Factors Associated With Fatigue in Patients Undergoing Hemodialysis

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Abstract

Background and objective
Fatigue is frequently experienced by patients undergoing hemodialysis and it has a negative effect on their quality of life. The aim of this study was to investigate the factors associated with fatigue in patients undergoing hemodialysis.

Methods
In this quantitative cross-sectional study, 100 patients on hemodialysis participated. Fatigue was evaluated via the Modified Fatigue Impact Scale (MFIS). Participants also completed a questionnaire about demographics and clinical characteristics. The Kruskal-Wallis test, the Mann-Whitney U test, and Spearman’s rho criterion were used to assess the association between fatigue score and patient characteristics. Multiple linear regression was performed to assess the effect of the characteristics on patients’ fatigue.

Results
Statistically significant high levels of physical or mental fatigue were found in older patients (p=0.001 and p=0.001), divorced/widowed patients (p=0.001 and p=0.014), those who had children (p=0.019), those who had primary education (p=0.015), those who were not informed about their health problems (p=0.003 and p=0.006), those who had comorbid diseases (p=0.001 and p=0.001), those who believed that regular information did not help to reduce stress (p=0.005 and p=0.004), patients who had insomnia (p=0.001 and p=0.001), patients who felt tired after hemodialysis (p=0.001 and p=0.001), those who thought they had a change in body image (p=0.001 and p=0.001), those who often felt stiffness (p=0.001 and p=0.001), those who sometimes felt nausea (p=0.015 and p=0.038), and those who had limitations in the clothes they could wear (p=0.001 and p=0.001).

Conclusions
The findings of this study showed that physical or mental fatigue had a strong association with advanced age, comorbidities, marital status, level of education, inadequate information about the disease, insomnia, and change in body appearance. Hence, renal professionals need to properly educate dialysis patients on the complicated nature of fatigue in order to manage it effectively and improve their physical, cognitive, and social wellbeing.

Introduction
Fatigue is commonly experienced by patients undergoing hemodialysis and has a negative effect on their quality of life [1]. Its prevalence rate ranges from 60-97% among hemodialysis patients [2]. These patients suffer from decreased levels of physical activity, low functional capability, and general muscle weakness, which results in a general feeling of fatigue [3]. Mental fatigue is characterized by lack of concentration and inability to remain focused under certain conditions while physical fatigue entails muscle weakness [4].

Symptoms of fatigue are tiredness, weakness, lack of energy [5,6], declined cognitive function, loss of memory, and poor concentration [7], which make patients unable to participate in daily activities. Lack of energy is a source of stress and frustration since patients have limited functional capability [7], which affects their ability to work, look after their families, and achieve personal goals [8]. Thus, fatigue negatively affects their physical, cognitive, and social wellbeing and life satisfaction [2].
Fatigue is a multidimensional problem caused by anemia, uremia, dialysis inadequacy, sleep disorders, pain in bones and muscles, poor nutritional status, inflammation, depression, anxiety, advanced age, and comorbid diseases. Depression is the most significant psychological factor that is strongly related to fatigue. Similarly, feelings of negative affect, including depressive mood, are reportedly related to significantly high rates of fatigue in dialysis patients. Additionally, it has been found that renal patients who suffer from restless leg syndrome have increased levels of fatigue.

However, fatigue among dialysis patients is often unrecognized and untreated since symptoms are usually subjective and not clearly identifiable. In light of this, the aim of this study was to explore the factors associated with fatigue in patients undergoing hemodialysis.

**Materials And Methods**

**Study sample**

The study was conducted at a dialysis unit in Athens, Greece, with a convenience sample of 100 patients. The selection criteria for participants were as follows: aged 20 years or older, on hemodialysis for at least three months, and the ability to speak, read, and write Greek. The exclusion criteria were as follows: insufficient language ability, age of more than 85 years, cognitive deterioration, and drug or alcohol abuse. Patients who met the inclusion criteria were informed about the purpose and procedure of the study and confidentiality was assured. Before collecting data, we obtained approval from the Ethics Committee at the Laconia General Hospital (approval number: 9123/29-10-2020). The study was carried out from November 2020 to January 2021.

The Modified Fatigue Impact Scale (MFIS) was utilized for the evaluation of fatigue and a questionnaire that included the following factors were distributed among the participants: (a) demographic characteristics: gender, age, educational level, job, marital status, number of children, (b) clinical characteristics: the degree of awareness of their health problems, comorbid diseases, the stress they felt due to dialysis regimens, whether they desired to receive written information about the management of their condition, pain after hemodialysis, changes in body image, muscle cramps, joint stiffness, nausea, vomiting, and values of urea, creatinine, and phosphorus, (c) information about patients’ concerns: changes in social and personal life, changes in the amount of fluid and food intake, fear of the possibility of the shutdown of the hemodialysis machine, difficulties in movement, and concerns about the clothes they could wear. The study was carried out in accordance with the Declaration of Helsinki (1989).

