

## Original Article

# Serum potassium and handgrip strength as predictors of sleep quality among hemodialysis patients in Malaysia

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**Background and Objectives:** Poor sleep quality is prevalent among hemodialysis (HD) patients and leads to adverse health outcomes. This study investigated the association of nutritional parameters with sleep quality among Malaysian HD patients. **Methods and Study Design:** A cross-sectional study was conducted among 184 Malaysian HD patients. Anthropometric measurements and handgrip strength (HGS) were obtained using standardized protocols. Relevant biochemical indicators were retrieved from patients' medical records. Nutritional status was assessed using the dialysis malnutrition score. The sleep quality of patients was determined using the Pittsburgh Sleep Quality Index questionnaire on both dialysis and non-dialysis days. **Results:** Slightly more than half of the HD patients were poor sleepers, with approximately two-third of them having a sleep duration of <7 hours per day. Sleep latency (1.5±1.2) had the highest sleep component score, whereas sleep medicine use (0.1±0.6) had the lowest score. Significantly longer sleep latency and shorter sleep duration were observed in the poor sleepers, regardless of whether it was a dialysis day or not ( $p<0.001$ ). Poor sleep quality was associated with male sex, old age, small triceps skinfold, hypoproteinemia, hyperkalemia, hyperphosphatemia, and poorer nutritional status. In a multivariate analysis model, serum potassium ( $\beta=1.41$ ,  $p=0.010$ ), male sex ( $\beta=2.15$ ,  $p=0.003$ ), and HGS ( $\beta=-0.088$ ,  $p=0.021$ ) were found as independent predictors of sleep quality. **Conclusions:** Poor sleep quality was evident among the HD patients in Malaysia. The sleep quality of the HD patients was associated with nutritional parameters. Routine assessment of sleep quality and nutritional parameters indicated that poor sleepers have a risk of malnutrition and may benefit from appropriate interventions.

**Key Words:** hemodialysis, sleep quality, nutritional parameters, hyperkalemia, Pittsburgh Sleep Quality Index

## INTRODUCTION

Sleep is the basic human physiological need that must be satisfied.<sup>1</sup> Poor sleep quality is more prevalent in hemodialysis (HD) patients than in the general population, ranging from 51% to 91% across studies.<sup>2-7</sup> Furthermore, poor sleep quality has been associated with several health consequences, including poor quality of life,<sup>7</sup> insomnia, irregularity in sleeping habits, poor nocturnal sleep, restless leg syndrome, sleep apnea, frequent awakening at night, early-morning awakening, daytime sleepiness, and others.<sup>8</sup> Sleep problems, such as sleep apnea and insomnia, may contribute to the development of cardiovascular complications and affect the survival of HD patients adversely.<sup>9</sup>

Multiple factors have been associated with sleep quality in HD patients, including metabolic factors, such as age, sex, and metabolic abnormalities; physiological factors, such as disability, pain, pruritus, muscle cramps, restless leg syndrome, fatigue, and sleep apnea; psychological factors, such as depression; and malnutrition.<sup>2,4,8,10,11</sup> Despite the literature indicating that the causes of sleep problems are multifactorial, the etiologies of

poor sleep quality among HD patients remain unclear.<sup>6</sup>

Although malnutrition has been reported to be highly prevalent among HD patients,<sup>12,13</sup> the relationship between their nutritional status and sleep is likely to be complex and can be different from that in the general population. To the best of our knowledge, all studies investigating the relationship between malnutrition and poor sleep quality have been conducted in Caucasian HD populations,<sup>12,14,15</sup> whose results may not be generalizable to non-Caucasian populations, including the Malaysian population. Therefore, this study investigated the potential effect of nutritional parameters and other factors on

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sleep quality among Malaysian HD patients.

