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Appetite Disorder in Hemodialysis Patients and its Impact on Dietary Intake; A Cross-sectional study

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Abstract

Background: Lack of appetite (anorexia) is a relatively common symptom among hemodialysis patients and contributes to the development of malnutrition; moreover, it is associated with unfavorable outcomes. This study aimed to explore the socio-demographic aspects, clinical characteristics, and appetite assessment in end-stage renal disease (ESRD) patients and study their impact on daily dietary intake. **Methods:** This was a cross-sectional study carried out at Mansoura Nephrology and Dialysis Unit (MNDU), Mansoura University, and Aga Hospital Dialysis Unit, Dakahlia, Egypt. The study was carried on patients with ESRD on hemodialysis. Patients who met inclusion and exclusion criteria were included in the study. Demographic and clinical characteristics were collected, and appetite was evaluated using subjective assessment of appetite then compared to dietary intake. **Results:** The current study included 162 hemodialysis patients whose age 48.72±12.64 years and males constituted 57.4% of them. The two main causes of ESRD in the present study were hypertension (51.9 %) and diabetic nephropathy (9.3 %). Hepatitis C virus (HCV) prevalence was found to be 36.4%. Median energy intake was 1348.5 kcal/day with (minimum-maximum) 519.78-3214.17 kcal/day, protein intake was 58.53 g/day. Significant lower values of dietary nutrient intake were observed among patients with diminished appetite category than those with normal appetite when assessed by subjective assessment of appetite. **Conclusion:** Diminished appetite is associated with decreased nutrient intake. Dietetic counseling is essential in HD patients to reduce rates of malnutrition.

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INTRODUCTION

ESRD is a permanent decline in a person's kidney function that necessitates timely renal replacement therapy (RRT) to prevent death. It refers to those patients whose estimated glomerular filtration rate (eGFR) / 1.73 m^2 falls below 15 mL/minute or those needing dialysis despite GFR. [1]

Hemodialysis (HD) is the routine RRT in our country. The aims of HD are restoring the body's internal environment and homeostasis. Prescribing an appropriate HD regimen that provides optimal care of the patient on chronic dialysis is adjusted according to machine-dependent variables and patient-related parameters. [2]

Appetite, a person's desire to eat, is often diminished in HD patients. This abnormally diminished appetite, also known as anorexia, decreases oral intake of protein and energy, thereby leading to malnutrition and cachexia. Undoubtedly, anorexia leads to lower quality of life perception and can be a risk factor for undesirable outcomes like poor erythropoietin response and high hospitalization and mortality rates. [3]

Malnutrition is common in patients with ESRD. In patients receiving dialysis, the most important factor causing malnutrition is decreased nutrient intake that is owing mainly to uremia resulting from the inadequacy of dialysis. Poor dietary intake of protein and energy is commonly noticed in patients on maintenance hemodialysis. [4]

Decreased nutrient intake may also be caused by non-anorexic factors such as insufficient finances for buying or preparing foods, surgical or medical morbidities that impair a person's capability of consuming, digesting, or processing the nutrients, cognitive impairment, and other mental disorders or physical disabilities. [5]

Assessment of appetite is generally accepted as an early warning of imminent morbidity and dietary concerns. Dietary restrictions aimed to maintain fluid, levels of serum potassium and phosphorus within normal ranges often lead to limited food options and unappetizing meals. [6]

To improve the outcome of dialysis, patients on dialysis need to follow a strict diet to lessen the accumulation of fluids and waste products between dialysis sessions. For patients receiving dialysis, it is important to have the proper amount intake of protein, calories, vitamins, minerals, and fluids every day. A healthy renal diet is low in sodium, potassium, and phosphorus, limited in fluids, and adequate in calories and protein. [7]

In this study, we aimed to explore the socio-demographic aspects, the clinical characteristics, and appetite assessment in ESRD patients receiving hemodialysis, of such patients and study their impact on daily dietary intake.