**Modified Fatigue Impact Scale (MFIS)**

The MFIS is a 21-item self-assessment scale. Participants indicate the fatigue they experienced throughout the last four weeks. Participants circle the corresponding number that best expresses how often their fatigue has affected them in the last four weeks on a 5-point Likert scale. In each of the grades of the 5-point scale, the scores range from 1 to 5. Ten of the 21 questions evaluate the mental fatigue of patients and the other 11 evaluate the physical fatigue of respondents. The scores assigned to the questions are summed up separately for the questions that assess mental fatigue and those that assess physical fatigue, leading to two scores ranging between 10 and 50 for mental fatigue and between 11 and 55 for physical fatigue. Higher scores indicate higher levels of mental and physical fatigue, respectively. The MFIS has high reliability and validity among the Greek population.

**Statistical analysis**

Nominal data are presented as absolute and relative (%) frequencies, while the continuous ones are presented as mean and standard deviation (SD), and median and interquartile range (IQR). The normality of the data was checked with the Kolmogorov-Smirnov criterion and graphically with histograms and Q-Q plots. The Kruskal-Wallis test, the Mann-Whitney U test, and Spearman’s rho criterion were used to evaluate the association between fatigue score and patient characteristics. Multiple linear regression was performed to assess the effect of characteristics on patients’ fatigue. The results are presented with β regression coefficients and 95% confidence intervals (CI). The observed significance level of 5% was considered statistically significant. All statistical analyses were performed with the SPSS Statistics program version 25 (IBM, Armonk, NY).

**Results**

**Sample description**

A total of 100 patients participated in the study. Most of the participants (75%) were men, while 73% of them were over 60 years old. The majority of the respondents (65%) were married, and pensioners (65%), while 42% had primary education. Most of the participants had two or more children (65%) (Table 1).
| Characteristics          | N (%) |
|--------------------------|-------|
| Gender                   |       |
| Male                     | 75 (75.0%) |
| Female                   | 25 (25.0%) |
| Age (years)              |       |
| 30-40                    | 2 (2.0%) |
| 41-50                    | 9 (9.0%) |
| 51-60                    | 16 (16.0%) |
| 61-70                    | 30 (30.0%) |
| >70                      | 43 (43.0%) |
| Marital status           |       |
| Single                   | 14 (14.0%) |
| Married                  | 65 (65.0%) |
| Divorced                 | 3 (3.0%) |
| Widowed                  | 17 (17.0%) |
| Living together          | 1 (1.0%) |
| Education level          |       |
| Primary school           | 42 (42.0%) |
| High school              | 46 (46.0%) |
| University               | 10 (10.0%) |
| MSc-PhD                  | 2 (2.0%) |
| Job                      |       |
| Unemployed               | 4 (4.0%) |
| Private employee         | 3 (3.0%) |
| Freelancer               | 16 (16.0%) |
| Household work           | 9 (9.0%) |
| Pensioner                | 65 (65.0%) |
| Other                    | 3 (3.0%) |
| Number of children       |       |
| 0                        | 14 (14.0%) |
| 1                        | 23 (23.0%) |
| 2                        | 45 (45.0%) |
| >2                       | 18 (18.0%) |

**TABLE 1: Demographic characteristics of patients (N=100)**

Additionally, 79% of the participants were very or sufficiently informed about their condition of health; 44% suffered from comorbid diseases and 66% had very or sufficient anxiety about the dialysis regimen. Moreover, 36% believed that regular updating was very helpful in reducing stress; 64% wanted to receive written information about management of their disease and 15% stated that they had insomnia. Furthermore, 34% felt tired after the dialysis session, 39% felt more tired at night, and 84% felt tired for a...
few hours; 37% sometimes felt pain during venous puncture, 73% believed that they had a change in body image, and 34% sometimes had itching. Also, 11% had frequent muscle cramps and 10% had stiffness, while 14% sometimes had nausea and vomiting. The mean values of patients’ recent urea, creatinine, and phosphorus were 124, 9, and 6.2, respectively.

Of note, 65% were bothered that they spent a lot of time on hemodialysis, 55% were concerned because they had limited social life due to hemodialysis, and 69% stated that they had experienced changes in their role as a husband/wife. Additionally, 75% stated that they were concerned about the fact that they had to take a limited amount of fluids, and 65% that they should avoid certain foods; 56% were also concerned about the possibility of disruption of arteriovenous anastomosis, and 16% of the possibility of disruption of the dialysis machine. Moreover, 86% stated that they had difficulty in going on vacations and 27% had restrictions on the clothes they could wear. Finally, 31% wanted to hide a part of their body and 70% said that they had a change in their body image.

Regarding the descriptive characteristics of the MFIS scale, the total mean score was 60.7 (SD: 18.0), while for the subscales of Physical and Mental Fatigue, it was 35.1 (SD: 9.9) and 25.5 (SD: 8.7), respectively. The median of the total score was 58.5 (IQR: 49-72.5) while the medians of Physical and Mental Fatigue were 33.5 (IQR: 28-42) and 24 (IQR: 20-31), respectively. At least 50% of patients scored <33.5 (median) and 25% scored <28 in physical fatigue, while 50% had <24 and 25% had <20 in mental fatigue. These values indicate moderate to low levels of patient fatigue.

