18). The ultimate goal of treatment, therefore, is to reduce the clinical activity and the severity of the disease and to prevent disability (19,20). In addition to drug therapy, lifestyle modifications to reduce anxiety and stress, appropriate exercises such as yoga and dietary modifications (taking vitamins, antioxidants, adequate

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Key Messages

- ▶ This study showed that disparaging and mechanical view of the treatment team staff towards patients, lack of compassion and disregard for patients' educational and treatment needs, lack of effort on staff's behalf to gain patient trust, poor cooperation and negative behaviors of patients' families, economic sanctions against Iran, and economic poverty and disappointment in the future are the most important reasons for non-adherence to the treatment regimen in Iranian patients with MS. The results of this article may help the treatment staff, families, and the MS Society eliminate or reduce these problems.

intake of vitamin D, unsaturated fatty acids, etc) also slow down the course of the disease and reduce the severity of symptoms and the degree of disability in the long term (13,21).

The essential factor in achieving the therapeutic goals for MS is long-term adherence to treatment regimens (22). Non-adherence to the treatment regimen can lead to more recurrence of the disease, increased complications, readmission, and escalated financial pressures on health care institutions (23-26). Despite the importance of adhering to the treatment regimen to control MS, studies have shown that one to five years after starting the treatments, 25%-40% of the patients receiving injectable medications, and 30% of patients receiving oral medications do not follow their treatment regimen (10,25,27-29). Research has shown that long-term adherence to DMT is a real challenge for MS patients (30). Reasons for non-adherence to treatment regimens vary in different countries, with studies showing the ineffectiveness of medications and their side effects (Sweden, Spain, Italy), the ineffectiveness of medications (Colombia and Canada), wrong medical decisions (Brazil), and forgetting (USA) as the most common causes of non-adherence to treatment regimens (31). Adherence to treatment regimens is a complex behavioral process that occurs in social interactions and is influenced by numerous factors. Therefore, the varying reasons for non-adherence to the treatment regimen among different countries are not surprising.

Most of the studies on Iranian MS patients are quantitative, and there is no qualitative study on MS patients' perceptions of the barriers to adherence to treatment regimens according to the Iranian culture. Also, identifying the underlying factors of non-adherence to treatment regimens can contribute to designing and developing targeted interventions. Therefore, the purpose of this study was to identify the problems of MS patients in adhering to their treatment regimens and to help the treatment staff, families, and the MS Society eliminate or reduce these problems. Accordingly, the present study was carried out with a qualitative content analysis approach to explain the barriers to adherence to treatment regimens in MS patients.

Materials and Methods

This qualitative study used qualitative content analysis. Purposive sampling was used to select the subjects and have maximum diversity (32). Since the purpose of this study was to identify the barriers to adherence to treatment regimens in MS patients, individuals who had profound and valuable experiences in this area were selected. Therefore, using purposive sampling method, we selected MS patients diagnosed for more than a year, who were willing to participate in the study. After the approval of the proposal and obtaining an ethics code from Tehran University of Medical Sciences and Tehran Health Care Services, sampling began until data saturation level (32).

Inclusion criteria

The inclusion criteria were as follows:

1. Definitive diagnosis with MS and at least one year passed since the diagnosis;
2. Iranian nationality and ability to understand and speak Persian;
3. At least 18 years old or older;
4. Willingness to participate in the study and express experiences and perceptions about adherence to the treatment regimen;
5. Not being in the recurrence and acute stages of the disease, and favorable mental and physical conditions to participate in the study;
6. No speech problems and the ability to express one's experiences and feelings;
7. No confirmed mental or cognitive disorders and incurable diseases such as cancer, AIDS, etc. that might affect adherence to the treatment regimen.

Also, there were two exclusion criteria: (a) recurrence of the disease and aggravation of the symptoms and (b) withdrawal of the participation from the study.

Ultimately, 24 people (12 MS patients, two parents, two spouses, one child, two experienced nurses in neurology wards, two neurologists, one physiotherapist, one pharmacy technician and MS medications supplier, and one director at MS Society) were interviewed. In-depth semi-structured interviews were held to get information from the participants. Since in qualitative research participants should be assessed in real-life environment, the location and duration of the interviews were decided according to the participants' consent and comfort (32). Therefore, they were interviewed in different locations, including private homes, doctors' offices, MS Society offices, physiotherapy clinics, pharmacies, and hospitals. Interviews lasted from 30 to 61 minutes, and in some cases, the participants were interviewed 2 or 3 times. Interview questions varied by case and purpose. Interviews would begin with a general open-ended question such as "Please tell your life story after developing MS" and then would continue based on the interviewees' experiences and, if necessary, supplementary, auxiliary, guiding. Exploratory questions would be asked to gain a deeper understanding

of the challenges and barriers patients faced in adhering to the treatment regimen (32), and to clarify, confirm or elaborate on their responses.

After explaining the research objectives, written consent forms were read and signed by the participants. They were informed that their participation in the research was completely voluntary and non-participation would have no effect on the medical services they received. They were also assured that they could refuse to answer any questions they did not want to and that they could leave the study at any time. It was also emphasized that all their information would remain confidential and only general findings would be published. If they agreed, the results would be made available to the participants and the MS Society. The interviews were recorded with the participant's consent and transcribed at most 24 hours later. The transcriptions were then analyzed word by word and line by line to extract the required information. To increase robustness, the data were analyzed simultaneously by two other authors of this paper and an external observer. To increase the credibility of the research, the researcher first tried to gain the subjects' trust and understand their perspectives by accompanying them for a long time. There were also long-term presence and follow-up observations for data immersion (33). In addition, the use of different data collection methods (observation, interview, etc.) helped enrich the data. For enhanced credibility, all stages of the study were reviewed by the research supervisors and advisor, as well as the external observer. An attempt was made to increase the study's credibility by engaging researchers with different specializations and high qualifications in conducting qualitative research. The search for rejecting and contradictory cases and using participants' opinions who had different views from others were further measures to validate the study. Extensive experience and previous studies on patients with MS were other positive aspects of this study. To increase dependability, an external observer was responsible for external control in all stages of the research. For transferability of results, a detailed description of the research background and conditions was provided to readers and other researchers so they could decide whether it is possible to transfer the results to other fields, understand the experiences, track the data, and achieve similar results.