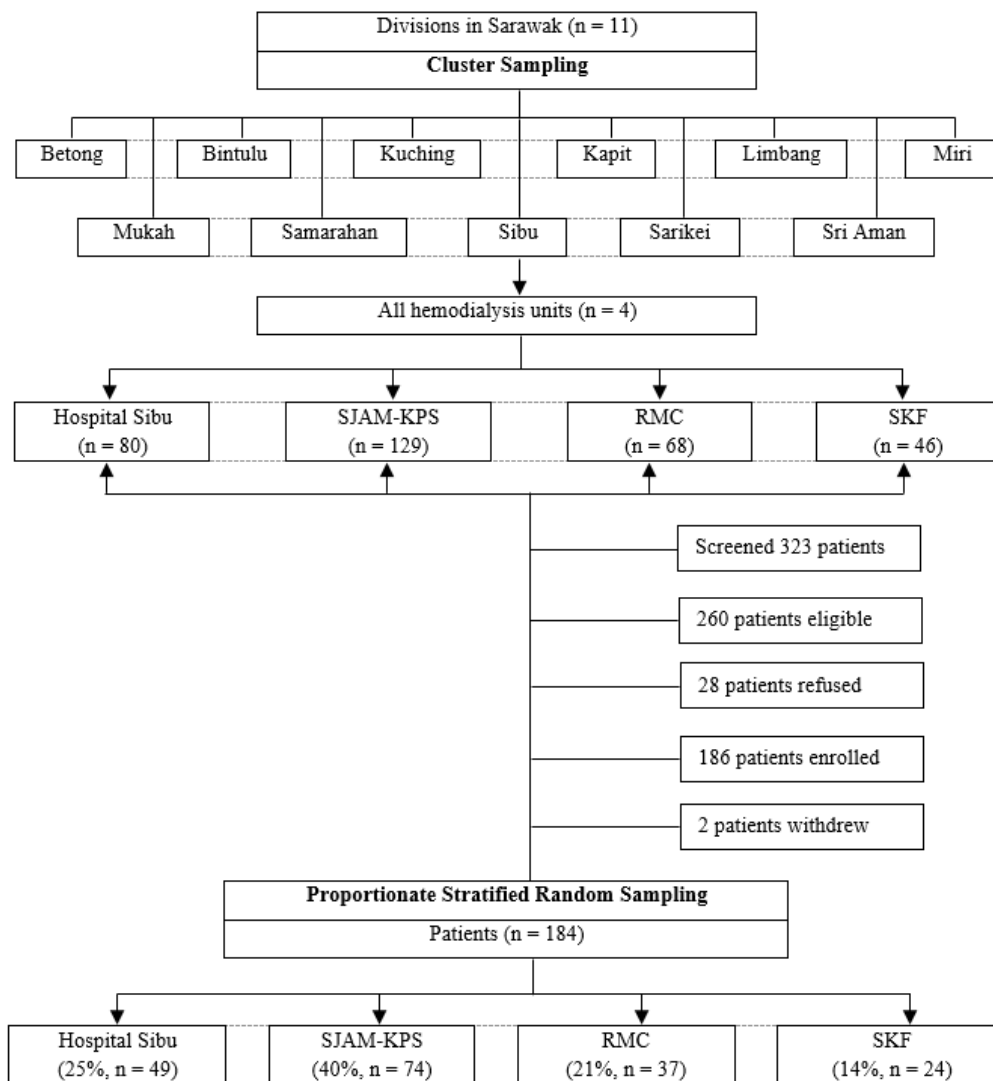
## METHODS

A cross-sectional study was conducted between February and June 2017 in four HD units in Sibü, which is an island town in Sarawak, the biggest state of Malaysia. Figure 1 shows the consort diagram of this study. Multistage sampling was performed using cluster sampling and stratified sampling methods, whereby cluster sampling was used to choose the division of Sibü. The number of patients chosen from each HD unit was proportional to the size of the HD unit. All patients in dialysis units were screened according to predefined criteria, and eligible patients were selected through simple random sampling. We included patients who were aged  $>21$  years and had undergone regular HD treatment thrice weekly for at least 3 months. Patients who presented with psychosocial problems, such as mental illness and dementia, or had hepatitis or were hospitalized within a month before the study were excluded. This study was performed in accordance with the principles of the Declaration of Helsinki and was approved by the Medical Research and Ethics Committee

of National Institutes of Health Malaysia with registration number NMRR-16-2238-33077. All patients provided informed consent to participate in the study, and patients' anonymity was preserved.

## Sleep quality

The sleep quality of patients in the past month was ascertained using the validated Pittsburgh Sleep Quality Index (PSQI) with permission from the author.<sup>16</sup> The PSQI is composed of seven components: subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, sleep medication use, and daytime dysfunction. In this study, sleep latency and sleep duration were measured for both HD days (HDDs) and non-HD days (NHDDs), and average values were used to compute the component score. Each sleep component has a scale factor from 0 to 3, and the seven components collectively form a global score ranging from 0 to 21. The higher the score is, the lower is the quality of sleep. A global PSQI score of  $\leq 5$  indicates satisfactory sleep quality, whereas a score of  $>6$  indicates poor sleep quality.<sup>16</sup> Cronbach's alpha of this index was 0.752, indicating that the instru-



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Figure 1. Consort diagram of the study.

ment has acceptable internal consistency.

### **Nutritional parameters**

Body height, dry weight, mid-upper arm circumference (MUAC), triceps skinfold (TSF), and handgrip strength (HGS) of patients were measured after dialysis to prevent the effect of excessive body fluids on body composition measurement. The MUAC and TSF were measured for the nonfistula arm at the midpoint of the upper arm between the acromion and olecranon process by using a nonstretchable measuring tape and Harpenden Skinfold Caliper, respectively. Mid-arm muscle circumference (MAMC) was calculated using the following formula:  $MUAC \text{ (cm)} - [\pi \times TSF \text{ (cm)}]$ . Furthermore, body mass index (BMI) was computed using the following formula:  $\text{dry weight (kg)} / [\text{height} \times \text{height}] \text{ (m}^2\text{)}$ . The HGS of the nonfistula arm rather than the fistula arm was assessed using Lafayette (Model 78010) Hand Dynamometer (Lafayette Instrument Company Inc., USA) to prevent bleeding of the arm with fistula due to overexertion after dialysis. Patients were instructed to perform warm-up exercises, such as shaking their hand three times before gripping the hand dynamometer with the maximum force.<sup>17</sup> The grip strength value reflected the muscle function of patients.

Biochemical indicators, including total protein, serum albumin, total cholesterol, serum creatinine, serum potassium, serum phosphorus, and hemoglobin levels, were retrieved from routine blood test records. All biochemical indicators were collected before dialysis. Three readings were documented to reflect the average reading of biochemical results for a period of 9 months, and mean values were calculated.

The nutritional status of patients was assessed subjectively by calculating the dialysis malnutrition score (DMS), a fully quantitative scoring system. The DMS consists of five components of medical history (weight change, dietary intake, gastrointestinal symptoms, functional capacity, and comorbidity) and two components of physical assessments (loss of subcutaneous fat and signs of muscle wasting).<sup>18</sup> Each component has a score ranging from 1 to 5, where 1 is normal and 5 is severe malnutrition risk. Summation of scores from the seven components provides a continuous score ranging from 7 (normal) to 35 (severely malnourished). Hence, a lower DMS score indicates better nutritional status, whereas a higher score is an indicator of malnutrition or protein-energy wasting.

### **Statistical analysis**

Data were analyzed using IBM SPSS Statistics version 22. Descriptive analysis was performed to describe the characteristics of patients, and results were expressed as the mean  $\pm$  standard deviation and number (n, %). The normality of data was assessed using skewness and Kurtosis. Mean differences between the groups were analyzed and compared using the independent sample t-test, whereas differences among variables within a group were compared using the paired sample t-test. Differences among categorical variables were analyzed using the chi-square test or Fisher's exact test as appropriate. However, correlations between continuous variables were examined using the Pearson product-moment correlation coefficient

or Spearman's rank correlation coefficient. Furthermore, to determine variables that were independently associated with the PSQI and sleep components, we performed multiple linear regression with stepwise selection of variables with a *p* value of  $<0.25$  in the univariate analysis. A *p* value of  $<0.05$  was considered statistically significant.

## **RESULTS**

### **Sociodemographic variables**

In total, 323 HD patients were screened, and 260 of them were eligible. Of 260 potential patients, 28 (10.8%) refused to participate, resulting in a response rate of 89.2%. A total of 186 patients agreed to participate, and two patients (1.1%) withdrew from the study. Thus, 184 sets of completed data were available. Table 1 shows the sociodemographic characteristics of the patients. The mean age of the patients was  $54.3 \pm 12.6$  years, ranging from 22 to 81 years, and 61% of the patients were men. Elderly patients, defined as those aged  $\geq 60$  years, comprised 37% of the patients, which reflected the aging phenomenon in Malaysia. By contrast, despite 63% of the patients belonging to the productive age group (20–59 years), three quarter of them were unemployed due to chronic kidney disease and chronic HD treatment. The majority of the patients were Chinese (52.7%), married (73.9%), qualified with equal or higher than secondary education level (65.2%), and having a low household income (66.8% of the bottom 40%). The median monthly household income of the patients was 30% lower than the median household income of approximately USD 1250 in Sarawak as reported by the Department of Statistics Malaysia.<sup>19</sup> The government was the main treatment funder. Due to economic downturn, subsidies from the government were limited to a certain amount, and patients had to pay the extra treatment fee on their own or from other funds. Compared with the good sleeper group, the poor sleeper group had more male, elderly, Chinese, married or divorced, and literate patients, with no significant differences between the groups. The distribution of patients according to employment status, household income, and source of treatment funding was similar in both the good and poor sleeper groups.

