Journal of
Clinical Nephrology and Renal Care

Original Article: Open Access

# Depression in Late-Life patients with End-Stage Renal Disease under Online-Haemodiafiltration is Associated with Low Social Support, Muscular Mass and Creatinine Serum Levels

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## Abstract

**Purpose:** Patients with end-stage renal disease (ESRD) under dialysis showed a higher prevalence of depression, which is independently associated with non-adherence, hospitalization and mortality. We aimed to evaluate the prevalence of depression and associated variables, among ESRD late-life patients under online-haemodiafiltration (OL-HDF).

**Methods:** An observational cross-sectional study that included 114 late-life patients under OL-HDF was conducted. Depression status was evaluated using the geriatric depression scale (GDS). Social support was also evaluated, as well as sociodemographic, comorbidities and haematological data, iron status, dialysis adequacy and nutritional markers.

**Results:** Our results showed that 43% (n = 49) of our dialysis patients showed a GDS score lower than 5, 28.1% (n = 32) showed a GDS score between 5 and 8, and 28.9% (n = 33) showed a score of 9 or more. When the three groups of patients were compared, we found significant differences in age, creatinine, substitution fluid volume, relative fat, fat tissue index (FTI), lean tissue index (LTI), lean tissue mass (LTM) and social support scores. Significant positive correlation was found between the GDS score and KTv, FTI and relative fat; and a negative correlation was found with social support score, creatinine, LTM and LTI.

**Conclusions:** Our results showed a high depression rate in dialysislate-life patients, which is associated with low social support and decreased muscular mass and creatinine serum levels. It will be important to consider social support as pivotal in non-pharmacological interventions to reduce depression in order to enhance adherence to medical plans, reduce health resource utilization and costs, and improve survival rates.

## Keywords

Depression, Dialysis, Predictors, Geriatric depression scale

## Introduction

Late-life patients with end-stage renal disease (ESRD) receiving chronic dialysis treatment experience many symptoms, of which depression is particularly common and potentially treatable [1-4], with a prevalence rate estimated at between 20% and 44% [5-9].

Depression has been associated with low quality of life and low adherence to prescribed dialysis treatments, including drugs regimen, prescribed dialysis sessions, dietetic recommendations and restriction of fluid intake, and increasing morbidity and mortality compared to the general population [5-7]. However, there is some controversy over whether depression is just a marker of increased associated comorbidities and disease severity or whether it has a direct causal role in poor treatment outcomes.

In spite of the social and economic burden of depression in patients with ESRD, there are not many pharmacological and/or non-pharmacological interventional controlled studies that have aimed to improve depression symptoms. A study by Blumenfield *et al.* [8], showed a very limited effect on symptoms associated with depression when comparing a group of patients with ESRD under dialysis treated with serotonin reuptake inhibitors with a group of patients receiving placebo. Another study using a non-pharmacological approach, showed an increased depression score in both a group of patients receiving a cognitive-behavioural intervention and a control group. However, the patients receiving the cognitive-behavioural intervention exhibited more improvements in quality of life when compared to the control group [9]. In a more recent study, an individual cognitive behavioural therapy has been used to reduce depression in patients with ESRD, and this intervention showed significant improvements in depression and quality of life [10].

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**Citation:** Amado L, Poveda V, Ferreira R, Ferreira N, Miranda V, Teixeira L, et al. (2016) Depression in Late-Life patients with End-Stage Renal Disease under Online-Haemodiafiltration is Associated with Low Social Support, Muscular Mass and Creatinine Serum Levels. J Clin Nephrol Ren Care 2:007

**Received:** April 05, 2016: **Accepted:** April 26, 2016: **Published:** April 28, 2016

Nutritional status in dialysis patients is routinely assessed with biochemical and clinical markers, including albumin, creatinine, nPCR and body mass index (BMI) [11,12]. In addition bio-impedance has been used, in recent years, to measure fat-related markers as a substitute for the calculation of BMI, which is considered a poor fat mass marker [13].

