



# Treatment Satisfaction of Patients Using Dimethyl Fumarate for Multiple Sclerosis: A Survey Study

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## Abstract

**Objective:** Multiple sclerosis (MS) is a chronic and progressive disease that affects the central nervous system. Dimethyl fumarate (DMF) is commonly used in the treatment of MS. This study examines the relationship between treatment adherence and quality of life (QoL) in patients undergoing DMF treatment.

**Materials and Methods:** The study included 227 patients using DMF. Demographic information, DMF usage duration, disease duration, and treatment adherence were obtained through surveys. Data were analyzed using the Statistical Package for the Social Sciences program. The effects of factors such as age, sex, disease duration, and treatment methods on treatment adherence and QoL were evaluated.

**Results:** Patients who had high adherence to DMF treatment had higher QoL. Moreover, younger patients adapted to the treatment more easily and had higher QoL. Female patients had higher treatment adherence than male patients. Additionally, treatment methods had varying effects on QoL.

**Conclusion:** DMF is an effective treatment for MS. The study results indicate that adherence to DMF treatment positively impacts patients' QoL and that increasing this adherence is crucial. Future studies should compare different treatment methods and comprehensively examine patients' experiences during the treatment process. Psychosocial support and education programs should be developed to enhance treatment adherence.

**Keywords:** Dimethyl fumarate, multiple sclerosis, treatment adherence, quality of life, demographic and clinical factors

## Introduction

Multiple sclerosis (MS) is a chronic, inflammatory disease affecting the central nervous system and is often seen in young adults (1). It is characterized by widespread demyelination and axonal loss throughout the central nervous system, leading to various neurological symptoms and functional impairments. MS treatment aims to slow disease progression, manage symptoms, and improve patients' quality of life (QoL).

Dimethyl fumarate (DMF) is an oral medication used to treat MS (2). DMF has anti-inflammatory and immunomodulatory properties and induces neuroprotective effects by protecting neurons from oxidative stress. However, the effectiveness of DMF is largely dependent on treatment adherence (3), which is defined as the degree to which patients follow their treatment plan and plays a critical role in MS management.

Existing literature shows that improving treatment adherence can significantly enhance the QoL of patients with MS (4). Treatment adherence can be influenced by various demographic and clinical factors, such as age, sex, disease duration, and treatment methods (5). This study aimed to evaluate the demographic and clinical characteristics of patients undergoing DMF treatment and analyze the relationship between treatment adherence and QoL.

The findings of the study may be beneficial in developing strategies that enhance the effectiveness of DMF treatment and improve patients' QoL. In 2015, Some studies emphasized the efficacy of DMF in patients with relapsing-remitting multiple sclerosis (RRMS) and highlighted the importance of conducting comparative studies with other treatment methods such as interferon beta and glatiramer acetate (6,7).

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The present study assessed the effectiveness of and patient adherence to DMF compared with these treatment methods. In addition, this study emphasizes the importance of adherence to DMF treatment and presents the support mechanisms to improve adherence. The current study hypothesized that patients with MS and high adherence to DMF treatment have higher QoL. To test this hypothesis, the effects of demographic and clinical characteristics on treatment adherence and QoL were analyzed.

## Materials and Methods

### Study Design

A cross-sectional research design was used to examine the relationship between treatment adherence and QoL in patients with MS undergoing DMF.

### Participants

The study included 227 patients followed at the MS clinic of University of Health Sciences Turkey, Sancaktepe Sehit Prof. Dr. Ilhan Varank Training and Research Hospital. All patients were diagnosed with RRMS according to the McDonald criteria (1). The inclusion criteria required that participants had been on DMF treatment for at least 6 months. The sample size represented 80% of the total number of patients followed in the MS clinic. The participants were aged 18-55 years, and the sample exhibited diversity in demographic variables such as age, sex, and disease duration.

The patients were examined in two separate ways according to their medication usage: The initiation treatment group, which included naive patients who started their treatment with DMF, and the switch group, comprising patients who had previously undergone other treatment protocols and later transitioned to DMF treatment (Figure 1). Additionally, the transition treatment group showed the initial treatments of the patients in the switch group (Figure 2).