Statistical Analysis

After data collection, all the demographic and clinical information were coded. The data entry was performed using an excel spreadsheet program. Afterwards, the statistical analysis was performed by SPSS version 21.0. The data were presented in tabular form showing the frequency and the relative frequency of distribution of different variables among the participants.

Results

Twenty-four people (12 MS patients, two parents, two

spouses, one child, two experienced nurses in neurology wards, two neurologists, one physiotherapist, one pharmacy technician and MS medications supplier, and one director at MS Society) were interviewed. Fourteen of the participants were female, and ten were male with an age range of 25-57 years (Tables 1 and 2). Interviews lasted from 30 to 61 minutes. Interviewees mentioned the following as the barriers to adherence to their treatment regimen (Table 3):

a. Discouraging treatment team: with the subcategories "similar symptoms and multiple differential misdiagnoses, delayed diagnosis and loss of treatment time, misinforming the patient, disparaging and mechanical view of the patient, damage to the trust-based relationship and developing defensive medicine, inappropriate interference of other medical team staff in doctors' job, lack of compassion and disregard for the patient's educational and medical needs, lack of effort to gain patient trust, doubts about adherence to the treatment regimen, doctor-patient disagreement about

Table 1. Demographic information of the participants

Variable	Category	No.	%
Gender	Male	10	41.66
	Female	14	58.34
Age	20-30	7	29.16
	30-40	5	20.83
	40-50	8	33.34
	50-60	4	16.67
	Single	6	25
Marital status	Married	17	70.83
	Divorced	1	4.17
	No high school diploma	2	8.33
Education	High school diploma	8	33.33
	Bachelor's	11	45.84
	Master's	1	4.17
	Doctorate and higher (medical specialty)	2	8.33
Employment	Unemployed	2	8.33
	Housewife	6	25
	Civil servant	11	45.83
	Self-employed	4	16.67
	Retired	1	4.17
	Patient	12	50
Participant's title	Patient's parent	2	8.33
	Patient's spouse	2	8.33
	Patient's offspring	1	4.17
	Neurology ward nurse	2	8.33
	Neurologist	2	8.33
	Physiotherapist	1	4.17
	Pharmacy technician	1	4.17
	Director at MS Society	1	4.17

Table 2. Clinical information of the MS patients (n=12)

Variable	Category	No.	%
Length of disease (year)	<5	2	16.67
	5-10	3	25
	10-15	5	41.67
	15-20	1	8.33
	>20	1	8.33
Number of hospitalizations	None	3	25
	1-5	7	58.33
	More than 5	2	16.67
Type of medication	Oral	1	8.33
	Injectable	8	66.67
	Combined (oral and injectable)	3	25

the treatment”

b. disappointing family: with the subcategories “poor cooperation, negative behaviors, misconduct of the spouse’s family, fear and misconceptions”

c. ignorant society: with the subcategories “hasty judgments, weak culture, economic sanctions”

d. personal problems: with the subcategories “devastating unemployment, debilitating economic poverty, disappointment in the future”.

The subcategories of each of these barriers refer to the reasons that, in the social and cultural context of Iran, would lead to non-adherence or poor adherence to the treatment regimen in patients with MS.

a. Discouraging Treatment Team

The treatment team can play a significant role in patients’ adherence to the treatment regimen by providing information, training, care, and motivation. However, the interviewees mentioned the following reasons for their confusion and non-adherence to their treatment regimen,

and therefore, the recurrence of MS.

Similar Symptoms and Multiple Differential Misdiagnoses

Patients, and the treatment team, stated that due to the similarity of the MS symptoms with several other diseases, at first, these patients would be often misdiagnosed with vision problems, physical weakness, and other conditions. This delays treatment and confuses the patients, which hurts starting the treatment and adhering to the treatment regimen. For example, a 33-year-old female patient with a 10-year history of MS said:

“I went to a doctor who said it might be anemia! My face was tingling under my eyes. I visited a doctor who said: “you are stressed out!” I woke up and saw that my whole face was tingling, my mouth was crooked, and my eyes were somehow half-open. Another doctor said there was a possibility of a stroke! After referring to different doctors, one doctor prescribed MRI. I had an MRI in 2010, and the definitive diagnosis was MS!” (S4).

A 26-year-old woman with a 3-year history of MS said:

“At first it was a tingling sensation on the right side of my body. I am a tailor, and I felt this was normal because of my job. Then my right side healed spontaneously, and my left side started to tingle. Then my left side healed again, and my right side started tingling. My right hand did not work anymore, it started from my feet until it reached my hands... I visited a doctor... they said I had sinusitis! They prescribed MRI first, but then said sinusitis!” (S6).