### **Nutritional parameters**

Data in Table 2 depict information on the nutritional parameters of the patients. The mean height, dry weight, and BMI of the patients were  $158.7 \pm 9.1$  cm,  $61.2 \pm 14.3$  kg, and  $24.2 \pm 4.6$  kg/m<sup>2</sup>, respectively. According to the World Health Organization classification, half of the patients had normal body weight status (BMI=18.5–24.9). By contrast, one and four of the 10 patients were underweight (BMI  $<18.5$ ) and overweight or obese (BMI  $\geq 25$ ), respectively. A higher proportion of the underweight patients were poor sleepers compared with those with normal BMI, overweightness, and obesity. However, no significant difference in BMI was observed between the poor and good sleepers. Almost all the patients had an MUAC of  $\geq 23$  cm. The mean values of TSF and MAMC were  $13.8 \pm 4.8$  mm and  $26.1 \pm 3.9$  cm, respectively. No significant differences were observed between the good and poor sleepers in terms of MUAC, TSF, and MAMC. Nevertheless, a significantly higher proportion of the poor

**Table 1.** Socio-demographic characteristics of patients stratified by sleep quality

Variables	Good sleepers (n=90)	Poor sleepers (n=94)	Total (n=184)	Statistics (p value)
Sex				$\chi^2=2.548$ (0.110)
Male	49 (54.4)	63 (67.0)	112 (60.9)	
Female	41 (45.6)	31 (33.0)	72 (39.1)	
Age group	53.2±13.2	55.3±12.0	54.3±12.6 <sup>†</sup>	t=-1.123 (0.263)
21–35 years old	12 (13.3)	8 (8.5)	20 (10.9)	$\chi^2=1.655$ (0.437)
36–59 years old	48 (53.4)	48 (51.1)	96 (52.1)	
≥60 years old	30 (33.3)	38 (40.4)	68 (37.0)	
Ethnicity				$\chi^2=1.358$ (0.244)
Chinese	43 (47.8)	54 (57.4)	97 (52.7)	
Non-Chinese	47 (52.2)	40 (42.6)	87 (47.3)	
Marital Status				$\chi^2=3.235$ (0.375)
Married	65 (72.2)	71 (75.5)	136 (73.9)	
Single	18 (20.0)	11 (11.7)	29 (15.8)	
Widow/ Widower	1 (1.1)	2 (2.2)	16 (8.7)	
Divorced/ Separated	6 (6.7)	10 (10.6)	3 (1.6)	
Educational level				$\chi^2=1.980$ (0.577)
No formal education	8 (8.9)	4 (4.3)	12 (6.5)	
Primary school	23 (25.6)	29 (30.8)	52 (28.3)	
Secondary school	49 (54.4)	51 (54.3)	100 (54.3)	
Tertiary	10 (11.1)	10 (10.6)	20 (10.9)	
Employment status				$\chi^2=0.000$ (1.000)
Unemployed	75 (83.3)	78 (83.0)	153 (83.2)	
Employed	15 (16.7)	16 (17.0)	31 (16.8)	
Household size	4.5±2.5	4.6±2.2	4.6±2.4	t=-0.148 (0.882)
Household monthly income (RM) <sup>‡</sup>			2,950 <sup>§</sup>	$\chi^2=0.153$ (1.000)
B40 (< 3,860)	60 (66.7)	63 (67.0)	123 (66.8)	
M40 (3,860 – 8,319)	26 (28.9)	63 (67.0)	52 (28.3)	
T20 (≥ 8,320)	4 (4.4)	5 (5.3)	9 (4.9)	
Per capita			890±1,085	
Source of treatment funding <sup>¶</sup>				
Government funded	78 (86.7)	80 (85.1)	158 (85.9)	
Self-funding	52 (57.8)	57 (60.6)	109 (59.2)	
NGO funded	6 (6.7)	6 (6.4)	12 (6.5)	
Employer subsidized	3 (3.3)	0 (0.0)	3 (1.6)	
Insurance	0 (0.0)	3 (3.2)	3 (1.6)	

Data was presented as mean±SD or n (%).

B40: bottom 40%; M40: middle 40%; T20: top 20%; NGO: non-government organization.

<sup>†</sup>Age ranged from 22 to 81 years.

<sup>‡</sup>Classified based on Eleventh Malaysia Plan (2016–2020), RM 1 was equivalent to approximately USD 0.3 at the time of data collection.

<sup>§</sup>Data was presented in median.

<sup>¶</sup>Multiple responses.

sleepers were observed to have an MUAC of <23 cm ( $p=0.035$ ). The HGS of the patients had a mean of 20.9±9.0 kg with comparable mean HGS between the good and poor sleepers ( $p>0.05$ ).

Approximately one in four patients had hypoalbuminemia. Slightly more than half of the patients had total cholesterol levels within the recommended range, whereas one-third and one of six patients had hypocholesterolemia and hypercholesterolemia, respectively. It is not uncommon for patients with kidney failure to have high serum creatinine levels. Although HD imitates the functions of the kidneys, the process does not remove all metabolic wastes from the body. The mean values of electrolytes, such as serum potassium and phosphorus, were within normal ranges. Approximately one-quarter of the patients experiencing hyperkalemia had failed to achieve the serum potassium level recommended by the Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines (2004).<sup>20</sup> Approximately 60% of the patients had serum phosphorus levels as per the K/DOQI recommendation, whereas one-third of them had hyperphosphatemia and

7% of them had hypophosphatemia. Furthermore, the mean hemoglobin level of the patients was 108±14 g/L, which was slightly lower than the normal value. Thirty percent of the patients had a hemoglobin level of <100 g/L, which indicated anemia, attributing to insufficient production of erythropoietin and red blood cells, as a health consequence of end-stage renal disease. In general, biochemical indicator readings of the good and poor sleepers were comparable. The nutritional status of the patients as assessed with DMS had a mean score of 11.3±2.3 and ranged from 7 to 21, suggesting a lower risk of malnutrition. No significant difference in mean DMS was observed between the good and poor sleepers.

#### **Sleep quality and its component scores**

The sleep quality and sleep component scores of the patients are summarized in Table 3. The mean PSQI score was 6.7±4.1 with a significantly higher PSQI score in the poor sleepers. Poor sleep quality was observed in >50% of the patients. Sleep latency had the highest PSQI subscore, whereas sleep medicine use had the lowest score.

