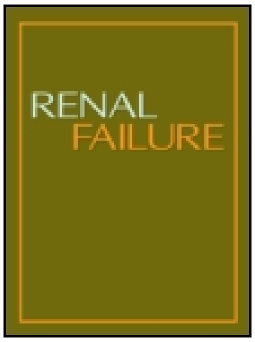

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CLINICAL STUDY

Prevalence of Protein-energy Wasting and Its Various Types in Iranian Hemodialysis Patients: A New Classification

Hadi Tabibi[1], Atefeh As'habi[1], Behnaz Nozary Heshmati[2], Mitra Mahdavi-Mazdeh[3], and Mehdi Hedayati[4]

[1]*Department of Clinical Nutrition & Dietetics, Shahid Beheshti University of Medical Sciences, Tehran, Iran;* [2]*Iranian Tissue Bank, Research & Preparation Center, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran;* [3]*Department of Nephrology, Tehran University of Medical Sciences, Tehran, Iran;* [4]*Cellular and Molecular Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

Abstract

Background: This study was designed to determine the prevalence of protein-energy wasting (PEW) and its various types in hemodialysis (HD) patients in Tehran, Iran. *Methods*: For this cross-sectional study, 291 HD patients were randomly selected. The nutritional status of the patients was determined by subjective global assessment (SGA) and their dietary intakes were assessed using a 4-day dietary recall. In addition, serum high-sensitive C-reactive protein (hs-CRP) was measured. *Results*: The prevalence of mild-to-moderate and severe PEW based on SGA was 60.5% and 1% in Tehran HD patients, respectively. The prevalence of various types of PEW in HD patients was 20.5% type I (inadequate energy or protein intake without inflammation), 65.5% type IIa (inadequate energy or protein intake with inflammation), and 14% type IIb (adequate energy and protein intake with inflammation). Of the total HD patients with no PEW based on SGA, about 3.5% had type 0 normal nutritional status (adequate energy and protein intake without inflammation), 34% had type I normal nutritional status (inadequate energy or protein intake without inflammation), 55.5% had type IIa normal nutritional status (inadequate energy or protein intake with inflammation), and 7% had type IIb normal nutritional status (adequate energy and protein intake with inflammation). *Conclusion*: PEW in Tehran HD patients is considerably prevalent and PEW type IIa is the most common type. In addition, HD patients with no PEW based on SGA should also be paid attention because they may be in the early stages of inadequate intake of energy and/or protein and inflammation.

Keywords: protein-energy wasting, subjective global assessment, inflammation, hemodialysis, Iran

INTRODUCTION

Protein-energy wasting (PEW), defined as reduced body protein mass and fuel reserves (body protein and fat mass), is prevalent in hemodialysis (HD) patients.[1–3] The etiology of PEW in HD patients is complex and its two major causes are inadequate intake of energy and/or protein and increased catabolism as a result of high production of inflammatory cytokines;[2,4–6] in these patients, there are three types of PEW: type I PEW (resulting from inadequate intake of energy and/or protein without inflammation); type IIa PEW (resulting from inadequate intake of energy and/or protein and inflammation), and the third type or type IIb PEW (resulting from inflammation without inadequate intake of energy and/or protein).[7–9] PEW results in a poor quality of life and increased morbidity and mortality in HD patients.[1,3,4,10,11] More complications result from type II PEW (IIa or IIb), which is associated with inflammation, than from type I PEW; the treatment of type II PEW is also more complicated and differs from that of type I PEW.[7,8]

Descriptive studies conducted in various countries have reported the prevalence of PEW in HD patients to range between 16% and 90%.[1–6,12] In addition, some studies show that the prevalence of energy and/or protein deficiency ranges between 51% and 70% in these patients.[13,14]

Address correspondence to Hadi Tabibi, Department of Clinical Nutrition & Dietetics, National Nutrition and Food Technology Research Institute, 46, West Arghavan St., Farahzadi Blvd., Shahrak Qods, PO Box 19395-4741, Tehran, Islamic Republic of Iran. E-mail: hadtabibi@yahoo.com

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Although most Iranian patients with end-stage renal disease are being hemodialyzed in Tehran (the capital of Iran), to our knowledge, no comprehensive study has yet been documented on the prevalence of PEW in Iranian HD patients. In addition, available literature reveals no investigation worldwide reporting the prevalence of the various types of PEW in HD patients. This study was therefore designed to determine the prevalence of PEW and its various types in HD patients in Tehran, Iran.

