Malnutrition, and anthropometric and biochemical abnormalities in end-stage renal disease patients

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ABSTRACT

Objective: To detect and compare the degree of malnutrition as well as the anthropometric and biochemical abnormalities among male and female patients with end-stage renal disease (ESRD).

Methods: A cross-sectional study was carried out at hemodialysis units in 7 Jordanian hospitals, between 2004 - 2005. Two hundred and seventeen ESRD outpatients who underwent hemodialysis were recruited using the convenience-sampling technique. A subjective global assessment (SGA) was used to assess the degree of malnutrition in both male and female patients. Anthropometric and biochemical measurements were also assessed in all patients.

Results: The SGA suggested that 50% of females were well nourished while 75% of the males were moderately to severely malnourished. The measured anthropometric variables showed a significant decrease in both male and female patients, except for triceps skinfold thickness. The hemoglobin as well as blood creatinine level were lower among females. In the biochemical parameters, there was a significant decrease in hemoglobin, albumin, and total protein blood levels in male patients. However, a significant decrease in hemoglobin only was detected in female patients with advanced malnutrition.

Conclusions: The nutritional status determined by SGA indicated a higher proportion of male patients with moderate to severe malnutrition as compared to female patients. Most of the anthropometric parameters could be used to assess the nutritional status of hemodialysis patients. The noticeable hemoglobin reduction, which increased with malnutrition degree, was significant in both male and female patients, while serum albumin and total protein reduction was significant among male patients only.

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Nutritional status influences the survival of patients on long-term hemodialysis, and malnutrition was found to be strongly associated with morbidity and mortality in end-stage renal disease (ESRD) patients who underwent hemodialysis.[1,2] Most surveys on nutritional status of patients undergoing maintenance hemodialysis or peritoneal dialysis indicate that there is a high incidence of protein-energy malnutrition, with a prevalence rate of 40%. Patients who have severe malnutrition account for 6-8% of cases.[3-6] The estimated prevalence of malnutrition varies due to the differences in methods used to assess patient's nutritional status, as well as other factors that can cause malnutrition. These factors include, although not limited to, age, recurrent illness, gastrointestinal problems, depression, inflammation, inadequate diet, anorexia, medications, taste abnormalities, and socioeconomic and cultural factors. Additionally, gender was found to markedly affect nutritional status.[7,8] Assessing nutritional status is difficult as there is no single test that can be considered as an indicator of protein-calorie malnutrition. It has been suggested that an assessment of malnutrition should rely on multiple indices of nutritional status, these indices comprise different anthropometric and biochemical measures. Anthropometric variables could be measured by different methods including dual energy x-ray absorptiometry or bioelectrical impedance analysis, and total body nitrogen (TBN).[8] The TBN quantifies body protein content and is considered as the "gold standard" of nutritional state in ESRD patients.[8,9] However, the previous methods are expensive, cumbersome, rarely available, and impractical for routine use.[8] In addition, assessment of malnutrition using common anthropometric and biochemical

measurements in isolation lacks specificity and reliability. Thus, using more than one type of measurement method (anthropometric and biochemical) may be more reliable and reflect the degree of malnutrition more accurately.[3] In hemodialysis patients, the common nutritional parameters that have been independently correlated with malnutrition included reduced body mass index (BMI), decreased fat mass and lean body mass, low serum albumin, prealbumin, transferrin, C-reactive protein, and more recently the subjective global assessment (SGA).[3] It has been reported that the use of SGA in detecting malnutrition is simple, valid, noninvasive and applicable, and correlates significantly with some nutritional parameters.[10] However, studies performed on ESRD to evaluate the degree of malnutrition using the average of some anthropometric (BMI, fat percent, fat mass, triceps skinfold thickness [TSF], mid arm circumference [MAC], mid arm muscle circumference [MAMC], and arm muscle area [AMA]), and biochemical parameters (albumin, total protein, hemoglobin, and creatinine) for both male and female patients may give inaccurate results.[8] Over- or underestimation may take place when unequal percentages of male and female patients are included in different study groups. Anthropometric and biochemical variations between male and female patients may be attributed to the differences of body composition, and the diversity of malnutrition and metabolic responses to ESRD and hemodialysis.[11] Only a limited number of studies have been conducted on renal diseases to reveal the effect of gender on some anthropometric and biochemical parameters, which could be used to assess the prevalence of malnutrition.[8,12] Therefore, the present study was conducted to assess the prevalence of malnutrition between male and female ESRD patients using SGA. Additionally, different anthropometric and biochemical parameters were measured and analyzed separately to detect gender effect on those parameters.

