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The burden of mental-physical fatigue and its correlates in patients undergoing hemodialysis and peritoneal dialysis

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Fatigue is a debilitating symptom in patients with end-stage renal disease. This study was aimed to determine the level and correlates of physical and also mental fatigue symptoms in addition to its effect on health related quality of life (HRQoL) in hemodialysis (HD) and peritoneal dialysis (PD) patients. A questionnaire-based cross-sectional study involving 318 patients was conducted in three dialysis centers. Data were collected using the Fatigue Severity Scale (FSS), Short-Form 36, Beck Depression Inventory (BDI) and Arizona Sexual Experiences Scale (ASEX). Patient groups were identified as having fatigue (FSS >4.0), depressive (BDI ≥17) and having sexual dysfunction (SD) (ASEX ≥12). Fatigue prevalence was 71.6% in HD patients and 66.9% in PD patients. Depression prevalence was 43.7% and most of the depressive patients (87.8%) had fatigue. SD prevalence was 77.8% and 75.2% of them had fatigue. MCS and PCS scores were markedly lower in fatigued patients. FSS was correlated with BDI, PCS and MCS scores in both HD and PD patients. Fatigue was similarly frequent and severe in both types of dialysis groups and this seriously impaired HRQoL. Depression and physical HRQoL were the major predictors of fatigue in both groups.

Key words: Kidney failure-chronic, renal dialysis, peritoneal dialysis, fatigue, mental fatigue, quality of life, chronic diseases and depression.

INTRODUCTION

Chronic Renal Failure (CRF) leads to progressive deterioration of fluid electrolyte balance and cardiovascular, hematopoietic or endocrinologic functions. CRF may also affect social, economic and physiological status directly (1). Fatigue is a complex phenomenon that involves physical, psychological, and emotional components which frequently experienced as a feeling of being tired, weak, exhausted, weary, worn

out, heavy or slow in patients with CRF (2). Recently, Hardy and Studensky identified two groups of fatigue qualities: mental, comprising emotional and cognitive qualities and physical, comprising sleepiness, lack of energy, and weakness (3). Mental fatigue which can present with somnolence, lethargy or directed attention dysfunction can be defined as impairment in cognitive performance. Physical fatigue or muscle fatigue is an inability of optimal muscle performance and it can abolish by resting (4). Fatigue is affected by a large number of demographic, socio-economic and biochemical factors but no specific pathogenesis

specifically has been identified in the literature so far (5).

Fatigue, with a prevalence of 45-55 % nationwide (2) and 60-97% worldwide (6) is one of the most common symptom in patients with ESRD which is often ignored and difficultly managed by health workers although it affects daily life activities, social relations and the professional life by impairing the quality of life. The prevalence of fatigue in HD patients ranges from 45 % to 80 % and 30 % to 88 in PD patients (7-9).

Several studies in ESRD patients report that fatigue is associated with depression sleep disorder, sexual dysfunction, and impaired quality of life (5, 10-12). Fatigue is negatively correlated with mental and physical health related quality of life in HD patients (13-15).

This study aims to: (1) evaluate the level of fatigue experienced by patients receiving HD and PD, (2) determine the possible correlations between fatigue and demographic, psychosocial and physiological factors in addition to the effect of fatigue on their HRQoL, and (3) compare the overlapping correlates of fatigue in both HD and PD patients.

MATERIALS AND METHODS

Participants

A questionnaire based study was performed by using face-to-face interview. 318 patients receiving HD or PD 3 times a week for at least one year from October 2007 to October-2008 at three centers in Kayseri, Turkey were included. 207 out of 246 (84. 1%) patients responded to the ASEX scale. The study was approved by the Ethics Committee of Erciyes University. Verbal confirmed consent was obtained from participants in the study.

Instruments

Data were collected using the patient interview form, FSS, SF-36, BDI and ASEX scales.