MATERIALS AND METHODS

For this cross-sectional study, using systematic sampling, we randomly selected 291 HD patients from among 2302 eligible adult HD patients in 50 HD centers in Tehran. The inclusion criteria were age $\geq$18 years and being on HD for at least 6 months, while the exclusion criteria were HIV infection and hepatitis B. The underlying causes of renal failure in the participating patients were diabetes mellitus (39%), hypertension (28%), urinary infection (9%), polycystic kidney disease (5.5%), nephrolithiasis (2.5%), nephrotic syndrome (2%), and other or unknown causes (14%).

Eighty-nine percent of participating patients were on HD treatments three times a week (4 h per session), while 11% patients had treatments twice weekly. All patients enrolled were hemodialyzed using polysulfone capillary dialyzers and bicarbonate dialysate. The study protocol was approved by the Ethics Committee of the National Nutrition and Food Technology Research Institute of Iran. The study was in adherence with the Declaration of Helsinki. Written informed consent was obtained from all patients.

Subjective global assessment (SGA), a valid, reliable, and commonly used tool was applied to determine the presence of PEW.[15–19] The original SGA form is based on a nutrition-related medical history and a brief physical examination;[17,19] medical history includes weight change during past 6 months, dietary intake, gastrointestinal symptoms, functional capacity, and co-morbidities, and the physical examination includes assessing loss of subcutaneous fat, muscle wasting, and nutrition-associated alterations in fluid balance (presence of edema and/or ascites).[17,19] Each of these components was scored separately as A, B, or C; an overall score of A (well nourished), B (mild-to-moderate PEW), or C (severe PEW), depended on the most predominant score (A, B, or C) obtained in the different sections of the SGA.[20–22]

Before beginning the study, for evaluating the degree of reproducibility the SGA form was completed by a trained physician for a subset of 16 HD patients. After 1 week, the SGA was repeated on the same subset without reference to the first evaluation. Spearman's correlation coefficient between the two sets of SGA was 0.71 ($p <$ 0.01), denoting an acceptable degree of reproducibility.

Dietary intakes of patients were assessed by a trained dietician using a 4-day diet diary-assisted recall (also referred to as a 4-day diet record), including two dialysis days and two nondialysis days. Patients' diets were analyzed by Nutritionist IV software (N Squared Computing, San Bruno, CA, USA) to determine daily intakes of energy and protein, which were compared with dietary guidelines for HD patients.[23] Dry postdialysis weight was used for calculating energy or protein intake per kg of body weight in HD patients with body mass index (BMI) $\leq$ 25 kg/m^2, whereas adjusted dry postdialysis weight was applied for patients with BMI > 25 kg/m^2.[18] Patients' height and weight were determined at the end of one of the dialysis sessions. In addition, after a 12- to 14-h fast, 4 mL blood was obtained from each patient before dialysis to measure serum urea, creatinine, albumin, and high-sensitive C-reactive protein (hs-CRP). Serum creatinine, urea, and albumin were assessed using commercial kits (Pars-Azmoon, Tehran, Iran) with the aid of a Selectra 2 Autoanalyzer (Vital Scientific, Spankeren, The Netherlands). Coefficients of variation (CVs) for these biochemical parameters were less than 3%. Serum hs-CRP was determined using enzyme-linked immunosorbent assay kits (Diagnostics Biochem Canada, London, Canada), with a CV of 4.6%.