**Association of the fatigue scale with patients' characteristics**

Statistically significant associations were found between patients’ physical fatigue score and age (p=0.001), marital status (p=0.004), number of children (p=0.019), degree of information about their health problem (p=0.003), whether they had another disease (p=0.001), whether they believed that regular updating helped reduce stress (p=0.005), insomnia (p=0.001), whether they felt tired after hemodialysis, and the duration of fatigue (p=0.001 and p=0.001, respectively), whether they had changes in body image (p=0.001), whether they felt stiffness and nausea/vomiting (p=0.001 and p=0.015, respectively), and whether they felt restricted about what they could wear (p=0.001).

More specifically, patients over the age of 70 had statistically significantly higher levels of physical fatigue (median: 41) than younger patients (median: 31 and 28). Divorced/widowed patients had statistically significantly higher levels of physical fatigue (median: 41) than married (median: 33) and single patients (median: 27). Patients who had children also had higher levels of physical fatigue (median: >34) than those without children (median: 26). Patients who were little or not at all informed about their health problems had higher levels of physical fatigue (median: 41) than those who were very or sufficiently informed (median: 32). Patients who had comorbid diseases had higher levels of physical fatigue (median: 40) than those who did not have comorbid diseases (median: 31). Patients who believed that regular updating did not help reduce stress had statistically significantly higher levels of physical fatigue (median: 42). In addition, high levels of physical fatigue were experienced by patients who had insomnia (median: 36), those who felt tired after dialysis (median: 42), those who believed they had a change in their body image (median: 38), those who often felt stiffness (median: 44), those who sometimes felt nausea (median: 37), and those who felt restricted about what they could wear (median: 38) (Table 2).

