

ASSOCIATION BETWEEN DEPRESSION AND HEMODIALYSIS IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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SUMMARY

Depression is the most common and serious psychiatric disorder that affects patients with chronic kidney disease and end-stage renal disease, and, has a significant impact on their quality of life. The aim of this study was to investigate and compare prevalence rates of depression among hemodialyzed patients, and non-dialyzed patients with a glomerular filtration rate <30 ml/min/1.73m² receiving conservative treatment or following kidney transplantation. A total of 50 hemodialyzed and 50 non-dialyzed patients with stage 4/5 of CKD was assessed using the following questionnaires: Hamilton Anxiety Rating Scale (HAM-A), Hamilton Depression Rating Scale (HAM-D), The Satisfaction with Life Scale (SWLS), The Acceptance of Illness Scale (AIS), and The Life Orientation Test-Revised (LOT-R). The use of steroids and immunosuppressant drugs was also investigated. Symptoms of depression and anxiety were present in both groups, however the proportion of persons with mild or severe depression was higher among dialyzed patients. The AIS, LOT-R and SWLS scores were very similar in both the groups. The patients using steroids and/or immunosuppressant drugs were more prone to develop mild or severe depression according to the HAM-D scores. The results indicated a high prevalence of depression and anxiety among patients with CKD. Furthermore, the fraction of patients with depression is greater among hemodialyzed patients. This indicates the importance of monitoring the mental state of the patients as well as the necessity of providing timely psychological care for patients with CKD.

Key words: chronic kidney disease – depression - hemodialysis

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INTRODUCTION

Depression is a well-known problem among both hemodialyzed and non-dialyzed patients with CKD that significantly contributes to the morbidity and mortality associated with CKD (Cukor et al. 2007). While the assessment of the prevalence of depression among patients with end-stage renal disease (ESRD) is challenging the problem has recently garnered much scientific attention (Cukor et al. 2014). Moreover only a few studies have compared the prevalence rate of depression between hemodialyzed and non-dialyzed patients. Even fewer studies have investigated the prevalence of other psychopathologies among patients with ESRD (Cukor et al. 2007).

Previous research has shown that mental disorders complicate the treatment of many chronic diseases. Furthermore, depression occurring with another illness such as CKD might be more resistant to treatment (Kimmel et al. 2005). Depression has been associated with a decreased quality of life (Drayer et al. 2006) and lower survival rate in patients with ESRD (Cukor et al. 2014). Although most of the studies concentrate on depression associated with hemodialysis and peritoneal dialysis, the problem is equally striking among non-dialyzed patients with CKD.

The aim of this study was to investigate the prevalence of depression among hemodialyzed patients and non-dialyzed patients with glomerular filtration rate (GFR) < 30 ml/min/1.73m² as well as to extend the

knowledge about how the method of treatment of CKD contributes to the patients' mental health.

SUBJECTS AND METHODS

The study was approved by the Bioethical Committee of the Medical University of Silesia. The participants were selected from adults on hemodialysis units and internal wards with GFR level below 30 ml/min/1.73m² in Katowice, Poznan and Bielsko-Biala. The patients were divided into two study groups each containing 50 patients; informed consent was obtained from every participant. The patients were tested using the following scales: The Hamilton Depression Rating Scale (HAM-D), The Hamilton Anxiety Scale (HAM-A), The Life Orientation Test Revised (LOT-R), The Satisfaction with Life Scale (SWLS), and The Acceptance of Illness Scale (AIS). The effect of steroids on depression was calculated by converting all the doses into their prednisone equivalent.

Measures

Hamilton Depression Rating Scale (HAM-D)

The HAM-D scale was for assessing patients suffering from affective disorders (Hamilton et al. 1960). The scale contains 21 questions and the patients are provided with 5 (or 3) possible responses with points varying from 0 to 4 (or 0 to 2). The HAM-D scale is frequently used in clinical trials, even though the results mainly depend on the interviewer (Pudlo et al. 2009).

Hamilton Anxiety Scale (HAM-A)

This scale was one of the first scales developed to assess the severity of anxiety (Hamilton et al. 1959). It contains 14 items that measure both somatic and psychological anxiety. Although the scale does not provide a standardized probe of questions it is widely used in clinical trials (Pudlo et al. 2009).

The Acceptance of Illness Scale (AIS)

The level of acceptance of a chronic illness is an important predictor of the quality of life of patients (Mazurek et al. 2014). Studies have shown that the greater the acceptance of illness the better the quality of the patient's life. As this scale assesses the acceptance of the disease fairly well, it is widely used in clinical trials.

The Satisfaction with Life Scale (SWLS)

The SWLS scale measures the global life satisfaction, which has favourable psychometric properties (Diener et al. 1985). The patients are presented with 5 statements, which they may or may not agree with. There responses range from 1 (I completely disagree) to 7 (I completely agree).