Dialysis adequacy, based on the K_t/V index was determined for each patient by a K_t/V calculator, using information recorded in patient files, including predialysis blood urea nitrogen (BUN) concentration, postdialysis BUN, the dialysis session length, postdialysis weight, and ultrafiltration volume[24]; of the 291 HD patients, information regarding their K_t/V index was available only for 246 HD patients.

In this study, HD patients who had PEW based on SGA, according to intakes of energy and protein and inflammation (hs-CRP > 3 mg/L), were classified into three groups[7–9]: (1) patients with type I PEW (inadequate energy and/or protein intake without inflammation), (2) patients with type IIa PEW (inadequate energy and/or protein intake with inflammation), and (3) patients with type IIb PEW (adequate energy and protein intake with inflammation).

It is important to note that HD patients without PEW based on SGA may be in the early stages of inadequate intakes of energy and protein or inflammation, which is why their nutritional status may still seem normal; these patients without PEW based on SGA, according to intakes of energy and protein and inflammation, were classified into four groups: (1) patients with type 0 normal nutritional status (adequate energy and protein intake without inflammation), (2) patients with type I normal nutritional status (inadequate energy and/or protein intake without inflammation), (3) patients with type IIa normal nutritional status (inadequate energy and/or protein intake with inflammation), and (4) patients with type IIb normal nutritional status (adequate energy and protein intake with inflammation).

Statistical Analysis

Statistical analysis of the data was performed using the Statistical Package for the Social Sciences (SPSS, Inc., Chicago, IL, USA) for windows version 16.0. A chi-square test was used to determine the associations between qualitative variables. Because all quantitative parameters had normal distribution according to the Kolmogorov–Smirnov test, we used a one-way analysis of variance (ANOVA) to compare quantitative parameters between the groups. If the result of ANOVA test was significant, the Bonferroni test was used for multiple comparisons. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

Characteristics of HD patients are shown in Table 1. In this study, based on SGA, 38.5% of HD patients were well nourished and the prevalences of mild-to-moderate and severe PEW were 60.5% and 1% in HD patients, respectively (Table 1).

There were significant associations between the prevalence of PEW with gender ($p < 0.01$), the age of patients ($p < 0.001$), microinflammation ($p < 0.01$), and dietary intakes of energy and protein ($p < 0.05$; Table 2). No significant associations however were found between the prevalence of PEW with HD vintage and dialysis adequacy (Table 2).

Results of this study showed that dietary intakes of energy and protein were lower than recommended intakes in 88% and 84.5% of HD patients, respectively (Table 1).

Table 1. Characteristics of the HD patients and prevalence of PEW, and inadequate intakes of energy and protein.

Characteristics	All patients ($n = 291$)
Age (year)	
18–40	45 (15.5%)
41–60	99 (34%)
>60	147 (50.5%)
Sex	
Men	164 (56%)
Women	127 (44%)
Dialysis vintage (year)	
$\leq$1	60 (21%)
1–5	149 (51%)
5–10	61 (21%)
>10	21 (7%)
Dialysis adequacy (K_t/V)	
<1.2	113 (46%)
$\geq$1.2	133 (54%)
Diabetes	114 (39%)
Hepatitis C	16 (5.5%)
Serum creatinine (mg/dL)	9 ± 0.2
Serum urea (mg/dL)	123 ± 1.7
Prevalence	
Well nourished	112 (38.5%)
Mild-to-moderate PEW	175 (60.5%)
Severe PEW	3 (1%)
Inadequate energy intake	275 (88%)
Inadequate protein intake	246 (84.5%)

Note: Serum creatinine and urea are presented as mean ± standard error (SE).

The prevalences of various types of PEW in HD patients were 20.5% for type I (inadequate energy and/or protein intake without inflammation), 65.5% for type IIa (inadequate energy and/or protein intake with inflammation), and 14% for type IIb (adequate energy and protein intake with inflammation; Table 3).