### Materials

The study was approved by the University of Health Sciences Turkey, Sancaktepe Sehit Prof. Dr. Ilhan Varank Training and Research Hospital Ethics Committee (number: E-46059653-050.99-215847885, date: 17.05.2023) and conducted according to the ethical principles of the Declaration of Helsinki. Written informed consent was obtained from the participants after providing information about the study.

Data were collected during routine clinical visits of the patients. Participants were informed about the study and gave their written consent. Surveys were performed through face-to-face interviews or electronic forms. Confidentiality and privacy of the data and participants were ensured. The tools used in data collection were as follows.

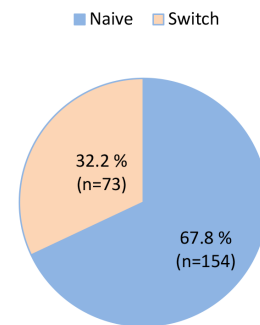
## Demographic Information Form

This form was used to obtain demographic information of the participants, such as age, sex, education level, marital status, and disease duration.

## Multiple Sclerosis Treatment Adherence Questionnaire

The Multiple Sclerosis Treatment Adherence Questionnaire (MS-TAQ) was developed by Barber. Its Turkish validity and reliability study was conducted by Yeşilbalkan et al. (8) in 2019

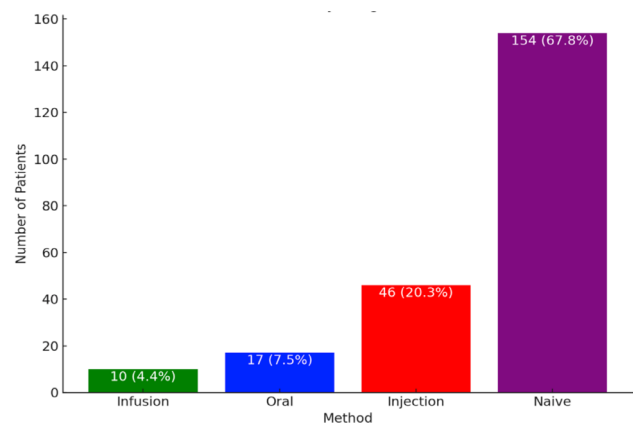
### Initiation Treatment Group



**Figure 1.** Distribution of naive and switch patients undergoing DMF treatment

The initial treatments of patients with multiple sclerosis who are either treatment-naïve or have switched to DMF from other therapies are shown. The initiation treatment group includes patients who started their treatment with DMF, whereas the switch group comprises patients who transitioned to DMF after previously undergoing other treatment protocols

DMF: Dimethyl fumarate



**Figure 2.** Initial treatments of patients in the switch group undergoing DMF treatment

The initial treatments received by patients with MS in the switch group before they transitioned to DMF are presented. It shows the distribution of patients who initially received injection, oral, or infusion therapies, providing insight into the treatment history and preferences prior to switching to DMF. The naive group represents patients who started treatment directly with DMF

DMF: Dimethyl fumarate, MS: Multiple sclerosis

The Cronbach's alpha internal consistency coefficient of the scale was 0.82. The MS-TAQ is a 5-point Likert-type scale used to determine the treatment adherence levels of individuals. High scores on the scale indicate high treatment adherence and greater attention to the treatment process.

### Treatment Adherence Form

This form was used to evaluate the DMF treatment adherence levels of the participants through subjective questions. The questions measure whether patients take their medications as prescribed and how adherent they are to the treatment.

### Short Form-36 Health Survey

This scale was used to assess the QoL and general health status of the patients. The Short Form-36 Health Survey (SF-36) was developed by Ware and Sherbourne (9) in 1987, and its Turkish validity and reliability study was conducted by Bilir Kaya and İçağasioğlu (10) in 2018. The SF-36 is a 36-question self-assessment scale and measures eight dimensions: Physical function, social function, physical role difficulty, emotional role difficulty, mental health, energy/vitality, pain, and general health perception. Scores range from 0 to 100, with higher scores indicating better health status.