DOPPS study showed that patients with increased lack of appetite have nutritional markers decreased. Moreover, they found an association between depression and lack of appetite with higher mortality risk [12]. Depression in ESRD patients under dialysis, has also be caused by metabolic disturbances, enhanced inflammatory and oxidative stress [14].

Online-haemodiafiltration (OL-HDF), an alternative to standard dialysis, was claimed to be more biocompatible, to increase dialysis efficacy and reduce the inflammatory response, which would, probably, contribute to decrease cardiovascular outcomes and mortality in ESRD. However, the recent randomized trials [15] showed that the potential benefits of convective modalities over standard dialysis for clinical cardiovascular outcomes or all-cause mortality remain unproved. There is still no evidence of a better effect on small-molecule clearance [15], although convective modalities appear to reduce the incidence of symptomatic hypotension and to increase middle-molecular clearance (assessed by β2-microglobulin).

**Table 1:** Comparison of studied variables between the three groups of ESRD patients, non-depression (GDS score ≤ 5), suggestive of depression (GDS score between 6 and 8) and depression (GDS score > 8).

| | Geriatric depression scale score less than or equal to 4 (n = 49) | Geriatric depression scale between 5 and 8 (n = 32) | Geriatric depression scale greater than or equal to 9 (n = 33) | P value |
|---|---|---|---|---|
| **Sociodemographic data** | | | | |
| Age, years | 64.6 ± 13.2 | 73.3 ± 10.4 a) | 65.1 ± 15.8 b) | 0.011 |
| Gender, % male | 67.3 | 40.6 | 36.4 | 0.090 |
| **Dialysis markers** | | | | |
| URR, % | 82.2 ± 5.8 | 81.8 ± 5.8 | 82.4 ± 6.6 | 0.910 |
| KTv | 1.9 ± 0.3 | 2.0 ± 0.4 | 2.0 ± 0.5 | 0.129 |
| Creatinine, mg/dL | 9.1 ± 2.7 | 7.5 ± 1.7 a) | 7.1 ± 2.3 a) | < 0.001 |
| Substitution fluid volume, L | 25.0 ± 8.0 | 21.0 ± 7.0 | 20.0 ± 7.0 a) | 0.009 |
| **Biochemical data** | | | | |
| Potassium, mmol/L | 5.1 ± 0.6 | 4.9 ± 0.6 | 4.8 ± 0.8 | 0.154 |
| Sodium, mmol/L | 137.6 ± 3.3 | 137.7 ± 2.7 | 137.2 ± 2.9 | 0.797 |
| Phosphorus, mmol/L | 4.3 ± 0.8 | 4.2 ± 1.4 | 4.0 ± 0.8 | 0.529 |
| Calcium, mg/dL | 8.9 ± 0.6 | 8.6 ± 1.7 | 8.8 ± 0.7 | 0.296 |
| Calcium phosphorus product | 38.2 ± 8.4 | 36.7 ± 11.9 | 35.4 ± 9.1 | 0.437 |
| **Lipid profile** | | | | |
| Total cholesterol, mg/dL | 156.5 ± 46.7 | 155.9 ± 37.3 | 154.5 ± 44.4 | 0.981 |
| Triglycerides, mg/dL | 157.7 ± 82.5 | 119.6 ± 76.1 | 129.3 ± 59.6 | 0.062 |
| HDLc, mg/dL | 42.7 ± 14.9 | 44.9 ± 13.2 | 44.5 ± 13.8 | 0.747 |
| LDLc, mg/dL | 82.2 ± 39.5 | 86.9 ± 32.9 | 84.2 ± 38.4 | 0.855 |
| **Hematological data** | | | | |
| Haemoglobin, g/dL | 11.5 ± 2.0 | 11.1 ± 1.5 | 11.6 ± 1.3 | 0.491 |