| Variables                  | Physical fatigue |                  |
|----------------------------|------------------|------------------|
|                            | Mean (SD)        | Median (IQR)     | P-value |
| Gender                     |                  |                  | 0.325   |
| Male                       | 34.7 (10.3)      | 32 (26-42)       |         |
| Female                     | 36.4 (8.6)       | 34 (31-42)       |         |
| Age (years)                |                  |                  | 0.001   |
| ≤60                        | 29.1 (7.1)       | 28 (24-32)       |         |
| 61-70                      | 33.1 (9.1)       | 31 (28-40)       |         |
| >70                        | 40.3 (9.4)       | 41 (32-49)       |         |
| Marital status             |                  |                  | 0.004   |
| Married/living together    | 34.7 (9.8)       | 33 (28-42)       |         |
| Single                     | 29.4 (8.8)       | 27 (24-34)       |         |
| Divorced/widowed           | 40.5 (8.9)       | 41 (32-47)       |         |
| Variable                                           | Mean (SD) | Min-Max |
|---------------------------------------------------|-----------|---------|
| **Education level**                               | 0.116     |         |
| Primary school                                    | 36.9 (6.6)| 36 (29-44) |
| High school                                       | 34.7 (9.4)| 35 (28-42) |
| University/MSc-PhD                                 | 31.0 (12.1)| 28 (22-36) |
| **Job**                                           | 0.087     |         |
| Unemployed/household work                         | 31.5 (6.8)| 31 (28-34) |
| Employee                                          | 32.4 (9.0)| 29 (26-36) |
| Pensioner                                         | 36.9 (10.5)| 37 (28-44) |
| **Number of children**                            | 0.019     |         |
| 0                                                 | 27.9 (7.4)| 26 (24-31) |
| 1                                                 | 37.1 (11.0)| 38 (28-47) |
| 2                                                 | 36.4 (8.9)| 34 (30-43) |
| >2                                                | 35.1 (10.7)| 36 (26-43) |
| **Informed about their health problems**          | 0.003     |         |
| Very                                              | 27.8 (11.1)| 24 (20-31) |
| Enough                                            | 35.1 (9.6)| 34 (28-42) |
| A little/not at all                               | 39.2 (8.3)| 41 (32-44) |
| **Other diseases**                                | 0.001     |         |
| Yes                                               | 39.5 (9.4)| 40 (32-47) |
| No                                                | 31.8 (9.0)| 31 (25-36) |
| **Are you nervous about the course of the disease?** | 0.466     |         |
| Very                                              | 35.3 (9.8)| 32 (27-42) |
| Enough                                            | 33.6 (9.1)| 32 (28-41) |
| A little/not at all                               | 36.7 (10.8)| 36 (28-47) |
| **Do you believe that regular updating helps reduce stress?** | 0.005     |         |
| Very                                              | 32.6 (10.8)| 30 (25-42) |
| Enough                                            | 33.9 (7.9)| 34 (28-38) |
| A little/not at all                               | 40.4 (9.6)| 42 (32-49) |
| **Do you wish to receive written information regarding the management of the disease?** | 0.104     |         |
| Yes/sometimes                                     | 34.3 (9.4)| 32 (28-41) |
| No                                                | 38.0 (11.3)| 41 (30-49) |
| **How often do you weigh yourself at home?**      | 0.327     |         |
| Daily                                             | 32.7 (8.1)| 33 (27-39) |
| Every 2-4 days                                    | 31.0 (10.5)| 32 (22-34) |
| Once a week                                       | 36.0 (10.1)| 36 (28-43) |
| **Do you have insomnia?**                        | 0.001     |         |
| Yes/sometimes/often                               | 36.5 (10.0)| 36 (29-43) |
| No                                                | 29.9 (7.8)| 29 (24-34) |
| **Do you feel tired after each dialysis session?**| 0.001     |         |
| Question                                                                 | Response          | Yes     | 95% CI    | No       | 95% CI   |
|-------------------------------------------------------------------------|-------------------|---------|-----------|----------|----------|
| When do you feel most tired?                                           | Morning/noon      | 35.8 (11.0) | 31 (28-43) | Afternoon | 33.0 (9.4) | 31 (26-39) |
|                                                                        | Night             | 36.7 (9.5)  | 36 (29-43) |           |          |           |
| What is the duration of fatigue?                                       | Continuous        | 47.3 (6.2)  | 47 (42-54) | A few hours | 33.2 (9.0) | 31 (27-40) |
|                                                                        |                   |          |           | Do you feel pain during venous punctures? | No | 34.2 (10.4) | 31 (25-42) | Rarely | 32.0 (8.7) | 31 (28-36) |
|                                                                        |                   |          |           | Sometimes | 37.2 (9.8) | 37 (31-43) | Often/yes | 36.4 (10.4) | 37 (28-44) |
| Do you think there has been a change in body image after the diagnosis of the disease? | Yes | 37.6 (9.9)  | 38 (31-44) | No       | 28.4 (6.3) | 28 (24-31) |
| Have you had itching in your body since you started dialysis?         | No                | 32.8 (9.3)  | 31 (26-38) | Rarely/sometimes | 35.6 (9.8) | 34 (28-43) |
|                                                                        | Often/yes         | 39.8 (10.6) | 41 (32-48) |           |          |           |
| Do you have muscle cramps?                                            | No                | 35.1 (10.0) | 36 (28-43) | Rarely/sometimes | 34.7 (9.8) | 32 (28-41) |
|                                                                        | Yes/often         | 37.1 (10.7) | 39 (29-44) |           |          |           |
| Do you have stiffness in your joints?                                 | No                | 28.0 (6.3)  | 28 (24-32) | Rarely/sometimes | 35.3 (9.0) | 33 (29-42) |
|                                                                        | Yes/often         | 44.4 (7.1)  | 44 (41-51) |           |          |           |
| Do you feel nauseous and vomiting?                                    | No                | 33.1 (9.7)  | 31 (26-40) | Rarely/sometimes | 38.1 (9.9) | 37 (31-48) |
| Are you concerned about the fact that you now have a limited social life compared to what you had before you started dialysis? | Yes/sometimes   | 35.0 (9.4)  | 34 (28-42) | No        | 35.9 (13.4) | 31 (24-49) |
| Are there any changes in your role as a husband/wife?                 | Yes/sometimes    | 34.9 (9.4)  | 33 (28-42) | No        | 36.4 (12.0) | 41 (24-49) |
| Are you worried about the possibility of the dialysis machine shutting down? | Yes/sometimes | 35.0 (9.4)  | 34 (28-42) | No        | 35.9 (13.4) | 31 (24-49) |
Statistically significant associations were found between the score of patients’ mental fatigue and age (p=0.001), marital status (p=0.014), educational level (p=0.015), degree of information about their health problem (p=0.006), whether they had another disease (p=0.001), whether they believed that regular updating helps reduce stress (p=0.004), insomnia (p=0.001), whether they felt tired after hemodialysis, and the duration of fatigue (p=0.001 and p=0.001, respectively), whether they had changes in body image (p=0.001), whether they felt stiffness and nausea/vomiting (p=0.001 and p=0.038, respectively), and whether they felt restricted about what they could wear (p=0.001).