Selection of covariates

Demographic factors (age, gender, education, and marital status), treatment related factors (type of dialysis and duration), biochemical parameters (hemoglobin, serum albumin, blood urea nitrogen (BUN), weekly Kt/V urea, creatinine) and psychological factors (SF-36 subscales, PCS and MCS scores, BDI score and ASEX scores) were examined to assess their influence on fatigue.

Statistical analysis

HD and PD patients were divided into two groups based on baseline FSS scores as "fatigue" (having >4.0 points) and "non-fatigue" (having 0-4 points). Statistical assessment of the data was performed using SPSS version 18.0 software package. Baseline sociodemographic and biochemical factors are

described as arithmetic means and standard deviations (Mean \pm SDs) for continuous variables and as frequencies for categorical variables. The independent sample *t*-test was used to examine the associations between SF-36 subscales and dimension scores and fatigue among independent groups. To determine the predictors of fatigue and its correlates univariate and multiple logistic regression analyses and Spearman's rank correlation coefficient (ρ) were used.

Fatigue constituted the dependent variable in regression analyses whereas age, educational level, serum albumin level, depression, PCS and MCS dimension scores, which display significant relations in univariate analyses, constituted the independent variables. ASEX scores were not included in the regression analyses since the scale was not applied to all the subjects.

RESULTS

155 patients (48.7 %) on HD and 163 patients (51.3 %) on PD treatment were included. Demographic data of the patients are summarized in table 1. There is no significant difference between in patients HD and PD in terms of socio-demographic variables. The mean duration of disease in the HD and PD groups were similar but, the mean duration of dialysis treatment was significantly higher in the HD group than in the PD group (5.05 \pm 4.17 vs. 3.63 \pm 2.84 years; p <0.001).

Fatigue in ESRD patients

The prevalence and degree of fatigue was similar among HD and PD patients (p =0.453). 166 of 220 patients (75.5 %) with fatigue reported severe fatigue and 46.3% of them complained substantial fatigue lasting 12-24 hours per day (p <0.001) (Table 2).

Fatigue and demographic factors

Table 1 shows the prevalence of fatigue according to demographic and clinical variables in both HD and PD groups. In our study the prevalence of fatigue was found to be significantly associated with mean age (p <0.001), the level of education (p =0.002), depression (p <0.001) and sexual dysfunction (p =0.001) in total patients. The mean age was significantly higher in patients having fatigue (p <0.001).

Fatigue and psychological factors

Prevalence of depression in ESRD patients was 43.7 %. The prevalence of depression were significantly higher in patients with fatigue compared to patients with no fatigue (88.9 % vs. 86.8 %, p <0.001). BDI score was higher in PD group than HD group (21.31 \pm 10.73 vs. 18.51 \pm 8.93, p <0.001) (Table 2).

Fatigue and sexual dysfunction

The overall prevalence of sexual dysfunction (SD) was 77.8 %. The prevalence of SD was significantly higher (75.2 %) in patients with fatigue (p =0.001). SD prevalence was 85.7 % for women with fatigue

Table 1. Demographic and clinical characteristics of the patients with and without fatigue.