| Haematocrit, % | 34.7 ± 6.5 | 33.9 ± 4.8 | 35.4 ± 4.4 | 0.562 |
| Erythrocytes, $x10^{12}$/L | 3.8 ± 0.8 | 3.7 ± 0.6 | 3.9 ± 0.5 | 0.418 |
| RDW, % | 13.7 ± 2.2 | 14.4 ± 1.7 | 14.1 ± 0.8 | 0.182 |
| Platelets, $x10^9$/L | 205.9 ± 76.0 | 214.7 ± 76.6 | 210.5 ± 56.0 | 0.859 |
| White blood cells, $x10^9$/L | 6.3 ± 1.8 | 6.9 ± 2.9 | 6.8 ± 2.4 | 0.379 |
| Neutrophils, $x10^9$/L | 3.9 ± 1.4 | 4.5 ± 2.0 | 4.7 ± 2.2 | 0.184 |
| Lymphocytes, $x10^9$/L | 1.7 ± 0.6 | 1.8 ± 1.5 | 1.6 ± 0.6 | 0.679 |
| Neutrophil/Lymphocyte ratio | 2.7 ± 1.8 | 3.3 ± 1.9 | 3.7 ± 3.1 | 0.160 |
| **Iron status** | | | | |
| Iron, mg/dL | 71.8 ± 31.2 | 65.2 ± 24.7 | 63.5 ± 33.7 | 0.431 |
| Transferrin, mg/dL | 179.1 ± 30.6 | 167.3 ± 26.7 | 173.4 ± 27.8 | 0.200 |
| Transferrin saturation, % | 28.9 ± 12.9 | 28.5 ± 13.7 | 26.5 ± 15.5 | 0.736 |
| Ferritin, ng/mL | 435.3 ± 168.9 | 549.1 ± 230.0 | 456.7 ± 264.5 | 0.067 |
| **Nutritional markers** | | | | |
| Total proteins, g/dL | 6.9 ± 0.4 | 6.9 ± 0.4 | 6.7 ± 0.6 | 0.114 |
| Albumin, g/dL | 3.8 ± 0.6 | 3.6 ± 0.7 | 3.5 ± 0.7 | 0.351 |
| BMI, Kg/m2 | 26.7 ± 6.9 | 27.2 ± 6.6 | 27.4 ± 7.2 | 0.877 |
| nPCR, g/kg/day | 1.2 ± 0.2 | 1.1 ± 0.2 | 1.1 ± 0.2 | 0.271 |
| Relativefat, % | 34.7 ± 12.0 | 39.1 ± 11.0 | 43.1 ± 10.6 a) | 0.006 |
| FTI, kg/m2 | 13.5 ± 5.9 | 15.4 ± 5.8 | 17.1 ± 6.8 a) | 0.043 |
| LTI, kg/m2 | 13.6 ± 3.4 | 11.9 ± 2.6 | 10.4 ± 3.1 a) | < 0.001 |
| LTM, kg | 37.6 ± 11.6 | 30.6 ± 8.1 a) | 27.4 ± 10.8 a) | < 0.001 |
| ATM, kg | 36.5 ± 15.2 | 39.1 ± 14.0 | 42.3 ± 13.5 | 0.214 |
| OH, L | 1.2 ± 1.3 | 1.2 ± 1.1 | 1.3 ± 1.5 | 0.871 |
| **Abbreviated Lubben Social Network Scale** | | | | |
| Abbreviated Lubben Social Network Scale, total score | 17.7 ± 7.1 | 16.3 ± 6.9 a) | 11.8 ± 5.4 a) b) | 0.001 |

a) P < 0.05 *vs.* group I; b) P < 0.05 *vs.* group II.

CVC: Central venous catheter; URR: Urea reduction ratio; PTHi: Parathyroid hormone; RDW: Red cell distribution width; HDLc: High-density lipoprotein cholesterol; LDLc: Low-density lipoprotein cholesterol; MCV: Mean cell volume; MCH: Mean cell haemoglobin; MCHC: Mean cell haemoglobin concentration; BMI: Body mass index; nPCR: Normalized protein catabolic rate; FTI: Fat tissue index; LTI: Lean tissue index; LTM: Lean tissue mass; ATM: Adipose tissue mass; OH: Pre-dialysis hydration state

In this work, we aimed to evaluate the prevalence of depression in a group oflate-life patients with ESRD under OL-HDF, based on the geriatric depression scale (GDS) score and its associated variables, in order to develop interventions to improve depression symptoms, quality of life, adherence to dialysis prescription treatments and to reduce morbidity and mortality rates and health-care costs.