Delayed Diagnosis and Loss of Treatment Time

Since MS symptoms are similar to those of some other diseases, it is difficult for doctors to diagnose patients with

Table 3. Main Themes and Subcategories of the Barriers to Adherence to Treatment Regimens in MS Patients

Main category	Themes	Subcategory
Barriers	a. Discouraging treatment team	Similar symptoms and multiple differential misdiagnoses
		Delayed diagnosis and loss of treatment time
		Misinforming the patient
		Disparaging and mechanical view of the patient
		Damage to the trust-based relationship and developing defensive medicine
		Inappropriate interference of other medical team staff in doctors’ job
		Lack of compassion and disregard for the patient’s educational and medical needs
		Lack of effort to gain patient trust
		Doubts about adherence to the treatment regimen
		Doctor-patient disagreement about the treatment
	b. Disappointing family	Poor cooperation
		Negative behaviors
		Misconduct of the spouse’s family
		Fear and misconceptions
	c. Ignorant society	Hasty judgments
		Weak culture
Economic sanctions		
d. Personal problems	Devastating unemployment	
	Debilitating economic poverty	
	Disappointment in the future	

MS. Therefore, most of these patients might be diagnosed with other diseases, which in turn would delay treatments, worsen patients' symptoms, and interrupt their adherence to treatment regimens. A 37-year-old man whose wife had been suffering from MS for 14 years stated:

"Her legs were shaking and she could not stand up at all! What can I say? She was unsteady and could not stand on her feet or go for a walk! We kept taking her to the doctor! This was our situation for six months. They gave us pills, and six months later, they said it was MS!" (S9).

A 25-year-old woman with an 8-year history of MS said:

"I visited a general practitioner. They said that because I did heavy exercise, the soles of my feet were tingling and that my muscles were weak, and I had to take painkillers for it. They said if I did not get better after three days, I would have to visit another doctor!" (S1).

Misinforming the Patient

There are different types of MS and not all patients have the same symptoms. Moreover, not all symptoms occur in all patients, but some doctors, by providing incorrect information, cause frustration in patients and therefore have a negative impact on their adherence to the treatment regimen. A 25-year-old woman with eight years of MS stated this:

"I went to a neurologist. He said "you are prone to MS". And I just asked "is it the disease that paralyzes?" and he said exactly, that's MS!" (S1).

Disparaging and Mechanical View of the Patient

Improper behavior of doctors and medical staff, looking at people only as patients and not human beings, disregard for human needs, and mechanical and disparaging views of the MS patients would discourage the patients. As a result, they might not adhere to their treatment regimen. A 25-year-old woman with an 8-year history of MS stated:

"The first time I went to the doctor, he told me "you must listen to me!" But I said to myself, why should I listen to the doctor? This is for me! I either inject it or I do not. There is no must! It should be for me to decide, maybe I do not want to! Doctors' behavior affects MS patients a lot; for example, it was here that I first went to see a doctor, and he offered me this, and I didn't accept!" (S1).

A 27-year-old woman with a 7-year history of MS also said:

"I will not go to doctor ---. I don't like his behavior at all! I went to see him too, but I did not go inside! I saw that he brought all the patients inside the room at once! (Researcher: Lack of respect for patients' privacy) I felt uncomfortable!" (S3).

Damage to the Trust-Based Relationship and Developing Defensive Medicine

In recent years, due to the negative publicity in social

networks and mass media, the trust-based relationship between the treatment teams and patients has been severely damaged in Iran. The number of patients' complaints against members of the treatment teams has significantly increased. This also has a great negative impact on patient's adherence to treatment regimens. A 53-year-old neurologist with 17 years of experience stated:

"Doctors used to have a patriarchal status! I mean, we decided on our own what treatment should be given to a patient! And we did the work ourselves! If the patient had complications, he would accept and say that the doctors had done their best and now these complications have occurred! But this is not the case today! Today, people are so provoked that they'd complain of any complication!!! These factors are called defensive medicine! This means that while we are thinking about the patients, giving them medicine and taking care of the complications, we are also taking care of ourselves! So that if a complication occurred, the patient would not complain! Or have bad behavior! You know that a complaint can take us to court for a couple of years! This means that sometimes we have to do more tests than necessary" (S14).

A 27-year-old woman with a 7-year history of MS also said:

"The doctor told me to eat cold-natured foods because, as they say, they are still testing things out! They see that eating cold-natured foods may have bad side effects and then they'd say no, eat hot-natured foods instead! Like a laboratory mouse (laughter) to be constantly tested on. I don't know. Do they have to keep saying this, eat this, eat that? After all, this is another kind of experiment, isn't it?" (S3).

A 47-year-old neurologist with 12 years of experience said:

"I have a general opinion about our people. People's trust in doctors has declined a little!!! I think it's because the doctors don't spend enough time examining the patients! And they do not pay much attention and are not sympathetic! Maybe it's because doctors' tariffs are low compared to the rest of the world!" (S15).

Inappropriate Interference of Other Medical Team Staff in Doctors' Job

Diagnosing the disease, informing the patient, and choosing the type of treatment are the doctors' job descriptions, but unfortunately, in Iran, some members of the medical staff interfere in the doctors' job and cause MS patients to become defensive and refuse to adhere to their treatment regimen. A 47-year-old neurologist with 12 years of experience stated:

"Usually, the patients who come to us have heard this word before! For example, unfortunately, when he is doing an MRI, the person in charge tells the patient that he has seen something in his brain! And he thinks it's MS! That is, he has already put that thought in the patient's mind! Patients have a background and go to the doctor

to make sure of the diagnosis and to hear the doctors confirm that word! That the diagnosis is correct.” (S15).

Similarly, a 26-year-old woman with a 3-year history of MS said:

“The doctor did not say it was MS at all! I was in a naughty mood, he told me I had inflammation in my head and had to be hospitalized, and I still did not know it was MS! A nurse looked at me and said: ‘you have MS! You are in bad condition!!!’ I was distraught, shocked, nervous, and the doctor had not diagnosed MS yet! My older sister came to the hospital and said how dare your nurse say such a thing when the doctor has not diagnosed her yet?” (S6).

