RELATIONSHIP BETWEEN DEPRESSION, CLINICAL AND BIOCHEMICAL PARAMETERS IN PATIENTS UNDERGOING HAEMODIALYSIS

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SUMMARY

In this paper, we investigated the incidence of depression and its relation to clinical, laboratory parameters and sleep disorders in 45 haemodialysis (HD) patients. They were divided into two groups. Group A (n = 29) had no depression, whereas Group B (n = 16) had clinically assessed depression. Subjects were compared in terms of socioeconomic, clinical, laboratory parameters and presence of sleep disorders. Groups were matched for age, sex, family status, education, self-esteem, coffee and alcohol consumption, psychiatric history, time on HD and laboratory (serum urea, creatinine, electrolytes, iron, albumin and lipids) parameters. Group B demonstrated significantly lower haemoglobin levels (11.13 $\pm$ 1.69 and 12.23 $\pm$ 1.31 g/dl, respectively; $p < 0.01$) and higher C-Reactive Protein (CRP) levels (1.82 $\pm$ 1.73 and 0.83 $\pm$ 0.6 mg/dl, respectively; $p < 0.005$) compared to Group A. Additionally, strong correlation was observed when Hamilton Depression Scale scores were related to haemoglobin ($r = -0.30$, $p < 0.05$), CRP ($r = 0.38$, $p < 0.001$) and AIS scores ($r = 0.54$, $p < 0.0001$). In conclusion, depression seems to be related to high CRP, low haemoglobin levels and sleep disorders.

KEY WORDS **C-reactive protein • Depression • Haemodialysis • Haemoglobin**

INTRODUCTION

Haemodialysis (HD) has prolonged the life of patients with renal failure by reversing several of the metabolic derangements associated with the uraemic state. The quality of life (QOL) perceived by end-stage renal disease (ESRD) patients, however, remains poorer than that of the general population (Kimmel 2000; Valderrabano *et al.* 2001; Patel *et al.* 2002; Kastrouni *et al.* 2010). Focusing on the QOL of these patients is now of increasing importance particularly in light of evidence that QOL may potentially impact mortality in a variety of

BIODATA

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conditions, including ESRD (Kimmel *et al.* 1998; Kimmel 2000; Kalantar–Zadeh *et al.* 2001; Valderrabano *et al.* 2001; Mapes *et al.* 2003). The Dialysis Outcomes and Practice Pattern Study, a large, international observational study, demonstrated that QOL indicators from the Medical Outcomes Study Short Form (SF-36) were associated with differential survival and morbidity (Mapes *et al.* 2003).

Depressive disorder is a medical condition associated with significant subjective suffering, impairment of social and occupational functioning and lower health-related quality of life (Kastrouni *et al.* 2010). Specifically, depressive disorder typically presents with a complex set of overlapping symptoms with varying degrees of severity that can be classified as psychological, behavioural and somatic (physical; Cassano & Fava 2002). Psychological symptoms of depression are typically viewed as the defining key features of the disease and include anxiety, irritability, reduced concentration and motivation, feelings of hopelessness, excessive guilt, suicidal thoughts, hypersensitivity to criticism, perfectionism and indecisiveness (Kimmel & Peterson 2006). In addition, common behavioural symptoms of depression are psychomotor retardation or agitation, crying spells, anger attacks and interpersonal confrontation, avoidant behaviour and social withdrawal, reduced productivity, compulsive or ritualistic behaviours, substance abuse and less commonly self-injury (Tossani *et al.* 2005).

Some of these symptoms overlap with those of a variety of medical conditions, complicating the differential diagnosis. However, for many depressed patients, these somatic symptoms are an important part of their initial presentation. Despite the severity of the symptoms described, many sufferers do not seek treatment and of those who do, significant numbers are improperly diagnosed or inappropriately treated because of existence of diagnostic problems that centre on adjustment, mood disorders and origin in the body systems.

The aim of this cross-sectional study is to determine the prevalence of depression in ESRD patients treated with HD, to investigate the association with demographic and lifestyle variables and to assess its relation to clinical and laboratory parameters.