Patients and Methods

Study design and participants' criteria:

This cross-sectional study was carried out at Mansoura Nephrology and Dialysis Unit (MNDU), Mansoura University, and Aga Hospital Dialysis Unit, Dakahlia, Egypt.

Inclusion criteria:

1- Patients older than 18 and below 65 years old.
2- On regular hemodialysis for at least six months.
3- Vitally and clinically stable.
4- Patients who were able to consume food orally and doesn't have dysphagia.

5- Patients who were able to report questionnaire (subjective assessment of appetite).
6- Patients who provided an informed consent.

Exclusion criteria:

1- Patients with extreme age (below 18 and above 65 years).
2- Patients who refused enrollment in the study or unable to give informed consent.
3- Patients with other diseases that associated with wasting, such as infection either, acute or chronic, and cancer.
4- Patients with recurrent illnesses or frequent history of hospital admissions in the six months before their enrollment in the study.

Methods:

The study was explained to all patients. Informed consent was obtained. Epidemiological, clinical, and laboratory characteristics of all patients were documented using specially prepared sheet.

- During this study, the followings were done:

1- Collection of demographic features including age, sex, gender, residence, marital status, years of education, and work.
2- Clinical characteristics were documented, especially the associated comorbidities (hypertension, diabetes mellitus, cardiovascular disease, etc.) and hepatitis C virus infection. Also, hemodialysis duration, history of renal transplantation, family history of kidney disease, and current dialysis access were reported.
3- Blood samples have been collected from each patient, and routine laboratory investigations such as serum creatinine, hemoglobin, albumin, high-sensitivity C-reactive protein (hs-CRP), urea reduction ratio (URR), calcium, phosphorus, and parathyroid hormone were done.
4- Weight in centimeters and body weight in kilograms were measured, and Body Mass Index (BMI) was calculated as weight (in kilograms) divided by the square of height (in meters). Average erythropoietin dose over three months was calculated and the mean of the three consecutive monthly doses was used in statistical analysis.
5- Dietary Assessment, patients were given a plain sheet, and they were asked to report the consumed diet over three days in a selected week. These days include a dialysis day, a day without dialysis, and a weekend day that is optional. [8] The total dietary energy (Kcal/day) and nutrients intake {protein (g/day), fat (g/day), carbohydrate (g/day), calcium (mg/day), phosphorus (mg/day), sodium (mg/day), potassium (mg/day), water (g/day)} were calculated. The mean energy and nutrients intake over these three days were used in statistical analysis.
6- Appetite was assessed using subjective assessment of appetite tool with the following question: "During the past week, how would you rate your appetite?" that was based on a Likert scale which contained 5 response options: (1) very good, (2) good, (3) fair, (4) poor, and (5) very poor. [9.10] . This questionnaire was

asked to all patients on mid-week dialysis day before starting hemodialysis session. It was compared to dietary intake. We translated the available English version of the above appetite question into Arabic and was given in printed sheet for each patient separately.

Statistical Analysis

Data were fed to the computer and analyzed using IBM SPSS Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. Qualitative data were described using number and percent. Chi-Square test for comparison of 2 or more groups. Fischer Exact test was used as correction for Chi-Square test when more than 25% of cells have count less than 5 in 2*2 tables. Quantitative data were described using median (minimum and maximum) for non-parametric data and mean, standard deviation for parametric data after testing normality using Kolmogorov-Smirnov test. The two independent groups were compared with Student t test for parametric data and Mann-Whitney U test for non-parametric data. For all the above-mentioned statistical tests done, the significance threshold is fixed at 5% level (p-value). The results were considered non-significant when the probability of error is more than 5% ($p > 0.05$) while significant when the probability of error is less than 5% ($p \leq 0.05$).