Demographic and clinical characteristics	Type of Renal Replacement Treatment								
	HD			PD			Total		
	Non-fatigue (n:44)	Fatigue (n:111)	P	Non-fatigue (n:54)	Fatigue (n:109)	P	Non-fatigue (n:98)	Fatigue (n:220)	P
%	%		%	%		%	%		
Gender									
Female	25.6	74.4	0.445	33.3	66.7	0.951	29.8	70.2	0.716
Male	31.2	68.8		32.9	67.1		32.0	68.0	
Age (years)									
18-44	43.3	56.7	0.003	40.3	59.7	0.111	41.7	58.3	<0.001
45-64	22.2	77.8		30.9	69.1		27.1	72.9	
≥65	12.5	87.5		13.3	86.7		12.8	87.2	
Mean age	42.93±16.55	51.85±14.63	0.001	43.70±14.41	48.74±14.09	0.034	43.35±15.53	50.30±14.41	<0.001
Education									
Primary school	22.2	77.8	0.004	29.2	70.8	0.109	25.7	74.3	0.002
Secondary school and over	47.4	52.6		42.0	58.0		44.3	55.7	
Marital status									
Single	36.8	63.2	0.507	55.0	45.0	0.073	46.2	53.8	0.053
Married	28.4	71.6		30.8	69.2		29.7	70.3	
Widow (er)/Divorced	20.0	80.0		23.1	76.9		21.2	78.8	
Depression									
Absent (0-16 p)	40.2	59.8	<0.001	50.6	49.4	<0.001	45.3	54.7	<0.001
Present (17-63 p)	11.1	88.9		13.2	86.8		12.2	87.8	
Mean BDI Score	10.15±6.32	18.51±8.93	<0.001	12.25±8.64	21.31±10.73	<0.001	11.31±7.72	19.90±9.94	<0.001
Sexual dysfunction									
Absent (0-11 p)	64.3	35.7	0.001	43.8	56.3	0.132	50.0	50.0	0.001
Present (12-30p)	20.0	80.0		29.1	70.9		24.8	75.2	
Mean ASEX score	14.33±6.94	19.53±6.93	0.003	16.35±8.64	16.86±6.60	0.750	15.58±8.03	18.05±6.86	0.025

($p=0.006$) and 77.1 % for men with fatigue ($p=0.053$). (Table 2).

Fatigue and biochemical parameters

Hemoglobin, BUN, weekly Kt/V urea and total cholesterol levels did not differ significantly between the patients with and without fatigue in both treatment groups ($p>0.05$). However, while serum albumin levels in the HD group (4.01 ± 0.76) were within reference values (3.5-5.5 mg/dl), in the PD group they were below the minimum threshold level (3.21 ± 0.53) ($p<0.001$). Serum albumin in patients with fatigue in the PD group was at a more lower (3.15 ± 0.50) ($p=0.042$). Serum creatinine levels were significantly higher in patients with fatigue than in those without fatigue in both total and HD group (13.03 ± 16.78 vs. 8.95 ± 4.44 , $p=0.001$, 14.50 ± 19.82 vs. 8.95 ± 3.42 ; $p=0.005$; respectively).

Fatigue and health related quality of life

The overall PCS score was 39.23 ± 11.05 and MCS score was 41.41 ± 10.95 . Comparison of the SF-36

scores among patients with and without fatigue in HD and PD were shown in table 3.

Fatigue and its correlates

The FSS scores in both treatment groups were positively correlated with BDI, but negatively correlated with PCS and MCS (Table 4 a-b). FSS was correlated with ASEX score in only HD group ($\rho=0.48$, $p<0.001$). Table 4a and 4b show the correlation between FSS scores and BDI, ASEX, PCS and MCS scores in both HD and PD patients.

Interrelated correlations:

The BDI displayed positive correlation with ASEX and inverse correlation with PCS and MCS in both dialysis modalities. Similarly, the ASEX score positively correlated with FSS and also positively correlated with BDI, but negatively with PCS. The PCS score, which was negatively correlated with FSS, was inversely correlated with BDI and ASEX scores; the MCS score, however, was only inversely correlated with BDI score (Table 4 a-b)

Table 2. Comparison of Fatigue Severity Score According to Type of Dialysis Treatment.

Type of Dialysis Treatment	Fatigue Severity Scale Score			Total n (%)	p
	Non-fatigue (0-4 p) n (%)	Moderate fatigue (4.1-4.9 p) n (%)	Severe fatigue (4.9-7 p) n (%)		
HD	44 (28.4)	30 (19.4)	81 (52.3)	155 (48.7)	
PD	54 (33.1)	24 (14.7)	85 (52.1)	163 (51.3)	
Total	98 (30.8)	54 (17.0)	166 (52.2)	318 (100.0)	0.453
Overall FSS Mean ± SD	1.97±1.13	4.57±0.20	5.92±0.40	4.48±1.97	<0.001

