p-ISSN: 2788-4961 | e-ISSN: 2788-418X

DOI(Journal): 10.31703/giddr

DOI(Volume): 10.31703/giidr/.2024(IX) DOI(Issue): 10.31703/giidr.2024(IX.III)





GLOBAL IMMUNOLOGICAL & INFECTIOUS DISEASES REVIEW

**HEC-RECOGNIZED CATEGORY-Y** 

**VOL. IX, ISSUE III, SUMMER (SEPTEMBER-2024)** 

Double-blind Peer-review Research Journal www.giddrjournal.com

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#### **Article Title**

## Frequency, Impact, and Risk Factors of Fatigue in Patients with Multiple Sclerosis

# Global Immunological & Infectious Diseases Review

p-ISSN: 2788-4961 e-ISSN: 2788-418X

DOI (journal): 10.31703/giidr

**Volume:** IX (2024)

**DOI (volume):** 10.31703/giidr.2024(IX)

Issue: Summer (September-2024)

DOI(Issue): 10.31703/giidr.2024(IX-III)

Home Page www.giidrjournal.com

Volume: IX (2024)

https://www.giidrjournal.com/Current-issues

Issue: III-Summer (September-2024)
https://www.giidrjournal.com/Current-issues/9/2/2024

### Scope

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#### **Abstract**

Fatigue is one of the most common and debilitating symptoms affecting 75–90% of individuals with multiple sclerosis (MS), significantly impacting their quality of life. This study aimed to assess the prevalence, effects, and risk factors of fatigue among MS patients in Quetta, Pakistan. A cross-sectional descriptive design involved 34 participants aged 20-50 years from Bolan Medical Complex Hospital and nearby facilities. The Fatigue Severity Scale(FSS) was used to evaluate the impact of fatigue on functionality and well-being. Findings revealed that II patients experienced severe fatigue due to lack of exercise, and 8 linked it to depression. MRI showed lesions in 4 out of 5 patients with severe fatigue. Additionally, 71% reported worsening of other symptoms due to fatigue. The study highlights fatigue in MS as a complex issue requiring integrated management strategies and contributes to addressing gaps in literature to improve healthcare policies and patient quality of

Keywords: Frequency, Impact, Risk Factors of Multiple Sclerosis in Patients, Pakistan

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Pages: 53-63

DOI: 10.3 | 703/giidr.2024(IX-III).07

DOI link: https://dx.doi.org/10.31703/giidrr.2024(IX-III).07
Article link: http://www.giidrrjournal.com/article/A-b-c
Full-text Link: https://giidrrjournal.com/fulltext/