### Statistical Analysis

Collected data were analyzed using the Statistical Package for the Social Sciences version 25.0 software. Descriptive statistics, such as frequency, percentage, mean, and standard deviation, were used to determine the distribution of demographic and clinical variables. Chi-square analysis was applied to investigate the relationship between DMF treatment adherence and QoL. Analyses examined the relationships between disease duration, sex, age, and initiation treatment group and transition treatment group variables and patients' physical activity, mental problems, experiences of side effects and body pain in the last 4 weeks, side-effect tolerance, treatment satisfaction, overall drug satisfaction, general health perception, social activity, drug use satisfaction, and overall QoL. Table 1 presents the demographic distribution of the participants, as well as disease duration, initial treatment, and DMF usage duration. The distribution of participants by treatment stage is shown in Table 2. Additionally, the chi-square analysis on the relationships between disease duration, sex, age, and the initiation and transition treatment groups with health and QoL variables is presented in Table 3.

## Results

### Disease Duration Analyses

Disease duration analyses revealed significant relationships between disease duration and drug satisfaction ( $\chi^2=0.007$ ) and overall QoL ( $\chi^2=0.050$ ). These findings indicate that disease duration has a significant impact on these variables. Detailed analyses showed that participants with a disease duration of

>5 years had higher levels of drug satisfaction compared to those with a disease duration of  $\leq 5$  years (mean satisfaction score:  $72.5 \pm 8.3$  vs.  $58.9 \pm 7.2$ ;  $p=0.007$ ). This shows that long-term patients are more satisfied with their treatments. Regarding overall QoL, participants with a disease duration of >5 years had a lower overall QoL compared to those with a disease duration of  $\leq 5$  years (mean QoL score:  $48.2 \pm 10.1$  vs.  $63.4 \pm 9.7$ ;  $p=0.050$ ). This finding indicates that disease duration negatively impacts overall QoL. Thus, the disease duration variable induces significant differences in drug satisfaction and overall QoL. While long-term patients show more positive results in drug satisfaction, they show more negative results in overall QoL. These findings demonstrate that disease duration critically affects health and QoL. No significant relationships were found between disease duration and other variables.

### Sex Analyses

According to the results, significant relationships were found between sex and physical activity ( $\chi^2=0.022$ ), general health perception ( $\chi^2=0.028$ ), overall QoL ( $\chi^2=0.041$ ), and body pain in the last month ( $\chi^2=0.005$ ). These reveal that sex has a significant impact on these variables. Detailed analyses showed that females were more successful than males regarding physical activity levels (mean physical activity score:  $42.3 \pm 6.1$  for females vs.  $35.2 \pm 5.7$  for males;  $p=0.022$ ). As regards general health perception, females rated themselves as healthier compared to males (mean scores:  $7.1 \pm 1.5$  vs.  $5.8 \pm 1.8$ ;  $p=0.028$ ), and females scored higher in overall QoL compared to males (mean QoL score:  $66.4 \pm 8.9$  vs.  $51.2 \pm 9.3$ ;  $p=0.041$ ). Additionally, females reported less body pain in the last month compared to males (median pain scores: 2 vs. 4;  $p=0.005$ ). Therefore, female participants showed more positive results in physical activity, general health perception, and overall QoL and experienced less body pain in the last month compared to male participants.

### Age Group Analyses

In the age group analyses, significant relationships were noted between age and mental problems ( $\chi^2=0.011$ ) and overall QoL ( $\chi^2=0.024$ ). These findings show that age has a significant impact on these variables. A significant relationship was found between age group and mental problems (mean mental problems score:  $62.0 \pm 8.2$  for  $\leq 29$  vs.  $45.5 \pm 7.4$  for 30-40 and  $50.3 \pm 8.1$  for >40;  $p=0.011$ ). This shows that the  $\leq 29$  age group experienced more mental problems compared to the older age groups. Regarding overall QoL, the 30-40 age group reported the highest QoL (mean score:  $72.1 \pm 9.4$ ) compared to the  $\leq 29$  (mean score:  $60.5 \pm 8.7$ ) and >40 (mean score:  $55.8 \pm 9.0$ ) ( $p=0.024$ ) age groups. Therefore, the age group variable caused significant differences in mental problems and overall QoL. Younger participants experienced more mental problems, whereas participants in the 30-40 age group showed more positive results in overall QoL.

### Initiation Treatment Group Analyses

In the present study, the results from the analyses of patients who had previously undergone another treatment and continued their treatment with DMF showed a significant relationship only between the initiation treatment group and treatment interruption variable ( $\chi^2=0.004$ ). This finding indicates that patients who had previously undergone another treatment and are currently using DMF more possibly interrupt their treatment compared to those who started their treatment with DMF (percentage of treatment interruption: 32% in the switch group vs. 10% in the naive group;  $p=0.004$ ).