The Life Orientation Test Revised (LOT-R)

This test measures dispositional optimism and its relationship with the psychological well-being, sense of mastery and sense of coherence (Chiesi et al. 2013). The test consists of 10 statements and the patients are provided with 5 possible answers ranging from 'I completely disagree' to 'I completely agree'. The test has been used in many trials conducted to demonstrate the clinical consequences of the patients' attitude.

Data analysis

The statistical analysis was performed using SPSS Statistics version 12.5. The results were considered statistically significant when the significance level (p) was lower than 0.05.

RESULTS

Of the 102 patients with CKD originally enrolled in this study, 2 hemodialyzed patients were excluded as they used antidepressants during the period of the study. The patients were divided into two groups, namely the hemodialyzed and the second of non-dialyzed groups. The first group consisted of 22 men and 28 women aged from 20 to 80 years (mean \pm SD 51.3 \pm 16.6 years). In this group 8 patients were undergoing steroid treatment during the study period. The second group consisted of 26 men and 24 women aged from 21 to 82 years (mean \pm SD 52.1 \pm 16.3 years). 8 patients received a kidney transplant, while 15 patients were undergoing steroid treatment during the study period.

The average HAM-D score of patients in hemodialyzed group was 11.88 (SD \pm 7.54 indicating mild depression). It is interesting that men scored higher 13.05 (SD \pm 6.95) then the women (10.96 SD \pm 7.98) in this

test. The mean HAM-D score of the patients in non-dialyzed group was 9.98 (SD \pm 6.13) also indicating mild depression. However the women in this group suffered from more severe depression (12.17 SD \pm 7.21) than men (7.96 SD \pm 4.12). Spearman's rank correlation coefficient revealed a statistically significant correlation between the age of the patient and the result in HAM-D score ($p=0.027$, $R=-0.313$) in the hemodialyzed group; the sign of correlation coefficient was reversed in the non-dialyzed group ($p=0.046$, $R=0.284$). Furthermore there was a significant correlation ($p=0.038$, $R=0.479$) between steroid dosage and the HAM-D score in both the groups; the mean prednisone dose was 30.43 mg (Figure 1-4).

The average HAM-A score of patients in the hemodialyzed group was 12.72 \pm 9.19, indicating a rare occurrence of anxiety in this group. The results were similar for women (12.64 \pm 9.77) and men (12.82 \pm 8.61). The average HAM-A score of patients in the non-dialyzed group was 10.16 \pm 7.56; the average score for women was 12.25 \pm 8.41, while that for men was 8.23 \pm 6.25.

The AIS scores were very similar in both the groups and are (25.12 SD \pm 7.31) and 26.67 (SD \pm 7.55) for hemodialyzed and non-dialyzed groups, respectively. The results match those obtained in different studies, as the mean value for the hemodialyzed patients was 25.32. Although neither the method of treatment nor sex had a statistically significant effect on the AIS scores of patients in both the groups, there was a trend of correlation between the AIS score and the duration of dialysis ($p=0.085$, $R=0.246$).

The LOT-R scores suggest that the method of treating CKD has no influence on the optimism levels of the patients. The average LOT-R score was 5.52 \pm 1.76 for patients in the hemodialyzed group and 6.18 \pm 1.99 for those in the non-dialyzed group.

The SWLS scores indicate that the treatment method does not influence the patients' satisfaction with life, and that the most important factor is age. The mean SWLS score was 5.00 \pm 2.31 for patients in the dialyzed group and 5.34 \pm 2.10 for those in the non-dialyzed group. Table 1 shows all correlations obtained by non-dialyzed patients while Table 2 demonstrates all correlations obtained by dialyzed patients.

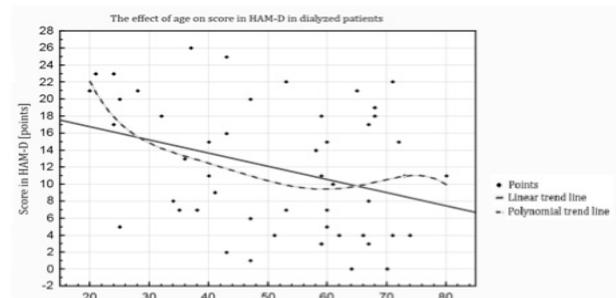


Figure 1. Correlations between age and HAM-D for dialyzed patients

Table 1. Correlations obtained by non-dialyzed patients

	HAM-D	HAM-A	AIS	SWLS	LOT-R
Age	0.283617	0.711211	0.026565	0.228699	-0.030797
Gender	-2.087480*	-1.912710	1.068151	0.970920	0.796150
Duration of the disease	-0.245866	-0.111946	0.012383	0.056388	0.051234