Predictors of fatigue

FSS score was significantly correlated with age, BDI, PCS and MCS scores in the HD and PD groups. In addition albumin was significantly correlated with FSS score in the PD group. In multiple logistic regression analysis depression and physical health QoL were found to be the most important determiners of fatigue. Depression raised fatigue on average 1.12 and 1.06 fold in HD and PD patients, respectively (BDI score; HD: OR=1.12, 95 % CI [1.04-1.19], p=0.001 and PD: OR=1.06, 95 % CI [1.01-1.11], p=0.010). However, the improvement of physical health QoL in both treatment groups played a recuperative role on fatigue (PCS score; HD: OR=0.93, 95 % CI [0.89-0.98], p=0.005 and PD: OR=0.90, 95 % CI [0.86-0.94], p<0.001).

DISCUSSION

The importance of the present study is being one of the few reports those examining the level and correlates of fatigue as well as its effects on HRQoL in two different dialysis modalities. Comparing and analyzing the interactions between a great numbers of different modalities effecting fatigue in ESRD patients enriched and increased the value of this study either.

Consistently with previous studies, in the present study, fatigue was the major problem among patients on dialysis treatment (6-10, 16, 17). The rates of fatigue was higher in HD (71.6 %) patients than PD (69.2 %) counterparts, however this was not significant. Two-thirds of patients with fatigue had severe fatigue based on increased number of days with fatigue within the last one month and its duration that prolonged gradually. Approximately half of these patients complained about severe fatigue symptoms lasting 12-24 hours per day (p<0.001).

Fatigue defined as an emotional exhaustion by patients. Multiple physiologic, psychosocial and socio-demographic factors may contribute to development of fatigue in ESRD patients but their complex and reciprocal interactions with fatigue are poorly understood (10, 18).

We detected relationship between fatigue and age, educational level, psychological health, sexual functioning, serum albumin and creatinine levels.

The mean age of the patients with fatigue (50.30±14.41) was significantly greater than non-fatigue (43.33±15.53) subjects (p<0.001). A similar relationship was also observed in the HD and PD groups, but the effect of age on fatigue was more prominent in HD group (p=0.001, 0.034, respectively). In line with our findings, some studies (8, 16-19) conducted in HD and PD patients demonstrated that age was associated with higher fatigue levels and older participants had more frequent and severe fatigue than younger participants. On the other hand Letchmi, Das (7) and Bossola, Luciani (10) had found a negative correlation between age and fatigue levels. The emergence and rise of fatigue in parallel with aging has been ascribed to bio-psycho-social problems caused by the burden of chronic diseases increasing in advanced age and reduced physical activity.

In general, educational level significantly affected the incidence of fatigue. Such that, patients with primary school education had much more fatigue than patients with further education (74.3 % vs. 55.7 %; p=0.002). Similarly in the HD group, the patients with primary education reported more frequent fatigue (77.8 % vs. 52.6 %, p=0.004). On the other hand, educational status did not affect the level of fatigue in patients receiving PD (p=0.109). Consistent with our study, Liu (17) showed that in patients receiving HD, as the level of education decreased, the incidence of fatigue increased. They also reported that fatigue occurred more frequently in patients who were illiterate and primary school graduates. In contrast to our study, Kim and Son (20) concluded that educational level was not associated with fatigue in patients treated with HD. We considered that educational level increase a person's general perception of health and self awareness, while it is facilitating compliance to treatment and the development of methods to deal with fatigue more successfully.

In our study serum albumin and creatinine levels had a significant effect on fatigue. Compared with HD group, serum albumin levels in the PD group were under the

Table 3. SF-36 scale scores according to hemodialysis and peritoneal dialysis patients with and without fatigue.