**Table 2.** Nutritional parameters of patients stratified by sleep quality

Parameters	Good sleepers (n=90)	Poor sleepers (n=94)	Total (n=184)
<b>Anthropometric data</b>			
Height (cm)	157.4±9.3	159.8±8.7	158.7±9.1 (134–184)
Dry weight (kg)	60.8±13.1	61.5±15.5	61.2±14.3 (33.3–102.8)
BMI (kg/m <sup>2</sup> ) <sup>†</sup>	24.5±4.4	23.9±4.7	24.2±4.6
<18.5	3 (3.3)	13 (13.8)	16 (8.7)
18.5–24.9	49 (54.5)	43 (45.8)	92 (50.0)
25.0–29.9	28 (31.1)	29 (30.9)	57 (31.0)
30.0–34.9	7 (7.8)	8 (8.5)	15 (8.1)
≥35.0	3 (3.3)	1 (1.1)	4 (2.2)
MUAC (cm)	30.8±4.6	30.0±4.9	30.4±4.7 (19.6–40.4)
<23	1 (1.1)	8 (8.5) <sup>‡</sup>	9 (4.9)
≥23 ref	89 (98.9)	86 (91.5)	175 (95.1)
TSF (mm)	14.3±4.8	13.3±4.8	13.8±4.8 (2.4–31.0)
MAMC (cm)	26.4±3.9	25.9±3.9	26.1±3.9 (17.8–35.6)
Handgrip strength (kg) <sup>§</sup>	20.9±9.6	20.8±8.5	20.9±9.0 (0.5–51.0)
Low	19 (21.8)	28 (30.4)	47 (26.3)
Normal	68 (78.2)	64 (69.6)	132 (73.7)
<b>Biochemical data</b>			
Total protein (g/L)	72.7±4.7	72.3±4.9	72.5±4.8 (61.3–88.0)
Serum albumin (g/L) <sup>¶</sup>	40.1±3.2	40.0±3.5	40.0±3.3 (26.3–46.7)
<40	35 (38.9)	37 (39.4)	72 (39.1)
≥40 ref	55 (61.1)	57 (60.6)	112 (60.9)
Total cholesterol (mmol/L) <sup>¶, ††</sup>	4.3±0.8	4.3±1.0	4.3±0.9 (2.3–6.7)
<3.9	29 (32.2)	31 (33.0)	60 (32.6)
3.9–5.2 ref	50 (55.6)	45 (47.9)	95 (51.6)
>5.2	11 (12.2)	18 (19.1)	29 (15.8)
Serum creatinine (µmol/L)	959.4±212.7	938.4±258.3	948.7±236.7 (395.7–1621.7)
Serum potassium (mmol/L) <sup>‡‡</sup>	4.6±0.5	4.7±0.6	4.6±0.6 (3.2–6.3)
≤5.0 ref	68 (75.6)	68 (72.3)	136 (73.9)
>5.0	22 (24.4)	26 (27.7)	48 (26.1)
Serum phosphorus (mmol/L) <sup>§§</sup>	1.7±0.4	1.7±0.4	1.7±0.4 (0.8–3.0)
<1.13	7 (7.8)	6 (6.4)	13 (7.1)
1.13–1.78 ref	52 (57.8)	56 (59.6)	108 (58.7)
>1.78	31 (34.4)	32 (34.0)	63 (34.2)
Hemoglobin (g/L) <sup>¶¶</sup>	106.2±13.0	108.9±14.7	107.6±13.9 (69.3–150.0)
<100	30 (33.3)	26 (27.7)	56 (30.4)
100–120 ref	50 (55.6)	49 (52.1)	99 (53.8)
>120	10 (11.1)	19 (20.2)	29 (15.8)
Dialysis Malnutrition Score	11.0±2.0	11.6±2.4	11.3±2.3 (7–21)

Data was presented as mean ± SD, range or n (%).

BMI: body mass index; MUAC: mid-upper arm circumference; TSF: triceps skinfold; MAMC: mid-arm muscle circumference.

<sup>†</sup>BMI classification based on WHO.

<sup>‡</sup>Significant association between MUAC ( $p=0.035$ ) with sleep quality was determined by Fisher's Exact Test at 0.05 level of significance.

<sup>§</sup>Total patients=179, Low HGS: ≤20 kg for male, ≤10 kg for female.

<sup>¶</sup>National Kidney Foundation Kidney Disease Outcomes Quality Initiative (K/DOQI) Clinical Practice Guidelines for nutrition in chronic renal failure (2000)

<sup>††</sup>National Kidney Foundation K/DOQI Clinical Practice Guidelines for management of dyslipidemias in patients with kidney disease (2003)

<sup>‡‡</sup>National Kidney Foundation K/DOQI Clinical Practice Guidelines on hypertension and antihypertensive agents in chronic kidney disease (2004)

<sup>§§</sup>National Kidney Foundation K/DOQI Clinical Practice Guidelines for bone metabolism and disease in chronic kidney disease (2003)

<sup>¶¶</sup>Renal Association Clinical Practice Guidelines (2009–2012) (5th edition) (Mactier, Davies, Dudley, Harden, & Jones, 2011)

The poor sleepers had significantly higher scores in all sleep components than did the good sleepers. In addition, sleep latency and sleep duration on both HDDs and NHDDs were determined. A paired sample t-test was conducted to compare sleep latency and sleep duration of the patients on NHDDs and HDDs. A significantly longer sleep latency was observed on NHDDs (53.1±57.6 minutes) than on HDDs (22.1±28.0 minutes) ( $p<0.001$ ). Likewise, a significantly shorter sleep duration was noted on NHDDs (5.5±2.0 hours) than on HDDs (6.2±2.1 hours) ( $p<0.001$ ). Similarly, significantly longer sleep latency

and shorter sleep duration were noted on NHDDs in both the good and poor sleepers ( $p<0.001$ ). These results suggested that HD treatment can affect sleep latency and sleep duration. Specifically, the results suggested that on HDDs, the patients could fall asleep faster and sleep longer. These results were supported by the finding that the patients took approximately 30 minutes less to fall asleep and had an extra 0.7 sleep hours on HDDs than on NHDDs. Moreover, the poor sleepers had significantly longer sleep onset time and shorter sleep duration than did the good sleepers, regardless of whether it was a HDD