Mean dietary intakes of energy and protein did not differ significantly between HD patients with PEW types I and IIa (Table 3); however, dietary intakes of energy and protein were significantly lower in HD patients with PEW type I or type IIa, when compared to HD patients with PEW type IIb ($p < 0.01$; Table 3).

Mean serum CRP was significantly higher in HD patients with PEW type IIa or type IIb, when compared to HD patients with PEW type I ($p < 0.001$; Table 3).

In HD patients with PEW type I, who do not have inflammation, mean serum albumin was in the normal range (>4 g/dL), whereas in HD patients with PEW type IIa or type IIb, who have inflammation, this concentration was in the mildly deficient range (3.5–3.99 g/dL; Table 3).

There were no significant differences among HD patients with PEW type I, IIa, and IIb with regard to HD vintage and dialysis adequacy (Table 3).

Of all the HD patients without PEW, based on SGA, about 3.5% had type 0 normal nutritional status (adequate energy and protein intake without inflammation), 34% had type I normal nutritional status (inadequate energy and/or protein intake without inflammation), 55.5% had type IIa normal nutritional status (inadequate energy and/or protein intake with inflammation), and 7% had type IIb normal nutritional status (adequate energy and protein intake with inflammation; Table 3).

Mean dietary intakes of energy and protein were significantly lower in HD patients with normal nutritional statuses types I and IIa, when compared to HD patients with normal nutritional statuses types 0 and IIb ($p < 0.01$; Table 3).

Mean serum CRP was significantly higher in HD patients with normal nutritional statuses types IIa and IIb, when compared to HD patients with normal nutritional statuses types 0 and I ($p < 0.001$; Table 3).

In HD patients with normal nutritional statuses types 0, I, IIa, and IIb, the mean serum albumin concentration was in the normal range (>4 g/dL), with no significant differences (Table 3). In addition, no significant differences were observed among HD patients with normal nutritional statuses types 0, I, IIa, and IIb with regard to HD vintage and dialysis adequacy (Table 3).

DISCUSSION

This study showed that the prevalences of mild-to-moderate and severe PEW were 60.5% and 1%, respectively, in adult HD patients of Tehran HD centers in Iran, a finding in agreement with those of previous studies from

Table 2. Prevalence of PEW in the HD patients based on different factors.

Variable	PEW Yes	PEW No	p-Value
Sex			
Men	89 (54%)	75 (46%)	<0.01
Women	89 (71%)	37 (29%)	
Age (year)			
<60	59 (45%)	73 (55%)	<0.001
≥60	119 (75%)	39 (25%)	
Dialysis vintage (year)			
≤5	122 (59%)	86 (41%)	NS
>5	56 (68%)	26 (32%)	
Dialysis adequacy (K_t/V)			
≥1.2	86 (65%)	47 (35%)	NS
<1.2	67 (60%)	45 (40%)	
Microinflammation			
Yes (hs-CRPP > 3 mg/L)	140 (67%)	69 (33%)	<0.01
No (hs-CRP ≤ 3 mg/L)	37 (46%)	43 (54%)	
Dietary intakes of energy and protein			
Adequate energy and protein intake	6 (33%)	12 (67%)	<0.05
Inadequate energy and/or protein intake	172 (63%)	100 (37%)	

Note: NS, nonsignificant.

Table 3. Prevalence of various types of PEW and normal nutritional statuses in the HD patients and a comparison of their characteristics.