SF-36 Dimensions	Type of Renal Replacement Treatment				Total Score	
	HD		PD		Non-fatigue	Fatigue
	Non-fatigue	Fatigue	Non-fatigue	Fatigue		
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
Role physical	68.37±38.82	37.83±44.5	62.50±45.4	38.30±44.9	65.13±42.5	38.06±44.66
p	<0.001		0.002		<0.001	
Physical func.	72.15±28.31	43.15±32.3	72.68±25.1	44.40±26.4	72.44±26.4	43.77±29.48
p	<0.001		<0.001		<0.001	
Bodily pain	74.88±27.73	40±34.80	82.92±26.2	56.94±36.8	79.31±27.0	56.67±35.77
p	0.001		<0.001		<0.001	
General health	55.38±18.33	39.19±19.9	56.33±23.8	31.90±21.4	55.90±21.4	35.58±20.96
p	<0.001		<0.001		<0.001	
Vitality	63.06±20.20	37.43±20.1	65.92±20.5	38.11±23.8	64.64±20.3	37.77±22.03
p	<0.001		<0.001		<0.001	
Social function	62.12±39.10	38.81±42.8	74.30±25.8	54.01±35.0	68.83±32.8	46.34±39.81
p	0.002		<0.001		<0.001	
Role emotional	73.01±26.12	59.00±31.2	40.06±46.6	58.64±46.2	65.09±39.0	49.62±40.65
p	0.006		0.018		0.001	
Mental health	65.00±16.86	48.72±19.8	67.70±20.2	56.18±23.7	66.48±18.7	52.41±22.11
p	<0.001		0.002		<0.001	
PCS	46.23±9.17	36.66±10.2	35.09±10.2	47.19±8.70	46.76±8.88	35.88±10.25
p	<0.001		<0.001		<0.001	
MCS	46.46±9.12	38.38±9.51	46.21±11.1	40.08±11.0	46.33±10.2	39.22±10.56
p	<0.001		0.001		<0.001	

minimum threshold level (3.5 mg/dl). It was lower in patients with fatigue ($p=0.042$). Bonner, Wellard (21) reported that albumin levels under 4 mg/dl resulted in higher fatigue ratio, which is compatible with our finding. Some researchers (21) reported that hypo-albuminemia is an indicator of malnutrition-inflammation complex syndrome and a strong predictor of infection, fatigue and poor quality of life. In line with our findings, Bossola, Luciani (10) found that the level of creatinine is associated with fatigue in HD patients. On the contrary, McCann and Boore (14) showed that BUN and creatinine levels are not associated with fatigue.

In our study, overall depression prevalence was 43.7%. The majority of the depressive patients reported much more fatigue in both treatment groups (88.8% vs. 86.8%, $p<0.001$). Depression has been acknowledged positively associated with fatigue in dialysis patients (14, 17, 18, 20, 22). This relation was attributed to the deterioration of the immune system and high levels of pro-inflammatory cytokines (10). Beside this, ESRD patients suffering from depression usually have lack of physical exercise and poor diet which also induce fatigue.

The incidences of sexual dysfunction in patients with fatigue were 77.1% in men and 85.7% in women similar to the literature (23, 24). Dialysis modality may

have impact on the development of sexual dysfunction. In the studies by Diemont, Vrugink (25) and Kettas, Cayan (26) sexual dysfunction is more prevalent in patients on HD than patients on PD. In our study HD patients had higher frequency of sexual dysfunction (84.3% vs. 72.9%) and this difference was almost statistically significant ($p=0.051$). The great majority of patients with SD had been suffering from fatigue (75.2%; $p<0.001$), and women reported more symptoms of fatigue than men notably (77.9% vs. 72.6%; $p=0.006$). Consistent with our results, some studies (24, 27) indicated that sexual dysfunction was more prevalent in women with chronic fatigue syndrome. Fatigue was positively correlated with sexual dysfunction only in the HD group. Chronic fatigue syndrome has a direct influence on sexual dysfunction, particularly hypoactive sexual desire. From other point of view, inadequate sexual performance may lead to anxiety, lack of sexual desire and even depression which may aggravate fatigue (27, 28).

In our study, regardless of the type of treatment, fatigue was related to deteriorate health related QoL. In both treatment groups, all the subscale scores were nearly 1.5-2 fold less in patients with fatigue, this reduction was more markedly in areas of general health, vitality and role physical, constituting physical

Table 4a. Analysis of correlation between SF-36 scale and FSS, BDI, ASEX scores in hemodialysis patients.