Results:

In the current study, we evaluated one hundred seventy-seven ESRD patients on regular HD and only one hundred sixty-two patients were included (4 patients refused enrollment, 7 patients were on dialysis for less than six months duration, 2 patients had infections, and 3 patients were older than 65 years, and 1 patient had cancer,). The baseline demographic data are listed in table 1. The age of included sample ranged from 20 to 65, with mean 48.72 years. Sixty-nine (42.6%) of them were females, and 93 (57.4%) were males. One hundred five cases (71%) were rural residence, while 47 (29%) were from urban ones. One hundred thirty-nine cases (85.8%) were not working, 134 (82.7%) were married, with the median number of offspring was 3.

Table 2 illustrates the clinical data of the studied patients. Fifty-nine patients (36.4%) had chronic HCV. The whole sample screened negative for hepatitis B and HIV. Regarding etiology, hypertension was found in 84 patients (51.9%), diabetic nephropathy in 15 patients (9.3%), analgesic nephropathy in 14 patients (8.6%). 29 patients (17.9%) showed a positive family history of renal disease. Duration of dialysis ranged from 12-213 months, with a median of 57 months. 6 patients (3.7%) had a history of kidney transplantation. Regarding dialysis access, 155 patients (95.7%) had Arteriovenous Fistula, 4 patients (2.5%) had Arteriovenous Graft, 2 patients (1.2%) had permcath, and only one patient (0.6%) had a temporary catheter. Regarding distribution of associated co-morbidities; 88 patients (54.3%) were hypertensive, 28 patients (17.3%) were diabetic, 32 patients (19.8%) had cardiovascular disease**.**

The laboratory data of the studied patients are listed in table 3. Mean serum albumin was 3.99 gm/dl with standard deviation ±0.47, while mean calcium level was 8.75 mg/dl with standard deviation ±0.86, and mean phosphorus was 4.59 mg/dl with standard deviation ±1.71. On the other

hand, the mean urea reduction ratio was 68.35%, with a standard deviation of ±11.95. The mean hemoglobin level was 9.84 gm/dl with standard deviation ± 1.49, and the hs-CRP level was 6.0 mg/L with (minimum-maximum) 0.0-252 mg/L., Additionally, the mean BMI was 27.81 Kg/m2 with a standard deviation ±5.52, and the median average erythropoietin dose was 24.66 *103 IU/month with (minimum-maximum) 0.0-78.33 *103 IU/month. Table 4 shows dietary intake among studied cases. Median energy intake was 1348.5 kcal/day with (minimum-maximum) 519.78-3214.17 kcal/day, protein 58.53 g/day, fat 40.53 g/day, carbohydrate 187.66 g/day, calcium 381.7 mg/day, phosphorus 707.74 mg/day, sodium 2051.4 mg/day, potassium 1789.3 mg/day and water 507.21 g/day.

Table 5 illustrates the association between subjective assessment of appetite* and dietary intake of the cases included in the study. There were statistically significant lower values of dietary nutrient intake among patients with diminished appetite category than patients with a normal appetite as assessed by subjective assessment of appetite tool.

Table 6 illustrates the association between subjective assessment of appetite and co-morbidities & URR among studied cases. There was statistically significant higher frequency of hypertension among cases with diminished appetite category than those with normal appetite by subjective assessment of appetite (p=0.007). Other co-morbidities and URR showed no significant difference between the two appetite categories.

Table (1): Socio-demographic characteristics of the studied cases.

	n=162	**%**
Age (years) **mean± SD** **(Range)**	48.72±12.64 (20.0-65.0)	
Sex **Male** **Female**	 93 69	 57.4 42.6
Residence **Rural** **Urban**	 115 47	 71.0 29.0
Occupation **Not working** **Working**	 139 23	 85.8 14.2
Education duration (years) **median (range)**	10.5(0.0-16.0)	
Marital status **Unmarried** **Married**	 28 134	 17.3 82.7
Number of offspring **median (range)**	3.0(0.0-8.0)	
Special habits **Not smoking** **Smoking**	 138 24	 85.2 14.8

Table (2): Medical history data of the studied cases.

