Responsiveness of Pain and Fatigue of Patients with Multiple Sclerosis to the Zone Foot Reflexology Massage

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Abstract

Background: Patients with multiple sclerosis (MS) have symptoms that affect all facets of their lives; the most prevalent of these symptoms are pain and fatigue, which significantly lower their quality of life. The disease's complexity, the challenge of determining appropriate treatment, and the variety of symptoms underscore the gravity of the situation and the importance of including complementary interventions along with pharmacological therapy. The Zone foot reflexology massage (ZFRM) is one of the most popular complementary interventions that seem to be low-risk, adaptable, inexpensive, easy to use, and quite effective at decreasing pain and fatigue in several trials. ***Study aim:*** Evaluate the responsiveness of pain and fatigue of patients with MS to the Zone foot reflexology massage. ***Design:*** A quasi-experimental design. ***Setting:*** Multiple Sclerosis clinic belonging to the Neurological Diseases Outpatient Clinic, Zagazig University Hospitals, Al Sharqia Governorate, Egypt. ***Subject:*** A purposive sample of 60 adult patients with MS randomly assigned into two equal groups. ***Tools:*** A structured interview questionnaire, a visual analog scale, and a fatigue severity scale. ***Results:*** A statistically significant difference and decrease were observed in pain mean scores ($p = 0.005$ & 0.001) and fatigue mean scores ($p = 0.004$ & 0.001) of study group patients compared to the control group post-8^{th} and 12^{th} week, respectively, of Zone foot reflexology massage intervention. ***Conclusions:*** The pain and fatigue of patients with MS respond positively to Zone foot reflexology massage sessions, which reflect the significant effect of Zone foot reflexology massage in decreasing and improving the pain and fatigue of those patients. ***Recommendations:*** Zone foot reflexology massage should be a key component of provided care for patients with MS in addition to pharmacological treatments.

Keywords: Multiple sclerosis, Pain, Fatigue, Zone foot reflexology massage.

Introduction:

Multiple sclerosis (MS) is a long-term autoimmune condition linked to inflammation mediated by the central nervous system. The immune system targets the myelin sheath that surrounds nerve fibers in multiple sclerosis, which impairs brain-to-body communication. One of the main pathological characteristics of MS that affect the brain and have a variety of consequences on nerve impulse conduction is inflammation and demyelination of spinal nerve cells **(Gaballah et al., 2023)**. MS causes a variety of functional abnormalities, including fatigue, pain, incontinence, cognitive issues, psychosocial issues, and physical impairment (such as weakness, stiffness, sensory dysfunction, and visual loss) **(Amatya et al., 2019)**. In MS patients, the most prevalent complaints and symptoms that lower their quality of life (QoL) are fatigue and pain **(Gaballah et al., 2023)**.

Fatigue is one of MS's most incapacitating symptoms, which frequently appears as the initial symptom and persists throughout the illness **(Power et al., 2021)**. Up to 90% of MS patients have been reported to experience it; which might be cognitive (slowed processing speed or mental exhaustion) or physical (arm or leg fatigue). Its exact cause is unclear. On the other hand, some forms of fatigue might be brought on by pain, nighttime waking from bladder malfunction, or the effort required to carry out daily tasks **(Alain L. Fymat, 2023)**. Furthermore, according to earlier research, between 40 to 80 percent of MS patients reported having excruciating pain, and 44 percent reported having trouble carrying out daily

tasks **(Jensen et al., 2009; Johansson et al., 2007)**.

Chronic MS symptoms, perceived ineffectiveness, and negative reactions to immune-modulating treatments may raise interest in complementary and alternative therapies like reflexology, acupuncture, yoga, heliotherapy, and exercise, which are frequently used to manage symptoms and enhance the quality of life (QoL) **(Claflin et al., 2018)**. According to **Sari et al., (2020)**, individuals with numerous chronic conditions can benefit from complementary therapies, which are risk-free, safe, and effective methods that can be used alone or in conjunction with other approaches.

Instead of providing patients with traditional nursing care, nursing is now frequently using complementary therapy as part of nursing care to enhance and implement holistic care **(Naseri-Salahshour et al., 2019)**. Nursing complementary interventions are considering noninvasive techniques without negative effects that can improve everyday living activities, reduce fatigue severity, and offer patients greater safety. They use in conjunction with standard nursing care. Examples of these techniques include energy conservation, therapeutic exercises, and reflexology **(Arji et al., 2022)**.

One of the most often used complementary and alternative therapies that can be helpful when used alongside other treatments for a chronic condition is reflexology **(Venugopal et al., 2023).** Reflexology is a type of massage therapy that targets particular body points. It is based on the theory that applying pressure to these points affects the health of the body part that corresponds to each point **(Ebrahimi et al., 2020)**. According to **Kartka & Ulfa (2020)**, the technique's method of action entails stimulating specific body parts to promote circulation, vitality, and relaxation while preserving homeostasis.

Zone foot reflexology massage is the most popular kind of reflexology, sometimes referred to as foot reflexology or reflexology massage. It is founded on the idea that particular regions on the soles of the feet represent various bodily parts and functions. It is thought that these reflex zones can be triggered by appropriately applying pressure and stimulation to specific locations, which would promote therapeutic effects by boosting blood flow, nutrients, nerves, etc. **(He MY et al., 2024)**. There are a number of theories regarding the possible mechanisms of zone foot reflexology massage. They mostly focus on how electromagnetic fields allow energy to freely move throughout the body. According to one idea, foot reflexology can help heal obstructed energy so that the organs and the body's other energy fields can communicate more effectively. Another idea holds that lactic acid crystals that impede energy flow can be broken up by applying pressure to particular foot locations during reflexology **(Embong et al., 2016)**.

MS symptomatic management plays a crucial role in improving a patient's QoL on a daily basis; however, it is important to understand that symptomatic management does not alter the course of the disease; rather, it focuses on specific symptoms, offering relief and improving functionality. Complementary interventions alongside constant therapy are often still essential to MS management, allowing patients to effectively control their symptoms and maintain their overall QoL **(Al-ma'mouri, 2024)**. So, these interventions should be implemented for MS patients to achieve a positive health outcome by preventing consequences from the disease's progression and negative drug effects **(Hauser & Cree, 2020)**. The research indicates that ZFRM is a simple, non-invasive, inexpensive, and side-effect-free therapy that can help with cancer symptoms, sleep disruptions, and other health issues **(He MY et al., 2024)**; thus, with the right training, nurses can do it as easily as professional practitioners in order to promote relaxation and healing of those patients **(Gaballah et al., 2023)**.