More specifically, patients over the age of 70 years had statistically significantly higher levels of mental fatigue (median: 30) than younger patients (median: 22 and 20). Divorced/widowed patients had statistically significantly higher levels of mental fatigue (median: 30) than married (median: 22) and singles (median: 24) patients. Patients with primary education had higher levels of mental fatigue (median: 28) than those with secondary (median: 22) and university level (median: 20) education. Patients who were little or not at all informed about their health problems had higher levels of mental fatigue (median: 29) than those who were very or sufficiently informed (median: 11). Patients with comorbid diseases had higher levels of mental fatigue (median: 27) than those without comorbid diseases (median: 22). Patients who believed that regular information did not help reduce stress had statistically significantly more mental fatigue (median: 30). In addition, higher levels of mental fatigue were experienced by patients who had insomnia (median: 27), those who felt tired after dialysis (median: 30), and those who experienced persistent fatigue (median: 32), those who thought that they had a change in their body image (median: 28), those who often felt stiffness (median: 31), and those who sometimes felt nausea (median: 29), and those who felt restricted about what they could wear (median: 28) (Table 3).
| Category                          | Very          | Enough        | A little/not at all | No            |
|----------------------------------|---------------|---------------|---------------------|---------------|
| Informed about their health problems | 18.3 (11.0)   | 25.5 (7.7)    | 29.4 (8.2)          | 23.3 (8.0)    |
| Other diseases                   |               |               |                     |               |
| Yes                              | 28.3 (8.8)    | 25.0 (7.3)    | 27.4 (10.9)         | 23.3 (8.0)    |
| No                               |               |               |                     |               |
| Are you nervous about the course of the disease? |               |               |                     |               |
| Yes                              | 24.0 (7.0)    | 25.0 (7.3)    | 27.4 (10.9)         | 24.5 (7.6)    |
| No                               |               |               |                     | 29.0 (11.1)   |
| Do you believe that regular updating helps reduce stress? |               |               |                     |               |
| Yes                              | 23.3 (8.6)    | 24.1 (6.6)    | 30.7 (9.6)          | 20.9 (7.3)    |
| No                               |               |               |                     |               |
| How often do you weigh yourself at home? |               |               |                     |               |
| Daily                            | 21.4 (10.5)   | 20.9 (7.3)    | 20.9 (7.3)          | 21.4 (10.5)   |
| Every 2-4 days                   |               |               |                     |               |
| Question                                                                 | Yes | Yes/sometimes/often | No | No/rarely/sometimes/often | Yes/often | p-value |
|-------------------------------------------------------------------------|-----|---------------------|----|---------------------------|-----------|---------|
| Once a week                                                             | 26.9 (8.4) | 26 (20-32)          | 19.3 (6.3) | 19 (16-23)               |           | 0.001   |
| Do you have insomnia?                                                   |     |                     |    |                           |           |         |
| Yes/sometimes/often                                                     | 27.2 (8.5) | 27 (21-32)         | 23.4 (7.3) | 22 (20-29)               |           |         |
| No                                                                      | 19.3 (6.3) | 20 (16-23)         | 19.3 (6.3) | 19 (16-23)               |           |         |
| Do you feel tired after each dialysis session?                          |     |                     |    |                           |           | 0.001   |
| Yes                                                                     | 30.3 (9.1) | 30 (25-36)         | 26.6 (9.5) | 24 (20-33)               |           |         |
| Sometimes/often                                                         | 23.8 (7.4) | 23 (20-30)         | 23.8 (7.4) | 23 (20-30)               |           |         |
| When do you feel most tired?                                           |     |                     |    |                           |           | 0.472   |
| Morning/noon                                                            | 26.6 (9.5) | 24 (20-33)         | 26.6 (9.5) | 24 (20-33)               |           |         |
| Afternoon                                                               | 23.8 (7.4) | 23 (20-30)         | 23.8 (7.4) | 23 (20-30)               |           |         |
| Night                                                                   | 26.5 (9.2) | 27 (20-31)         | 26.5 (9.2) | 27 (20-31)               |           |         |
| What is the duration of fatigue?                                        |     |                     |    |                           |           | 0.001   |