Lack of Compassion and Disregard for the Patient’s Educational and Medical Needs

Unfortunately, the lack of compassion and inattention of some treatment team members to the educational and medical needs of MS patients, as well as no instructions on how to take medications and prevent side effects can cause complications in these patients. These, in turn, will have negative effects on adherence to the treatment regimen. A 27-year-old woman with seven years of MS stated:

“Early on, I didn’t know what to eat for the injection! We went to my dad’s, and he said: ‘take this ibuprofen to reduce your pain.’ I took it and my pain went away. We went to the doctor the next night... my mother explained my condition and the doctor said he had forgotten to tell me to take pills!” (S3).

Also, a 33-year-old woman with a 10-year history of MS said:

“It was my doctor’s fault! He didn’t explain it to me at all! He didn’t say that, for example, I had MS, and if I took injections once a week or every other day, I might get better! He just said that I had MS! He didn’t tell me anything that I could cope with my disease!” (S4).

Lack of Effort to Gain Patient Trust

Some members of treatment teams may not establish proper relationships with MS patients and may not even try to gain their trust. This would undermine patients’ adherence to the recommendations and their treatment regimen. A 26-year-old woman with a 3-year history of MS stated:

“They had an angiocatheter (angiocath) attached to my hand, which bothered me a lot. When I went to the bathroom and wanted to fix my scarf, my right hand didn’t work, and I couldn’t flex my left hand either! I asked the nurses to change the location of the angiocatheter, but they didn’t! I was admitted at nine in the morning and three o’clock in the afternoon; we left the hospital with my husband’s permission! I told them that they had to respect and take care of their patients, that I was being bothered, and I couldn’t do anything! I was very ill.” (S6).

A 43-year-old female nurse with 18 years of experience caring for MS patients said:

“It is a fact that when a patient sees a nurse who works compassionately for him, even if she makes the slightest mistake in her work, because the patient trusts her, he accepts her work and may even tell others that the nurse has done nothing wrong! For example, if a little of the drug went under his skin, he’d say no problem! But if the patient does not accept and does not see us by his side, he may magnify this issue! He may think that he has been seriously injured and refuse to accept the treatment. At the next visit, he’d also say that he wouldn’t want that particular person to be his nurse.” (S12).

Doubts About Adherence to the Treatment Regimen

By questioning the treatments and medications prescribed by their colleagues, some members of the treatment team make MS patients and their families doubtful about continuing to adhere to the treatment regimen. A 57-year-old man whose son had MS for 21 years said:

“Seven years later, we went to see Dr. ---. He said that we should not have taken Cinnovex at all. Or the other medication, I don’t know its name! Yes, Recigen. Those seven years that we went to Dr. ---, they said it was a mistake! They said they should not have injected this medicine at all! My son had visited the doctor, which I found out when talking to him. Due to his illness, he said that other medicines should have been prescribed for him.” (S10).

Doctor-Patient Disagreement About the Treatment

In addition to medical treatments, some MS patients and their families also tend to use traditional medicine simultaneously. This would lead to doctor-patient disagreements regarding the treatments and, as a result, would undermine the adherence to the treatment regimen. A 25-year-old woman having MS for eight years of MS stated:

“If my doctor tells me not to do something, I’ll do my best not to do it, but then I’ll go back to my thoughts! If I see that it’s perfect for me because I know my body better than anyone else, and I realize that it’s not harmful to my body, I’ll do it. And I would recommend other patients to see a traditional medicine doctor, something I didn’t do for six years! I was talking to my doctor, and I said I heard traditional medicine doctors say that MS patients like me should eat hot-natured foods and never eat cold-natured foods. Then my doctor, who is a neurologist, said: I can’t entirely agree with this. I can’t say, for example, go to a traditional medicine doctor, and he will tell you what to eat for your MS to go away!” (S1).

b. Disappointing Family

Families can play a critical role in patient’s adherence or non-adherence to the treatment regimen. Poor cooperation, negative behaviors, fears & misconception, and misconducts of the spouse’s family provided conditions that prevented the patients from adhering to the treatment regimen.

Poor Cooperation

The consent and cooperation of patients' families is essential in the diagnosis and treatment of MS. Also, after the onset of symptoms, most of these patients need the help of family members in performing some self-care activities. Still, unfortunately, the poor cooperation of family members prevents them from adhering to the treatment regimen. A 25-year-old woman with an 8-year history of MS said:

"Doctors said they had to take cerebrospinal fluid (CSF) to diagnose the disease, but my family disagreed! Because I was 20 years old at the time, and my family said it was too soon for that!" (S1).

A 43-year-old female nurse with 18 years of experience caring for MS patients said:

"From the family's point of view, these issues may also be ignored. When patients' problems increase and it gets difficult for them to move, they need others for going to bathroom, personal hygiene, and daily chores... and this leads to negligence of their health. I have seen cases where, for example, a young woman's hair was shaved because they could not take care of her health! They could not take care of her bath! And the family doesn't see the mental and psychological damages they cause to their patient." (S12).

A 47-year-old neurologist with 12 years of experience said:

"There are people who abandon their patients the moment they are diagnosed with MS! As if they have an incurable disease, a contagious disease!" (S15).

Negative Behaviors

Family members can support MS patients to encourage them to adhere to their treatment regimens. Unfortunately, some family members with negative behaviors and language discourage and lower their motivation to adhere with the treatment regimen. A male patient having MS for 12 years stated:

"I had an argument with my father, and he said yes you are sick! You are so and so! You deserve to be sick!!! It broke my heart that day! And I haven't forgotten it yet!" (S2).

A 27-year-old woman with a 7-year history of MS also said:

"I'd love for my parents to be happy to do this, but if I want to do something again, my mother says they won't do it... don't be like that! Her does and don'ts lower my motivations" (S3).