Significant of study:

Approximately 2.8 million people worldwide suffer from MS, with women being twice as likely to receive a diagnosis **(Walton et al., 2020)**. MS significantly impacts function, economics, and QoL and typically affects people in their early adult years **(Ando et al., 2022)**. Pain and fatigue are the worst symptoms of MS, affecting 55% to 90% of patients worldwide **(Salehi et al., 2020)**. Between 10% and 15% of people may experience negative side effects or find pharmaceutical therapies ineffective **(Claflin et al., 2018)**. The everyday QoL of patients with MS is greatly enhanced by symptomatic management; thus, to

help persons with MS live better lives, alongside disease-modifying therapies, complementary interventions are essential for improving symptomatic control **(Al-ma'mouri, 2024)**. Zone foot reflexology massage is the most effective way to treat various chronic disease symptoms without posing any risks or being expensive, according to numerous studies conducted in the US and other nations **(Mirhosseini et al., 2019; Sajadi et al., 2020)**.

Aim of the study:

The aim of the study was to evaluate the responsiveness of pain and fatigue of patients with multiple sclerosis to the Zone foot reflexology massage through:

- Assessing the baseline levels of pain and fatigue in patients with multiple sclerosis.
- Designing and implementing zone foot reflexology massage sessions on the patients with multiple sclerosis who are suffering from pain and fatigue.
- Evaluating the effect of zone foot reflexology massage on the pain and fatigue levels of patients with multiple sclerosis.

Research hypotheses:

To achieve the study's aim, the following research hypotheses were formulated:

- **H1:** The pain level in study group patients will respond positively and decrease after Zone foot reflexology massage sessions intervention compared to control group patients.
- **H2:** The fatigue level in study group patients will respond positively and decrease after Zone foot reflexology massage sessions intervention compared to control group patients.

Subjects and Methods

Research design:

A quasi-experimental two-group research design with pre- and post-tests (repeated measurements) on the study and control groups was utilized to conduct the study. A cause-and-effect relationship between the independent and dependent variables is investigated using the quasi-experimental study approach. The dependent variable is the one that is impacted, whereas the independent variable is the one that is influenced **(Loewen & Plonsky, 2016)**.

Setting:

The study was conducted in the Multiple Sclerosis (MS) clinic belonging to the neurological diseases outpatient clinic at Zagazig University Hospitals, Al Sharqia Governorate, Egypt. The MS clinic present on the second floor of the outpatient clinics building at Zagazig University Hospitals comprises an examination room (This area is used for routine examination and follow-up visits for MS patients) and a physical therapy room (This room provides physiotherapy and rehabilitation services, which are crucial for managing MS symptoms, including mobility issues).

Subjects:

A purposeful sample of 60 MS patients who are being treated or monitored in the aforementioned location; the following were requirements for inclusion: being at least eighteen years old, both male and female, having been diagnosed with MS at least six months prior, being able to walk without assistance, experiencing pain and fatigue, not having visual or hearing impairment, not having previously used complementary and alternative therapies, having both right and left feet, not having vascular disease, ulcers, infections, fractures, sprains, or surgical procedures in either foot and not being pregnant. Patients who are currently receiving other forms of therapy for pain or fatigue that could skew results, those with severe cognitive impairment or health conditions that could interfere with the study, those with foot injuries or conditions that prevent Zone foot reflexology massage and patients who are unwilling to continue the study were all excluded.

Sample size:

The following parameters were used to estimate the sample size using the Epi Info 7 program: population size 300, 50% prevalence rate, 95% confidence coefficient, and 10% tolerable error. A minimum of 60 patients was needed for the sample. They were split into two equal groups of 30 patients each at random: 30 patients in the study group received the Zone foot reflexology massage in addition to their routine treatment, and 30 patients in the control group received routine treatment with no additional intervention. The sample size was calculated based on **Ronser, (2016)** using the following equation:

$$n = \left(\frac{Z_{1-\alpha/2} + Z_{1-\beta}}{ES} \right)^2$$

Data collecting tools include:

Tool I: A structured interview questionnaire: It was designed by the researchers after reviewing related pertinent literature **(Ma et al., 2023; Racke et al., 2022; Dikmen et al., 2019)** to assess the patients' demographic and medical history. It had the following two parts:

- **Part 1: Socio-demographic characteristics:** Five items concerning the patient's age, gender, degree of education, marital status, and occupation were included in this part.
- **Part 2: Medical history information:** This part was used to evaluate the patient's medical history; it included information on the type of MS, neurological symptoms, and drug use status.

Tool II: The Visual Analog Scale (VAS): It was created by **Bond & Pilowsky (1966)** and is used to convert numerical values that are not quantitatively measurable. The researchers adopted it to assess the pain level of the studied patients. The scale has gained acceptance in international literature and has shown itself to be a very dependable tool. "No pain = 0 points" and "unbearable pain = 10 points" are written on a 10-cm horizontal line. By having each patient actively participate and rate their pain on a scale from 0 to 10, with specific implications for each score, researchers can determine the degree of pain experienced by the individuals under study.

Tool III: The Fatigue Severity Scale (FSS): The FSS is adopted from **Krupp et al., (1989)** to evaluate the degree and effect of fatigue, especially in MS patients. The scale addresses fatigue's effects on daily functioning, querying its relationship to motivation, physical activity, work, family, and social life, and asking respondents to rate the ease with which they are fatigued and the degree to which the symptom poses a problem for them. ***FSS scoring system:*** There are nine items in the FSS, and each one is rated from 1 to 7, a low value (e.g., 1) indicates strong disagreement with the statement, whereas a high value (e.g., 7) indicates strong agreement. A higher degree of fatigue is suggested by a score of 4 or higher, whilst lower degree is indicated by a score of less than 4. The degree of fatigue increases with the score's proximity to 7. A final score is calculated by averaging the scores for each of the nine items.

Tools validity and reliability:

Five experts from different nursing and medical specialties were consulted once the data collection instruments were finalized in order to evaluate their content validity. This panel, which included two professors of neurology, two professors of medical-surgical nursing, and one professor of physiotherapy, proved essential to the validation process. These experts evaluated the tools for applicability, thoroughness, clarity, and ease of use, and minor adjustments were made in response to their suggestions. The internal consistency reliability of every item in the tools was evaluated using a Cronbach's Alpha test; the results for VAS (tool II) and FSS (tool III) were 0.94 and 0.89, respectively.

Ethical considerations:

The study began with approval from the dean of Zagazig University's nursing faculty and the ethics committee, in addition to official agreement from the directors of the aforementioned study location. Additionally, prior to data collection, oral consent was obtained from participating patients to guarantee their full cooperation and to make arrangements for their attendance. These patients received explanations of the study's nature, methods, and goal. The participants were also made aware of their freedom to withdraw from the study at any moment. Throughout the whole study, complete confidentiality was maintained, and all patients were assured that their information would only be utilized for research purposes.