	n=162	%
Hepatitis C Virus	59	36.4
Hepatitis B Virus	0	0.0
HIV	0	0.0
Etiology of Renal Failure:		
Hypertension	84	51.9
Diabetic Nephropathy	15	9.3
Analgesic Nephropathy	14	8.6
Chronic Glomerulonephritis	13	8
Obstructive Nephropathy	13	8
Lupus Nephritis	4	2.5
Polycystic disease of kidney	8	4.9
Unknown etiology	8	4.9
Contrast-induced nephropathy	2	1.2
Amyloidosis	1	0.6
Family history of renal disease:		
Negative	133	82.1
Positive	29	17.9
Duration of dialysis (Months) median (range)	57.0 (12.0-213)	
History of kidney transplantation:		
No	156	96.3
Yes	6	3.7
Current dialysis access:		
Arteriovenous Fistula	155	95.7
Arteriovenous Graft	4	2.5
Permcath	2	1.2
Temporary catheter	1	0.6
Co-morbidities:		
Hypertension	88	54.3
Diabetes	28	17.3
Cardiovascular disease	32	19.8
Peripheral vascular disease	56	34.6
COPD	6	3.7
Stroke	13	8.0
Gastrointestinal bleeding	11	6.8
Autoimmune disease	5	3.1
HIV= Human immunodeficiency virus, COPD= chronic obstructive pulmonary disease		

Table (3): Laboratory data, BMI and EPO dose of the cases included in the study.

	n=162
Serum albumin (g/dl)	3.99±0.47
Serum creatinine (mg/dl)	8.21±2.56
Calcium (mg/dl)	8.75±0.86
Phosphorus (mg/dl)	4.59±1.71
Parathyroid hormone (pg/ml)	347.42±42.15
URR (%)	68.35±11.95
Hemoglobin (g/dl)	9.84±1.49
hs-CRP (mg/l)	6.0(0.0-252)
BMI (Kg/m^2)	27.81±5.52
Average EPO dose over 3 months*10^3 (IU/month)	24.66 (0.0-78.33)
All parameters described as mean± SD except hs-CRP and EPO dose described as median (minimum-maximum). **URR= Urea reduction ratio, hs-CRP= high sensitivity C-reactive protein, BMI= Body mass index, EPO= Erythropoietin**	

Table (4): Dietary intake among studied cases.

	n=162
Energy (kcal/day)	1348.5(519.78-3214.17)
Protein (g/day)	58.53(18.76-184.38)
Fat (g/day)	40.53(11.09-198.04)
Carbohydrates (g/day)	187.66(72.15-534.9)
Calcium (mg/day)	381.7(60.62-965.88)
Phosphorus (mg/day)	707.74(102.32-3097.3)
Sodium (mg/day)	2051.4(289.87-8817.6)
Potassium (mg/day)	1789.3(467.42-4610.1)
Water (g/day)	507.21(168.21-1445.3)
All parameters described as median (min-max)	

Table (5): Association between subjective assessment of appetite* and dietary intake of the cases included in the study.

	Subjective assessment of appetite		**test of significance**
	Normal n=91	**Diminished n=71**	
Energy (kcal/day)	1580.8±473.5	1143.3±335.52	t=6.59 p<0.001*
Protein (g/day)	68.09±20.42	49.91±16.52	t=6.10 p<0.001*
Fat (g/day)	46.16 (14.79-198.04)	34.57 (11.09-169.02)	z=4.77 p<0.001*
Carbohydrate (g/day)	224.41±80.73	160.07±50.59	t=5.87 p<0.001*
Calcium (mg/day)	424.57 (60.62-965.88)	318.27 (91.72-877.67)	z=3.98 p<0.001*
Phosphorus (mg/day)	799.25 (307.7-3097.3)	562.97 (102.32-1332.7)	z=5.12 p<0.001*
Sodium (mg/day)	2339.4 (289.87-8817.6)	1650.92 (507.4-3695.27)	z=4.56 p<0.001*
Potassium (mg/day)	2099.8±687.64	1570.0±552.30	t=5.29 p<0.001*
Water (g/day)	639.08±204.0	445.13±138.06	t=6.87 p<0.001*

*(after categorization into 2 categories: Normal; very good, good & Diminished; fair, poor, very poor)
All parameters described as mean± SD except Fat, Calcium, Phosphorus, Sodium described as median (range)
Z: Mann Whitney U test t: Student t test *statistically significant p: probability

Table 6: Association between subjective assessment of appetite and co-morbidities & URR among studied cases.