Pdf link: https://www.giidrjournal.com/jadmin/Auther/31rvlolA2.pdf







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www.humapub.com

Doi: https://dx.doi.org/10.31703



# Citing this Article

	Frequency, Impact, and Risk Factors of Fatigue in Patients with Multiple Sclerosis						
07	Author	Mahmood khan Muhammad Abbas Khan Gohar Shah Sana Ullah Muhammad Nawaz		DOI	10.31703/giidr.2024(IX-III).07		.4(IX-III).07
Pages	53-63	Year	2024	Volume	IX	Issue	III
	APA	and Risk	khan, M., Khan, M. A., Shah, G., Ullah, S., & Nawaz, M. (2024). Frequency, Impact, and Risk Factors of Fatigue in Patients with Multiple Sclerosis. <i>Global Immunological &amp; Infectious Diseases Review</i> , IX(III), 53-63. <a href="https://doi.org/10.31703/giidr.2024(IX-III).07">https://doi.org/10.31703/giidr.2024(IX-III).07</a>				
	CHICAGO	Nawaz. 2 Multiple S	hmood, Muhammad 2024. "Frequency, Im Sclerosis." <i>Global Im</i> 1703/giidr.2024(IX-I	pact, and Rismunological &	sk Factors of Fa	itigue in Pat	ients with
ıg Styles	HARVARD	KHAN, M., KHAN, M. A., SHAH, G., ULLAH, S. & NAWAZ, M. 2024. Frequency, Impact, and Risk Factors of Fatigue in Patients with Multiple Sclerosis. <i>Global Immunological &amp; Infectious Diseases Review IX</i> , 53-63.					
Referencing & Citing Styles	MHRA	khan, Mahmood, Muhammad Abbas Khan, Gohar Shah, Sana Ullah, and Muhammad Nawaz. 2024. 'Frequency, Impact, and Risk Factors of Fatigue in Patients with Multiple Sclerosis', Global Immunological & Infectious Diseases Review, IX: 53-63.					
Referenc	MLA	khan, Mahmood, et al. "Frequency, Impact, and Risk Factors of Fatigue in Patients with Multiple Sclerosis." <i>Global Immunological &amp; Infectious Diseases Review IX.III</i> (2024): 53-63. Print.					
	OXFORD	khan, Mahmood, et al. (2024), 'Frequency, Impact, and Risk Factors of Fatigue in Patients with Multiple Sclerosis', Global Immunological & Infectious Diseases Review IX (III), 53-63.					
	TURABIAN	khan, Mahmood, Muhammad Abbas Khan, Gohar Shah, Sana Ullah, and Muham Nawaz. "Frequency, Impact, and Risk Factors of Fatigue in Patients with Multiple Sclerosis." <i>Global Immunological &amp; Infectious Diseases Review IX</i> , no. III (2024): 5 <a href="https://dx.doi.org/10.31703/giidr.2024(IX-III).07">https://dx.doi.org/10.31703/giidr.2024(IX-III).07</a> .				vith Multiple	







# Global Immunological & Infectious Diseases Review

www.giidrjournal.com
DOI:http://dx.doi.org/10.31703/giidr



Pages: 53-63 <u>URL:https://doi.org/10.31703/giidr.2024(IX-III).07</u>

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#### Title

# Frequency, Impact, and Risk Factors of Fatigue in Patients with Multiple Sclerosis

### **Abstract**

Fatigue is one of the most common and debilitating symptoms affecting 75–90% of individuals with multiple sclerosis (MS), significantly impacting their quality of life. This study aimed to assess the prevalence, effects, and risk factors of fatigue among MS patients in Quetta, Pakistan. A cross-sectional descriptive design involved 34 participants aged 20-50 years from Bolan Medical Complex Hospital and nearby facilities. The Fatigue Severity Scale(FSS) was used to evaluate the impact of fatigue on functionality and well-being. Findings revealed that II patients experienced severe fatigue due to lack of exercise, and 8 linked it to depression. MRI showed lesions in 4 out of 5 patients with severe fatigue. Additionally, 71% reported worsening of other symptoms due to fatigue. The study highlights fatigue in MS as a complex issue requiring integrated management strategies and contributes addressing gaps in literature to improve healthcare policies and patient quality of life.

**Keywords:** Frequency, Impact, Risk Factors of Multiple Sclerosis in Patients, Pakistan

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# Introduction

The inflammatory disease known as multiple sclerosis (MS) is caused by the demyelination of nerve fibers in the central nervous system, which results in a variety of

neurological symptoms (Yewande & Olawunmi, 2023). Of all of these symptoms, fatigue is perhaps the most common and most disabling. Studies show that fatigue is present in 75-90% of all multiple sclerosis patients





and this greatly impacts their quality of life and functional status (Ramirez et al., 2021). This tiredness is not a type of fatigue that results from physical work, it can manifest when the person has done very little work and may be in direct opposition to the amount of work done. The factors contributing to fatigue in MS are multiple and have neuro-inflammatory origin, psychogenic, and metabolic causes (Cordone et al., 2023).

The findings of the study show that fatigue in MS goes beyond individuals' physical capacity impairment though it has some effects on the social roles they occupy; it also causes social isolation, anxiety and depression, and activity restriction (Newton et al., 2016). Common experiences that patients describe include complaints and poor motivation from work or social isolation because they cannot work or socialize at the level they desire. Moreover, fatigue leads to higher healthcare costs because more often and extensive visits require additional assistance services.