Pilot study:

The clarity, relevance, comprehensiveness, comprehension, applicability, and ease of use of the tool were assessed on six patients or 10% of the primary study sample. It also aided in calculating the time needed to do the paperwork (tools). Patients who participated in the pilot study were included in the actual study population because the instruments had not been changed.

Felid of work:

The current study was carried out in the following order:

A. Preparatory stage (Assessment stage):

- Data for this study was gathered over a six-month period, from early April 2024 to September 2024. The dean of Zagazig University's nursing faculty and the director of Zagazig University hospitals provided the researchers with the required formal approval before the study was conducted during the assessment phase. After that, researchers visited the study site and met with the head nurses and directors to discuss the goals and procedures of the study to gain their participation and agreement. Additionally, following an explanation of the study's goal and an explanation of their rights, including the freedom to withdraw from the study at any time, patients who met the eligibility conditions were encouraged to participate.
- After giving their agreement, patients were randomly assigned to either the study or the control group, and to make sure that the Zone foot reflexology massage doesn't conflict with other therapies, the researchers speak with a study group patient's physicians before starting the study and applying Zone foot reflexology massage and take their consent.
- At the start of the study, a baseline assessment was conducted for each patient in both groups. This involved interviewing each participant separately to determine their demographics, medical history, degree of pain, and fatigue. The completion of the data-collecting tools took between 25 and 35 minutes, respecting the patients' time and ensuring a comprehensive comprehension of their condition.

B. Planning stage:

- The researcher created the program's goals; priorities, contents, and expected outcomes based on the information gathered during the assessment phase and the examination of relevant literature, taking into account the requirements and issues of the patients. To ensure that all patients are educated and involved to promote their cooperation during the intervention, the researcher also created a booklet about MS disease and Zone foot reflexology massage, which was given to every patient in the study group throughout the implementation stage and given to control group patients at the end of the study.

C. Implementation stage (intervention stage):

- Regard to patients in the control group had their usual routine treatment or care and received no intervention. While study group patients had two sessions of Zone foot reflexology massage weekly for a total of twelve weeks in addition to their usual routine treatment or care. Also, prior to beginning Zone foot reflexology massage sessions, the researchers designed a 30- to 40-minute basic health education session for the study group patients. The benefits of Zone foot reflexology massage for MS patients were briefly discussed throughout the session, along with the disease's symptoms, which focused on pain and fatigue. In order to improve the patient's participation and cognitive function during the intervention, the researchers also gave out the booklet.
- The researchers distrusted printed schedules clarifying Zone foot reflexology massage sessions with date and time as well as place and text messaging to increase the patients' cognition. The Zone foot reflexology massage sessions were applied at the physical therapy room that belonging to Multiple Sclerosis (MS) clinic. Each patient has two times sessions per week for twelve weeks. The Zone foot reflexology massage sessions were applied to the study group as follows:

a. Before the Zone foot reflexology massage session:

- Prior to beginning applying Zone foot reflexology sessions, a tub of warm water with salt or apple cider vinegar was prepared, and patients were instructed to soak their feet in it for five to ten minutes prior to the session.
- To gain access to the soles of both feet, the patient was told by the researchers to lie supine with their feet outstretched and a pillow beneath their knees.
- To maintain the patient's safety and comfort, the researcher who conducted the reflexology massage took off all hand accessories, clipped his nails, then washed and warmed his hands to body temperature before beginning the session.

b. During the Zone foot reflexology massage session:

- The researcher kept the patient's feet at a comfortable distance while seated in a chair close to the end of the bed. First, the reflexology massage was performed on the right foot and then on the left foot. A total of

15- ≤ 20 minutes of reflexology massage were performed for each foot with a total of 30 min for both feet.

- Initially, the researcher applied a generous amount of olive oil to both palms and spread it evenly; the process began with a minute of warm-up exercises on the patient's feet, which included rotation, Achilles tendon stretching, sole of the foot release, running the toe on the soles of the feet, and laundry wringing techniques; then pressure was applied to the feet's solar plexus to finish the warm-up exercises.
- Using the thumb, the researcher next massaged and applied pressure to the top of the patient's toes for four minutes, focusing on the brain region locations in the toes. The point of the toes represents the pituitary gland, the master gland responsible for the release of endorphins, which alleviate pain and fatigue as well as lessen stress and mood swings.
- The researcher then proceeded to the patient's middle foot region and used the thumb-walking technique to massage these zones for eight minutes at a moderate pace and steady rhythm while applying manageable pressure with his thumb or finger index joint. After that, the spinal reflex points at the patient's foot were subjected to reflexology for two minutes.
- Lastly, a minute was spent doing foot-loosening exercises for patients. In fifteen to twenty minutes, the one-foot session was finished by applying pressure to the solar plexus. For the other foot, identical procedures were then taken.

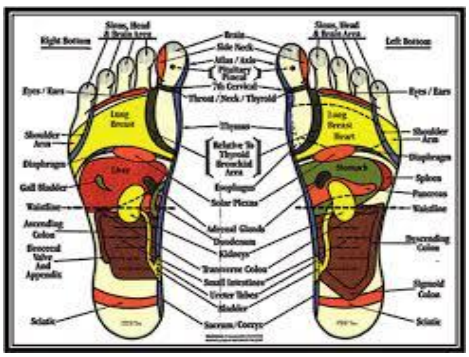

Fig (1): Foot Reflexology Chart **(Rooney, 2019)**

c. After the Zone foot reflexology massage session:

- To help the patient stay alert and prevent any drowsiness as well as maintain a safe exit from the session, the researcher massages the patient's feet gently with both thumbs for a few minutes after the session ends. Encourage them to complete each session with a cup of water. Because it aids in the body's removal of toxins that might be brought on by muscle contraction, it is a crucial point.

D. Evaluation stage:

- After 8 and 12 weeks of Zone foot reflexology massage application to the study group and after standard treatment or care for the control group, the same data collection tools (Tool II & Tool III) used at the pre-test were used post-test for both groups in order to assess the responsiveness of MS patients' pain and fatigue to the Zone foot reflexology massage, which reflects its efficacy in reducing both complaints. The basis for this efficacy was the observation of variations (or changes) in the baseline assessment scores for pain and fatigue levels between the pre-intervention and post-intervention phases.

Data analysis:

SPSS software version 25 was used to analyze the data. According to the patients' descriptive features, chi-square analysis was used to compare the study and control groups, and the "$\chi 2$" value was provided. Two independent group t-tests were used to compare the study and control groups in the measurement of pain and fatigue. Less than 0.05 p-values were considered statistically significant (S), less than 0.001 p-values were considered highly statistically significant (HS), and higher than 0.05 p-values were considered statistically insignificant (NS).