Misconduct of the Spouse's Family

Some family members of MS patients' spouses, by pointing out their illness and disability, secretly encourage their spouses to remarry, which negatively affects these patients and reduces their motivation to adhere to the treatment regimen. A 26-year-old woman with a 3-year history of MS said:

"My husband's family, for example, had a meeting at my brother-in-law's house and said we don't want a sick woman! We'll find another woman for him." (S6).

A 43-year-old female nurse with 18 years of experience caring for patients with MS said:

"Most of these patients who came to the hospital would ask us not to write the name of the disease on the board above their beds! Because they didn't want anyone, especially their husbands' families if they were married, to know their disease! And we did this for them! We would even write another diagnosis or leave the diagnosis blank!" (S12).

Fear and Misconceptions

Some family members of patients have misconceptions about MS and think that it is a dangerous and incurable disease like cancer, leading to a negative effect on these patients and their adherence to the treatment regimen. A 57-year-old man whose son had MS for 21 years said:

"I had only heard its name! From family and friends. I had heard more about cancer; I had also heard about MS. I had heard the names of several incurable diseases, and I was distraught!! I was worried that my son had an incurable disease, and the doctor confirmed that it was MS! I said, God forbid, he would be paralyzed or die! God forbid, such a feeling! His mother was upset because it was an incurable disease!" (S10).

A 47-year-old neurologist with 12 years of experience said:

"In the case of MS patients, our problem is more with the patients' families than with the patients themselves! They are more afraid than the patients! (Doctor laughs)" (S15).

c. Ignorant Society

The conditions and culture of the society can have a great impact on the adherence or non-adherence to the treatment regimen, which will be discussed in the following lines.

Hasty Judgments

Some people make hasty judgments about MS and therefore cause a lot of stress in patients, reducing their confidence and high spirits. A 43-year-old female nurse with 18 years of experience caring for MS patients said:

"Because many of these patients have difficulty walking, some families do not have a good idea of this. They think, for example, what a frivolous person she is when she hits a man while walking! But they don't know that this is out of her control! She hits someone because of the imbalance problem! These doubts may arise for others as well!" (S12).

Weak culture

The cultural and social weakness of society causes many MS patients to turn to soothsayers and fortune-tellers

instead of adhering to their treatment regimen. A 47-year-old neurologist with 12 years of experience said:

“A few things are critical to our people: religious beliefs. Rural or religious people go to prayer healers! Or they seek healing from Imams and Imamzadehs! I don’t say they are ineffective, but they are not the cure! They induce a feeling of confidence so that patients can handle their illnesses. People of higher social classes, like the rich people, believe in other things like fortune tellers, pray healers, soothsayers! Like other beliefs we see in society! These are wired into our culture so that people prefer superstition first and then go after scientific and knowledge-based ideas! All patients often have the same preference for the treatments.” (S15).

A 47-year-old female nurse with 24 years of experience caring for MS patients said:

“Families’ reactions are different! Some families support their patients and provide spiritual and financial support, while others may not support their patients enough! It also depends on the family situation! Their economic and cultural situation, well, they are all influential!” (S13).

Economic Sanctions

Although the United States has not sanctioned the selling of medications and medical equipment to Iran, the US economic sanctions have made it difficult for Iranian companies to transfer money for their purchases from foreign countries, which has led to an occasional shortage of medications for particular diseases, including MS. As a result, patients will not be able to adhere to a regular treatment regimen. A 41-year-old pharmacy technician and MS medications supplier with ten years of experience said:

“Unfortunately, because of the current economic conditions in Iran, MS patients have difficulty finding their medications! Sometimes sanctions cause their medication to be past due! But we try to contact the pharmaceutical companies to prevent such delays. But unfortunately, sometimes it happens! See, we had a medication I knew some patients were using and I knew the company would not supply it for a month! So, we rationed the supply we had, and if a woman used 24 Copamers, we’d give her the medications for a couple of weeks. We would even borrow them so that we could cover the shortage in that month!” (S17).

d. Personal Problems

Some MS patients have personal problems that make it more challenging to adhere to a treatment regimen. The following are instances of such issues.

Devastating Unemployment

Some MS patients are unemployed before their diagnosis, and some are unable to continue working after the symptoms are manifested and therefore become unemployed. This creates a lot of discomfort and stress

in the patients, which firstly causes recurrence and worsening of the signs and secondly, reduces their income and financial ability to buy the necessary medications and adhere to the treatment regimen. A 43-year-old female nurse with 18 years of experience caring for MS patients said:

“The government should cooperate with these patients so that they can work as much as they can and be useful for the society. They can handle office jobs as long as they can work, so they should use them. This will help the patients feel they are useful for their families and society and avoid despair and hopelessness. They shouldn’t be left alone and unemployed. It would disrupt their treatments and their emotions. It would worsen their condition!” (S12).

A 53-year-old mother whose son had MS for three years stated:

“I cried a lot! I said, what could I do with no money! Where could I take him! His dad is unemployed! I don’t know what will happen! He’s young, and I won’t be around forever! His dad won’t be around forever! He always stays at home! He’s so upset he can’t stand on his feet anymore! He can’t go to work! (Her eyes filled with tears, and she wiped them with her chador)” (S11).

Debilitating Economic Poverty

The economic and financial situation of MS patients and their families plays a significant role in their abilities to provide the necessary medications, participate in physiotherapy sessions, and adhere to the treatment regimen. Poverty and economic problems prevent some patients from adhering to their treatment regimen against their will. A 47-year-old neurologist with 12 years of experience said:

“The choice of medication for the patient depends on our initial assessment of the patient’s social and economic level. I often don’t recommend many medications to patients because I know they can’t buy them at all! Once I even asked a patient how much his income was? We had to ask! It’s a personal thing, for God’s sake! There is no reason for any patient to tell their doctor how much they earn! So that we could decide on the medication! We had to see if he could save up to buy his medications. We have patients who don’t even visit because of the high prices of medications and don’t receive any treatments, and their conditions worsen! No institutions or organizations support them!” (S15).