| Continuous                                                              | 34.5 (9.0) | 32 (30-41)         | 24.0 (7.9) | 23 (20-30)               |           |         |
| A few hours                                                             | 24.0 (7.9) | 23 (20-30)         | 24.0 (7.9) | 23 (20-30)               |           |         |
| Do you feel pain during venous punctures?                               |     |                     |    |                           |           | 0.146   |
| No                                                                      | 25.4 (8.8) | 23 (20-32)         | 25.4 (8.8) | 23 (20-32)               |           |         |
| Rarely                                                                  | 22.5 (6.9) | 22 (20-26)         | 22.5 (6.9) | 22 (20-26)               |           |         |
| Sometimes                                                               | 27.9 (9.0) | 28 (21-33)         | 27.9 (9.0) | 28 (21-33)               |           |         |
| Often/yes                                                               | 24.4 (9.2) | 26 (17-30)         | 24.4 (9.2) | 26 (17-30)               |           |         |
| Do you think there is a change in body image after the diagnosis of the disease? |       |                     |    |                           |           | 0.001   |
| Yes                                                                     | 27.3 (8.8) | 28 (21-32)         | 27.3 (8.8) | 28 (21-32)               |           |         |
| No                                                                      | 20.7 (6.2) | 20 (17-24)         | 20.7 (6.2) | 20 (17-24)               |           |         |
| Have you had itching in your body since you started dialysis?           |     |                     |    |                           |           | 0.258   |
| No                                                                      | 23.9 (6.8) | 22 (20-30)         | 23.9 (6.8) | 22 (20-30)               |           |         |
| Rarely/sometimes                                                        | 26.0 (9.4) | 26 (20-31)         | 26.0 (9.4) | 26 (20-31)               |           |         |
| Often/yes                                                               | 28.5 (10.1) | 29 (20-35)        | 28.5 (10.1) | 29 (20-35)               |           |         |
| Do you have muscle cramps?                                             |     |                     |    |                           |           | 0.622   |
| No                                                                      | 24.5 (7.0) | 23 (21-30)         | 24.5 (7.0) | 23 (21-30)               |           |         |
| Rarely/sometimes                                                        | 25.6 (9.0) | 25 (20-31)         | 25.6 (9.0) | 25 (20-31)               |           |         |
| Yes/often                                                               | 27.6 (10.4) | 28 (22-35)        | 27.6 (10.4) | 28 (22-35)               |           |         |
| Do you have stiffness in your joints?                                   |     |                     |    |                           |           | 0.001   |
| No                                                                      | 21.1 (6.8) | 21 (17-26)         | 21.1 (6.8) | 21 (17-26)               |           |         |
| Rarely/sometimes                                                        | 25.5 (8.9) | 24 (20-30)         | 25.5 (8.9) | 24 (20-30)               |           |         |
| Yes/often                                                               | 31.5 (7.0) | 31 (25-39)         | 31.5 (7.0) | 31 (25-39)               |           |         |
| Do you feel nauseous and vomiting?                                      |     |                     |    |                           |           | 0.038   |
| No                                                                      | 23.8 (7.6) | 22 (20-29)         | 23.8 (7.6) | 22 (20-29)               |           |         |
| Rarely/sometimes                                                        | 28.3 (10.0) | 29 (20-36)        | 28.3 (10.0) | 29 (20-36)               |           |         |
| Are you concerned about the fact that you now have a limited social life compared to what you had before you started dialysis? |       |                     |    |                           |           | 0.157   |
| Yes/sometimes                                                           | 24.9 (7.9) | 23 (20-30)         | 24.9 (7.9) | 23 (20-30)               |           |         |
Regarding physical fatigue, we observed that patients who sometimes felt tired after dialysis had a statistically significantly lower score of 4.8 points compared to patients who felt tired after each session ($\beta=-4.81$, 95% CI: -8.78 to -0.83, $p=0.018$). In addition, patients who felt tired for a few hours had a statistically significantly lower score of 6.5 points compared to those who felt continuous fatigue ($\beta=-6.53$, 95% CI: -11.91 to -1.15, $p=0.018$). Also, patients who often felt joint stiffness and those who sometimes felt nauseous had 7 and 3.7 points, respectively, which were higher scores for physical fatigue compared to those who did not feel stiffness and nausea ($\beta=7.08$, 95% CI: 1.64-12.53, $p=0.012$ and $\beta=3.67$, 95% CI: 0.18-7.17, $p=0.040$, respectively).