PATIENTS AND METHODS

Our unit has 61 HD patients.

Inclusion criteria for study:

On HD for at least six months;
In a clinically stable condition;
Being ambulant.

Exclusion criteria were:

Clinically evident cerebrovascular disease;
Major psychiatric illness;
Major visual or hearing impairment.

Twelve patients were excluded because they met one or more of the exclusion criteria. Four patients declined to participate. Thus, 45 patients (32 male and 13 female with mean age 59 $\pm$ 16.2 years) on chronic HD were evaluated. Consent was required before entering the study.

Patients were screened for depression using the Hamilton Depression Scale (HAMD; Snaith 1996). This scale was introduced by Max Hamilton in 1960 and includes 17 questions. Each answer is rated on a five-point scale. Total scores 0–6 are considered normal, 7–17 mean mild depression, 18–24 moderate or average depression and $\geq$24 represent severe depression (Snaith 1996). According to HAMD scores, the patients were then divided into two groups. Group A with score 0–7 (absence of depression) and Group B that included patients scoring higher than 7 (clinically assessed disorder).

The selection of covariates was guided by parameters that were found to be associated with the presence of depression in the general population and among dialysis patients. Depression has been associated with demographic factors such as age and gender. It is also likely that socioeconomic factors affect mood, an effect that is possibly stress-induced. Therefore, marital status, employment, level of education, psychological well-being, self esteem and lifestyle factors such as current cigarette smoking, alcohol (at least one unit of alcohol per day) and coffee (at least one cup of coffee per day) use seem to influence the incidence of depressive disorders and as such, they were considered during our study. Individual and family psychiatric histories that were significant elements have been investigated. Dialysis treatment-related factors and demographics (Table 1) and laboratory tests (Table 2) were evaluated. Patients undergoing dialysis often have substantial comorbidity and exhibit elevated levels of inflammatory markers, both of which have been associated with depressive disorder. Therefore, we examined the coexistence of diabetes and ischemic heart disease evaluating C-Reactive Protein (CRP) levels. Lastly, the Athens Insomnia Scale (AIS) was used to assess

	Group A	Group B	*p*
Patients	29 (65%)	16 (35%)	–
Gender (M/F)	22/7	10/6	0.546
Age (years)	58.3 ± 17.4	60.6 ± 14.4	0.657
Mode of dialysis (HD/HF)	22/7	10/6	0.228
Time in HD (years)	5.4 ± 4.2	6.1 ± 3.7	0.647
Smoking (Y/N)	11/18	4/12	0.582
Alcohol (Y/N)	12/17	7/9	1.0
Coffee (Y/N)	25/4	12/4	0.593

Table 1: Demographic dialysis-related and lifestyle factors.

	Group A	Group B	*p*
Haemoglobin (g/dl)	12.2 ± 1.3	11.1 ± 1.6	0.009
Ferrum (mg/dl)	83.1 ± 42.6	80.4 ± 34.2	0.843
Urea (mg/dl)	144 ± 29.2	158.4 ± 35.3	0.150
Creatinine (mg/dl)	8.5 ± 2.2	7.2 ± 1.7	0.502
Potassium (mEq/l)	5.9 ± 1.1	6.1 ± 0.8	0.475
Albumin (g/dl)	3.9 ± 0.24	3.73 ± 0.38	0.115
Cholesterol (mg/dl)	169.1 ± 45.9	177.3 ± 35.4	0.542
Triglycerides (mg/dl)	170.8 ± 101.2	198.7 ± 82.2	0.351
HDL (mg/dl)	34.7 ± 7.3	34.5 ± 8.9	0.906
LDL (mg/dl)	99.5 ± 30.6	103.4 ± 27.9	0.680
VLDL (mg/dl)	34.1 ± 20.2	39.8 ± 16.4	0.345
CRP (mg/dl)	0.83 ± 0.6	1.82 ± 1.73	0.005

Table 2: Laboratory factors.

sleep quality. More specifically, the former has been used to assess individual sleep complaints, measure overall sleep quality and to identify cases of clinically significant insomnia. The AIS consists of eight items. The first five items cover night-time symptoms of insomnia (difficulty initiating sleep, difficulty maintaining sleep and early morning awakening) and three items probe daytime consequences of disturbed sleep (well-being, functioning capacity and daytime sleepiness). Score ≥6 is considered insomnia (Soldatos *et al.* 2003).