Parameters	Various types of PEW: PEW type I ($n = 36$)	PEW type IIa ($n = 115$)	PEW type IIb ($n = 25$)
Prevalence (%)	20.5	65.5	14.0
Dietary energy intake (kcal/kg_{bw}/d)	22 ± 1.2*	21 ± 0.5*	33 ± 1.0
Dietary protein intake (g/kg_{bw}/d)	0.85 ± 0.05*	0.79 ± 0.02*	1.30 ± 0.04
Serum CRP (mg/L)	1.2 ± 0.1	7.5 ± 0.2**	7.1 ± 0.4**
Serum albumin (g/dL)	4.15 ± 0.04	3.98 ± 0.03***	3.98 ± 0.07
Dialysis vintage (month)	59 ± 10	53 ± 5.0	55 ± 7.5
Dialysis adequacy (K_t/V)	1.4 ± 0.07	1.2 ± 0.03	1.2 ± 0.07

Parameters	Various types of normal nutritional statuses: Type 0 ($n = 4$)	Type I ($n = 38$)	Type IIa ($n = 62$)	Type IIb ($n = 8$)
Prevalence (%)	3.5	34.0	55.5	7.0
Dietary energy intake (kcal/kg_{bw}/d)	40 ± 3.9	25 ± 1.2****	22 ± 0.8****	42 ± 3.1
Dietary protein intake (g/kg_{bw}/d)	1.5 ± 0.17	0.9 ± 0.05****	0.8 ± 0.03****	1.6 ± 0.11
Serum CRP (mg/L)	0.9 ± 0.4	1.3 ± 0.1	6.6 ± 0.3*****	6.2 ± 0.7*****
Serum albumin (g/dL)	4.4 ± 0.08	4.4 ± 0.06	4.2 ± 0.04	4.2 ± 0.10
Dialysis vintage (month)	69 ± 17	51 ± 11	42 ± 4	61 ± 23
Dialysis adequacy (K_t/V)	1.1 ± 0.09	1.3 ± 0.06	1.17 ± 0.04	1.14 ± 0.15

Notes: All values are presented as mean ± SE, except prevalence.
*$p < 0.01$ versus type IIb; **$p < 0.001$ versus type I; ***$p < 0.05$ versus type I; ****$p < 0.01$ versus types 0 and IIb; and *****$p < 0.001$ versus types 0 and I.

various countries; Tayyem et al., in a study from Jordan, showed that 56.2% of HD patients had mild-to-moderate PEW and 5.6% had severe PEW.[25] In the study by Tapiawala et al., the prevalences of mild-to-moderate and severe PEW were 58 and 0%, respectively.[26] Morais et al., in a study from Brazil, reported that based on a modified SGA, 90.9% HD patients had moderate PEW and 4.6% had severe PEW.[6] In a study conducted in Stockholm, Sweden, Qureshi et al. reported the prevalences of mild and moderate-to-severe PEW to be 51% and 13%, respectively.[27]

PEW leads to a poor quality of life and increased morbidity and mortality in HD patients.[10] Inadequate energy and protein intakes are among the main causes of PEW in HD patients.[4] Our study showed that dietary intakes of energy and protein in a large percentage of HD patients (88% and 84.5%, respectively) were lower than recommended intakes and there was a significant association between the prevalence of PEW with dietary intakes of energy and protein. Available literature shows that the most significant cause for these inadequate intakes in HD patients is anorexia.[5] Evidence shows that anorexia may be induced by uremic toxins, inflammation, altered serum amino acid patterns, changes in secretion of hormones and neurotransmitters affecting the appetite, and by underlying illnesses such as infections and emotional disorders, particularly depression, which occurs commonly in patients with chronic renal failure.[5,28] Other causes of inadequate energy and protein intakes in HD patients are the physical or economic inability to purchase food, dental problems, reduced food consumption to prevent hyperkalemia or hyperphosphatemia, and further dietary restrictions because of underlying illnesses such as diabetes.[5,23,29]

Another important cause of PEW in HD patients is inflammation,[7] and in our study, there was a significant association between the prevalence of PEW with inflammation. In HD patients, chronic inflammation may result from the repeated contact of blood mononuclear cells with dialysis tubes and dialyzer membranes, impurities in the dialysis water and/or dialysis solution, decreased clearance of inflammatory cytokines, and oxidative and carbonyl stress.[30] Inflammation may mediate PEW through suppressing appetite and increasing skeletal muscle protein breakdown.[7,31]