## Material and Methods

An observational cross-sectional study was carried out to evaluate the GDS score in patients with ESRD under OL-HDF. We evaluated 114 patients from a dialysis clinic in the north region of Portugal (66.8 ± 13.6 years; 50.88% males) under dialysis three times a week, for 3-5 hours. Synthetic high-flux polysulfone dialysers (Fresenius Medical Care, Bad Hamburg, Germany) were used. The aetiology of renal disease was diabetes in 58 (50.9%) and hypertension in 62 (54.4%) patients. Patients were excluded if they: did not agree to participate; were younger than 55 years old; had been receiving dialysis for less than three months; had malignancies, autoimmune diseases or acute inflammatory or infectious diseases. All participants gave their informed consent to participate in this work, previously approved by the Ethics Committee of the dialysis clinic. Anonymity of the patients was ensured, and all data were confidentially processed and stored.

## Data Collection

On the same day as the analytical evaluation of patients, they were invited to complete the questionnaires for the measurement of social support, using the abbreviated Lubben Social Network Sale (LSNS-6), and depression, using the GDS. When disabled or blind, patients would then have the help of a family member/friend or a physician of dialysis clinic to fill in the questionnaires. Patients' depression scale scores were assessed using the GDS previously adapted for Portugal [16]. Social support was measured with the Portuguese version of the abbreviated LSNS-6 [17]. Reliability, calculated with Cronbach's α, was higher than 0.73 for total score and for subscales of the abbreviated LSNS-6 scale [17], and 0.83 for the GDS scale [16]. In addition, sociodemographic data, comorbidities, time under dialysis and aetiology of kidney disease were collected from medical records. The analytical evaluation, which included haematological data, iron status and nutritional markers, performed on the same day as the questionnaire was also included as variables.

Blood was collected immediately before dialysis session. Hematological studies were performed by using an automatic blood cell counter (Sysmex K1000; Sysmex, Germany). Differential leukocyte count was evaluated by microscopy. Serum iron concentration was determined using a colorimetric method (Iron, Randox Laboratories Ltd., North Ireland, UK), whereas serum ferritin and transferrin were measured by immunoturbidimetry (Ferritin, Laboratories Ltd., North Ireland, UK; Transferrin, Laboratories Ltd., North Ireland, UK). Serum albumin levels were measured using a colorimetric assay end-point method (Albumin Plus; Roche GmbH, Mannheim, Germany). Serum total cholesterol and triglycerides concentrations were performed by enzymatic colorimetric tests (cholesterol oxidase-phenol aminophenazone and glycerol-3-phospate oxidase-phenol aminophenazone methods, Roche, respectively). High-density lipoprotein cholesterol (HDLc) and low-density lipoprotein cholesterol (LDLc) levels were measured using enzymatic colorimetric tests (Direct HDL Cholesterol and Direct LDL Cholesterol, Roche). Relative fat, fat tissue index (FTI), lean tissue index (LTI), lean tissue mass (LTM), adipose tissue mass (ATM) and overhydration (OH) were also evaluated using the Body Composition Monitor (BCM Fresenius Medical Care D GmbH) [13].

## Statistical Analysis

All variables are reported as mean ± standard deviation or as proportions. Data were analysed using the program SPSS 21.0 for Windows (SPSS, Inc., Chigago, IL). The normality of data was tested using the Kolmogorov-Smirnov test. Differences between groups were analysed by using one-way ANOVA test. Pearson or Spearman's rank correlation coefficients were used to evaluate relationships between sets of data. The association between categorical variables was analysed using the chi-squared test or Fisher's exact test. $P < 0.05$ was accepted as statistically significant.