Results:

Table 1 reveals that the study group patients' mean age was 33.36 ± 15.07 years, and the control group was 37.97 ± 9.5 years. The largest percentage of the patients in both groups was female (73.2% and 80.0%, respectively), had high education (56.3% and 60.0%, respectively), and were married (66.7%). The bulk of the patients were working (73.2% and 80.0%, respectively). Generally, all demographic variables show no statistically significant differences between the study and control groups. This suggests that both groups are well-matched in terms of demographic characteristics, which is a key factor in ensuring the validity of our study. This robust validity

instills confidence that any observed effects can be attributed to the intervention rather than to demographic differences.

Table 2 shows a highly statistically significant difference in the types of MS between the study and control groups ($p < 0.001$). This means the distribution of MS types is not equal between the two groups, with a higher proportion (70.0%) of RRMS in the study group and more PPMS in the control group (53.0%). Moreover, there is a statistically significant difference ($p = 0.003$) in sensory symptoms between the two groups, as the lowest percentage (13.4%) of the study group had numbness and tingling compared to the control group. On the other hand, there was no statistically significant difference ($p = .754$) between the study and control group patients regarding drug use status, as 63.3% and 70.0%, respectively, of them took medication for MS.

According to Table **3**, there was no statistically significant difference (p=0.491) in the two groups' pain levels during the pre-intervention phase. While the study group patients' pain level mean scores were 3.45 ± 0.63 at the pre-intervention phase and dropped to 2.04 ± 0.90 post the 12th week of intervention, there is a statistically significant difference and decrease ($p = 0.005$ & 0.001, respectively) between the study group patients' pain level mean scores post-8 and 12 weeks of intervention Zone foot reflexology massage compared to the control group, whose baseline pain level mean score was 3.62 ± 1.12 and decreased to 3.03 ± 1.02 after 12 weeks of traditional care. Even while both groups' mean pain levels decreased, the study group's pain level clearly improved and decreased post-intervention of ZFRM, as compared to the control group. Additionally, the study group had a highly statistically significant decrease in pain scores between the pre- and post-intervention phases of ZFRM ($P^0 = 0.001$).

Table **4** shows that the study group patients' fatigue level mean score was 6.30 ± 1.13 in the pre-intervention phase, which dropped to 3.59 ± 1.35 post-12th week of the Zone foot reflexology massage intervention, this indicates a statistically significant difference and decrease ($p = 0.004$ & 0.001, respectively) in fatigue levels between the study and control groups post-8th and 12th weeks of the intervention. Although both groups' fatigue level mean scores decreased, the study group's fatigue level showed a more noticeable improvement and decrease post-intervention of ZFRM than the control group, whose baseline fatigue level mean score was 5.88 ± 1.61 and decreased to 5.52 ± 1.80 after 12 weeks of traditional care. Additionally, the study group had a highly statistically significant decrease in fatigue scores between the pre- and post-intervention phases of ZFRM ($P0 = 0.001$).

Table (1): Frequency and Percentage Distribution of Demographic Characteristics for Patients with Multiple Sclerosis in the Study and Control Groups (n = 60):

Items	Study group (n=30)		Control group (n=30)		χ^2	P-vale
	No	%	No	%		
Age (years):						
<30	9	30.0	10	33.3	1.062	1.000
≥ 30	21	70.0	20	66.7		
Mean ±SD	33.36 ± 15.07		37.97 ± 9.5			
Gender:						
Male	8	26.8	6	20.0	0.373	0.542
Female	22	73.2	24	80.0		
Education level:						
Read/write	6	20.0	3	10.0	1.370	0.763
Intermediate/basic	7	23.7	9	30.0		
High education	17	56.3	18	60.0		
Marital status:						
Married	20	66.7	20	66.7	1.265	1.000
Unmarried	10	33.3	10	33.3		
Occupation:						
Working	22	73.2	24	80.0	4.244	0.120
Not working	8	26.8	6	20.0		

χ^2: Chi-square test; Insignificant (p>0.05).

Table (2): Frequency and Percentage Distribution of Studied Patients according to their Medical History (n = 60):

Items	Study group (n=30)		Control group (n=30)		χ^2	P-vale
	No	%	No	%		
MS Type:						
Relapsing-Remitting MS (RRMS)	21	70.0	13	43.3	4.200	(<0.001**)
Primary Progressive MS (PPMS)	7	23.3	16	53.3		
Secondary Progressive MS	2	6.7	1	3.4		
Neurological Symptoms:						
Mobility Issues (muscle weakness)	13	43.3	11	36.7	2.949	(0.003*)
Visual Issues (Blurred or double vision)	13	43.3	13	43.3		
Sensory Issues (Numbness, tingling)	4	13.4	6	20.0		
Multiple Sclerosis drug use status:						
Yes	19	63.3	21	70.0	0.098	.754
No	11	36.7	9	30.0		

χ^2: Chi-square test; ***** Highly statistically significant (p<0.001);***
**** Statistically significant (p<0.05);*** ***Insignificant (p>0.05)***

Table (3): Comparison between Study and Control Group Patients with Multiple Sclerosis regarding Pain Mean Scores throughout Zone Foot Reflexology Massage Intervention Phases (n = 60)

Items	Study group (n=30)	Control group (n=30)	Paired t-test value	*p-value*
	Mean±SD	Mean±SD		
Pain level measurements:				
Pre intervention phase (baseline phase)	3.45 ± 0.63	3.62 ± 1.12	0.694	0.491
Post 8th weeks of Zone foot reflexology intervention.	2.32 ± 0.94	3.09 ± 1.08	2.926	0.005*
Post 12th weeks of Zone foot reflexology intervention.	2.04 ± 0.90	3.03 ± 1.02	3.951	0.001*
Test value	χ^2 = 140.643	χ^2 = 22.386		
Significance	P^0 =0.001*	*P0* =0.003*		

Paired t-test was used; ***** Highly statistically significant (p<0.001);*** **** Statistically significant (p<0.05);***
Insignificant (p>0.05) ***χ2: Chi-square test;***
p^0: p value for comparing between before and after foot reflexology in each group.

Table (4): Comparison between Study and Control Group Patients with Multiple Sclerosis regarding Fatigue Mean Scores throughout Zone Foot Reflexology Massage Intervention Phases

Items	Study group (n=30)	Control group (n=30)	Paired t-test value	*p-value*
	Mean±SD	Mean±SD		
Fatigue level measurements:				
Pre intervention phase (baseline phase)	6.30 ± 1.13	5.88 ± 1.61	3.018	0.004*
Post 8th weeks of Zone foot reflexology intervention.	4.22 ± 1.70	5.56 ± 1.73	3.018	0.004*
Post 12th weeks of Zone foot reflexology intervention.	3.59 ± 1.35	5.52 ± 1.80	5.681	0.001*
Test value	χ^2 = 167.996	χ^2=14.869		
Significance	*P0* =0.001*	*P0*=0.249		

Paired t-test was used; ***** Statistically highly significant (p<0.001);*** **** Statistically significant (p<0.05);***
Insignificant (p>0.05) ; ***χ2: Chi-square test;***
p0: p value for comparing between before and after foot reflexology in each group.