In our study, a significant association was found between PEW and gender. The frequency of PEW in female HD patients was significantly higher when compared to their male counterparts, which may be due to a higher prevalence of emotional disorders, particularly depression, in women,[5] resulting in reduced food consumption and consequently PEW. The frequency of PEW was significantly higher in HD patients, aged $\geq$60 years, compared to those below the age of 60 years, which may be due to a higher prevalence of infections, emotional disorders, particularly depression, physical or economic inability to purchase food, and dental problems.[5]

Since the two main causes of PEW in HD patients are inadequate energy and/or protein intakes and inflammation, HD patients found to have PEW based on SGA, according to their energy and protein intakes and inflammation, can be classified into three groups[7–9]: (1) HD patients with type I PEW (inadequate energy and/or protein intake without inflammation), (2) HD patients with type IIa PEW (inadequate energy and/or protein intake with inflammation), and (3) HD patients with type IIb PEW (adequate energy and protein intake with inflammation). Available literature reveals no investigation documented worldwide on the prevalence of various types of PEW in HD patients.

In our study, the prevalences of various types of PEW in HD patients were 20.5% for type I, 65.5% for type IIa, and 14% type IIb, indicating that PEW in the majority of HD patients results from inadequate energy and/or protein intakes in combination with inflammation.

Considering the differences in the three types of PEW in HD patients, treatment strategies for each type are different; in HD patients with PEW type I, nutrition counseling and adequate intakes of energy and protein are probably sufficient for treatment;[8] however, HD patients with PEW type IIb, for adequate treatment, require the chronic inflammation to be eliminated.[8] In recent years, several studies demonstrated that l-carnitine supplement could reduce inflammatory markers in HD patients.[32–36] In HD patients with PEW type IIa, nutrition counseling and adequate intakes of energy and protein in combination with elimination of chronic inflammation are necessary for treatment.

Serum albumin concentration was lower in HD patients with PEW types IIa and IIb, when compared to HD patients with PEW type I, most probably because of chronic inflammation in HD patients with PEW types IIa and IIb. Serum albumin is a negative, acute phase protein and inflammatory cytokines reduce albumin synthesis in liver.[30]

In this study, HD patients without PEW based on SGA, according to intakes of energy and protein and inflammation, were classified into four groups: (1) patients with type 0 normal nutritional status (adequate energy and protein intake without inflammation), (2) patients with type I normal nutritional status (inadequate energy and/or protein intake without inflammation), (3) patients with type IIa normal nutritional status (inadequate energy and/or protein intake with inflammation), and (4) patients with type IIb normal nutritional status (adequate energy and protein intake with inflammation). Our results demonstrated the prevalence of various types of normal nutritional statuses in HD patients to be 3.5% type 0, 34% type I, 56% type IIa, and 6.5% type IIb. Hence, this study showed that the majority of HD patients without PEW had inadequate energy and/or protein intake without inflammation or in combination with inflammation; however, because the inadequacy of intakes of energy and protein or inflammation are in the early stages, the nutritional status of these HD patients based on SGA appears to be still normal. Therefore, even if HD patients based on SGA have no PEW, nutrition specialists should assess their energy and protein intakes and inflammation in these patients; the nutritional counseling, adequate intakes of energy and protein, and elimination of any inflammation could be effective in helping them to prevent PEW.

In conclusion, PEW in Iranian HD patients is considerably prevalent, with PEW type IIa being the most common type. It is important that HD patients without PEW based on SGA also be monitored because they may be in the early stages of energy and protein intake inadequacy and inflammation.

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REFERENCES

[1] Dukkipati R, Kopple JD. Causes and prevention of protein-energy wasting in chronic kidney failure. *Semin Nephrol.* 2009;29:39–49.

[2] Mak RH, Ikizler AT, Kovesdy CP, Raj DS, Stenvinkel P, Kalantar-Zadeh K. Wasting in chronic kidney disease. *J Cachex Sarcopenia Muscle.* 2011;2:9–25.