Methods. Using the convenience sampling technique in 253 patients, 217 (102 males and 115 females; age mean ± SD: 43.4 ± 13.2 years) ESRD outpatients who underwent hemodialysis were recruited from dialysis units of 7 Jordanian hospitals in 3 main cities (Amman, Irbid, and Zarqa) in Jordan between the years 2004 - 2005. The response rate of the participants at the current study was 86%. Of the potential participants, 36 patients refused to participate due to their anthropometric measurements and their unwillingness to answer some questions of the SGA. The inclusion criteria of the sample were patients undergoing hemodialysis for at least 6 months and aged 17 years or older. Patients with acute morbidity such as infections, elevated body temperature, respiratory and gastrointestinal distresses or wounds, as well as patients above 75 years old were excluded. The main causes for renal failure in those patients were primary hypertension (32%), diabetic nephropathy (28%), chronic glomerulonephritis (20%), polycystic kidney disease (9%), and other causes (11%). The standard socio-demographical characteristics of the patients (age, gender, marital status, educational status, and occupation) were collected. Also, hemodialysis duration was recorded for every patient and presented in months. The patients' anthropometric variables were collected, these included body weight (weight, pre- and post-dialysis session), BMI (weight [kg]/height^2 [m]^2), fat percent (body fat %), fat mass (body fat content [kg]), TSF, MAC, MAMC, and AMA. The TSF measurements were taken to the nearest 0.1 mm using a Lange Skinfold Caliper, while the mid arm circumferences were measured with Sammons Preston tape. The percentage of fat was determined using body fat monitor (Omron BF 306, Japan).[13] Percentiles of TSF, MAC, MAMC, and AMA for each patient were calculated referring to Frisancho.[14] All measures (except pre-dialysis weight) were taken post-dialysis on the right arm. In some cases, the measurements were taken on the left arm, as the right arm was functionally impaired due to the presence of an arterio-venus shunt. All patients were subjected to biochemical assessment as a part of their routine care. Means of serum albumin, total protein, hemoglobin, creatinine, urea, cholesterol, phosphorus, calcium, sodium, and potassium were taken from 3 consecutive preceding months. Blood samples were withdrawn immediately before starting the dialysis session. An SGA was completed for every patient by recording the history and performing physical examination. These 2 main components were classified from A - C.[15] Some of the required information in the SGA was collected from the patient or from the patient's medical record, or both. The overall scoring of A (well-nourished), B (moderately-malnourished), and C (severely-malnourished) was decided depending on the most predominant score (A, B, or C) in the different parts of the SGA. The anthropometric parameters as well as the SGA grades were obtained by a qualified renal dietitian experienced in performing the SGA to minimize errors of measurement. In addition, a pilot study for measuring the consistency of SGA was performed for 37 patients in 2 different occasions (2 weeks apart) by the same dietitian. Intra-rater reliability was measured using Cohen's Kappa; it was reported to be 0.92 at a significance level of $p<0.05$.

The research and its methodology were funded and approved by the research and ethical committee of the Hashemite University, Zarqa, Jordan, where the researchers are currently working. Approvals for collecting data were obtained from the different hospitals'

administrators. Informed consent was obtained from patients for the purpose of documenting the biochemical values and measuring the anthropometric parameters, and filling the SGA.

The results of the continuous variables included age, hemodialysis duration as well as the anthropometric and biochemical parameters were expressed as mean and standard deviations. Data of continuous variables for male and female patients were compared using independent t-test. However, differences between SGA grades A-C for each anthropometric and biochemical parameter were determined using one-way analysis of variants. Categorical variables using percentages and proportions were analyzed using Chi-square. Statistical analyses were conducted using the Statistical Package for Social Sciences, version 11 (SPSS Inc, 2001). A statistical significance was considered at the $p<0.05$ level.[16]

Table 1 - Nutritional status and time on hemodialysis in both male and female ESRD patients (N=217).

Parameters	Male (n=102)	Female (n=115)	*P* value
Age (years) (Mean ± SD)	44.2 ± 14.9	42.5 ± 12.6	0.170
Nutritional status by SGA (%)			
A	23.8	51.1	<0.001
B	72.6	41.5	
C	3.6	7.4	
Time on hemodialysis (months)			
Mean ± SD	73.3 ± 56.8	84.0 ± 63.8	0.247

ESRD - end-stage renal disease, SGA - subjective global assessment, A - well-nourished, B - moderately malnourished, C - severely malnourished.