**Table 3.** Comparison of sleep quality and sleep components scores of patients

Sleep components	Good sleepers (n=90)	Poor sleepers (n=94)	Total (n=184)	t value
Global PSQI score	3.2±1.5	10.0±2.8	6.7±4.1 (0–19)	-20.646**
≤5 (Good sleepers)			90 (48.9)	
>5 (Poor sleepers)			94 (51.1)	
Subjective sleep quality	0.7±0.5	1.3±0.7	1.0±0.7 (0–3)	-6.303**
Sleep latency	0.7±0.9	2.2±1.0	1.5±1.2 (0–3)	-10.833**
On NHDD (minutes)	25.4±32 <sup>†</sup>	79.7±63 <sup>†</sup>	53.1 ± 57.6 (2–360) <sup>†</sup>	-7.346**
On HDD (minutes)	13.2±15.3	30.6±34.2	22.1 ± 28.0 (2–240)	-4.475**
Sleep duration	0.4±0.7	2.3±1.0	1.4±1.3 (0–3)	-14.814**
On NHDD (hours)	7.0±1.3 <sup>‡</sup>	4.1±1.6 <sup>‡</sup>	5.5±2.0 (1.0–11.5) <sup>‡</sup>	13.158**
On HDD (hours)	7.7±1.5	4.7±1.6	6.2±2.1 (1.0–12.0)	12.696**
Sleep efficiency	0.3±0.7	2.3±1.0	1.3±1.3 (0–3)	-15.569**
Sleep disturbances	0.9±0.3	1.2±0.5	1.1±0.5 (0–3)	-4.708**
Use of sleep medicine	0.0±0.0	0.2±0.8	0.1±0.6 (0–3)	-2.902*
Daytime dysfunction	0.2±0.4	0.6±0.8	0.4±0.6 (0–3)	-4.287**

Data was presented as mean ± SD, range or n (%).

NHDD: non-hemodialysis day; HDD: hemodialysis day.

Difference between continuous data was determined by independent sample t-test at significance level of 0.05.

<sup>†</sup>Paired sample t-test were used to compare sleep latency on NHDD and HDD, with significant differences shown for good sleepers (t (89)=4.578, p<0.001), poor sleepers (t (93)=7.774, p<0.001) and all patients (t (183)=8.321, p<0.001), respectively.

<sup>‡</sup>Paired sample t-test were used to compare sleep duration on NHDD and HDD, with significant differences shown for good sleepers (t (89)=-6.671, p<0.001), poor sleepers (t (93)=-5.883, p<0.001) and all patients (t (183)=-8.879, p<0.001), respectively.

\*p<0.01; \*\*p<0.001.

or NHDD. Thus, dialysis treatment may affect sleep quality.

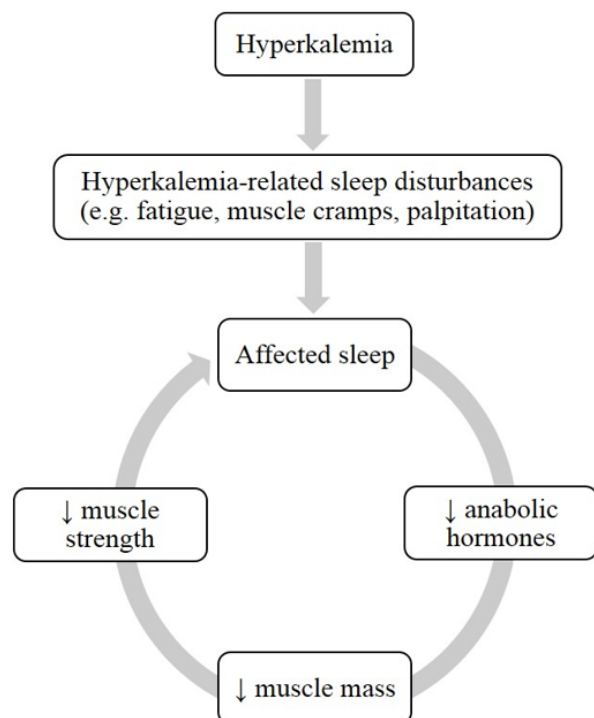
#### Association between sleep quality and nutritional parameters

Demographic and nutritional parameters were explored for a potential correlation with sleep quality (Table 4). Age; sex; TSF; total protein, serum potassium, and serum phosphorus levels; and DMS were found to correlate significantly with sleep quality or its components. Old age was correlated with less sleep efficiency (r=0.157, p=0.033). Furthermore, compared with the women, the men had poorer sleep quality (r=0.160, p=0.030), shorter sleep duration (r=0.161, p=0.029), and lower sleep efficiency (r=0.150, p=0.043). Smaller TSF was correlated with poorer sleep quality (r=-0.147, p=0.047), whereas hypoproteinemia was correlated with poorer subjective sleep quality (r=-0.186, p=0.012). Hyperkalemia was correlated with poorer sleep quality (both global and subjective sleep quality scores) and longer sleep latency (r=0.150, p=0.042). Moreover, hyperphosphatemia was correlated with longer sleep latency (r=0.154, p=0.037). Poorer nutritional status (as indicated with higher DMS) was correlated with poorer sleep quality (r=0.152, p=0.039), less sleep efficiency (r=0.167, p=0.024), and more frequent daytime dysfunction (r=0.150, p=0.043). Other sleep components and nutritional parameters were not significantly correlated. In a nutshell, the current findings indicate that old age, men, and poor nutritional markers of low body fat, hypoproteinemia, hyperkalemia, hyperphosphatemia, and high DMS are factors for poor sleep quality.

#### Predictors of sleep quality

The multivariate analysis model indicated 8.1% variance in the global PSQI score. The significant independent predictors of sleep quality were serum potassium level

( $\beta=1.408$ ,  $p=0.010$ ), male sex ( $\beta=2.149$ ,  $p=0.003$ ), and HGS ( $\beta=-0.088$ ,  $p=0.021$ ) (Table 5). The global PSQI score was primarily predicted by HGS, followed by the serum potassium level and, to a lesser extent, male sex. On the basis of the multivariate analysis model, Figure 2 shows the proposed mechanism of determining independent predictors and sleep. The suggested equation for the global PSQI score is as follows:  
 Global PSQI = 0.694 + 1.408 serum potassium (mmol/L) + 2.149 if male patient - 0.088 handgrip strength (kg).