Regarding mental fatigue, we observed that patients who did not have insomnia had a statistically significantly lower score of mental fatigue at 6.3 compared to patients who had insomnia ($\beta=-6.31$, 95% CI: -10.01 to -2.61, $p=0.001$). In addition, patients who felt tired for a few hours had a statistically significantly lower score for mental fatigue 8 points than those who felt constant fatigue ($\beta=-8.04$, 95% CI: -15.01 to -3.07, $p=0.002$). In addition, patients who sometimes felt nauseous had a higher score of mental fatigue at 5 points than those who did not ($\beta=5.01$, 95% CI: 1.62-8.40, $p=0.004$) (Table 4).

**TABLE 3: Association of mental fatigue scale with patients' characteristics**

| Variables                                      | Physical fatigue | Mental fatigue |
|------------------------------------------------|------------------|----------------|
|                                               | $\beta$ coefficient (95% CI) | P-value | $\beta$ coefficient (95% CI) | P-value |
| Age (years)                                    |                  |                |                              |         |
| ≤60 Ref. Cat.                                  |                  |                |                              |         |
| >60                                            |                  |                |                              |         |

**Effect of patients' characteristics on the fatigue scale**

Multiple linear regression was performed to assess the effect of patient characteristics (independent factors) on the fatigue they experienced (dependent variable).
| Group          | Ref. Cat. | Ref. Cat. | Ref. Cat. | 95% CI     | p-value |
|----------------|-----------|-----------|-----------|------------|---------|
| 61-70          | -0.09     | 0.962     | -0.48     | -4.48-3.53 | 0.814   |
| >70            | 3.82      | 0.068     | 3.41      | -0.68-7.50 | 0.101   |
| **Status**     |           |           |           |            |         |
| Married/living together | Ref. Cat. | Ref. Cat. |           |            |         |
| Single         | 2.32      | 0.726     | -0.70     | -5.13-3.74 | 0.755   |
| Divorced/widowed | 0.27      | 0.893     | 1.46      | -2.47-5.39 | 0.461   |
| **Education level** |           |           |           |            |         |
| Primary school | -         | Ref. Cat. |           |            |         |
| High school    |           | 1.95      | -1.14     | -5.04      | 0.213   |
| University/MSc-PhD | -        | 0.80      | -0.51     | -7.10      | 0.802   |
| **Number of children** |           |           |           |            |         |
| 0              | Ref. Cat. | -         |           |            |         |
| 1              | 6.10      | 0.375     | -         |            |         |
| 2              | 6.51      | 0.33      | -         |            |         |
| >2             | 2.99      | 0.659     | -         |            |         |
| **Informed about their health problems** |           |           |           |            |         |
| Very           |           | Ref. Cat. | Ref. Cat. |            |         |
| Enough         | 3.53      | 0.18      | 5.82      | -0.69-12.34| 0.079   |
| A little/not at all | 1.34      | 0.692     | 3.37      | -4.48-11.21| 0.395   |
| **Other diseases** |           |           |           |            |         |
| Yes            | Ref. Cat. | Ref. Cat. |           |            |         |
| No             | 2.49      | 0.14      | 2.53      | -0.73-5.78 | 0.126   |
| **Do you believe that regular updating helps reduce stress?** |           |           |           |            |         |
| Very           |           | Ref. Cat. | Ref. Cat. |            |         |
| Enough         | -1.91     | 0.28      | -1.77     | -5.06-1.52 | 0.286   |
| A little/not at all | 4.23      | 0.122     | 4.90      | -0.29-10.09| 0.064   |
| **Do you have insomnia?** |           |           |           |            |         |
| Yes            | Ref. Cat. | Ref. Cat. |           |            |         |
| No             | -1.93     | 0.321     | -6.31     | -10.01 to -2.61| 0.001  |
| **Do you feel tired after each dialysis session?** |           |           |           |            |         |
| Yes            | Ref. Cat. | Ref. Cat. |           |            |         |
| Sometimes/often | -4.81     | 0.016     | -1.75     | -5.63-2.12 | 0.369   |
| **What is the duration of fatigue?** |           |           |           |            |         |
| Continuous     |           | Ref. Cat. | Ref. Cat. |            |         |
| A few hours    | -6.53     | 0.018     | -8.04     | -13.01 to -3.07| 0.002  |
| **Do you think there is a change in body image after the diagnosis of the disease?** |           |           |           |            |         |
| Yes            | Ref. Cat. | Ref. Cat. |           |            |         |
| No             | -2.44     | 0.266     | -1.89     | -5.93-2.16 | 0.355   |
| **Do you have stiffness in your joints?** |           |           |           |            |         |
| No             | Ref. Cat. | Ref. Cat. |           |            |         |
TABLE 4: Effect of patients’ characteristics on the fatigue scale

| Rarely/sometimes | 0.25 (-4.24-4.74) | 0.913 | -1.15 (-6.42-3.11) | 0.591 |
|-------------------|-------------------|-------|-------------------|-------|
| Yes/often         | 7.08 (1.64-12.53) | 0.012 | 1.13 (-4.16-6.42) | 0.672 |
| No                | 3.67 (0.18-7.17)  | 0.04  | 5.01 (1.62-8.40)  | 0.004 |

Discussion

The present study found that patients over the age of 70 years and those with comorbid diseases had statistically significantly high levels of physical or mental fatigue. It is well known that patients of advanced age have decreased levels of physical functioning due to comorbid diseases, which lead to complications, disabilities [16], and loss of energy [17]. Given that the prevalence of renal failure is increasing in individuals over 65 years old, it is understandable that elderly people need closer attention. They frequently have to overcome several challenges such as the complexity of therapy, the severity of the disease, and greater effort to follow the therapeutic regimen [18].

Fatigue in patients with advanced age is a multifactorial problem due to depression, anxiety, and subjective sleep quality. Furthermore, illness perception, coping mechanisms, and self-efficacy are gradually deteriorating in them. An equally important factor is that the elderly are frequently unable to adhere to treatment, which leads to the deterioration of their physical state [17]. Meanwhile, loss of skeletal muscle, which constitutes the largest type of tissue mass and accounts for 40-45% of total body weight, leads to functional failure, resulting in poor outcomes, especially in elderly individuals [19]. However, fatigue is often under-recognized and under-treated by healthcare providers as its symptoms are often not visible. Healthcare professionals frequently attribute fatigue to the advanced age or side effects of hemodialysis [20]. At the same time, age is one of the strongest predictors of depression among hemodialysis patients, which may explain the fatigue in the elderly to some extent [21].

Moreover, this study showed that divorced/widowed patients had statistically significantly higher levels of physical or mental fatigue than married and single patients. A possible explanation for this finding is that patients who lead their lives without support are exposed to worse clinical outcomes. It is well documented that social support consists of a modifiable psychosocial factor of significant importance for survival. The need for social support varies among patients undergoing hemodialysis according to the quality and quantity of their social network or the severity of the disease [22]. It is important to take into account that patients undergoing long-term hemodialysis usually face problems with marital relationships since spouses feel emotional and psychological distress due to problems arising from hemodialysis [23].

It can be assumed that this vulnerable group of patients (no spouse/pattern) are deprived of the benefits associated with social support. Social support improves the quality of life through various mechanisms such as increasing patients’ satisfaction from the provided care, enhancing adherence to the therapeutic regimen including diet and fluid restrictions, or alleviating symptoms of fatigue. This finding may provide guidance to the healthcare providers, family members, and social services about the importance of social support in dialysis patients [22].