Patients | with multiple sclerosis experience significant physical and mental deficits as a result of this chronic illness (Hosseini et al., 2022). Among these challenges, fatigue is probably one the most recurrent and among the ones with the biggest impact to the patient. However, fatigue which is present in over 90% of MS patients does not receive the attention or management it deserves, and patients are often left with inadequate support (Macaron et al., 2023). This issue is expected to be addressed by this study by exploring the prevalence, severity, and possible predictors of fatigue among MS patients. It is with the aim of offering direction to effective clinical practices and recommendations necessary for reducing fatigue in MS patients that this study aims to offer a comprehensive understanding of these factors.

Up to 90% of people with multiple sclerosis experience fatigue, which has a significant negative influence on their functioning and quality of life (Eizaguirre et al., 2020). However, the pathophysiology of this complaint is not well characterized, and its treatment has received suboptimal attention. In this study, the existence severity, and potential antecedents of fatigue in MS will be examined with the aim of closing the gap between the clinical research findings and the patient's perspective. Comparing the current and past literature related to fatigue in MS has multiple implications for nurses, healthcare professionals, family caregivers, patients, and the government.

Research shows that in the America, about 36.5% to 34%, of people with MS suffer from fatigue (Ramirez

et al., 2021). Additionally, it has been estimated that the overall prevalence of fatigue in MS patients is around 59.1%; however, there are some moderate variations in the results obtained from different measurement instruments and patient demographics (Yi et al., 2024). The details of how pervasive MS-associated fatigue is in Asia are still scarce because of inadequate research. However, it is estimated that between 36.5 % – 34 % of patients experience fatigue in Asia MS countries (Ismail & Saqr, 2022).

In certain works, done in countries such as Saudi Arabia the percentage of MS patients complaining, of fatigability was 48.3% (AlSaeed et al., 2022). There is a scarcity of detailed information regarding fatigue surveys conducted for Multiple Sclerosis patients in Pakistan. However, there is the possibility of having obtained data that has relied on individuals with MS making testimonies of their lives and experiences in the region; fatigue has been identified as one of the big challenges that most people with MS will grapple with in their day to day activities Zeine, 2023.

According to Oliva Ramirez et at (2021) fatigue levels are reported to be different among MS patients with a varying level that ranges from 36.5% to 34%. An analysis of several articles revealed that fatigue is cited as the most burdensome symptom by between 30-60 percent of patients. A sample of 1,446 participants was followed up for 2.5 years, during which the overall prevalence of fatigue had risen from 56% at the baseline to 62.5% (Ramirez et al., 2021). According to Razazian et al. (2021), fatigue is a major factor in determining quality of life (QoL) in individuals with multiple sclerosis (MS). These studies show that fatigue is associated with lower QoL scores and has an uneven effect on the physical, cognitive, psychological-social domains. Research using the Fatigue Impact Scale revealed that of all the MS patients, 71% complained that their fatigue worsened other symptoms they were experiencing, suggesting that fatigue significantly affected functioning (Razazian et al., 2020).

Marchesi et al. (2022) found that the EDSS neurological impairment index was positively related to fatigue levels, which usually indicates that higher indexes of neurological barrier mean that patients are experiencing higher levels of fatigue. One study has found that patients with progressive forms of MS, especially those with primary progressive MS, report greater degrees of fatigue than patients with relapsing-remitting MS (Marchesi et al., 2022). Ayache et al. (2022) said that depression and anxiety are other

symptoms often associated with MS and their presence affects fatigue levels. In the literature, studies have proposed that some aspects of fatigue could be reduced through improved mental health (Ayache et al., 2022). Gianni (2023) stated that the mechanisms that underlie fatigue in persons with MS are multiple and interrelated. It includes 11 central and 14 peripheral mechanisms. It is believed that central fatigue is caused by neurotransmitter abnormalities and the disruption of circadian rhythms. Peripheral fatigue may be attributed to the muscle abnormalities due to the disease process. This article also gives information on causes that have a role to play in the experience of fatigue by the patients and they include side effects of medications and other related issues like for instance inactivity Gianni, E. (2023).

# **Research Methodology:**

# Research Design/ Research Area

The Bolan Medical Complex Hospital (BMCH), Sandeman Provincial Hospital (SPH), and Sheikh Khalifah Bin Zayyad Hospital Quetta were the sites of this study's descriptive cross-sectional survey. This research was completed between October 2022 and October 2024 to clinically define acute multiple sclerosis disease in a single time point. In total, 34 patients aged from 20 to 50 were selected.