Discussion:

As they are unrelated to the severity or duration of MS, fatigue, and pain are among the most prevalent symptoms that might manifest at any point in the disease's progression **(Ng & Kishimoto, 2021)**. Given that MS is currently incurable, healthcare providers should employ various approaches that can help patients achieve positive health outcomes, treat relapses, manage symptoms, improve independence, function, and safety, and alter or slow the disease's progression **(Alain L. Fymat, 2023)**. Complementary therapy has been shown in prior research to be useful in managing a variety of symptoms, including stress, fatigue, and bowel and bladder dysfunction, as well as improving patients' QoL and sleep **(Dilek Doğan & Tan, 2021)**.

A popular complementary therapy among people with severe illnesses, particularly those with MS, is Zone foot reflexology massage, which is safe and gentle and involves applying pressure, usually with the thumb and fingers, to certain reflex points on the feet **(Toukabri et al., 2021)**. Those who support reflexology suggest that exerting pressure on these points can affect how the relevant organs react physiologically **(Mazloum et al., 2024)**. Because applying pressure to these reflex zones activates many nerve terminals in the soles, endorphins are released, so this procedure promotes comfort, eases tension, and creates a feeling of calm by preventing the transmission of pain signals **(Xiao & Tao, 2017)**. Therefore, this study aimed to evaluate the responsiveness of the pain and fatigue of patients with MS to the Zone foot reflexology massage. A discussion of the current results will cover four main areas in the following sequence:

Firstly, the demographic characteristics of studied patients:

Regarding the demographic characteristics of the patients under study, the current study revealed that the study group patients' mean age was 33.36 ± 15.07 years, and the control group was 37.97 ± 9.5 years. The largest percentage of the patients in both groups was female, had high education, was married, and working. Generally, all demographic variables show no statistically significant differences between the study and control groups. This suggests that both groups are well-matched in terms of demographic characteristics, which is a key factor in ensuring the validity of our study. This robust validity instills confidence that any observed effects can be attributed to the intervention rather than to demographic differences. From the researchers' point of view, the lack of a significant difference between the two groups in their demographic data reflects that the baseline of pain and fatigue disturbances was similar in the two groups.

These results align with those of **Mazloum et al., (2024)**, who found that there was no statistically significant difference between the two groups under study in terms of age, gender, and marital status ($p > 0.05$). Additionally, they found that women made up 59.4% of patients in the reflexology group and 46.7% of patients in the footbath group. According to **Özdelikara et al., (2024)**, the majority of participants in both groups were married. Furthermore, **Zidan et al., (2022)** explained that there was no statistically significant difference ($p > 0.05$) between the two groups (control and study) in age, gender, marital status, and employment. These findings are consistent with their findings.

The present results also concur with those of **SehatNejad (2021)**, who explained that the average age of the participants was 31.87±7.83 years (Reflexology = 33.17±7.51 and Control = 29.73±7.61) and that there was no significant difference in this variable between the groups ($p=0.1$). Additionally, 53% had an academic educational degree. Age, length of sickness, marital status, sex, and educational attainment did not significantly differ among the two groups.

Secondly, the medical history of studied patients:

Regarding the medical history of the patients under study, the current study showed that there was a highly statistically significant difference in the types of MS between the study and control groups. This means the distribution of MS types is not equal between the two groups, with a higher proportion of relapse-remitting MS (RRMS) in the study group and more PPMS in the control group. Moreover, there is a statistically significant difference in sensory symptoms between the two groups, as the lowest percentage of the study group had numbness and tingling compared to the control group. On the other hand, there was no statistically significant

difference between the study and control group patients regarding drug use status, as the highest percentage in both groups took medication for MS.

The findings of the current study are similar to those of **Zidan et al., (2022)**, who showed that the largest percentage of the study group had RRMS. However, the current study differs from them in one point, as there is no statistically significant difference ($p > 0.05$) between the two groups being studied in terms of their MS types (Chi-square = 1.002). As well, **Dilek Doğan & Tan (2021)** found that 80% of the patients in the intervention group had relapsing-remitting multiple sclerosis (MS) and that 76.7% of the patients in the intervention group and 80% of the patients in the control group were taking medication. The current study results are also in line with their findings.

Thirdly, study and control group patients' pain mean scores throughout Zone Foot Reflexology Massage Intervention Phases:

Regarding the pain level of the studied patients, the current study found that there was no statistically significant difference in pain level between both groups at the pre-intervention phase (baseline phase) of Zone foot reflexology massage. While there was a statistically significant difference and decrease in pain level mean scores of study group patients post 8^{th} and 12^{th} weeks of intervention Zone foot reflexology massage compared to the control group, as the study group patients had a pain level less than the control group. Although the pain level mean scores of both groups were decreased, the study group's pain level showed a more obvious decrease and improvement post-intervention of Zone foot reflexology massage compared to the control group. Also, for the study group, a highly statistically significant difference and decrease had occurred in the pain mean scores between the pre-intervention phase, or baseline, and post-intervention phase.

From the perspective of the researchers, these results might be explained by the fact that the Zone foot reflexology massage can stimulate the pituitary gland through foot reflex points to release beta-endorphins, which are proteins that are primarily synthesized by it and have sedative and analgesic effects. It alleviates pain through a variety of mechanisms in the central and peripheral nervous systems when it binds to its mu-opioid receptors, which lowers sympathoadrenal system activity. These were confirmed through the notable changes that occurred in the study group patients' pain levels compared to the control group.

These results are corroborated by **Deenadayalan et al., (2024)**, who clarified that the most commonly reported outcomes of foot reflexology intervention in MS patients were improvements in QoL and bowel and bladder functions as well as decreases in pain, fatigue, muscle spasms, stiffness, and psychological symptoms. The present results also support those of **Vindis et al., (2024)**, who showed that reflexology helps lessen post-operative pain in patients. Additionally, it was explained by **Ma et al., (2023)** that their systematic review revealed that reflexology therapy for MS patients can enhance pain, exhaustion, and QoL. These results are also consistent with those of an Iranian study by **Eftekhari & Moradmand (2023)**, which discovered that foot reflexology was the most efficient massage modality in reducing pain when various massage techniques were applied for the same amount of time each session.