The present study also found that patients with primary education and those who were little or not at all informed about their health problems had statistically significantly high levels of physical or mental fatigue. The association with the level of education can be viewed in the context of patients’ capability to understand health-related information. Patients’ knowledge is regarded as an important factor in the management of their disease since those who are knowledgeable understand their condition better and comply with the restrictions of their treatment [16]. However, individuals with low education levels have more difficulty in accepting or comprehending recommendations related to the therapeutic regimen, disease management, and necessary alterations in everyday living. Possibly, these individuals fail to recognize the importance of alleviating fatigue [24]. The mechanism by which low levels of education are linked to fatigue is complex. Possibly, these patients are less likely to have access to healthcare or have difficulty retrieving health information due to a lack of understanding. They may also experience difficulties in learning self-care skills, which leads to exacerbations and a higher burden of symptoms [25,26].

The present study also found that patients who had insomnia had statistically significantly high levels of physical or mental fatigue. These findings are in line with those of a previous study [27]. It can be assumed that sleep disorders have a strong relationship with fatigue since they lead to daytime sleepiness, poor concentration, and increased levels of inflammatory cytokines in patients’ blood [10]. Additionally, the findings of this study showed that patients who had a change in body image had statistically significantly
high levels of physical or mental fatigue. Body image is one of the most stressful factors for patients on hemodialysis, often affecting their psychological status. Changes in body image after the initiation of dialysis can be caused by weight loss, muscle wasting, changes in skin color, and marks caused by venous puncture [28].

The results of this study offer important information to renal professionals about the factors related to fatigue in patients on hemodialysis. The findings of this study indicated that fatigue had a strong relationship with advanced age, comorbidity, marital status, level of education, inadequate information about the disease, insomnia, and changes in body appearance. Therefore, this study highlights the importance of early diagnosis of fatigue by renal professionals and the provision of the appropriate information to dialysis patients about the complicated nature of fatigue.

Conclusions

Fatigue is a common problem among hemodialysis patients, leading to poor quality of life. The findings of the present study indicated high levels of fatigue in patients aged over 70 years, those with comorbidities, divorced/widowed patients, those with primary education, those having inadequate information about the disease, and patients with insomnia and changes in body image. Renal health professionals need to educate patients about the symptoms of fatigue and help them combat it effectively in order to improve their physical, cognitive, and social wellbeing.

Appendices

Modified Fatigue Impact Scale (MFIS)

|   |                                                                                     | 0 | 1 | 2 | 3 | 4 |
|---|-------------------------------------------------------------------------------------|---|---|---|---|---|
| 1 | I have been less alert                                                               |   |   |   |   |   |
| 2 | I have had difficulty paying attention for long periods of time                      | 0 | 1 | 2 | 3 | 4 |
| 3 | I have been unable to think clearly                                                  | 0 | 1 | 2 | 3 | 4 |
| 4 | I have been clumsy and uncoordinated                                                | 0 | 1 | 2 | 3 | 4 |
| 5 | I have been forgetful                                                                | 0 | 1 | 2 | 3 | 4 |
| 6 | I have had to pace myself in my physical activities                                 | 0 | 1 | 2 | 3 | 4 |
| 7 | I have been less motivated to do anything that requires physical effort              | 0 | 1 | 2 | 3 | 4 |
| 8 | I have been less motivated to participate in social activities                       | 0 | 1 | 2 | 3 | 4 |
| 9 | I have been limited in my ability to do things away from home                        | 0 | 1 | 2 | 3 | 4 |
| 10| I have trouble maintaining physical effort for long periods                          | 0 | 1 | 2 | 3 | 4 |
| 11| I have had difficulty making decisions                                              | 0 | 1 | 2 | 3 | 4 |
| 12| I have been less motivated to do anything that requires thinking                     | 0 | 1 | 2 | 3 | 4 |
| 13| My muscles have felt weak                                                            | 0 | 1 | 2 | 3 | 4 |
| 14| I have been physically uncomfortable                                                | 0 | 1 | 2 | 3 | 4 |
| 15| I have had trouble finishing tasks that require thinking                             | 0 | 1 | 2 | 3 | 4 |
| 16| I have had difficulty organizing my thoughts when doing things at home or at work   | 0 | 1 | 2 | 3 | 4 |
| 17| I have been less able to complete tasks that require physical effort                 | 0 | 1 | 2 | 3 | 4 |
| 18| My thinking has been slowed down                                                     | 0 | 1 | 2 | 3 | 4 |
| 19| I have had trouble concentrating                                                    | 0 | 1 | 2 | 3 | 4 |
| 20| I have limited my physical activities                                                | 0 | 1 | 2 | 3 | 4 |
| 21| I have needed to rest more often or for longer periods                               | 0 | 1 | 2 | 3 | 4 |

TABLE 5: Modified Fatigue Impact Scale (MFIS)
Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. Ethics Committee at the Laconia General Hospital issued approval 9123/29-10-2020. Animal subjects: All authors have confirmed that this study did not involve animal subjects or tissue. Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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