	Subjective assessment of appetite		Test of significance
	Normal N=91(%)	Diminished N=71(%)	
Hypertension	41(45.1)	47(66.2)	χ^2=7.18 p=0.007*
Diabetes	14(15.4)	14(19.7)	χ^2=0.524 p=0.469
Cardiovascular disease	18(19.8)	14(19.7)	χ^2=00.0 p=0.992
Peripheral vascular disease	27(29.7)	29(40.8)	χ^2=2.20 p=0.138
Chronic obstructive pulmonary disease	5(5.5)	1(1.4)	χ^2=1.87 p=0.17
Stroke	5(5.5)	8(11.3)	χ^2=1.80 p=0.18
Gastrointestinal bleeding	9(9.9)	2(2.8)	χ^2=3.15 p=0.07
Autoimmune disease	2(2.2)	3(4.2)	FET p=0. 654
URR (%)	69.21±11.85	67.25±12.07	t=1.034 p=0.303

URR was described as mean± SD
χ^2=Chi-Square test FET: Fischer exact test t; student t test
P; probability *statistically significant

Discussion

The current study included 162 patients with ESRD on dialysis, 57.4 of them were males and the mean age of the patients was 48.72 years. The high percentage of male patients in this study was in concordance with Hecking et al., who reported that more men were on hemodialysis than women (59% versus 41% overall). [11] Moreover, Nagata et al. reported that ESRD was more prevalent in males, particularly after 50 years. [12] Furthermore, some female patients refused enrollment in the study. On the other hand, our result was matched with Afifi et al. who reported that the mean age of HD patients in Egypt increased from 45.6 years in 1996 to 49.8 years in 2008 [13] and the 9th Annual Report of The Egyptian Renal Registry, which showed that the mean age of HD patients was about 49.8 ± 19 years and 55.2% of them were males. [14] Also, this was in agreement with the study performed by Yu et al., who reported a rise in the prevalence of CRF with aging. [15]

In the present study, hypertension was the main cause of ESRD (51.9%), followed by diabetic nephropathy (DN) (9.3 %) and this came in agreement with Ghazaly et al. who reported that in Mansoura Nephrology and Dialysis Unit (MNDU), Mansoura University, Dakahlya, hypertension was the main cause of ESRD (41%), followed by diabetes (25%). [16] Also, a similar result is reported in a number of governorates in Egypt. El-Zorkany reported that in Menoufia, the leading cause of ESRD was hypertension (33.4%), followed by DN (9.2%). [17] Ahmed et al. reported that in Beheira the major cause of ESRD was hypertension (27.8%), followed by DN (20.1%). [18] El Minshawy reported that in Cairo hypertension was the major cause of ESRD with 29.7%, followed by DN 12.5%; in Canal governorates hypertension was the leading cause of ESRD with 27.3% followed by DN (10.7%) and in El-Minia governorate the main cause was also hypertension (20%), followed by DN (8%). [19] This high prevalent etiology of hypertension in this current study may be attributed to lower rates of awareness, lack of early screening through hypertension-screening programs and negligence of hypertension treatment, especially in areas of low socioeconomic status.