### Transition Treatment Group

In the transition treatment group analysis, patients who had previously received injection, oral, and infusion treatments were compared with naive patients who started treatment directly with DMF. The chi-square test showed significant relationships between the transition treatment group and general health perception ( $\chi^2=0.009$ ) and body pain in the last month ( $\chi^2=0.039$ ). These show that patients who started their treatment with DMF had distinct differences in general health perception and body pain experiences. Specifically, patients who started treatment with DMF had a more positive general health perception (mean scores:  $78.5\pm 7.6$  for injection,  $65.3\pm 6.9$  for infusion, and  $52.8\pm 7.0$  for oral;  $p=0.009$ ) and reported less body pain in the last month (median pain scores: 1 for injection, 3 for infusion, and 5 for oral;  $p=0.039$ ). Hence, different drug usages (initiation and transition treatment groups) caused significant differences in certain health and QoL variables.

### Linear Regression Analysis

Linear regression analysis was performed to examine the factors affecting overall QoL. First, based on the Pearson correlation analysis, significant relationships were found between social activity ( $r=-0.42$ ,  $p<0.05$ ) and general health perception ( $r=1.03$ ,  $p<0.05$ ) and overall QoL. According to the regression model, social activity alone explained 21.3% of the variance in overall QoL ( $R^2=0.213$ , adjusted  $R^2=0.209$ ). A decrease in social activity was significantly associated with a decline in overall QoL (coefficient:  $-0.4199$ ,  $p=0.000$ ). When general health perception was added to the model, it explained 42.6% of the variance in overall QoL ( $R^2=0.426$ , adjusted  $R^2=0.421$ ), with an increase in general health perception significantly associated with an improvement in overall QoL (coefficient:  $1.0293$ ,  $p=0.000$ ). Other variables such as sex, age, disease duration, medication satisfaction, physical activity, and mental health

problems were not statistically significant in this model. These results are presented in Table 4.

Another linear regression analysis was performed to assess the explanatory power of sex, age, disease duration, medication satisfaction, physical activity, and mental health problems on general health perception. Pearson's correlation analysis indicated that physical activity ( $r=0.457$ ,  $p<0.05$ ) and mental health problems ( $r=-0.358$ ,  $p<0.05$ ) were moderately correlated with general health perception. As physical activity increased, general health perception significantly improved, whereas an increase in mental health problems was associated with a decline in general health perception. The regression model explained 27.4% of the variance in general health perception ( $R^2=0.274$ , adjusted  $R^2=0.251$ ), with the highest explanatory power attributed to physical activity and mental health problems. These findings also are detailed in Table 4.

### Discussion

This study examined the effects of DMF treatment on treatment adherence and QoL in patients with MS and presented significant findings. The results are consistent with those in the existing literature, supporting the positive effects of DMF treatment adherence on QoL. A study by Gold et al. (11) indicated that younger patients adapted to treatment more easily and had higher QoL, which aligns with our findings.

In this study, patients with high adherence to DMF treatment were found to have higher QoL. Similarly, some studies suggest that medication adherence positively affects QoL in MS treatment (12,13). Considering the side effects of DMF and the adaptation process of patients to the treatment, it is understood that treatment adherence directly impacts treatment outcomes. This aligns with the findings of a study by Nieto González et al. (14), wherein the nasal application of DMF was explored to reduce side effects, which could further

**Table 1. Demographic characteristics of all participants**

Demographic feature	Value
Average age (years)	33.08
Age range (years)	18-55
Average disease duration (years)	6.43
Average DMF usage duration (months)	16.74
Female (n, %)	180 (79.3%)
Total participants (n)	227

DMF: Dimethyl fumarate

**Table 2. Distribution of participants by treatment stage**

Treatment stage	Injection (n, %)	Oral (n, %)	Infusion (n, %)	Naive (n, %)
Initiation treatment (naive)	-	-	-	154 (67.8%)
Transition treatment (switch)	46 (20.3%)	17 (7.5%)	10 (4.4%)	-
Total patients (n, %)	46 (20.3%)	17 (7.5%)	10 (4.4%)	154 (67.8%)

**Table 3. Chi-square analysis results of the relationships between disease duration, sex, age group, initiation treatment group, and transition treatment group with health and quality of life variables**