Statistically significant results are marked by *. Relationships between age/duration of the disease and HAM-D, HAM-A, AIS, SWLS, LOT-R are calculated by Spearman rank correlation coefficient. Connection between gender and HAM -D, HAM-A, AIS, SWLS, LOT-R are calculated by Man-Whitney U test

Table 2. Correlations obtained by dialyzed patients

	HAM-D	HAM-A	AIS	SWLS	LOT-R
Age	-0.130568	-0.113805	0.067724	-0.007100	0.123018
Gender**	0.947890	0.371340	-1.895789	-0.592970	0.527690
Duration of the dialysis	-0.313007*	-0.245362	0.246252	0.054239	0.220376

Statistically significant results are marked by *. Relationships between age/duration the disease and HAM-D, HAM-A, AIS, SWLS, LOT-R are calculated by Spearman rank correlation coefficient. Connection between gender and HAM-D, HAM-A, AIS, SWLS, LOT-R are calculated by Man-Whitney U test

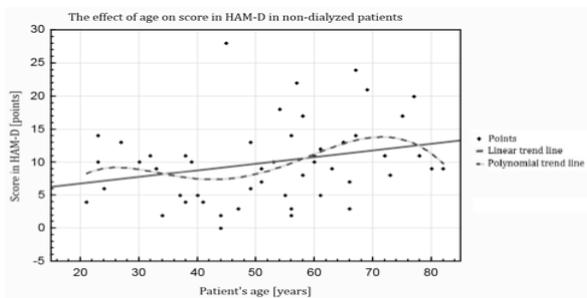


Figure 2. Correlations between age and HAM-D for non-dialyzed patients

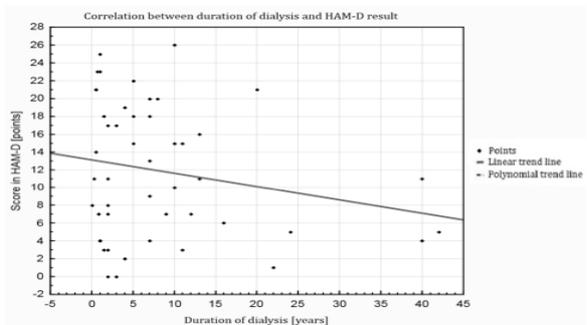


Figure 3. Correlations between duration of dialysis and HAM-D result

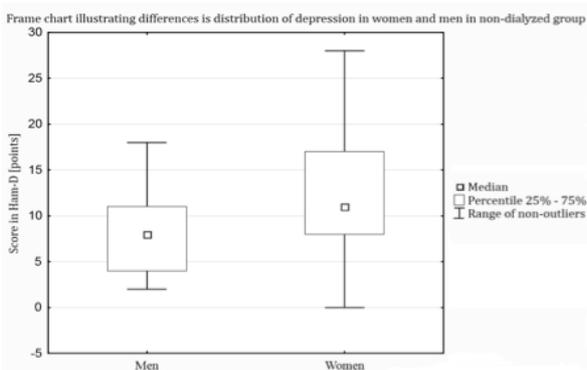


Figure 4. Differences in distribution of depression in women and man in non-dialyzed group

DISCUSSION

While the occurrence of depression among dialyzed patients is well established, only a few studies have compared the prevalence rates of depression between hemodialyzed and non-dialyzed patients with CKD. The current estimates suggest a 20-30% prevalence rate of depression in hemodialyzed patients with CKD (Cukor et al. 2007). However, the numbers based on this study were dramatically different as 60% of the patients in the hemodialyzed group met the diagnostic criteria for depression. One of the reasons for such a difference might be the different diagnostic instruments used in different studies (Cukor et al. 2007); the Beck Depression Inventory, a self-assessment scale, was used in the earlier study, as opposed to the Hamilton Depression Rating Scale used in this study. Another reason may be the fact that the effect of steroid use on depression was also calculated, while the studies mentioned above did not take into account the effect of steroids.

Another study (Diener et al. 1985) has reported a similar prevalence rate of depression in patients as that reported in this study, indicating the possible role of steroids in the development of depressive symptoms. The percentage of patients with depression in the non-dialyzed group was 64%, although mild depression was the most common type of depression seen in approximately 70% of the patients with depression.

The sample contained 2 hemodialyzed patients who were taking antidepressants during the study period; these patients were excluded from the analysis. None of the patients showing symptoms of depression were undergoing any psychiatric treatment, which not only highlights how under-recognized depression and anxiety are, but also hints at the insufficient attention from the medical personnel on the nephrology wards. The authors assume that the high prevalence of depression among hemodialyzed patients is an effect of many biological and psychological factors.