A 47-year-old female nurse with 24 years of experience caring for MS patients said:

“We had cases who were not supported and wouldn’t get hospitalized! And it was because of their economic situation... they had no choice. They didn’t want to, but because their family was poor, and they saw themselves as a burden on the family! That’s why they’d put off! They’d say they didn’t need treatment that it wasn’t necessary. And their situation worsened!” (S13).

Disappointment in the Future

Hope in the future and treatment of the symptoms reinforces MS patients' motivation to adhere to their treatment regimen. However, their disappointment in the future and the treatment of symptoms have a very destructive impact on their motivation to adhere to the treatment regimen. A 29-year-old woman with 12 years of MS said:

"The MS Society is excellent. The financial support and these classes they have are amazing. They have club, things like these are perfect for our mood. Though I haven't gone to the gym since September, it's amazing, and I encourage others to join it too. But I don't go anymore; I don't have hope in my life. I got very disappointed after I my MS" (S5).

Discussion

This study showed that the challenges perceived by MS patients are discouraging treatment teams, disappointing family, ignorant society, and personal problems. The participants perceived the following as the barriers to adhering to their treatment regimens regarding the treatment teams: similar symptoms and multiple differential misdiagnoses, delayed diagnosis and loss of treatment time, misinforming the patient, disparaging and mechanical view of the patient, damage to the trust-based relationship and developing defensive medicine, inappropriate interference of other medical team staff in doctors' job, lack of compassion and disregard for the patient's educational and medical needs, lack of effort to gain patient trust, doubts about adherence to the treatment regimen, and doctor-patient disagreement about the treatment.

The results of our study also showed that, in most cases, the treatment team not only facilitates treatment adherence, but also reduces patients' motivation. The results of other studies also confirm the present findings. For example, in a study in Spain, Verdugo et al. showed that providing accurate information about the disease and greater satisfaction with treatments played an important role in adhering to the treatment regimen in MS patients (6). Ibrahim et al. also found that long waitlists for hospital visits, poor understanding of the disease mechanism, and poor doctor-patient relationship were the reasons for non-adherence to the treatment regimen in some MS patients in Qatar (1). De Seze et al reported that higher awareness of patients with MS led to more adherence to their treatment regimen (34). Battista et al. focused on doctor-patient communication to control the desired and realistic goals, motivating the MS patient to adhere to their treatment regimen (35). Costello et al also argued that the treatment team and MS patients need to interact with each other to build an open, trust-based relationship regarding the treatments to ensure that the patients will have sufficient knowledge and skills necessary to adhere to a long-term treatment regimen (22). It seems that the treatment team

can help increase adherence to the treatment regimen through more careful examination of patients, spending more time for examination, patient training, human rather than mechanical view, and designing a comprehensive and multidimensional treatment plan.

The findings of this study indicated that families play a crucial role in facilitating or preventing adherence to the treatment regimen. These include poor cooperation of the family members in adhering to the treatment regimen, their negative behaviors, misconduct of the spouse's family, and their fear and misconceptions. The cooperation of the patients' families is essential at the time of diagnosis and treatment. Family members can support MS patients and encourage them to follow their treatment regimen. However, negative behaviors and words of family members will discourage them and reduce their motivation to adhere to the treatment regimen. Verdugo et al. reported a relationship between family support for patients with MS and their adherence to the treatment regimen (6). In their study to explore the experience of families of Iranian MS patients, Roshangaran found that family had little knowledge about MS at the beginning of diagnosis. This caused severe stress, confusion, and conflicts in the family members (36). Hence, educating family members about MS and its possible treatments and encouraging them to support their patients can be very helpful.

The present study suggested that the ignorant society also has a very important role in facilitating or preventing adherence to the treatment regimen in patients with MS, ranging from hasty judgments, weak culture, and economic sanctions. Ibrahim et al. also stated that the reasons for non-adherence to the treatment regimen in several MS patients in Qatar were stigma and unfavorable attitude towards MS, poor social support, and cultural and family pressures (1). Social and mass media can play a constructive role in raising public awareness and correcting these negative attitudes and misconceptions. The economic sanctions are also involved in the poor adherence to treatment regimens. Although the United States has not sanctioned the selling of medications and medical equipment to Iran, the US economic sanctions have made it difficult for Iranian companies to transfer money for their purchases from foreign countries, which has led to an occasional shortage of medications for special diseases, including MS. However, the central banks of other countries are not sanctioned by the US; and they have no problem providing the required medications. Therefore, sanctions are not mentioned barriers to adherence to treatment regimens in studies carried out in those countries.

The results of this study also indicated that some MS patients had personal problems that made it much more difficult to adhere to the treatment regimen, such as unemployment, poverty, and poor economic and financial status, which play a very important role in

their abilities to provide the necessary medications, participate in physiotherapy sessions, and adhere to the treatment regimens. Poverty and economic problems prevent some patients from adhering to their treatment regimen against their will. Koltuniuk and Rosińczuk referred to forgetting to take drugs due to busy daily work and interference of medications with daily activities as the barriers. Remington mentioned economic and financial challenges and lack of insurance as the barriers to adherence to treatment regimens in MS patients (2,37). In some countries, however, economic problems are not mentioned as barriers to MS patients' adherence to treatment regimens, due to the strong comprehensive insurance coverage in those countries. Disappointment in the future is another important factor because hope and treatment of the symptoms reinforce MS patients' motivation to adhere to their treatment regimen. However, their disappointment in the future and the treatment of symptoms have a very destructive impact on their motivation to adhere to the treatment regimen. Several studies also reported depression, disappointment, and neuropsychiatric problems as factors that undermine adherence to a treatment regimen (2,38-40). Câmara and Gondim also argued that giving hope to these patients would increase their adherence to the treatment regimen (41). Introducing these patients to the MS Society, financial support from the Society and charities, and referring the MS patients to psychologists can help reduce their financial problems and frustration. Finally, the findings of this study can be of help members of the treatment team and medical institutions in Iran and other countries that accept Iranian MS patients to understand the barriers and help the patients to further adhere to their treatment regimen.