Variable	Comparison	Values	p-value
Disease duration	>5 years vs. ≤5 years	Satisfaction: 72.5±8.3 vs. 58.9±7.2 QoL: 48.2±10.1 vs. 63.4±9.7	0.050
Sex	Female vs. male	Physical activity: 42.3±6.1 vs. 35.2±5.7 Health perception: 7.1±1.5 vs. 5.8±1	0.022*
Age group	≤29 years vs. 30-40 years vs. >40 years	Mental problems: 62.0±8.2 vs. 45.5±7.4 vs. 50.3±8.1 QoL: 72.1±9.4 vs. 60.5±8.7	0.011*
Initiation treatment group	Naive vs. switch	Treatment interruption: 32% vs. 10%	0.004*
Transition treatment group	Oral vs. infusion vs. injection	Health perception: 78.5±7.6 vs. 65.3±6.9 vs. 52.8±7.0 Pain: 1 vs. 3 vs. 5	0.009*

Note: The symbol (\*) indicates statistical significance ( $p \leq 0.05$ ).

QoL: Quality of life

**Table 4. Regression results for quality of life and general health perception**

Model variables	R <sup>2</sup>	Adjusted R <sup>2</sup>	Coefficient	p-value
Social activity	0.213	0.209	-0.4199	0.0*
General health perception	0.436	0.421	1.0293	0.0*
Physical activity	0.274	0.251	0.457	0.05*
Mental health problems	0.274	0.251	-0.358	0.05*

Note: The symbol (\*) indicates statistical significance ( $p \leq 0.05$ ).

support treatment adherence. This novel approach highlights the need for personalized DMF administration methods to improve patient comfort and adherence outcomes.

In this study, demographic and clinical factors such as age, sex, and disease duration were found to be determinants of treatment adherence and QoL. The finding that younger patients adapted to treatment more easily and had higher QoL is consistent with the results of other studies (15). Additionally, the higher treatment adherence of female patients compared to male patients supports findings in the literature regarding sex differences (16).

The different impacts of DMF administration methods (e.g., injection, oral, and infusion) on QoL highlight the psychological and physical burden of treatment methods on patients. A study on the impact of treatment methods on patients' QoL revealed that injection treatments cause more stress and discomfort in patients, whereas oral treatment methods provide higher patient satisfaction (17).

In the current study, a significant portion of patients experienced side effects related to DMF treatment; however, their overall satisfaction was high. This indicates that the balance between the effectiveness and side effects of DMF is tolerable for patients. Furthermore, the study by Gold et al. (18) in 2017 also reported that the side effects of DMF treatment were manageable, and overall patient satisfaction was high. This is consistent with the findings of Jožef et al. (19) in 2024, which highlighted the

influence of mental health on DMF adherence and QoL in patients with MS. It showed that mental health status, including levels of depression and anxiety, directly influences treatment adherence and satisfaction with DMF.

The findings of this study reveal that increasing treatment adherence in DMF treatment can improve the QoL of patients. Future studies should include comparative analyses of different treatment methods and a more detailed examination of patients' experiences during the treatment process. Additionally, the development of psychosocial support and education programs to enhance treatment adherence is recommended.

Moreover, in the current study, it was found that social activity and general health perception had significant relationships with overall QoL. These findings are consistent with those in the existing literature, which emphasize the crucial impact of social and health perceptions on the QoL of patients with MS. Particularly, physical activity was widely acknowledged as a key factor in improving physical functioning and mental health, which in turn leads to higher QoL for patients with MS (20,21). However, our study did not find a direct significant relationship between physical activity and QoL, which contrasts with some findings in the literature (22). This discrepancy may be due to differences in disease severity or physical activity levels within our sample. For example, patients with higher levels of disability may face difficulties in participating in regular physical activity, which could reduce its impact on QoL (23).

Similarly, mental health issues such as depression and anxiety were not found to be directly related to QoL. In contrast, several studies emphasized that mental health is a key determinant of QoL in patients with MS (24). This could be attributed to the homogeneity of the mental health status within our sample or the influence of mediating factors including social support. Furthermore, as demonstrated in a 2023 study by Moccia et al. (25), consistent physical activity was found to have a positive impact on physical and mental well-being among DMF-treated patients with MS, underscoring the importance of promoting physical activity within this patient group.