**Figure 2.** Proposed mechanism of hyperkalemia, handgrip strength and sleep quality.

**Table 4.** Correlation between variables and sleep components

Variables	Global PSQI	SSQ	SL	SD	SE	SDB	SM	DD
Socio-demographic								
Age	0.112	-0.053	0.115	0.103	0.157*	0.049	0.075	-0.066
Sex (male)	0.160*	0.023	0.047	0.161*	0.150*	0.039	0.008	0.134
Anthropometric data								
BMI	-0.086	-0.091	0.004	-0.098	-0.110	0.009	-0.087	0.015
MUAC	-0.117	-0.100	-0.025	-0.094	-0.117	-0.020	-0.128	-0.066
TSF	-0.147*	-0.115	-0.061	-0.123	-0.134	-0.062	-0.123	-0.048
MAMC	-0.082	-0.078	-0.009	-0.056	-0.090	-0.002	-0.111	-0.068
Handgrip strength	-0.060	0.018	-0.040	-0.018	-0.026	-0.010	-0.110	-0.144
Biochemical data								
Total protein	-0.110	-0.186*	-0.070	0.014	-0.099	-0.123	-0.100	-0.081
Serum albumin	0.031	0.112	-0.052	0.032	-0.033	0.066	0.036	0.083
Total cholesterol	0.046	-0.004	0.027	0.109	0.064	-0.006	0.048	-0.065
Serum creatinine	-0.027	-0.027	0.009	0.001	-0.071	-0.045	-0.008	-0.045
Serum potassium	0.161*	0.154*	0.150*	0.099	0.069	0.095	0.137	0.023
Serum phosphorus	0.098	0.019	0.154*	0.066	0.050	0.137	0.093	-0.062
Hemoglobin	0.027	-0.007	0.047	0.057	0.058	-0.022	0.062	-0.121
Dialysis Malnutrition Score	0.152*	0.089	0.097	0.103	0.167*	0.079	-0.020	0.150*

PSQI: Pittsburgh Sleep Quality Index; SSQ: subjective sleep quality; SL: sleep latency; SD: sleep duration; SE: sleep efficiency; SDB: sleep disturbance; SM: use of sleep medication; DD: daytime dysfunction; BMI: body mass index; MUAC: mid-upper arm circumference; TSF: triceps skinfold; MAMC: mid-arm muscle circumference.

\* $p < 0.05$ .

**Table 5.** Multiple linear regression model with global PSQI score as variable outcome (n = 178)

Variables	$\beta$	SE	Beta	R	R <sup>2</sup>	$\Delta R^2$	p value
Constant	0.694	2.596					
Serum potassium	1.408	0.543	0.189	0.164	0.027	-	0.010
Sex (Male)	2.149	0.703	0.254	0.229	0.053	0.026	0.003
Handgrip strength	-0.088	0.038	-0.193	0.284	0.081	0.028	0.021

PSQI: Pittsburgh Sleep Quality Index; SSQ: subjective sleep quality; SL: sleep latency; SD: sleep duration; SE: sleep efficiency; SDB: sleep disturbance; SM: use of sleep medication; DD: daytime dysfunction; BMI: body mass index; MUAC: mid-upper arm circumference; TSF: triceps skinfold; MAMC: mid-arm muscle circumference.

\* $p < 0.05$ .

## DISCUSSION

This study explored determinants for sleep quality among the HD patients. The mean global PSQI score of this study is in agreement with those reported in previous studies conducted in HD patients in Canada<sup>21</sup> and Turkey<sup>22</sup> but is lower than that reported by studies conducted in Iran.<sup>3,6</sup> Using the same sleep measure, the literature has consistently shown a high prevalence of poor sleep quality among HD patients (51%–91%) throughout the decade. The prevalence of poor sleep quality in the current study is comparable to that reported in studies conducted by Chang and Yang<sup>2</sup> and Köse et al<sup>4</sup> but lower than that reported in other studies.<sup>3,5-7,21</sup> The discrepancy could be due to social and lifestyle diversities. Although the current studied cohort had a lower prevalence of poor sleep quality, preventive measures are required to improve the sleep quality of patients because poor sleep quality is universally associated with decreased quality of life through negative impacts on energy, emotional balance, and health status.<sup>23</sup>

The sleep latency and sleep duration of the patients in this study are comparable to those reported in a previous study conducted by Mehrabi et al.<sup>7</sup> In this study, the poor sleepers had a significantly longer sleep latency and shorter sleep duration than did the good sleepers. Such

phenomenon has also been observed in non-HD patients, such as students of tertiary institutions and Caucasians with type 2 diabetes.<sup>24,25</sup> Furthermore, the patients in this study had less sleep onset latency and longer sleep duration on HDDs. This could be due to rapid physiological changes such as rapid fluid, electrolyte, and acid–base changes during chronic daytime HD treatment and induced fatigue.<sup>26</sup> As a result, the patients usually could fall asleep faster and sleep more on HDDs to get adequate rest. Conversely, physiological changes due to HD treatment may increase daytime sleep, which can reduce the quantity and quality of subsequent nocturnal sleep.<sup>26</sup> This can explain why the patients had a shorter sleep duration on NHDDs. Furthermore, a shorter sleep duration on NHDDs could be due to longer sleep latency at night and waking up early on the next day, especially for those with a morning dialysis session to prepare for HD treatment. In addition, shorter sleep on the night before HD session (NHDD), especially during a long interdialytic interval, could be the possible effect of high interdialytic weight gain.

The study finding of the association of old age with poor sleep quality is in congruence with the findings reported by Tel.<sup>27</sup> Less engagement in daily or physical activities, primary sleep disorders, changes in the sleeping

habit, shorter sleep duration, increased sleep latency and arousals, and psychological disorders are factors that can interfere with sleep among elderly people and reduce sleep quality.<sup>2,5,23</sup> Although studies have consistently reported a higher prevalence of poor sleep in women,<sup>2,3,6,11</sup> the current study results showed a higher prevalence of poor sleep quality in the men. This discrepancy could be due to a higher proportion of older men than women in the study. Furthermore, the uniqueness of the biological conditions of women, for example, female hormones and menstrual cycle, may regulate the sleep pattern and sleep duration of each individual differently.<sup>28</sup> More studies are warranted to delineate how sex may influence sleep quality.

In the current study, TSF, total protein, serum potassium, serum phosphorus, and DMS were associated with sleep quality. TSF is commonly used to estimate the subcutaneous fat of the body<sup>29</sup> and is negatively associated with DMS (data not shown), indicating that patients with a higher TSF value had a lower DMS value and hence better nutritional status.<sup>29,30</sup> To the best of our knowledge, the association between TSF and sleep quality among HD patients is underexamined. However, the result may suggest that a high TSF value is an indication of a good nutritional status, which could result in better sleep. Nutritional status as assessed subjectively with a reliable DMS tool revealed a lower DMS associated with better sleep quality. However, the pathological relationship between nutritional status and sleep quality is unclear. Bilgic et al<sup>12</sup> reported that malnourished HD patients were more depressed and had lower sleep quality than normal HD patients. Although depression is not examined in this study, it can be postulated that poor sleep quality among malnourished HD patients is due to depression because Firoz et al<sup>3</sup> reported that depression was one of the predictors of poor sleep quality in HD patients. More studies are needed to confirm and explore the plausible associations of TSF and nutritional status with sleep quality, specifically among HD patients.