# **Data or Sample Collection**

Data collection involved a multi-stage sampling technique to provide a representative sample of the MS population of Quetta. To be more precise, the sample size will be estimated employing an adequate formula to reach a 95% confidence interval and 5% margin of error. Potential participants will be approached from local hospitals and support groups, with an estimated target sample size of 34 with an MS diagnosis The following participants were included with the estimated target sample size of approximately 34 with diagnosed MS were collected following the institutional ethics committee approval and all participants' informed consents. The data collection was conducted for eight months, and only patients were included in the study through purposive sampling, which makes the sample as diverse as possible.

### **Inclusion Criteria**

For this study the eligibility criteria were set in a way that the participant had to be an adult and/or above 18 years of age since the purpose of most of the questions given were to self-report symptoms, therefore only

those with the capacity to voluntarily give such information were considered. Furthermore. participants had to have a clinical diagnosis of multiple sclerosis according to a neurological expert to exclude other neurological or medical disorders. Lastly, some participants had to display fatigue in such a way in order to fully respond to the questions that could be answered only in the case when the persons themselves indicated that they suffer from fatigue, as the study was geared primarily towards the analysis of the prevalence, effects, and potential causes of fatigue in the MS patient pool. This set of criteria assisted keep the relation and specificity of data retrieved to the objectives of the study.

# **Exclusion Criteria**

People with other neurological or mental conditions that can cause exhaustion, such as depression or chronic fatigue syndrome, were thus excluded from this study due to its exclusion criteria. These conditions could have masked other variables that may have affected fatigue thereby complicating the possibility of determining the true impact of Multiple Sclerosis (MS). It's also important to note that participants who did not come to the supported decision-making for holding informed consent or for answering the survey questions because of moderate to severe dementia were also excluded. This made it possible to have participants who were able to comprehend the objective and approach of the study, respond to questions to self-rate their levels of fatigue. Doing so allowed the study to effectively focus on fatigue in individuals with MS without confounding factors of other medical conditions of cognitive impairment getting in the way.

# Questionnaire

A semi-structured questionnaire was developed to assess fatigue level and how it affects their daily activities. The questionnaire consisted of closed-ended and open-ended questions, categorized into the following sections:

- 1. Demographic information: Age, gender, duration of diagnosis, and current treatment.
- 2. Fatigue measurement: The Fatigue Severity Scale (FSS), a common questionnaire, was used to gauge the degree of exhaustion.
- Impact of fatigue: Participants were requested to say how far fatigue impacted their daily living, work, and general well-being by answering a set of Likert scale questions.

4. Risk factors: Additional questions inquiring about lifestyle factors, presence of other diseases, mood disorders, sleep problems, and medications taken were employed as queries that might predispose the patient to fatigue.

The questionnaire was developed and pre-tested on a significant sample to determine its relevance and comprehensible structure. Changes were made depending on the results obtained to increase the stability of the instrument.

#### Lab tests

To evaluate the existence and course of Multiple Sclerosis (MS), as well as potential causes of fatigue, the following diagnostic procedures were carried out:

#### **MRI Brain with Contrast**

An MRI with contrast was done to outline the brain and Pick out any MS-related lesions, these are signs of disease activity and progression. The existence of lesions that affect either the area linked with movement or the cognitive areas may coincide with the extent of fatigue in MS patients. They often include regions of demyelination which cause interruption of the neuronal signal flow and can cause fatigue.

# **Visual Evoked Potential (VEP)**

VEP testing is a neuro-diagnostic procedure that assesses electrical potentials on the brain screen in relation to visual stimulation. It also aids in assessing the performance of the optic nerves; this can be impacted by MS It is used in the VEP, and delays in response may point toward demyelination in the connections of the visual pathway; fatigue is correlated with sensory impairment here because when the visual pathways are impaired by MS the quantity of signal enhances the mental load and makes a fatigue contribution.