[3] Guarnieri G, Barazzoni R. Fighting protein-energy wasting in chronic kidney disease: A challenge of complexity. *J Ren Nutr.* 2011;21:2–6.

[4] Mehrotra R, Kopple JD. Causes of protein-energy malnutrition in chronic renal failure. In: Kopple JD, Massry SG, eds. *Kopple and Massry's Nutritional Management of Renal Disease.* 2nd ed., Philadelphia, PA: Lippincott Williams & Wilkins; 2004: 168–182.

[5] Kopple JD. McCollum Award, 1996: Protein-energy malnutrition in maintenance dialysis patients. *Am J Clin Nutr.* 1997;65:1544–1557.

[6] Morais AAC, Silva MAT, Faintuch J, et al. Correlation of nutritional status and food intake in hemodialysis patients. *Clinics.* 2005;60:185–192.

[7] Stenvinkel P, Yeun JY. Role of inflammation in malnutrition and atherosclerosis in chronic renal failure. In: Kopple JD, Massry SG, eds. *Kopple and Massry's Nutritional Management of Renal Disease.* 2nd ed., Philadelphia, PA: Lippincott Williams & Wilkins; 2004:199–212.

[8] Stenvinkel P, Heimburger O, Lindholm B, Kaysen GA, Bergstrom J. Are there two types of malnutrition in chronic renal failure? Evidence for relationships between malnutrition, inflammation and atherosclerosis (MIA syndrome). *Nephrol Dial Transplant.* 2000;15:953–960.

[9] O'Keefe A, Daigle NW. A new approach to classifying malnutrition in the hemodialysis patient. *J Ren Nutr.* 2002;12:248–255.

[10] Kalantar-Zadeh K, Kopple JD. Malnutrition as a risk factor of morbidity and mortality in patients undergoing maintenance dialysis. In: Kopple JD, Massry SG, eds. *Kopple and Massry's Nutritional Management of Renal Disease.* 2nd ed., Philadelphia, PA: Lippincott Williams & Wilkins; 2004:183–198.

[11] Kalantar-Zadeh K, Kopple JD. Relative contributions of nutrition and inflammation to clinical outcome in dialysis patients. *Am J Kidney Dis.* 2001;38:1343–1350.

[12] Aparicio M, Cano N, Chauveau P, et al. Nutritional status of hemodialysis patients: A French national cooperative study. *Nephrol Dial Transplant.* 1999;14:1679–1686.

[13] Jacob V, Carpentier JEL, Salzano S, et al. IGF-1, a marker of undernutrition in hemodialysis patients. *Am J Clin Nutr.* 1990;52:39–44.

[14] Bossola M, Muscaritoli M, Tazza L, et al. Variables associated with reduced dietary intake in hemodialysis patients. *J Ren Nutr.* 2005;15:244–252.

[15] de Mutsert R, Grootendorst DC, Boeschoten EW, et al. Subjective global assessment of nutritional status is strongly associated with mortality in chronic dialysis patients. *Am J Clin Nutr.* 2009;89:787–793.

[16] Vegine PM, Fernandes AC, Torres MR, Silva MI, Avesani CM. Assessment of methods to identify protein-energy wasting in patients on hemodialysis. *J Bras Nefrol.* 2011;33:55–61.

[17] Steiber AL, Kalantar-Zadeh K, Secker D, McCarthy M, Sehgal A, McCann L. Subjective global assessment in chronic kidney disease: A review. *J Ren Nutr.* 2004;14:199–200.

[18] Hull A. *Renal Nutrition.* 5th ed., Ashland: Nutrition Dimension; 2004:87, 88, 117, 125, 178, 179, 190.

[19] Pupim LB, Ikizler TA. Assessment and monitoring of uremic malnutrition. *J Ren Nutr.* 2004;14:6–19.