Furthermore, the present results are in alignment with those of **Yakout et al., (2022)**, who found that the study group's mean score for pain, stiffness, and function capacities sharply improved following the second, third, and fourth foot reflexology sessions. Too, the present results correspond with **Kapıkıran & Özkan (2021)**, who discovered that following the application of foot reflexology, the intervention group's pain level decreased statistically significantly in comparison to the control group (Cohen's $d = 1.95$, 95% confidence interval (CI): -2.7261 to -1.8738; $p < 0.001$), and that both comfort and beta-endorphin levels increased statistically post-test compared to the initial test ($p < 0.05$) and were higher in the intervention group than the control group.

More distant, the results of this study are consistent with those of **Nazari et al., (2015),** who demonstrated in a Turkish study on the impact of reflexology versus conventional relaxation techniques on pain in women with multiple sclerosis that reflexology interventions had a significantly greater impact on pain reduction than the other conventional techniques.

However, the present results are not in line with those of **Salarvand et al., (2021)**, who discovered that a foot reflexology massage as a supplemental nursing intervention can have a minor pain-reduction impact. Similarly, **Albert et al., (2009)** demonstrated that there was no statistically significant difference in the average pain levels of patients undergoing heart surgery following the reflexology intervention as compared to their pre-intervention scores.

Fourthly, study and control group patients' fatigue mean scores throughout Zone Foot Reflexology Massage Intervention Phases:

Regarding the fatigue level of the studied patients, the current study displays that there was a statistically significant difference and decrease in fatigue level mean scores between the study and control groups of patients post 8^{th} and 12^{th} weeks of intervention Zone foot reflexology massage, as the study group patients had a fatigue level less than the control group. Although the fatigue level mean scores of both groups were decreased, the study group's fatigue level showed a more obvious decrease and improvement post-intervention of Zone foot reflexology massage compared to the control group. Additionally, for the study group, a highly statistically significant difference and decrease had occurred in the fatigue mean scores between the baseline and post-intervention phase.

From the researcher's point of view, the physiological benefits of Zone foot reflexology massage, which can release endorphins and serotonin (which elevate mood) and can increase autonomic nervous system activity, may be responsible for the study group patients' decreased level of fatigue following the intervention. This would have a combined effect on the hypothalamic level and relaxation response. Additionally, these results can be related to the fact that Zone foot reflexology massage can lessen nervous system excitability and muscle stress. It can also help eliminate toxins by promoting energy circulation, which can enhance one's sense of well-being and lessen fatigue sense.

The present results are consistent with those of **Mohamed et al., (2024)**, who explained that there were notable decreases in fatigue among 30 subjects after reflexology. Of these, 20% reported no fatigue following the intervention, severe and excessive fatigue significantly decreased (from 40% and 50% to 6.7% and 0%, respectively), and the average fatigue score significantly decreased from 105.7 to 64.1. These changes were statistically significant ($P < 0.001$), demonstrating the effectiveness of foot reflexology in lowering fatigue levels. Also, **Mazloum et al., (2024)** found that foot reflexology is very helpful in reducing the mental and physical symptoms of the illness and its treatment, such as stress, fatigue, and pain. Likewise, these findings are in agreement with **Mohammed et al., (2022)**, who found that the intervention group's fatigue scores were lower than those of the control group, indicating a highly significant difference and improvement in fatigue levels between the two groups.

Moreover, the present results are in the same line with **Zidan et al., (2022)**, who demonstrated that the study group significantly outperformed the control group in terms of overall fatigue (Chi-square=9.30, $p<0.01$) and that the study group's fatigue levels improved following massage. Furthermore, following reflexology therapy, **Dilek Doğan & Tan (2021)** found that patients with MS experienced a considerable drop in their fatigue and pain scores. Additionally, by promoting energy circulation, reflexology eliminates pollutants and lessens weariness, according to **Sajadi et al., (2020)**. Too, the current findings align with those of **Ozdelikara & Agcadiken (2018)**, who found that the reflexology intervention group experienced a lower fatigue score than the control group.

Conclusion:

It can be concluded that the pain and fatigue of patients with MS respond positively to Zone foot reflexology massage sessions, which reflects the significant effect of Zone foot reflexology massage in decreasing and improving the pain and fatigue of those patients. This is evidenced by the presence of a statistically significant difference and decrease in the mean scores of pain and fatigue level in study group patients compared to the control group in the post-intervention phase of Zone foot reflexology massage, also between the pre-and post-intervention phase of it. Thus, incorporating Zone foot reflexology massage into nurses' work as an additional nursing intervention can improve the quality of care for patients with MS, particularly since it is a simple, inexpensive, non-invasive,

readily available, and uncomplicated intervention that can be used alongside other medical care to control symptoms and improve the well-being of those patients.

Recommendation:

Based on the results of this study, the following recommendations can be proposed:

1. Zone foot reflexology massage should be a key component of provided care for patients with MS in addition to pharmacological treatments or used as a part of early strategies for controlling the pain and fatigue symptoms of those patients.
2. Developing and implementing a training program for nurses and other healthcare professionals in Zone foot reflexology massage may aid in recognizing it as an essential part of routine care procedures.
3. In order to enable a broader generalization of the results, the study should be replicated with a larger sample size and a longer duration of exposure to Zone foot reflexology massage.

References:

Alain L. Fymat, (2023): Multiple Sclerosis: II. Diagnosis and Symptoms Management. Journal of Neurology and Psychology Research; 4 (1): pp. 1-21. https:// doi. org/ 10. 12968/ ijtr. 2020.0144

Albert NM, Gillinov AM, Lytle BW, Feng J, Cwynar R, Blackstone EH, (2009); A randomized trial of massage therapy after heart surgery. Heart Lung; 38(6):pp.480-90. doi: 10.1016/j.hrtlng.2009.03.001. PMID: 19944872.

Al-ma'mouri M Y, (2024): Article Review: Multiple Sclerosis. Journal for Research in Applied Sciences and Biotechnology; 3 (1): pp. 177-186. https:// doi. org/ 10. 55544/ jrasb. 3. 1.29

Amatya B, Khan F, Galea M, (2019): Rehabilitation for people with multiple sclerosis: an overview of Cochrane Reviews. Cochrane Database of Systematic Reviews; 1(CD012732). DOI: 10.1002/ 14651858. CD012732. pub2.

Ando H, Cousins R, Young CA, (2022): Understanding quality of life across different clinical subtypes of multiple sclerosis: a thematic analysis. Qual Life Res; 31(7):pp.2035-2046. doi: 10.1007/s11136-021-03041-7. PMID: 34822047.