# Lumbar Puncture (Cerebrospinal Fluid Oligoclonal Bands)

CSF was tested for oligoclonal bands after performing lumbar puncture to evaluate intrathecal antibody synthesis. These bands are abnormal proteins that suggest an immune response activity within the Central Nervous System (CNS), common in Multiple Sclerosis. These bands are present in CSF but not in sera and their presence indicates MS. There is a suggestion that

higher levels may indicate increased disease activity and subsequently, increased fatigue.

# **Serum Oligoclonal Bands**

Serum electrophoresis and oligoclonal bands analysis were also conducted for the sera obtained from the patient's peripheral blood. Conversely, OBs detected in the serum are not exclusive to MS and might be suggestive of another disease. However, it is useful to compare serum and CSF oligoclonal bands, to evaluate the presence and activity of immune abnormalities in the CNS. The presence of oligoclonal bands is the most compelling evidence and is supported by recent findings when CSF results differ from serum in patients with active MS pathology.

These diagnostic results have been used by me to explore the bio-mechanisms of fatigue in MS patients and identify potential biomarkers that could exacerbate the severe feeling of fatigue.

# **Statistical Analysis**

### **Results**

A total of 34 patients were selected with PTSD, out of which 9 were male (26.47%) and 25 patients were female (73.52%). The patients belonged to three different age groups: The participants in the current study were males, aged between 20-30 years, 31-40 years, and 41-50 years from different villages in Quetta District. The total number of males was 9 similar, among them 20-30 years were 2 patients, 31-40 years were 4 patients, and 41-50 years patients were 3There were 25 female patients in all, 8 of whom were between the ages of 31 and 40, and 7 of whom were between the ages of 41 and 50.

**Table I**Study Participants' Demographic Distribution by Age Group and Gender

Age Group (years)	Total Patients (n=34)	Male Patients (n=9)	Female Patients (n=25)	Frequency %
20-30	10	2	8	29.41%
31-40	14	4	10	41.17%
41-50	10	3	7	29.41%
Total	34	9 (26.47%)	25 (73.52%)	100%

**Figure 1**Study Participants' Demographic Distribution by Age Group and Gender

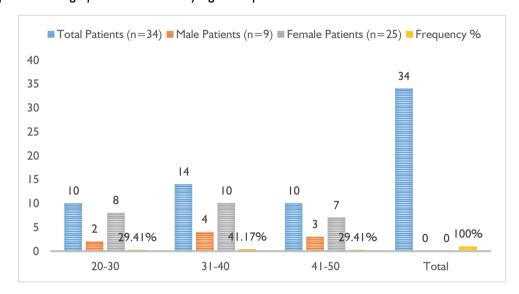


Table and Figure I indicate that the study had 34 participants and among them, more were females (73.52%) as compared to control males (26.47%). Age groups included 20-30, 31-40, and 41-50-year age bracket with the age bracket of 31-40 accounting for

41.17% of the participants. The 20-30 and 41-50 categories attracted 29.41 % of participants each. This breakdown shows a rather good representation of female personnel in all age groups.

 Table 2

 Impact Level of Fatigue Associated with Each Risk Factor

Risk Factor	Low Impact (n=8)	Moderate Impact (n=15)	High Impact (n=11)
Physical Inactivity	2	6	6
Depression	3	7	8
Sleep Disorders	I	4	7
Medication Side Effects	2	5	3
Chronic Pain	0	6	4
Total	8	15	<u> </u>

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Figure 2
Impact Level of Fatigue Associated with Each Risk Factor

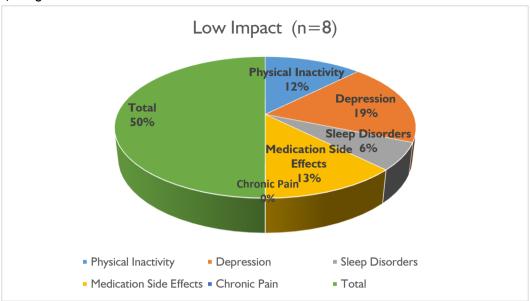


Table and Figure 2 present fatigue magnitude with risk factors among 34 participants. Inactivity and depression exhibit the most impact as 6 patients each highlighted a high impact of both. Others too play a very significant role including sleep disorders of which 7 stay at high

impact. Further, medication side effects and chronic pain are two of the lowest high-impact counts of 3 and 4 respectively. Altogether, the number of moderate impacts in total is greatest related to depression in 7 patients.