Table 2 - Differences in anthropometric parameters between male and female patients (N=217).

Parameters	Male (Mean ± SD)	Female (Mean ± SD)	*P* value
Pre-dialysis weight (kg)	69.0 ± 15.6	59.9 ± 17.2	<0.001
Post-dialysis weight (kg)	65.9 ± 15.4	56.7 ± 16.5	<0.001
BMI	23.7 ± 4.5	22.4 ± 5.8	0.150
Fat percent	19.3 ± 7.9	23.7 ± 10.0	0.005
Fat mass (kg)	14.7 ± 8.6	14.5 ± 9.2	0.879
TSF (mm)	11.0 ± 8.2	14.5 ± 7.2	<0.001
MAC (cm)	25.9 ± 3.9	25.1 ± 4.6	0.206
MAMC (cm)	23.4 ± 3.6	20.6 ± 3.3	<0.001
AMA (cm^2)	30.5 ± 11.7	28.7 ± 11.6	0.114

BMI - body mass index, TSF - triceps skinfold thickness, MAC - mid arm circumference, MAMC - mid arm muscle circumference, AMA - arm muscle area.

Results. In the present study, 52.9% of the patients were females and 47.1% were males. In their marital status, 77.4% of the male patients were married, 20.1% were single, 1.3% were divorced, and 1.2% were widowed, while 46.8% of the female patients were married, 35.1% were single, 5.3% were divorced, and 12.8% were widowed. **Table 1** shows that there was no gender differences with regards to age and time of being on hemodialysis therapy. However, a significant difference ($p=0.001$) was detected between male and female patients in the SGA grades. The frequencies of SGA grades indicated that 23.8% of the male patients were classified as grade A, 72.6% were in grade B and 3.6% in grade C, according to the rating of SGA. However, a higher proportion (51.1%) of female patients were found to be well nourished when compared to male patients, and 7.4% of female patients were severely malnourished.

Table 2 shows some significant differences ($p<0.001$) in some measured anthropometric parameters (including pre- and post-dialysis weight, fat percent, TSF, and MAMC) in males compared to females. Hence, the values of pre- and post-dialysis weight and MAMC were lower in females as compared to males. However, in regard to fat percent, TSF were found to be higher in females when compared to males. When correlated with SGA grades, the results of anthropometric parameters showed a significant reduction ($p<0.001$) in almost all among SGA grades. As shown in **Table 3**, TSF was significantly reduced in grade C male patients as compared to grades A and B.

Cross-classification of patients by gender and percentile in each of fat percent, TSF, MAMC, and AMA is shown in **Table 4**. The percentiles of fat percent, TSF, MAC, MAMC, and AMA for every patient were computed according to Frisancho.[13] The differences among TSF, MAC, MAMC, and AMA percentiles were found to be significant when percentages of male and female patients were compared to each other. While 71-75% of male patients are in the ≤5 percentile for both of MAMC and AMA measurements, 27-33% of female patients are in the same percentile. In contrast, 41% of female, and 23% of male patients were found in the ≤5 percentile of TSF.

As shown in **Table 5**, hemoglobin and creatinine values were significantly lower in female patients than in male patients. However, there were no significant differences among the other measured biochemical variables. Hemoglobin was the only biochemical variable, which decreased significantly with the increased malnutrition degree in both male ($p=0.045$) and female ($p=0.005$) patients. Although, there was a significant difference in creatinine level ($p<0.001$) between male and female patients, however, this difference could not

Table 3 - Differences in anthropometric parameters among the SGA grades in male and female patients (N=217).