Total protein is a parameter that is under investigated in HD patients as compared with serum albumin. The association between total protein and sleep quality is unexplored. Possible mechanisms that could explain the relationship between low total protein (hypoproteinemia) and sleep quality include edema, inadequate dietary intake, and immune function. Protein loss through HD and inadequate dietary protein intake could result in hypoproteinemia.<sup>31</sup> Reduction in the oncotic pressure due to hypoproteinemia increases tissue hydrostatic pressure and leads to accumulation of fluid in the body or edema.<sup>31</sup> Edema increases blood pressure, and edema in the lungs leads to difficulty in breathing and thus influences sleep quality. Moreover, sleep deprivation or a shorter sleep duration could suppress the immune function through the upregulation of circulating proinflammatory mediators.<sup>32</sup> The inflammation status due to kidney failure itself and sleep deprivation depletes the serum protein for antibody production. Nevertheless, additional studies are warranted to confirm the proposed mechanisms.

The relationship between hyperphosphatemia and poor sleep quality observed in the HD patients in this study is consistent with the findings reported by Sabry et al<sup>33</sup> and

Zeydi et al<sup>34</sup> but contradicts those reported by Köse et al<sup>4</sup> and Mehrabi et al.<sup>7</sup> Despite inconsistent findings, patients with hyperphosphatemia may have poor sleep quality due to sleep disturbances and prolonged sleep onset time. Frequent reported symptoms of sleep disturbances related to hyperphosphatemia are itchiness, joint pain, and restless leg syndrome.<sup>33</sup> Excessive dietary phosphorus intake may lead to hyperphosphatemia as Kalantar-Zadeh<sup>35</sup> and colleagues noted an interrelationship between serum phosphorus and dietary phosphorus. The significant correlation between serum potassium and sleep quality observed in this study contradicts previous findings.<sup>36</sup> Poor sleep quality in hyperkalemic patients is probably due to hyperkalemia-related sleep disturbances, such as fatigue, limb muscle numbness or cramps, and palpitation, which might affect the quality of sleep at night.<sup>33</sup> Compliance to medication and dietary restriction could however be the confounders of hyperphosphatemia and hyperkalemia. Therefore, future studies may explore patients' compliance while investigating the association between sleep quality and serum phosphorus and potassium.

Although HGS did not show a significant correlation with sleep quality in the correlation analysis, it appeared to be an independent negative predictor of sleep quality in the multivariate analysis. Studies on the association between grip strength and sleep quality among HD population are scant. Studies have documented the association between HGS and sleep duration.<sup>37-39</sup> It is speculated that sleep affects muscle strength through hormonal regulation.<sup>38</sup> Insufficient sleep reduces anabolic hormones and thus muscle mass synthesis, which leads to decreased muscle strength and causes muscle weakness, possibly impairing daytime functioning. However, the relationship between sleep and HGS appears to be a causality dilemma; hence, more studies are required to rule out the association between HGS and sleep.

The current study has several limitations. First, the cross-sectional study design could not determine whether poor nutritional markers caused poor sleep quality, or vice versa. Prospective longitudinal studies are required to confirm the association between sleep quality and nutritional markers while controlling for confounding variables. Second, biochemical data were collected from routine blood test records of each HD unit; thus, the values of biochemical indicators might have slight differences due to different laboratory test kits used in the biochemistry analysis. Future studies should consider collecting blood samples and performing standardized biochemistry analyses. Third, assessments of MUAC, TSF, and HGS were performed on the nonfistula arm and not the dominant hand, which may have contributed to variations in results. Dietary intake was not included in this study due to limited human resources. Lastly, gold standards, such as polysomnography and actigraphy, were not used for sleep measurements owing to financial constraints. However, the PSQI, which is validated as a high accuracy and reliable subjective sleep measurement tool, was used in this study.

### Conclusion

This study emphasizes the high prevalence of poor sleep quality among HD patients and suggests that routine



evaluation of sleep quality is required. Furthermore, parameters, namely TSF, HGS, total protein, serum potassium, serum phosphorus, and nutritional status, were found to affect the sleep quality of dialysis patients. Therefore, appropriate interventions should be formulated to improve nutritional status and other aspects, such as diet, physical activity, psychological factors, and sleep hygiene, to enhance sleep quality among HD patients.