Limitations

The limitation of our study is that patients in the acute stages of the disease did not cooperate and were therefore excluded from the study.

Authors' Contribution

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Conflict of Interests

Authors have no conflict of interest.

Ethical Issues

The study was approved by the Committee of Ethics in Research (IR.TUMS.FNM.REC.1396.3233).

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References

1. Ibrahim F, Deleu D. Assessment of non-adherence of multiple sclerosis patients to medication and follow up clinic. *Health Sci J*. 2018;12(2):1-5. doi:10.21767/1791-809x.1000554
2. Remington G, Rodriguez Y, Logan D, Williamson C, Treadaway K. Facilitating medication adherence in patients with multiple sclerosis. *Int J MS Care*. 2013;15(1):36-45. doi:10.7224/1537-2073.2011-038
3. Imani A, Golestani M, Omrani A, et al. Analysis of therapeutic expenditure in patients with multiple sclerosis in Iran. *J Ilam Univ Med Sci*. 2014;21(7):169-177. [Persian].
4. Campbell JD, Ghushchyan V, Brett McQueen R, et al. Burden of multiple sclerosis on direct, indirect costs and quality of life: national US estimates. *Mult Scler Relat Disord*. 2014;3(2):227-236. doi:10.1016/j.msard.2013.09.004
5. Masoudi R, Mohammadi I, Nabavi SM, Ahmadi F. The effect of Orem based self-care program on physical quality of life in multiple sclerosis patients. *J Shahrekord Univ Med Sci*. 2008;10(2):21-29. [Persian].
6. Morillo Verdugo R, Ramírez Herráiz E, Fernández-Del Olmo R, Roig Bonet M, Valdivia García M. Adherence to disease-modifying treatments in patients with multiple sclerosis in Spain. *Patient Prefer Adherence*. 2019;13:261-272. doi:10.2147/ppa.s187983
7. Tavakkol M, Yousefi S. Studying demographic grounds and characteristics of the patients suffering from multiple sclerosis (MS) a member of Tehran MS society in 2011. *Bioethics Journal*. 2013;3(8):79-100.
8. Elhami SR, Mohammad K, Sahraian MA, Eftekhari H. A 20-year incidence trend (1989-2008) and point prevalence (March 20, 2009) of multiple sclerosis in Tehran, Iran: a population-based study. *Neuroepidemiology*. 2011;36(3):141-147. doi:10.1159/000324708
9. Sadat SJ, Allimohammadi N, Sardisiri M, Zoladl M. Experience of patients with multiple sclerosis about physical effects of their illness; a phenomenological study. *Dena J*. 2006;1(1):51-63.
10. Yermakov S, Davis M, Calnan M, et al. Impact of increasing adherence to disease-modifying therapies on healthcare resource utilization and direct medical and indirect work loss costs for patients with multiple sclerosis. *J Med Econ*. 2015;18(9):711-720. doi:10.3111/13696998.2015.1044276
11. Eftekhari E, Nikbakht H, Rabiei K, Etemadifar M. Effect of endurance training on aerobic power and quality of life in female patients with multiple sclerosis. *J Olympic Acad IR*. 2008;16(1):37-46. [Persian].
12. Masoudi R, Khayeri F, Safdari A. Effect of self-care program based on the Orem frame work on self concept in multiple sclerosis patients. *J Gorgan Univ Med Sci*. 2010;12(3):37-44. [Persian].
13. Rashvand F, Moshtagh-Eshgh Z, Soleimani M, Abtahi M, Nasiri M, Madani H. Effects of designed feeding patterns on fatigue in multiple sclerosis patients. *J Shahrekord Univ Med Sci*. 2013;15(2):77-85. [Persian].
14. Gold LS, Suh K, Schepman PB, Damal K, Hansen RN. Healthcare costs and resource utilization in patients with multiple sclerosis relapses treated with HP Acthar Gel®. *Adv Ther*. 2016;33(8):1279-1292. doi:10.1007/s12325-016-0363-0