Parameters	SGA Grade	Male		Female	
		Mean ± SD	*P* value	Mean ± SD	*P* value
Pre-dialysis weight (kg)	A	86.6 ± 13.2	0.001	69.4 ± 18.0	0.001
	B	65.9 ± 11.9		50.7 ± 1.3	
	C	39.8 ± 11.4		47.1 ± 3.9	
Post-dialysis weight (kg)	A	82.5 ± 12.4	0.001	65.5 ± 17.3	0.001
	B	62.5 ± 11.8		48.2 ± 10.1	
	C	37.5 ± 10.8		44.1 ± 3.9	
BMI	A	27.5 ± 4.4	0.001	25.5 ± 6.1	0.001
	B	22.6 ± 3.7		19.2 ± 2.8	
	C	15.6 ± 4.2		17.3 ± 1.3	
Fat percent	A	24.8 ± 7.5	0.001	29.2 ± 9.3	0.001
	B	17.5 ± 7.0		18.2 ± 6.1	
	C	6.1 ± 2.7		11.2 ± 5.7	
Fat mass (kg)	A	21.2 ± 9.9	0.001	19.3 ± 9.6	0.001
	B	12.5 ± 6.5		9.4 ± 4.5	
	C	2.9 ± 0.9		4.9 ± 2.6	
TSF (mm)	A	12.2 ± 5.5*	0.183	16.6 ± 7.4	0.001
	B	10.0 ± 7.9*		13.5 ± 6.2	
	C	2.8 ± 1.3*		5.9 ± 3.1	
MAC (cm)	A	30.2 ± 3.2	0.001	28.3 ± 3.9	0.001
	B	25.1 ± 2.7		22.7 ± 2.4	
	C	17.3 ± 3.8		17.9 ± 2.2	
MAMC (cm)	A	27.3 ± 1.9	0.001	23.1 ± 26.9	0.001
	B	21.5 ± 2.5		18.5 ± 17.4	
	C	16.4 ± 3.5		16.0 ± 15.4	
AMA (cm^2)	A	45.7 ± 8.5	0.001	36.4 ± 10.3	0.001
	B	27.4 ± 8.1		21.1 ± 5.2	
	C	12.2 ± 8.7		14.1 ± 3.9	

SGA - subjective global assessment, BMI - body mass index, TSF - triceps skinfold thickness, MAC - mid arm circumference, MAMC - mid arm muscle circumference, AMA - arm muscle area, A - well-nourished, B - moderately malnourished, C - severely malnourished,*significant difference (p<0.05) between SGA grades within the measured parameter.

Table 4 - Cross-classification of patients by gender and reference percentile[13] of fat percent, TSF, MAMC, and AMA (N=217).

Percentile	Fat percent		TSF		MAMC		AMA	
	Male	Female	Male	Female	Male	Female	Male	Female
≤5 - <10	39.9	46.9	23.1	41.3*	71.1	27.3*	75.1	32.9*
10 - 25	29.6	32.9	38.5	39.0*	20.1	31.8*	18.8	28.4*
>25 - 75	20.6	9.3	25.6	17.4*	8.8	21.8*	6.1	28.4*
>75 - 95	5.9	6.2	10.2	2.3*	-	5.6*	-	6.8*
>95	13.2	4.7	2.6	-	-	3.4*	-	3.5*

TSF - Triceps skinfold thickness, MAC - mid arm circumference, MAMC - mid arm muscle circumference, AMA - arm muscle area,*the difference between male and female in the same percentile is significant at p<0.001. Data were expressed as percentage.

be detected when creatinine level was compared among the SGA grades in both male and female patients separately. Serum albumin (p=0.003) and total protein values (p=0.016) were found to decrease significantly in male patients only as the malnutrition degree increased (**Table 6**).

Discussion. In the present study, we estimated the prevalence of malnutrition among male and female hemodialysis patients in 7 Jordanian hospitals in 3 main cities in Jordan. Association of some measured anthropometric and biochemical parameters with SGA grades were performed for both male and female patients. Additionally, only one trained renal dietitian was assigned to estimate the SGA grades and the anthropometric measurements.

According to the SGA classification, 75% of male and 50% of female ESRD patients on hemodialysis were moderately to severely malnourished. Marcen et al[17] illustrated that 51.6% of the female patients were classified to have a moderate degree of malnutrition, and 46.3% with severe. However, it has been reported that the estimates of prevalence of malnutrition varied with a universal average of 40%. Mehrotra and Kopple[3] reported that the majority of those patients were classified to have mild to moderate malnutrition; specifically 6-8% of patients had severe malnutrition. Although the prevalence of malnutrition among Jordanian hemodialysis patients is high, it is still within the average of other countries. Many factors play a role in causing variations in the prevalence of malnutrition among different studies. These factors

Table 5 - Differences in biochemical parameters between male and female patients (N=217).

Parameter	Male (Mean ± SD)	Female (Mean ± SD)	*P* value
Albumin (g/L)	38.8 ± 4.7	39.0 ± 4.3	0.804
Total protein (g/L)	69.8 ± 7.9	71.1 ± 8.4	0.367
Hemoglobin (g/dL)	10.1 ± 1.5	9.0 ± 1.3	<0.001
Creatinine (mg/dL)	11.8 ± 2.7	9.7 ± 2.2	<0.001
Urea (mg/dL)	54.6 ± 14.7	59.0 ± 14.8	0.092
Cholesterol (mg/dL)	183.3 ± 60.6	165.6 ± 40.7	0.228
Phosphorus (mg/dL)	4.9 ± 1.9	4.7 ± 1.52	0.487
Calcium (mg/dL)	9.3 ± 0.91	9.2 ± 0.98	0.388
Sodium (mg/dL)	139.0 ± 4.2	138.7 ± 3.9	0.572
Potassium(mg/dL)	19.9 ± 2.7	20.3 ± 2.70	0.478

Table 6 - Differences in biochemical parameters among the SGA grades in male and female patients (N=217).