[20] Sacks GS, Dearman K, Replogle WH, Cora VL, Meeks M, Canada T. Use of subjective global assessment to identify nutrition-associated complications and death in geriatric long-term care facility residents. *J Am Coll Nutr.* 2000;19:570–577.

[21] McCann L. *Pocket Guide to Nutrition Assessment of the Patient with Chronic Kidney Disease.* 3rd ed., New York: National Kidney Foundation; 2005:1–34–1-40.

[22] Burleigh KS. *Associations among Plasma Homocysteine, Amino Acids and Nutritional Status in Hemodialysis Patients [dissertation].* Toronto: University of Toronto; 2001.

[23] Kalantar-Zadeh K, Kopple JD. Nutritional management of patients undergoing maintenance hemodialysis. In: Kopple JD, Massry SG, eds. *Kopple and Massry's Nutritional Management of Renal Disease.* 2nd ed., Philadelphia, PA: Lippincott Williams & Wilkins; 2004:432–457.

[24] Daugirdas JT, Stone JCV. Physiologic principles and urea kinetic modeling. In: Daugirdas JT, Blake PG, Ing TS, eds. *Handbook of Dialysis.* 3rd ed., Philadelphia, PA: Lippincott Williams & Wilkins; 2001:15–45.

[25] Tayyem RF, Mrayyan MT. Assessing the prevalence of malnutrition in chronic kidney disease patients in Jordan. *J Ren Nutr.* 2008;18:202–209.

[26] Tapiawala S, Vora H, Patel Z, Badve S, Shah B. Subjective global assessment of nutritional status of patients with chronic renal insufficiency and end stage renal disease on dialysis. *J Assoc Physician India.* 2006;54:923–926.

[27] Qureshi AR, Alvestrand A, Danielsson A, et al. Factors predicting malnutrition in hemodialysis patients: A cross-sectional study. *Kidney Int.* 1998;53:773–782.

[28] Bossola M, Giungi S, Luciani G, Tazza L. Appetite in chronic hemodialysis patients: A longitudinal study. *J Ren Nutr.* 2009;19:372–379.

[29] Laville M, Fouque D. Nutritional aspects in hemodialysis. *Kidney Int.* 2000; 58(Suppl. 76):S133–S139.

[30] Kalantar-Zadeh K, Ikizler TA, Block G, Avram MM, Kopple JD. Malnutrition-inflammation complex syndrome in dialysis patients: Causes and consequences. *Am J Kidney Dis.* 2003;42:864–881.

[31] Brodsky IG. Hormone, cytokine, and nutrient interactions. In: Shils ME, Olson JA, Shike M, Ross AC, eds. *Modern Nutrition in Health and Disease.* 9th ed., Philadelphia, PA: Lippincott Williams & Wilkins; 1999:716–719.

[32] Pertosa G, Grandaliano G, Simone S, Soccio M, Schena FP. Inflammation and carnitine in hemodialysis patients. *J Ren Nutr.* 2005;15:8–12.

[33] Bellinghieri G, Santoro D, Calvani M, Savica V. Role of carnitine in modulating acute-phase protein synthesis in hemodialysis patients. *J Ren Nutr.* 2005;15:13–17.

[34] Shakeri A, Tabibi H, Hedayati M. Effects of L-carnitine supplement on serum inflammatory cytokines, C-reactive protein, lipoprotein (a), and oxidative stress in hemodialysis patients with Lp (a) hyperlipoproteinemia. *Hemodial Int.* 2010;14:498–504.

[35] Hakeshzadeh F, Tabibi H, Ahmadinejad M, Malakoutian T, Hedayati M. Effects of L-Carnitine supplement on plasma coagulation and anticoagulation factors in hemodialysis patients. *Ren Fail.* 2010;32:1109–1114.

[36] Tabibi H, Hakeshzadeh F, Hedayati M, Malakoutian T. Effects of L-carnitine supplement on serum amyloid A and vascular inflammation markers in hemodialysis patients: A randomized controlled trial. *J Ren Nutr.* 2011;21:485–491.