## Results

The results were analysed in order to evaluate the prevalence of depression, and differences in sociodemographic, comorbidities and haematological data, iron status, dialysis adequacy, nutritional and inflammatory markers between the three groups of ESRD patients: non-depression (GDS score < 5), suggestive of depression (GDS score 5-8) and depression (GDS score ≥ 9).

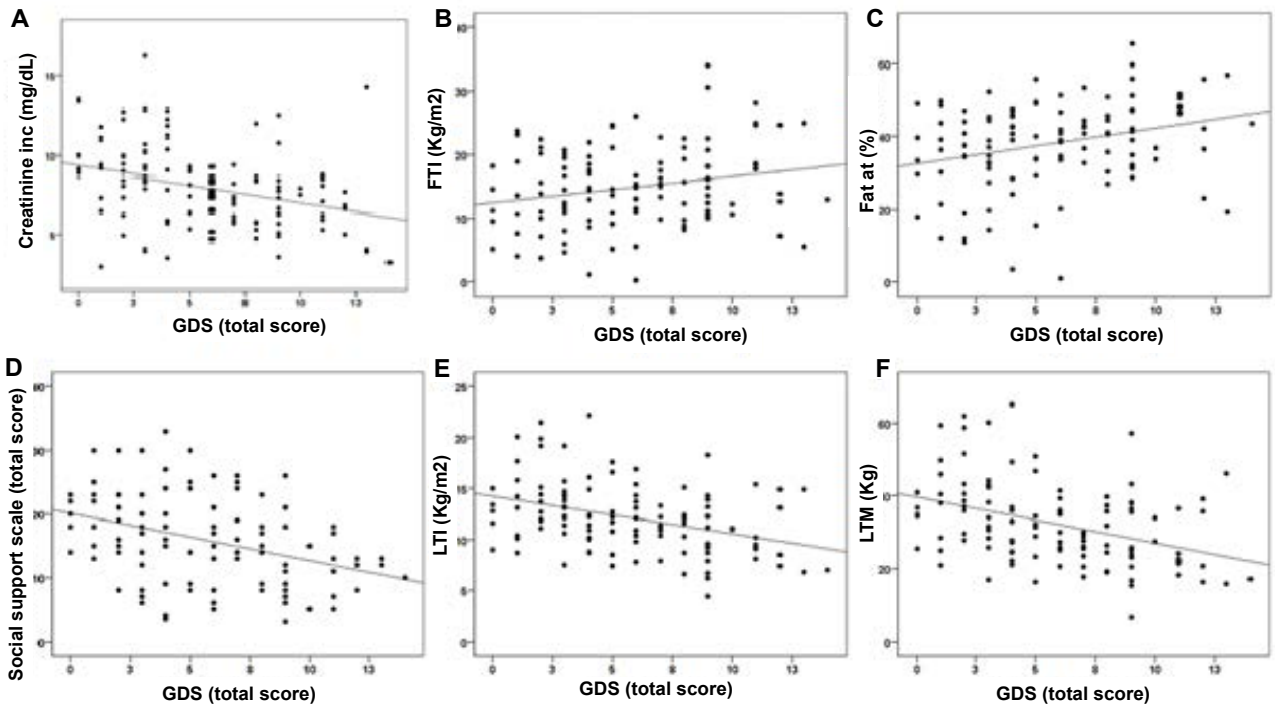


**Figure 1:** Significant positive correlation was found between GDS score and creatinine (A), FTI (B) and relative fat (C) and significant negative correlation was found with social support score (D), LTI (E) and LTM (F).

Thirty-three patients were included in the depressed group (28.9%), 32 in the suggestive of depression group (28.1%) and 49 in the non-depressed group (43%). When comparing the three groups of patients with ESRD, no significant differences were found in proportion of diabetic and hypertensive patients, diastolic and systolic pressure, number of drug prescribed, time under dialysis, central venous catheter use and BMI. However, significant differences were found in creatinine, substitution fluid volume, LTI and LTM, showing lower values in depressed patients (Table 1). On the other hand, relative fat and FTI showed higher values in depressed patients; age showed a higher value in patients with a suggestion of depression.