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#### AUTHOR DISCLOSURES

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#### REFERENCES

- Maslow AH. A theory of human motivation. *Psychol Rev.* 1943;50:370-96.
- Chang S, Yang T. Sleep quality and associated factors in hemodialysis patients. *Acta Nephrol.* 2011;25:97-104.
- Firoz MN, Shafiqpour V, Jafari H, Hosseini SH, Charati JY. Sleep quality and depression and their association with other factors in hemodialysis patients. *Glob J Health Sci.* 2016;8:121.
- Köse E, Turgutalp K, Kiykim A, Çelik F. The association between feeding habits, nutritional parameters and quality of sleep in hemodialysis patients. *Turkish Nephrol Dial Transplant.* 2014;23:14-9.
- Masoumi M, Naini AE, Aghaghazvini R, Amra B, Gholamrezaei A. Sleep quality in patients on maintenance hemodialysis and peritoneal dialysis. *Int J Prev Med.* 2013;4:165-72.
- Sabet R, Naghizadeh MM, Azari S. Quality of sleep in dialysis patients. *Iran J Nurs Midwifery Res.* 2012;17:270-4.
- Mehrabi S, Sarikhani S, Roozbeh J. Sleep quality in patients undergoing long-term hemodialysis using the Pittsburgh Sleep Quality Index. *Nephrourol Mon.* 2017;9:e44278.
- Trbojević-Stanković J, Stojimirović B, Bukumirić Z, Hadžibulić E, Andrić B, Đorđević V, Jovanović D. Depression and quality of sleep in maintenance hemodialysis patients. *Srp Arh Celok Lek.* 2014;142:437-43.
- Fonseca NT, Urbano JJ, Nacif SR, Silva AS, Peixoto RAO, Urbano GJ, Oliveira EF, Santos IR, Oliveira CS, Insalaco G, Oliveira LVF. A systematic review of sleep disorders in patients with chronic kidney disease undergoing hemodialysis. *J Phys Ther Sci.* 2016;28:2164-70.
- Burrowes JD, Russell GB, Unruh M, Rocco M V. Is nutritional status associated with self-reported sleep quality in the HEMO study cohort? *J Ren Nutr.* National Kidney Foundation, Inc.; 2012;22:461-71.
- Einollahi B, Motalebi M, Rostami Z, Nemati E, Salesi M. Sleep quality among Iranian hemodialysis patients: A multicenter study. *Nephrourol Mon.* 2015;7:e23849.
- Bilgic A, İbisi A, Tural E, Koc S, Sezer S, Ozdemir N. Association of nutritional status with depression and sleep disorders in elderly end stage renal disease patients - Does chronic inflammation cause it all? *Turkish Nephrol Dial Transplant.* 2012;21:148-55.
- Harvinder GS, Chee WSS, Karupaiah T, Sahathevan S, Chinna K, Ghazali A, Bavanandan S, Goh BL. Comparison of malnutrition prevalence between haemodialysis and continuous ambulatory peritoneal dialysis patients: A cross-sectional study. *Malays J Nutr.* 2013;19:271-83.
- Noori N, Kopple JD, Kovesdy CP, Feroze U, Sim JJ, Murali SB, Luna A, Gomez M, Luna C, Bross R, Nissenson AR, Kalantar-Zadeh, K. Mid-arm muscle circumference and quality of life and survival in maintenance hemodialysis patients. *Clin J Am Soc Nephrol.* 2010;5:2258-68.
- Trbojevic-Stankovic JB, Marjanović Z, Pesic S, Andric B, Hadzibulic E, Filipovic N, Birdjolic F, Djordjevic V. Relationship between malnutrition, inflammation and sleep quality in hemodialysis patients. *Nephrol Dial Transplant.* 2016;31:i298-99.
- Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: A new instrument psychiatric practice and research. *Psychiatry Res.* 1989;28:193-213.
- Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey (NHANES) muscle strength procedures manual. 2013 [cited 2016/12/12]; Available from: [https://wwwn.cdc.gov/nchs/data/nhanes/2013-2014/manuals/Muscle\\_Strength\\_2013.pdf](https://wwwn.cdc.gov/nchs/data/nhanes/2013-2014/manuals/Muscle_Strength_2013.pdf).
- Kalantar-Zadeh K, Kleiner M, Dunne E, Lee GH, Luft FC. A modified quantitative subjective global assessment of nutrition for dialysis patients. *Nephrol Dial Transplant.* 1999;14:1732-8.
- Department of Statistics Malaysia. Report of household income and basic amenities survey 2016. Department of Statistics Malaysia. 2017 [cited 2018/05/02]; Available from: [https://www.dosm.gov.my/v1/index.php?r=column/ctwoByCat&parent\\_id=119&menu\\_id=amVoWU54UT10a21NWm dhMjFMMWcyZz09](https://www.dosm.gov.my/v1/index.php?r=column/ctwoByCat&parent_id=119&menu_id=amVoWU54UT10a21NWm dhMjFMMWcyZz09).
- National Kidney Foundation K/DOQI Clinical Practice Guidelines on hypertension and antihypertensive agents in chronic kidney disease. *Am J Kidney Dis.* 2004;43:S1-290.
- Iliescu EA, Yeates KE, Holland DC. Quality of sleep in patients with chronic kidney disease. *Nephrol Dial Transplant.* 2004;19:95-9.
- Afsar B, Elsurur R. The relationship between sleep quality and daytime sleepiness and various anthropometric parameters in stable patients undergoing hemodialysis. *J Ren Nutr.* 2013;23:296-301.
- Azri MA, Dahlan A, Masuri MG, Isa KAM. Sleep quality among older persons in institutions. *Procedia - Soc Behav Sci.* 2016;234:74-82.
- Lai P, Say Y. Associated factors of sleep quality and behavior among students of two tertiary institutions in Northern Malaysia. *Med J Malaysia.* 2013;68:196-203.
- Mahmood WAW, Yusoff MSD, Behan LA, Di Perna A, Tun TK, McDermott J, Sreenan S. Association between sleep disruption and levels of lipids in Caucasians with type 2 diabetes. *Int J Endocrinol.* 2013;2013:341506.
- Ezzat H, Mohab A. Prevalence of sleep disorders among ESRD patients. *Ren Fail.* 2015;37:1013-9.
- Tel H. Sleep quality and quality of life among the elderly people. *Neurol Psychiatry Brain Res.* 2013;19:48-52.
- Krishnan V, Collop NA. Gender differences in sleep disorders. *Curr Opin Pulm Med.* 2006;12:383-9.
- Janardhan V, Soundararajan P, Rani NV, Kannan G, Thennarasu P, Chacko RA, Reddy CUM. Prediction of malnutrition using modified subjective global assessment-dialysis malnutrition score in patients on hemodialysis. *Indian J Pharm Sci.* 2011;73:38-45.
- Sedhain A, Hada R, Agrawal RK, Bhattarai GR, Baral A. Assessment of nutritional status of Nepalese hemodialysis patients by anthropometric examinations and modified

- quantitative Subjective Global Assessment. *Nutr Metab Insights*. 2015;8:21-7.
31. Scallan J, Huxley VH, Korthuis RJ. Pathophysiology of Edema Formation. In *Capillary Fluid Exchange: Regulation, Functions, and Pathology*. San Rafael (CA): Morgan & Claypool Life Sciences; 2010.
  32. Hurtado-Alvarado G, Pavón L, Castillo-García SA, Hernández ME, Domínguez-Salazar E, Velázquez-Moctezuma J, Gómez-González B. Sleep loss as a factor to induce cellular and molecular inflammatory variations. *Clin Dev Immunol*. 2013;2013:801341.
  33. Sabry AA, Abo-Zenah H, Wafa E, Mahmoud K, El-Dahshan K, Hassan A, Abbas TM, Saleh AEBM, Okasha K. Sleep disorders in hemodialysis patients. *Saudi J Kidney Dis Transpl*. 2010;21:300-5.
  34. Zeydi AE, Jannati Y, Khezri HD, Baradari AG, Espahbodi F, Lesani M, Yaghoubi T. Sleep quality and its correlation with serum C-reactive protein level in hemodialysis patients. *Saudi J Kidney Dis Transpl*. 2014;25:750-5.
  35. Kalantar-Zadeh K, Gutekunst L, Mehrotra R, Kovesdy CP, Bross R, Shinaberger CS, Noori N, Hirschberg R, Benner D, Nissenson AR, Kopple JD. Understanding sources of dietary phosphorus in the treatment of patients with chronic kidney disease. *Clin J Am Soc Nephrol*. 2010;5:519-30.
  36. Selvi Y, Ozdemir PG, Soyoral Y, Tasdemir M, Aslan M. The evaluation of dream anxiety and sleep quality in hemodialysis patients. *Sleep Hypn*. 2017;19:10-7.
  37. Chen HC, Hsu NW, Chou P. The association between sleep duration and hand grip strength in community-dwelling older adults: The Yilan study, Taiwan. *Sleep*. 2017;40.
  38. Chen Y, Cui Y, Chen S, Wu Z. Relationship between sleep and muscle strength among Chinese university students: A cross-sectional study. *J Musculoskelet Neuronal Interact*. 2017;17:327-33.
  39. Wang TY, Wu Y, Wang T, Li Y, Zhang D. A prospective study on the association of sleep duration with grip strength among middle-aged and older Chinese. *Exp Gerontol*. 2018; 103:88-93.