Arji G, Rezaeizadeh H, Moghadasi AN, Sahraian MA, Karimi M, Alizadeh M, (2022): Complementary and alternative therapies in multiple sclerosis: a systematic literature classification and analysis. Acta Neurol Belg; 122(2):281-303. doi: 10.1007/s13760-021-01847-3. PMID: 35060096.

Bond M R & Pilowsky I, (1966): Subjective assessment of pain and its relationship to the administration of analgesics in patients with advanced cancer. Journal of Psychosomatic Research; 10(2):pp. 203-208, ISSN 0022-3999,https://doi.org/10.1016/0022-3999 (66) 90064-X.

Claflin SB, van der Mei IAF, Taylor BV, (2018): Complementary and alternative treatments of multiple sclerosis: a review of the evidence from 2001 to 2016. J Neurol Neurosurg Psychiatry; 89(1):pp.34-41. doi: 10. 1136/ jnnp-2016-314490. PMID: 28768821.

Deenadayalan B, Venugopal V, Poornima R, Kannan VM, Akila A, Yogapriya C, Maheshkumar K, (2024): Effect of Foot Reflexology on Patients with Multiple Sclerosis: A Systematic Review of Current Evidence. Int J MS Care; 26(2):pp.43-48. doi: 10.7224/1537-2073.2022-093. PMID: 38482512; PMCID: PMC10930811.

Dikmen HA & Terzioglu F, (2019): Effects of Reflexology and Progressive Muscle Relaxation on Pain, Fatigue, and Quality of Life during Chemotherapy in Gynecologic Cancer Patients. Pain Manag Nurs; 20(1):47-53. doi: 10.1016/j.pmn. PMID: 29776873.

Dilek Doğan H & Tan M, (2021): Effects of Reflexology on Pain, Fatigue, and Quality of Life in Multiple Sclerosis Patients: A Clinical Study. Altern Ther Health Med; 27(5):pp.14-22. PMID: 33789252.

Ebrahimi N, Loripour M, Sayadi A, et al., (2020): Effect of foot reflexology on fatigue, stress, and serum cortisol levels in women with multiple sclerosis. J Evolution Med Dent Sci;9 (35):pp. 2497-2501, DOI: 10.14260/ jemds/ 2020/543

Eftekhari E & Moradmand E, (2023): The effect of massage as a complementary therapy on fatigue and quality of life in females with Multiple Sclerosis. Exercise Physiology and Performance; 1(1):pp.49-63. DOI: 10.30486/ epp.1968404.1006

Embong NH, Soh YC, Ming LC, Wong TW, (2016): Perspectives on reflexology: A qualitative approach. J Tradit Complement Med; 7(3):pp.327-331. doi: 10.1016/j.jtcme. PMID: 28725628; PMCID: PMC5506646.

Gaballah S, El-Deen DS, Hebeshy MI, (2023): Effect of effleurage massage therapy on sleep disturbance, fatigue, pain, and anxiety in patients with multiple sclerosis: A quasi-experimental study. Appl Nurs Res; 73: (151719). PMID: 37722787. DOI: 10. 1016/ j. apnr. 2023.151719

Hauser SL & Cree BAC, (2020): Treatment of Multiple Sclerosis: A Review. Am J Med; 133(12):pp.1380-1390.e2. doi: 10.1016/ j. amjmed. Epub 2020 Jul 17. PMID: 32682869; PMCID: PMC7704606.

He MY, Ud Din MJ, Xu HF, Wang SY, Ying GH, Qian H, Wu B, Qi HD, Wang X, Zhang G, (2024): Effects of foot reflexology on disease. World J Clin Cases; 12(35):pp.6851-6854. doi: 10.12998/wjcc.v12.i35.6851. PMID: 39687647; PMCID: PMC11525917.

Jensen MP, Barber J, Romano JM, Molton IR, Raichle KA, Osborne TL, Engel JM, Stoelb BL, Kraft GH, Patterson DR, (2009): A comparison of self-hypnosis versus progressive muscle relaxation in patients with multiple sclerosis and chronic pain. Int J Clin Exp Hypn; 57(2):pp.198-221. doi: 10.1080/ 00207140802665476. PMID: 19234967; PMCID: PMC 2758639.

Johansson S, Ytterberg C, Claesson IM, Lindberg J, Hillert J, Andersson M, Widén Holmqvist L, von Koch L, (2007): High concurrent presence of disability in multiple sclerosis. Associations with perceived health. J Neurol. Jun; 254(6):pp.767-73. doi: 10.1007/s00415-006-0431-5. PMID: 17401746.

Kapıkıran G & Özkan M, (2021): The effect of foot reflexology on pain, comfort and beta endorphin levels in patients with liver transplantation: A randomized control trial, European Journal of Integrative Medicine, 45, (9): pp.101344. doi: 10. 1016/ j. eujim. 2021. 101344

Kartka I R & Ulfa M, (2020): Complementary of Nursing Care for an Elderly Family: Management of Hypertension and Smoking Behaviour. Journal of Geriatric Medicine; 2(3): pp.1–5. doi: https:// doi.org/ 10. 30564/ jgm.v2i3.2330

Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD, (1989): The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. Arch Neurol; 46(10):1121-3. doi: 10. 1001/ archneur. 1989.00520460115022. PMID: 2803071.

Loewen S & Plonsky L, (2016): An A-Z of applied linguistics research methods, 1st ed., London: Palgrave Macmillan, p.224.

Ma X, Yuan Z, Qian B, Guan Y, Wang B, (2023): Systematic review and meta-analysis of reflexology for people with multiple sclerosis: Systematic Review and Meta-Analysis. Medicine (Baltimore); 102(5): e32661. doi: 10.1097/ MD. 000000 0 0 0 0 0 32661. PMID: 36749275; PMCID: PMC9902001.

Mazloum SR, Rajabzadeh M, Mohajer S, Bahrami-Taghanaki H, Namazinia M, (2023): Comparing the Effects of Warm Footbath and Foot Reflexology on the Fatigue of Patients Undergoing Radiotherapy: A Randomized Clinical Trial. Integr Cancer Ther; 22: 1 5 3 4 7 3 5 4 2 3 1 1 7 2940. doi: 10.1177/15347354231172940. PMID: 37162156; PMCID: PMC10176550.