The scales overall scores	Type of Renal Replacement Treatment (HD)				
	FSS Score (n:155)	BDI Score (n:155)	ASEX Score (n:88)	PCS Score (n:155)	MCS Score (n:155)
FSS	1				
BDI	rho=0.54 p<0.001	1			
ASEX	rho=0.48 p<0.001	rho=0.43 p<0.001	1		
PCS	rho=-0.57 p<0.001	rho=-0.50 p<0.001	rho=-0.48 p<0.001	1	
MCS	rho=-0.52 p<0.001	rho=-0.58 p<0.001	rho=-0.11 p=0.284	rho=0.28 p<0.001	1

FSS: Fatigue Severity Scale
 PCS: Physical Component Summary, MCS: Mental Component Summary
 BDI: Beck Depression Inventory
 ASEX: Arizona Sexual Experiences Scale.

health QoL (p<0.001). In accordance with our results, a recent study (12) showed that fatigue was one of the symptoms independently associated with impaired QoL, both at the physical and mental level in PD patients. Some other studies (13-15) concluded that fatigue was negatively correlated with physical functioning, role limitations, and daily activities in HD patients.

In our study, correlations among FSS and BDI, ASEX and HRQoL scores were statistically significant. Fatigue was positively correlated with depression independent of dialysis modalities, and depression was shown to aggravate fatigue. Consistent with our results, many researchers (10, 14, 20, 22) revealed that depression was positively correlated with fatigue. We only observed similar correlation in the HD group, in accordance with previous studies (27, 28).

In both treatment groups, irrespective of the type of the dialysis treatment fatigue markedly impaired physical and mental health QoL (p<0.001) and displayed inverse correlation with physical and mental health QoL. This effect was more noticeably in the SF-36 physical function, vitality, general health subscales and PCS summary score. Deterioration in physical health QoL was more serious than mental health QoL. In comparison the quality of life of fatigued patients in HD and PD groups, general health status and role emotional in HD; social function and mental health status in PD patients were poorer. Depression is a comorbidity that may be observed frequently in patients on PD treatment. Both the disease itself and having a dependency on a machine may impair social functions and demoralize the patients which result in poorer mental health scores in quality of life. On the other hand, mental and physical fatigue modalities have a reciprocal interaction. For example, mental fatigue

affects physical performance negatively by reducing exercise tolerance through higher perception of effort (29).

We found that mental and physical fatigue independently associated with poorer quality of life as described before (10, 12, 15, 20). In addition, in line with previous studies (11, 30) our study showed that depression, sexual dysfunction and HRQoL which correlated with fatigue may have bi-directional interactions with each-other, except for the relationship between SD and fatigue. Such that, impaired quality of life may be caused by fatigue, depression and sexual dysfunction but it is also possible that poor quality of life may contribute to fatigue.

Depression and other mood disorders found to be a major predictive factor on fatigue previously (17). Conformably, in our study, significant predictors of fatigue were depression and physical health QoL. Depression had a positive predictive effect while improved physical health QoL had a protective effect.

In conclusion, fatigue levels did not differ by dialysis modality. It was highly prevalent and severe in both HD and PD patients and strongly associated with impaired HRQoL. Fatigue was closely related to older age, lower educational level and sexual function disorders in HD group. Depression had positively significant relationship with fatigue in each group. SF-36 scores of fatigued patients were significantly lower. General health status and role-emotional in HD, social function and mental health status in PD group were poorer. Depression and physical health QoL were the most important predictors of fatigue in patients on both HD and PD therapy. This result indicated that to improve the QoL in patients with ESRD comprehensive interventions is necessary to assess and manage depression and fatigue. We suggest

that education of awareness for patients and care givers on this complex phenomenon is very important issue in detecting in the early stage.

Conflict of interest: Authors have no conflict of interest to declare.

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