**Table 3**MRI Brain with Contrast Results for MS Patients

Patient ID	MRI Results (Lesions)	Location of Lesions	Severity of Lesions (Scale 1-10)	Correlation with Fatigue (Scale 1-10)
ı	Yes	Periventricular	7	8
2	Yes	Cervical spine	6	7
3	No	N/A	N/A	4
4	Yes	Periventricular	8	9
5	Yes	Cervical spine	5	6
Total	4/5 Positive	Periventricular and Cervical Spine	-	34

Figure 3
MRI Brain with Contrast Results for MS Patients

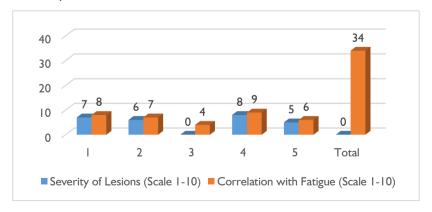


Table III and Figure 3 demonstrate five patients, the MRI results of four of the patients with lesions, preferably in the periventricular and cervical spine regions. Minimal to moderate disease is present as lesions rated on a scale of I-I0 ranging from 5 to 8.

Fatigue has a direct link with the severity of lesions in affected patients ranging from 6 to 9. The first patient participant had no lesions visible and their fatigue rating of 12 decreased to 4.

**Table 4**Visual Evoked Potential (VEP) Test Results

Age Range (years)	Entire Patients (n=34)	Male Patients (n=9)	Female Patients (n=25)	VEP Delay (ms)	Abnormal Response	Correlation with Fatigue (Scale 1-10)
20-30	10	2	8	135-150	Yes: Majority	6-8
31-40	14	4	10	120-160	Yes: Majority	7-9
41-50	10	3	7	120-160	Yes: Majority	5-9
Total	34	9	25	-	4/5 Abnormal	34

Table 4 shows the Visual Evoked Potential (VEP) test results data from 34 Multiple Sclerosis patients, consisting of 9 males and 25 females, divided into three age groups: Individuals in the following age ranges: 20–30 years (10); 31–40 years (14); and 41–50 years (10). The mean delay was seen to be around 130±40 ms,

and the majority of patients exhibited abnormal VEP delays of 120-160 ms. Fatigue scores varied by age group: For 20-30 years the frequency was 6-8, for 31-40 years – 7-9, for 41-50 years – 5-9. Altogether, VEP responses were pathologic in 4 of 5 patients with a total fatigue score of 34.

**Table 5**Lumbar Puncture (CSF Oligoclonal Bands) Results

Age Group (years)	Male Patients (n=9)	Female Patients (n=25)	Oligoclonal Bands in CSF (Yes/No)	Elevated Levels (Yes/No)	Correlation with Fatigue (Scale 1-10)
20-30	2	8	Yes: Majority	Yes: Majority	6-8
31-40	4	10	Yes: Majority	Yes: Majority	7-9
41-50	3	7	Yes: Majority	No	5-9
Total	9	25	4/5 Positive	3/5 Elevated	34

Table 5 shows the summary of the results of lumbar punctures of 34 patients; 5 of them tested positive for oligoclonal bands in their CSF, of which 3 displayed raised levels. Fatigue levels in the patients revealed average scores between patients 6 to 8 in the higher

fatigue groups and 5 to 9 in the lower fatigue groups. The patient who did not have oligoclonal bands noted a fatigue value of 4 below the initial measurement. In any case, the findings indicate that there is a strong relationship between oligoclonal bands and fatigue.