		Male		Female	
Parameters	**SGA Grade**	**Mean ± SD**	***P* value**	**Mean ± SD**	***P* value**
Hemoglobin (g/dL)	A	11.0 ± 1.2	0.045	9.7 ± 1.3	0.005
	B	10.1 ± 1.4		9.0 ± 1.4	
	C	8.5 ± 0.9		8.41 ± 1.1	
Creatinine (mg/dL)	A	11.1 ± 2.9	0.110	9.7 ± 2.6	0.060
	B	12.2 ± 2.7		9.9 ± 1.7	
	C	9.5 ± 1.8		7.8 ± 2.0	
Albumin (g/L)	A	41.1 ± 4.5	0.003	38.1 ± 4.3	0.156
	B	38.5 ± 3.9		39.9 ± 4.1	
	C	33.3 ± 11.2		37.6 ± 4.5	
Total protein (g/L)	A	73.4 ± 6.8	0.016	70.9 ± 7.1	0.223
	B	69.1 ± 9.7		71.7 ± 9.4	
	C	62.8 ± 9.3		65.3 ± 7.4	

SGA - Subjective global assessment, A - well-nourished, B - moderately malnourished, C - severely malnourished.

include differences between countries in which those studies were conducted, sample heterogeneity, diversity in dietary patterns, socioeconomic status, comorbidities, and differences in medical care hospitals from one country to another or even within the same country.[3] Additionally, the doses and conditions of dialysis may influence the rate of developing malnutrition.[18] The experience of the caregiver who administers the SGA may also influence the classification process.[19] In the present study, there was no significant difference in time on hemodialysis between male and female patients.

The differences between male and female patients in some measured anthropometric parameters (body weight, fat percent, TSF, and MAMC) are expected due to the differences in the body composition.[20,21] However, BMI, fat mass, MAC, and AMA were found to be similar without any significant differences between male and female patients. The present study showed that the loss of fat and muscular mass was higher in male than in female patients as malnutrition advances. A body fat mass was lost in both male and female patients classified in grade A (86%), as compared to grade C (74%). The same trend could be detected in AMA; AMA was lost in grade A (73%) as compared to grade C (61%) in male and female patients. Similarly, Stenvinkel et al[22] reported that the loss of muscular mass might be more significant in male than in female dialysis patients. Additionally, it has been described that fat depletion predominated in both genders, however protein depletion was higher in male patients.[17] As malnutrition advances, the reduction in patient's pre- and postdialysis body weight and BMI was found to be higher in male than in female patients. This reduction could be explained by the dramatic loss of fat mass as well as muscular mass in males when compared to female patients.

In conclusion, the cross classification of patients by gender and reference percentiles of MAMC and AMA revealed that 90% of male patients and 60% of female patients fall in or below the 25th percentile. However, the results of fat percent and TSF cross-classification showed that female patients were more influenced by malnutrition (80% of female patients at ≤25th percentile) than male patients (65% of male patients at ≤25th percentile). Hence, muscular mass was more inversely influenced by malnutrition degree in male patients, while adipose tissue loss was more in female than in male patients. On the biochemical analysis, there were significant differences between male and female patients in hemoglobin and blood creatinine levels. However, these results are expected due to the physiological differences between male and female patients.[9,23] It is well documented that blood creatinine level for males differ from females as creatinine is correlated with muscle mass.[9] Relating hemoglobin to SGA grades shows a significant decrease in both male and female patients. This trend of reduction with advances in malnutrition could not be seen in blood creatinine level. The results of albumin and total protein demonstrated a significant reduction as the malnutrition degree increased in male patients only. Thus, it could be recognized that serum albumin and total protein may be used as indicators for malnutrition in male patients except in female patients. Stenvinkel et al[24] pointed out that while serum albumin can predict outcome in male patients, no predictive effect of this parameter was found in female patients. However, more studies are warranted to investigate the reasons behind this elevated prevalence of malnutrition in hemodialysis patients.

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