In our study, sex, age, and disease duration did not show significant relationships with QoL. However, the literature shows that women and younger patients typically report higher QoL (26). This inconsistency may be due to the fact that the present study did not fully account for the varying disease progression and treatment modalities.

However, significant relationships were noted between general health perception and physical activity and mental health. Various studies have reported that physical activity improves general health perception by enhancing physical functioning, such as muscle strength, balance, and mobility (27). These findings explain the stronger association between physical activity and mental health with general health perception compared with QoL. While QoL is influenced by a wide range of factors, such as social relationships and emotional state, general health perception is more closely tied to how individuals assess their physical and mental health (28).

### Future Research Implications

The findings of this study highlight the positive effects of DMF treatment on adherence and QoL in patients with MS. However, future studies should consider several critical points for a more comprehensive understanding. Comparative studies directly evaluating DMF against other MS treatment methods are warranted to provide objective insights into its effectiveness and patient satisfaction relative to alternative therapies. Additionally, long-term follow-up studies are crucial to explore the sustained impact of DMF on patients' QoL and adherence over time and its long-term side effects. Furthermore, intervention studies that assess the benefits of psychosocial support and education programs designed to improve adherence to DMF should be pursued, focusing on their influence on patient outcomes. Further, investigation into how adherence to DMF and QoL vary across different demographic groups, including age, sex, socioeconomic status, and cultural backgrounds, is essential for personalizing treatment approaches. Moreover, control group studies using placebos or alternative treatments are required to objectively evaluate the efficacy and side effects of DMF. Implementing these research recommendations will deepen our understanding of DMF's role in MS treatment, enhancing

patient care and optimizing treatment strategies to improve the QoL of those affected by the disease.

### Study Limitations

The demographic and clinical characteristics of the 227 participants may not adequately represent the general population. Factors such as age, sex, and disease duration distribution can affect the generalizability of the results. Studies based on survey data assume that participants provide accurate and honest responses. However, factors including bias and misunderstanding can affect the results. In particular, data based on patients' self-reports may have reliability issues if not supported by objective measurements. The measurement of DMF usage duration and treatment adherence may not fully reflect long-term outcomes. Short-term side effects and long-term treatment-related variability can affect the accuracy of the results. It is possible that individuals who have discontinued the medication did not participate in the study. The present study evaluated the QoL of patients currently using the medication. The way patients experience and report side effects can be subjective, which can create variability in the evaluation of side effects and may not fully reflect the impact on treatment adherence. Comparing the effectiveness of DMF treatment and its effects on the QoL was challenging owing to the absence of a control group. Moreover, the inability to compare with placebo or other treatment methods makes it difficult to isolate treatment effects, and the cross-sectional study design makes it challenging to determine causal relationships. Not being able to identify the relationship between treatment adherence and QoL over time can overlook the dynamic nature of the results. Psychosocial factors that could affect patients' QoL (e.g., family support, socioeconomic status, and psychological support) were not detailed in this study. Ignoring these factors may not comprehensively present the results. General health status and presence of other chronic diseases can affect the effects of DMF treatment and patients' QoL. In this study, other health status variables were not adequately controlled.

DMF is considered an effective treatment option for patients with MS. The results of this study emphasize that adherence to DMF treatment positively impacts patients' QoL and that it should be increased. Consistent with the existing literature, the relationship between treatment adherence and QoL is critical for optimizing treatment processes and improving patients' QoL.

### Conclusion

High adherence to DMF treatment improves the QoL of patients with MS. Younger and female patients, in particular, showed higher adherence and QoL, highlighting the importance of demographic factors. Oral DMF treatments are associated with greater patient satisfaction compared to injection methods. Despite some side

effects, overall satisfaction remains high, indicating an adequate balance between treatment efficacy and side effects.

## Ethics

**Ethics Committee Approval:** The study was approved by the University of Health Sciences Turkey, Sancaktepe Sehit Prof. Dr. İlhan Varank Training and Research Hospital Ethics Committee (approval no: E-46059653-050.99-215847885, date: 17.05.2023).

**Informed Consent:** Written informed consent was obtained from the participants after providing information about the study.

## Footnotes

### Authorship Contributions

Concept: S.D., Design: M.T., Data Collection or Processing: E.H.U., I.G.D., Analysis or Interpretation: M.T., D.C.T., Literature Search: E.H.U., D.C.T., I.G.D., Writing: M.T.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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