15. Sicras-Mainar A, Ruíz-Beato E, Navarro-Artieda R, Maurino J. Impact on healthcare resource utilization of multiple sclerosis in Spain. *BMC Health Serv Res*. 2017;17(1):854. doi:10.1186/s12913-017-2807-x
16. Wingerchuk DM, Weinshenker BG. Disease modifying therapies for relapsing multiple sclerosis. *BMJ*. 2016;354:i3518. doi:10.1136/bmj.i3518
17. Rubin SM. Management of multiple sclerosis: an overview. *Dis Mon*. 2013;59(7):253-260. doi:10.1016/j.disamonth.2013.03.012
18. Torkildsen Ø, Myhr KM, Bø L. Disease-modifying treatments for multiple sclerosis - a review of approved medications. *Eur J Neurol*. 2016;23(Suppl 1):18-27. doi:10.1111/ene.12883
19. Scalfari A, Neuhaus A, Degenhardt A, et al. The natural history of multiple sclerosis: a geographically based study 10: relapses and long-term disability. *Brain*. 2010;133(Pt 7):1914-1929. doi:10.1093/brain/awq118
20. Goodin DS, Traboulsee A, Knappertz V, et al. Relationship between early clinical characteristics and long term disability outcomes: 16 year cohort study (follow-up) of the pivotal interferon β -1b trial in multiple sclerosis. *J Neurol Neurosurg Psychiatry*. 2012;83(3):282-287. doi:10.1136/jnnp-2011-301178
21. Krysko KM, Graves J, Rensel M, et al. Use of newer disease-modifying therapies in pediatric multiple sclerosis in the US. *Neurology*. 2018;91(19):e1778-e1787. doi:10.1212/wnl.00000000000006471
22. Costello K, Kennedy P, Scanzillo J. Recognizing nonadherence in patients with multiple sclerosis and maintaining treatment adherence in the long term. *Medscape J Med*. 2008;10(9):225.
23. Kafame F, Mohammadi F, Norouzi K, Rahgozar M. The effect of self-management program on the health status of multiple sclerosis patients. *J Res Dev Nurs Midwifery*. 2012;9(1):24-33. [Persian].
24. Tarrants M, Oleen-Burkey M, Castelli-Haley J, Lage MJ. The impact of comorbid depression on adherence to therapy for multiple sclerosis. *Mult Scler Int*. 2011;2011:271321. doi:10.1155/2011/271321
25. Tan H, Cai Q, Agarwal S, Stephenson JJ, Kamat S. Impact of adherence to disease-modifying therapies on clinical and economic outcomes among patients with multiple sclerosis. *Adv Ther*. 2011;28(1):51-61. doi:10.1007/s12325-010-0093-7
26. Ivanova JJ, Bergman RE, Birnbaum HG, Phillips AL, Stewart M, Meletiche DM. Impact of medication adherence to disease-modifying drugs on severe relapse, and direct and indirect costs among employees with multiple sclerosis in the US. *J Med Econ*. 2012;15(3):601-609. doi:10.3111/13696998.2012.667027
27. Agashivala N, Wu N, Abouzaid S, et al. Compliance to fingolimod and other disease modifying treatments in multiple sclerosis patients, a retrospective cohort study. *BMC Neurol*. 2013;13:138. doi:10.1186/1471-2377-13-138
28. Steinberg SC, Faris RJ, Chang CF, Chan A, Tankersley MA. Impact of adherence to interferons in the treatment of multiple sclerosis: a non-experimental, retrospective, cohort study. *Clin Drug Investig*. 2010;30(2):89-100. doi:10.2165/11533330-000000000-00000
29. Treadaway K, Cutter G, Salter A, et al. Factors that influence adherence with disease-modifying therapy in MS. *J Neurol*. 2009;256(4):568-576. doi:10.1007/s00415-009-0096-y
30. Evans C, Marrie RA, Zhu F, et al. Adherence and persistence to drug therapies for multiple sclerosis: a population-based study. *Mult Scler Relat Disord*. 2016;8:78-85. doi:10.1016/j.msard.2016.05.006
31. Wong J, Gomes T, Mamdani M, Manno M, O'Connor PW. Adherence to multiple sclerosis disease-modifying therapies in Ontario is low. *Can J Neurol Sci*. 2011;38(3):429-433. doi:10.1017/s0317167100011823
32. Corbin J, Strauss A. *Basics of Qualitative Research: Techniques and Procedures for Developing Grounded Theory*. SAGE Publications; 2014.
33. Polit DF, Beck CT. *Essentials of Nursing Research: Appraising Evidence for Nursing Practice*. 8th ed. Philadelphia: Lippincott Williams & Wilkins; 2014.
34. de Seze J, Borgel F, Brudon F. Patient perceptions of multiple sclerosis and its treatment. *Patient Prefer Adherence*. 2012;6:263-273. doi:10.2147/ppa.s27038
35. Di Battista G, Bertolotto A, Gasperini C, Ghezzi A, Maimone D, Solaro C. Multiple sclerosis state of the art (SMART): a qualitative and quantitative analysis of therapy's adherence, hospital reliability's perception, and services provided quality. *Mult Scler Int*. 2014;2014:752318. doi:10.1155/2014/752318
36. Roshangaran F. *Lived Experience of MS Patients' Families Exposure to Disease in 2015*. Isfahan: Islamic Azad University of Isfahan (Khorasgan Branch); 2015.
37. Kołtuniuk A, Rosińczuk J. Adherence to disease-modifying therapies in patients with multiple sclerosis. *Patient Prefer Adherence*. 2018;12:1557-1566. doi:10.2147/ppa.s175095
38. Munsell M, Fream M, Menzin J, Phillips AL. An evaluation of adherence in patients with multiple sclerosis newly initiating treatment with a self-injectable or an oral disease-modifying drug. *Patient Prefer Adherence*. 2017;11:55-62. doi:10.2147/ppa.s118107
39. Lee J, McPherson D, D'Ambrosi M, Stutsky M. Correlates and barriers to medication adherence in multiple sclerosis patients and their impact on clinical outcomes. *J Drug Assess*. 2019;8(Suppl 1):39. doi:10.1080/21556660.2019.1658319
40. Gromisch ES, Turner AP, Leipertz SL, Beauvais J, Haselkorn JK. Risk factors for suboptimal medication adherence in persons with multiple sclerosis: development of an electronic health record-based explanatory model for disease-modifying therapy use. *Arch Phys Med Rehabil*. 2020;101(5):807-814. doi:10.1016/j.apmr.2019.11.005
41. Câmara NA, Gondim AP. Factors associated with adherence to immunomodulator treatment in people with multiple sclerosis. *Braz J Pharm Sci*. 2017;53(1):e16132. doi:10.1590/s2175-97902017000116132

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