The statistical methods used were chi-square test with Yates correction (Table 1) and Student's t-test (Table 2) as appropriate. Statistically significant difference between the means of the two samples at the 95% confidence level $p < 0.05$. A linear model was used to describe the relation between the examined values (R^2 statistics).

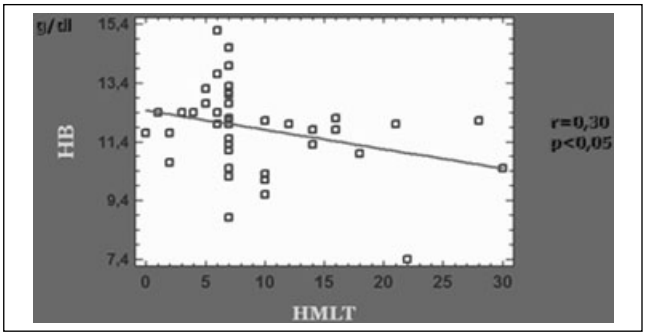

Figure 1: Correlation of haemoglobin levels with Hamilton score.

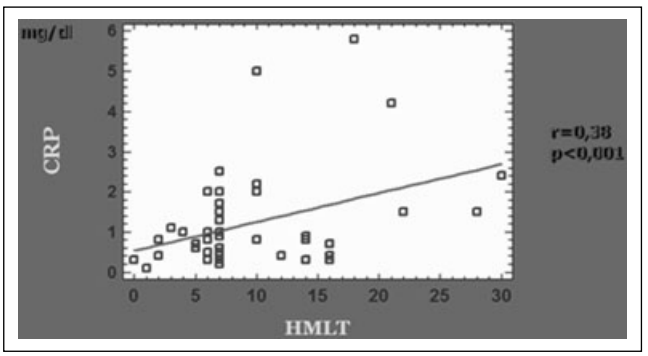

Figure 2: Correlation of CRP levels with Hamilton score.

RESULTS

Sixteen (35%) out of 45 patients were diagnosed as suffering from clinically assessable depressive disorder. Non-significant difference was observed with respect to demographics and duration and mode of HD (Table 1) and the various laboratory parameters examined (Table 2). Group B compared to Group A demonstrated significantly lower haemoglobin levels (11.13 ± 1.69 and 12.23 ± 1.31 g/dl, respectively; $p < 0.01$) and higher CRP levels (1.82 ± 1.73 and 0.83 ± 0.6 mg/dl, respectively; $p < 0.005$). Additionally, strong correlation was observed when HAMD scores were related to haemoglobin ($r = -0.30$, $p < 0.05$), CRP ($r = 0.38$, $p < 0.001$) and AIS scores ($r = 0.54$, $p < 0.0001$; Figures 1–3).

DISCUSSION

There is a substantial body of literature documenting the increased prevalence of depression in several chronic medical illnesses, with some evidence for depression amplifying the deleterious effects of medical illness and even leading to increased mortality. Particularly, in the last decade, increased

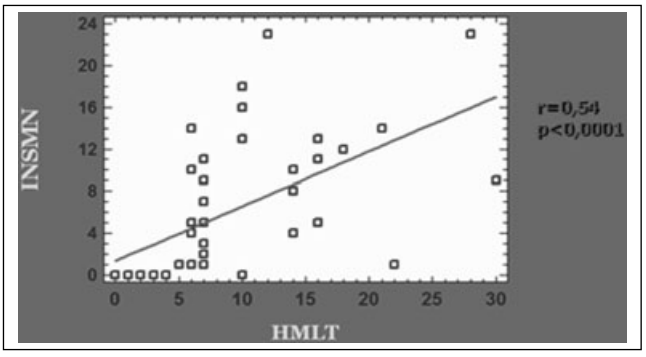

Figure 3: Correlation of insomnia score with Hamilton score.

interest in the study of depression in patients with ESRD has been observed because it represents the most frequent psychiatric disorder in patients suffering from kidney disease (Fabrazzo & De Santo 2006).