Mirhosseini S, Mohammadi A, Rezaei M, Mirbagher Ajorpaz N, (2019): The Effect of Benson Relaxation Technique on the Fatigue Severity of Patients With MS. JCCNC; 5 (3): pp. 175-182 URL: http:// jccnc. iums. ac. ir/ article- 1-219-en.html

Mohamed AH, Shaban M, Mohammed HH, Abobaker RM, Alsaqri SH, Allam RA, (2024): The impact of foot reflexology on fatigue and sleep quality in school-aged children undergoing hemodialysis. J Integr Nurs; 6(2):pp.76-82. doi: 10. 4103/ jin. jin_3_24

Mohammed A AE, Ayed M M A, Hegazy A E A, El-husseiny H S A, Amin F M , (2022): Effect of Foot Massage on Physiological Indicators, Fatigue, and Pain among Children undergoing Chemotherapy. Egyptian Journal of Health Care, 13(4):pp. 26-39. doi: 10.21608/ejhc.2022.257856

Naseri-Salahshour V, Sajadi M, Abedi A, Fournier A, Saeidi N, (2019): Reflexology as an adjunctive nursing intervention for management of nausea in hemodialysis patients: A randomized clinical trial. Complement Ther Clin Pract; 36:pp.29-33. doi: 10.1016/j.ctcp.2019.04.006. PMID: 31383439.

Nazari F, Shahreza MS, Shaygannejad V, Valiani M, (2015): Comparing the effects of reflexology and relaxation on fatigue in women with multiple sclerosis. Iran J Nurs Midwifery Res; 20 (2):pp.200-4. PMID: 25878696; PMCID: PMC4387643.

Ng J Y & Kishimoto V, (2021): Multiple sclerosis clinical practice guidelines provide few complementary and alternative medicine recommendations: A systematic review. Complementary Therapies in Medicine; Volume 56,102595, ISSN 0965-2299, https:// www. sciencedirect. com/ science/ article/ pii/ S096522992031862 8

Ozdelikara A & Agcadiken Alkan S, (2018): The Effects of Reflexology on Fatigue and Anxiety in Patients with Multiple Sclerosis. Altern Ther Health Med; 24(4):pp.8-13. PMID: 29332021.

Özdelikara, Afitapa, Alkan, Seval Ağaçdikenb; Terzi, Muratc, (2024): The effect of reflexology and pelvic floor muscle (Kegel) exercises on urinary incontinence in people with multiple sclerosis. Urological Science 35(3): pp. 147-152. DOI: 10. 1097/ us9. 0000000000000027

Power M, Arafa N, Wenz A, Foley G, (2021): Perceptions of fatigue and fatigue management interventions among people with multiple sclerosis: a systematic literature review and narrative synthesis. International Journal of Therapy and Rehabilitation; 28(6):pp. 1-21. https:// doi. org/ 10. 12968/ ijtr.2020.0144

Racke MK, Frohman EM, Frohman T, (2022): Pain in Multiple Sclerosis: Understanding Pathophysiology, Diagnosis, and Management through Clinical Vignettes. Front Neurol; 12:799698. doi: 10.3389/ fneur. 799698. PMID: 35095742; PMCID: PMC8794582.

Rooney A, (2019): Foot reflexology: principles and practice. Massage Therapy. E-Book: Principles and Practice, p.241.

Rosner B, (2016): Fundamentals of Biostatistics. 8th ed. Duxbury Press; p. 281.

Sajadi M, Davodabady F, Ebrahimi-Monfared M, (2020): The effect of foot reflexology on fatigue, sleep quality and anxiety in patients with multiple sclerosis: a randomized controlled trial. Archives of Neuroscience, 7(3). doi:10.5812/ans.102591.

Salarvand S, Heidari ME, Farahi K, Teymuri E, Almasian M, Bitaraf S, (2021): Effectiveness of massage therapy on fatigue and pain in patients with multiple sclerosis: A systematic review and meta-analysis. Mult Scler J Exp Transl Clin; 7(2):20552173211022779. doi: 10.1177/20552173211022779. PMID: 341 88950; PMCID: PMC8209836.

Salehi Z, Almasi-Hashiani A, Sahraian MA, Ashtari F, Baghbanian SM, et al., (2022): Epidemiology of familial multiple sclerosis in Iran: a national registry-based study. BMC Neurol; 22(1):p.76. doi: 10.1186/s12883-022-02609-1. PMID: 35248009; PMCID: PMC8897924.

Sari N, Yuswanto T J A, Fatmasari D, (2020): Complementary nursing intervention of acupressure and bay leaf extract (Syzygium polyanthum) on reducing pain among patients with arthritis gout. International Journal of Nursing and Health Services (IJNHS); 3(6):pp.pp.700-708.

Sehat Nejad S, Pour Samad A, Behnam Moghadam M, Mousavi zadeh A, kaidani N, (2021): Comparing the Effect of Reflexology and Effleurage Massages on Fatigue and Insomnia in Multiple Sclerosis Patients. J Clinic Care Skill; 2 (3) :139-144 URL: http://jccs.yums.ac.ir/article-1-111-en.html

Toukabri I, Said AB, Hamdi A, Mokrani A, Gabsi A, Ayed WB, Tounsi K, Limayem I, (2021): Patterns of complementary and alternative medicine use among Tunisian cancer patients. J Oncol Pharm Pract; 27(8): pp. 1948- 1957. doi: 10. 1177/ 107 8 1 5 5 2 20980131. PMID: 33323022.

Venugopal V, Yogapriya C, Deenadayalan B, Akila A, Poonguzhali S, Poornima R, Maheshkumar K, (2023): Foot reflexology for reduction of blood pressure in hypertensive individual: A systematic review. Foot (Edinb); 54:101974. doi: 10. 1016/ j. foot. 2023. 101974. PMID: 36804683.

Vindis K, Hozan C T, Coțe A, Szilagyi G (2024): A Review of the Effect of Foot Reflexology on Pain in Patients. Archives of Pharmacy Practice; 15(1): pp.12-16. https:// doi. org/ 10. 51847/7egqJLQbwh

Walton C, King R, Rechtman L, Kaye W, Leray E, (2020): Rising prevalence of multiple sclerosis worldwide: Insights from the Atlas of MS, third edition. Mult Scler; 26(14): pp.1816-1821. doi: 10.1177/ 135 2 4 5 8 5 2 0 9 70841. PMID: 33174475; PMCID: PMC7720355.

Xiao LJ & Tao R, (2017): Traditional Chinese Medicine (TCM) Therapy. Adv Exp Med Biol; 1010:261-280. doi: 10.1007/978-981-10-5562-1_13. PMID: 29098677.

Yakout R, Seyam N, Mohamed Eldesoky H, (2022): Effect of Reflexology Foot Massage on Pain intensity and Physical Functional Abilities among Patients with Knee Osteoarthritis. Egyptian Journal of Nursing and Health Sciences; 3(1):pp.17-40. doi: 10.21608/ejnhs.2022.227785.

Zidan S, Mohamed H S, Iskander L I, (2022): Effect of aromatherapy massage on fatigue and perceived stress of multiple sclerosis patients. International Journal of Health Sciences; 6(S7):pp.1045–1061. https:// doi. org/ 10. 53730/ijhs.v6nS7.11515