Moreover, a significant positive correlation was found between the GDS score and FTI ($r = 0.234$; $p = 0.014$) and relative fat ($r = 0.300$; $p = 0.001$); and a significant negative correlation was found with the social support score ($r = -0.372$; $p < 0.001$), creatinine ($r = -0.337$; $p < 0.001$), LTM ($r = -0.400$; $p < 0.001$) and LTI ($r = -0.390$; $p < 0.001$) (Figure 1).

## Discussion

Late-life patients with ESRD under dialysis showed a high prevalence of depression symptoms, which are independently associated with non-adherence, including drug therapy, fluid intake, diet and visits to health professionals, hospitalizations and mortality [1,3,18,19]. These findings highlight the potential clinical significance of depression symptoms, and the need for symptom-alleviating interventions in order to improve adherence and reduce health-care utilization and mortality rates. Several studies of late-life depressed patients showed that prognosis and outcomes in late-life depression patients appear to be lower when compared with younger depressed patients [20].

In this work, we found that 43% of patients presented a GDS score compatible with non-depression, (28.1%) suggestive of depression and (28.9%) depression. This prevalence is similar to that found in previous studies [3].

Slight or moderate increase in serum creatinine has been shown to be an independent risk factor of cardiovascular disease in the general population. However, in dialysis patients, it is dependent on muscle mass or meat ingestion and/or on the degree of dialysis efficiency, and it has been found to be inversely correlated with the risk of death. The results obtained in this study showed that high GDS scores were associated with low muscle mass, as suggested by the low levels of creatinine, LTI and LTM, and by the high relative fat and FTI. Indeed, depressed patients have less desire to eat [13] and so their muscle mass decreases, which makes their creatinine levels lower too, as well as the LTI and LTM, and the high relative fat and FTI. Indeed, our work showed a relationship between the GSD score and bio-impedance measurements, but not with BMI.

An association between substitution fluid volume and the GDS score was also found, suggesting that depression is associated with a decrease in dialysis adequacy. Dialysis adequacy markers are not independent variables, as they are influenced by protein intake and body composition. Patients with ESRD exhibit a weaker nutritional status with an increasing GDS score that may underlie the reduction in dialysis adequacy.

Social support has been shown to be a significant variable associated with the GDS score. Actually, social support affects health through behavioural, physiological and psychological mechanisms [18,19]. The characteristics of disease-associated symptoms and its treatments are functionally debilitating, affecting social relationships and activities of daily living. Moreover, it has been described that lower social support is associated with low survival and well-being [18,19]. Our results showed that lower social support is an important variable associated with a high GDS score, which is associated with depression. For these reasons, in clinical practice the promotion or improvement of patients' support networks, namely through emotional means, tangible efforts, information sharing or advice giving is of extreme importance [9,10]. This social support is important to improve depression status, and consequently the survival and quality of life of patients.

In conclusion, our results showed a high depression rate in patients with ESRD under dialysis, which is associated with low social support, decreased muscular mass and creatinine serum levels. It is important to consider social support as pivotal in non-pharmacological interventions to reduce depression, in order to enhance the adherence to medical plans, reduce health resource utilization and costs, and improve patient survival rates.

## Funding

Verónica A. Poveda P., MD, received support from the National Secretary of Higher Education, Science, Technology and Innovation (SENESCYT) No. 2259-ARG5-2014 and by the University Peninsula of Santa Elena, Ecuador. This work is supported by FCT/MEC through national funds and co-financed by FEDER under the Partnership Agreement (PT2020UID/MULTI/04378/2013 – POCI/01/0145/FERDER/007728, Norte-01-0145-FEDER-000024) and by FCT (UID/Multi/04378/2013), COMPETE-FEDER.

## Ethical Statement

**Conflict of Interest:** The authors report no conflicts of interest.

**Informed consent:** Informed consent was obtained from all individual participants included in the study.

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