The findings of the current study are also compatible with results from other Arab countries. Banaga et al. reported that in Sudanese, the most common cause of ESRD was hypertension (34.6%), followed by chronic glomerulonephritis (17.6%), then DN (12.8%). [20] Additionally, Moukeh et al. who reported that in Syrian, hypertension represented the main cause of ESRD (21.5%), followed by chronic glomerulonephritis (20.5%), then DN (19.5%) and counts the third cause. [21]

In contrast to the current result, Saran et al. reported that in USA, the main cause of ESRD was DM. [22] Also, Hassanien et al. reported that in the Gulf Cooperation Council countries, the leading cause of ESRD was DN (17). [23]

There is an increased risk for catching HCV infection among HD patients. [24] In our study, the prevalence of HCV was found to be 36.4%. Ghazaly's et al. study carried out in the nephrology and dialysis unit in Mansoura University Hospital, Dakahlya, Egypt, showed that 26 of 100 ESRD patients (26%) were tested positive for HCV Antibody. [25] Elmowafy et al. reported that in the Urology and Nephrolgy Center, Mansoura

University, Dakahlya, 46 of 96 HD patients (47.9%) had HCV Antibody. [26] Also, Anber et al. reported that in Mansoura University Hospital, Dakahlya, 48 of 93 chronic HD patients (51.8%) had HCV Antibody. [27] Kerollos et al. reported that in Assiut governorate the prevalence of HCV among HD patients was 34.8%. [28] El-Zorkany reported that in Menoufia the prevalence of HCV in the ESRD patients was found to be 36.8%. [29] The high prevalence of HCV in this current study may be attributed to lack of implementing standard precautions for infection control in dialysis centers or transmission of infection outside dialysis centers e.g., at barbershop during hair cutting and shaving, especially in low-income areas. In Egypt, the prevalence of HCV in HD patients in 2015 survey was estimated to be 50.7%. [30]

In the current study, median daily energy intake was 1348.5 kcal/day, protein 58.53 g/day, carbohydrate 187.66 g/day. Cupisti et al. reported that mean dietary energy intake was 1900 Kcal/day, mean protein was 70 g/day, mean carbohydrate was 238 g/day. [31]

The recommended dietary energy intake for HD patients is 35 Kcal/kg/day, and 30-35 Kcal/kg/day if below 60 and 60 years or older, respectively; dietary protein intake 1.2 g/kg/d for clinically stable patients (at least 50% should be of high biological value); total fat 25-35% of total energy intake; potassium 2000-2750 mg/day; sodium 750-2000 mg/day; phosphorus 800-1000 mg/day; calcium <1000 mg/day; water 750-1500 ml/day. [32]

We observed that there were significant lower values for dietary energy and protein intakes among patients with diminished appetite than patients with normal appetite. Low dietary intake of energy and protein in those patients with diminished appetite may be due to inadequate dialysis as some patients were not compliant to receive the full time of dialysis session. Moreover, other factors might contribute such as psychological disorders, and working status as 85.8 of the studied patients were not working and this participate in poverty and low socio-economic status.

Burrowes et al. reported significant lower values for dietary energy and protein intakes among patients with fair, poor/very poor appetite than patients with very good, good appetite. [33] Also, Sahathevan et al. reported that patients with the poorer appetite ratings (fair, poor) had significantly lower dietary energy and protein intakes. [34] Hajira et al. observed that the dietary intake of energy and protein are often low due to uremic anorexia, underlying disease, and psychological factors. [35]

We observed that frequency of hypertension comorbidity was statistically significant among patients with diminished appetite category than patients with normal appetite by subjective assessment of appetite. The reason for this finding is not clear. On the contrary, this disagreed with Sahathevan et al. and Kalanter-Zadeh et al. who observed that there was no significant association between underlying hypertension comorbidity and subjective assessment of appetite. Also, we observed that frequency of diabetes and cardiovascular disease comorbidities showed no statistically significant difference across the two appetite categories (normal & diminished), and this agreed with

Sahathevan et al. and Kalanter-Zadeh et al. who observed no significant association between diabetes and cardiovascular disease among the two appetite categories [36,37]

We observed that URR was not statistically differ across the two appetite categories (normal, diminished), this may be attributed to the fact the subjective assessment of appetite is limited-time frame assessment tool (the past week only) [38,39] and this agreed with Sahathevan et al. and Kalanter-Zadeh et al. who observed no statistically difference between Kt/V showed no statistically difference across appetite categories. (very good, good, fair, poor, very poor) [40,41]

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