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**Table 6**Serum Oligoclonal Bands Testing Results

Age Range (Years)	Gender	Number of Patients	Oligoclonal Bands in Serum (Yes/No)	CSF vs Serum Discrepancy (Yes/No)	Average Fatigue Correlation (1- 10)
20-30	Male	2	No	No	7
20-30	Female	8	No	No	6.5
31-40	Male	4	No	No	6.25
J1-10	Female	10	No	No	6.5

Age Range (Years)	Gender	Number of Patients	Oligoclonal Bands in Serum (Yes/No)	CSF vs Serum Discrepancy (Yes/No)	Average Fatigue Correlation (I- I0)
41-50	Male	3	No	No	7
<del>1</del> 1-30	Female	7	No	No	6.71

Table 6 summarizes serum oligoclonal bands testing results for 34 patients with multiple sclerosis. Patients are grouped by age range and gender. No oligoclonal bands were detected in serum across all groups, and no CSF vs serum discrepancies were observed. Fatigue correlation scores ranged from 6.25 to 7, with higher scores seen in males. Females aged 20-30 and 31-40 showed a slightly lower average fatigue score (6.5).

### **Discussions**

Of the 34 MS patients in the study, 25 (73.52%) were female. The study was carried out at three hospitals: Sheikh Khalifah Bin Zayyad Hospital in Quetta, Bolan Medical Complex Hospital, and Sandeman Provincial Hospital. Numerous participants were between the ages of 31 and 40, according to the demographic research. which showed proportionate representation. This demographic insight is important since it allows one to understand how fatigue may differ with regard to age and gender among the MS population The inclusion criteria ensured that all participants had an MS diagnosis and indicated that they experience MS-related fatigue, thereby keeping the study on target with important symptoms.

It is only important to discuss fatigue in Multiple Sclerosis (MS), on account of the effects that this symptom has on the lives of patients. Up to 90% of people with MS experience fatigue, making it one of the most prevalent complaints among them. Unlike other symptoms that are normally attributed to physical activity this symptom can present itself even after little physical activity is carried out which makes it a complex one. As with many aspects of MS, fatigue is multiple factors, by including inflammatory, psychological, and metabolic, and thus may be more challenging to treat. The most frequent emotional outcome of fatigue is the withdrawal from social contacts and reduced social functioning accompanied by frustration and lack of hope experienced by MT patients (Ayache & Chalah, 2017).

Sellitto et al. (2021) pointed out that a literature review shows that fatigue affects various aspects of life for individuals with MS including physical, cognitive, and psychosocial (Sellitto et al., 2021). Thus, it has been

established that various symptoms tend to worsen due to fatigue in nearly 71% of the patients, and the general quality of life has decreased as well. The Expanded Disability Status Scale (EDSS) may be used to define neurological deficiency, which is linked to fatigue levels, according to other studies based on self-assessed reported exhaustion. There is strong evidence that individuals with progressive forms of MS experience more severe fatigue than those with relapsing forms, according to Herring et al. (2021). This implies that the disease may cause increased fatigue symptoms and that there is a need to design interventions on how to cope with this debilitating aspect of MS (Herring et al., 2021).

Evaluation of the risk factors that predispose a patient to fatigue showed that both physical inactivity and depression were possibilities. Of the participants, six people expressed high-impact fatigue resulting from both aspects. Furthermore, sleep disorders were recognized as one more regularly occurring risk factor affecting 7 patients with severe outcomes. Altogether, these results stress the need to establish complex approaches to the problem of fatigue in MS patients, including its psychological aspect. When these risk factors are eventually recognized, it can support measures aimed at preventing patients' everyday weariness and reduced quality of life.

Rooney et al. (2019) have also revealed that fatigue is higher among progressive MS patients and linked to worse physical, cognitive, and psychological conditions no matter the type of MS Fatigue is among the most frequent symptoms reported by 81% of the patients with MS. The prevalence, risk factors, and effects of fatigue in contemporary MS patients are the main topics of this review, which thoroughly extracts recent research. Results pertaining to gender, degree of impairment, psychosocial factors, and excessive daytime sleepiness are covered in depth (Rooney et al., 2019).

According to Oliva Ramirez et al. (2021), with a cross-sectional prevalence ranging from 36.5% to 97%, fatigue is also one of the most common symptoms of multiple sclerosis. According to a systematic review conducted by Hobart and colleagues, fatigue ranged from 36.5% to 78% according to the

assessment tools used Another cross-sectional study of 1401 people with MS established that fatigue escalated from 56% at the baseline to 62.5% after 2.5 years; thus, fatigue is a chronic condition. In addition, the

patients with MS report fatigue to be worse and interfere with the quality of life for the patients (Ramirez et al., 2021).

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