Patients with ESRD, receiving HD, have to adapt to a chronic physical illness and the necessity for dependence on a dialysis machine to stay alive. Adjustment in cognitive, emotional and behavioural terms is required by patients and their families. The period of adjustment occurs over weeks and months and may be likened to a grief reaction with depressive symptoms sometimes developing as part of this process (Tossani *et al.* 2005).

Several studies report an incidence rate of depression in HD patients that varies between 10% and 100% (Lee *et al.* 2004). The reasons for these variations are considered to be: (1) depressive symptoms have many similarities with uraemia symptoms and (2) the different methodologies between studies (Christensen 1997; Tossani *et al.* 2005).

This study is in accordance within these findings as we report an incidence of 35% of depression in our HD patients. Moreover, in a similar study conducted by Dogan *et al.* (2005) in 43 HD patients, an attempt was made to correlate depression with various biochemical parameters. Participants were divided into two groups according to HAMD score. Comparisons were made in regard to QOL, CRP levels, haemoglobin and serum albumin. Patients suffering from depression were found to have lower QOL scores, haemoglobin and albumin levels and higher CRP levels.

We also found that CRP is elevated in dialysis patients suffering from depression while haemoglobin is lower. Elevated CRP has also been found in obese men with depression (Ford & Erlinger 2004).

Contrary to the study performed by Dogan *et al.* (2005), our study found no significant difference in serum albumin levels between the two groups. It is possible that the low albumin level in the Dogan study represents a poor nutritional status of the depressive patients. The absence of difference in our study may well reflect the greater supportive role of the family in Greek population (Kastrouni *et al.* 2010).

Because some authors believe that increased cytokine levels in the blood can trigger depressive symptoms, whereas others support a causal relationship between increased cytokine production and depression, a correlation between pro-inflammatory cytokines and depression in dialysis patients has been attempted (Abdel-Rahman *et al.* 2011). More specifically, IL-6 is elevated both in patients undergoing HD (Pereira *et al.* 1994; Capelli *et al.* 1998) and in patients with depression but otherwise healthy (Ladwig *et al.* 2003).

On the other hand, anti-depressive treatment appears to decrease the secretion of the pro-inflammatory cytokines. Among them, baseline IL-6 blood levels seem to be related with the outcome of this treatment, and failure to decrease levels is associated with a lack of response to anti-depressants (Kimmel *et al.* 1993; Abdel-Rahman *et al.* 2011). Furthermore, high levels of IL-6 and CRP have been related to anxiety and anorexia in HD individuals (Bossola *et al.* 2010). We have attempted to correlate depression and cytokine levels, but the method is very costly and sensitive to errors. For these reasons, this study is ongoing and the results are awaited with interest.

CONCLUSION

Our study demonstrates that clinically overt depression is common in HD patients and seems to be related to high CRP and low haemoglobin levels. Moreover, a strong correlation to sleep disorders, which are equally common to such patients, appears to be present. However, because this is a cross-sectional study and has only a small number of participants this study does have limitations. More research with larger numbers of participants is needed.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION STATEMENT

Dr. Bornivelli, Dr. Aperis and Dr. Paliouras wrote the Patients and Methods section, Dr. Bornivelli and Dr. Aperis wrote the Introduction, Dr. Giannikouris, Dr. Paliouras and Dr. Aperis wrote the Discussion, Dr. Alivanis and Dr. Aperis revised the manuscript, Dr. Alivanis and Dr. Aperis prepared the Abstract.

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