Many recent studies investigate the correlation between the levels of inflammatory cytokines and depressive symptoms. One of these studies (Diener et al. 1985) suggests that the imbalance between the levels of pro- and anti-inflammatory cytokines, rather than the absolute levels of pro-inflammatory cytokines, is associated with depression in hemodialyzed patients. However, this hypothesis cannot be confirmed at present as the authors only discuss the psychological origins of the disease. Hemodialyzed patients mostly complained of a lack of independence and being a burden to a family. Moreover, a majority of them was unable to work which only intensified the feeling of uselessness. In case of non-dialyzed patients, the uncertainty about the future treatment, which caused constantly increasing stress levels, could be a major reason for the depression.

Many factors that could have an impact on the severity of depression such as sex, age, and the length of the treatment, were analyzed. Of these, only the correlation between age and the HAM-D score was statistically significant. Spearman's rank correlation revealed that while younger dialyzed patients struggle with more severe depression, the direction (sign) of the correlation is reversed in non-dialyzed patients. When the patients are younger, dialysis impacts the quality of life and social functioning during the prime earning and child-rearing years; these patients also tend to accept dialysis as a part of their everyday life. In non-dialyzed patients, the result demonstrates that frequent examinations in the hospital and daily use of medication are much less limiting than dialysis. Furthermore, the effect of steroid use on depression was evaluated, and the results suggest that the severity of depression increases with an increase in the dose of steroids. These results match those from other studies that also claim that higher doses of prednisone might lead to the development of depressive symptoms. The detailed investigation of patient characteristics, differences between studies, demographic data, and laboratory data might make it possible to demonstrate a consistent prevalence rate of depression among patients with chronic kidney disease across studies.

As for the occurrence of anxiety, the results show that most of the patients in both the groups do not develop this condition. Only a small number of participants met the diagnostic criteria for mild anxiety, and the prevalence rates of severe and moderate anxiety were very low. However, these outcomes may be inaccurate as it was often difficult to determine if the somatic anxiety symptoms that the patients presented with were a result of a comorbid mental disorder or the primary disease itself. The results obtained in this study suggest that the test has poor predictive value in hemodialyzed patients or patients with stage 4 CKD, and other assessment strategies are necessary in order to improve the diagnosis of anxiety disorder (Cukor et al. 2008).

The mean AIS score of patients in the hemodialyzed group (25.12) matches the one observed in a previous Polish study investigating AIS scores in a similar group of patients (25.32). This study also assessed the AIS scores for other sub-groups: 28.13 for women with breast and uterus cancers; 22.14 for men after heart infarction; 18.46 for patients with chronic pain; and 24.81 for patients with diabetes. These findings indicate that hemodialysis may not be such an inconvenience to the patients; however, as mentioned earlier, the acceptance of the procedure comes with time. Although there was no statistically significant correlation between AIS scores and the duration of dialysis, there was a visible trend that was close to reaching a p value of 0.05.

The LOT-R test showed almost no difference between the scores of patients in the hemodialyzed and non-dialyzed groups, indicating that the patients' optimism levels are not affected by the method used to treat the CKD. Another Polish study investigating the impact of chronic diseases on the LOT-R scores also found that hemodialyzed patients had LOT-R scores of ~6 similar to that reported by us.

Finally, the SWLS scores were very similar in the two groups and also matched those reported by Juczynski et al. (2009) (~5), slightly lower than that observed among healthy adults and patients with diabetics, and a little higher than that observed among men after heart infarction.

CONCLUSIONS

The aim of this study was to investigate the prevalence rates of depression among hemodialyzed patients and patients with CKD with a GFR below 30 ml/min/1.73 m². The authors also sought to understand the impact of steroids on the depressive mood. The study has shown a correlation between age and the occurrence of depression in both the groups. Moreover, the results indicate that higher doses of prednisone are associated with higher prevalence of depressive symptoms. No psychiatric intervention was administered during the course of our study, given its observational nature. One limitation of our study is its relatively small sample size; all of the presented results should, therefore, be confirmed in a large prospective study.

These findings imply the necessity of training medical personnel working in nephrology wards to pay a closer attention to behavior of the patients. Timely psychiatric help may be essential in order to improve the patients' mental state and quality of life, both of which may contribute to the efficacy of the primary treatment.

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Contribution of individual authors:

Aleksandra Ćwiek: design and conception of the study, collection and analysis of data;
Marcelina Czok: design of the study, data collection
Bartłomiej Kurczab: data analysis, literature searches
Krzysztof Kramarczyk: data collection, literature searches;
Karolina Drzyzga: design and conception of the study, literature searches;
Krzysztof Kucia: design and conception of the study
All authors participated in the final revision of the manuscript and approved it.

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