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Relationship of Diabetes Mellitus and Dementia in Chronic Haemodialysis Patients

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Abstract

Introduction: Patients suffering from final stage kidney disease (ESRD) and undergo an inveterate haemodialysis often suffer from depression and dementia. Many of them were driven to ESRD through the disease of Diabetes Mellitus (DM). However, the relation between diabetes and depression and/or dementia to those patients who are subjected to dialysis has not yet been efficiently investigated.

Objective: The purpose of the study was to investigate the effect of diabetes on depression and dementia for the patients who undergo continuous dialysis.

Methodology: 53 patients of an average age 69.57 ± 13.02 years (Male/Female=38/15) out of which 27 were diabetic and 26 were not, who were undergoing chronic dialysis for 28.34±56,36 months. All the patients provided replies to the standardized questionnaires "Mini Mental State Examination" (MMSE) and "Hospital Anxiety and Depression Scale" (HADS) in the form of an interview during dialysis so that to ascertain the level of depression and dementia. Moreover, blood samples were taken in order to determine haemoglobin, the efficiency of the dialysis (kt/V) the levels of natrium, potassium, calcium and phosphorus in their blood, as well as the levels of C-reactive protein (CRP).

Results: The level of depression and dementia of the whole of the patients examined was correspondent to a moderate level of illness (13.91±10.56 and 15.00±5.49 respectively). In a comparison between the diabetics and the non-diabetics the results indicated a statistically notable difference for the patients suffering from diabetes who displayed a high-level depression (17.63±10.63 vs 10.04±9.15, $p<0.05$). The level of dementia was that of an average degree both for the diabetics and the non-diabetic, however there was a significant gap in numbers between the two groups (13.19±5.19 vs 16.88±5.23, $p<0.05$). The results of the non-diabetic patients showed a noteworthy difference regarding the depression level between men and women was established (8.79±7.70 vs 13.43±12.35, $p<0.05$). Nevertheless, the same distinguishable difference concerning the level of dementia was not statistically determined. Regarding the group of the diabetic patients a substantial difference between the two genders was not observed. A connection between the levels of CRP non-diabetic patients ($r=0.487$, $p<0.05$) but not of the diabetic patients has also been discovered. As far as the rest of the parameters are concerned, there was no noteworthy correlation.

Conclusions: Depression is closely related with the presence of diabetes for the patients undergoing dialysis, being of a higher degree for the diabetics. The degree of dementia is higher in those suffering from diabetes but not of an important level.

Keywords: Alzheimer's disease; Dialysis; Diabetes; MMSE; HADS

Abbreviations: DM: Diabetes Mellitus; WHO: World Health Organization; DR: Diabetic Retinopathy; DN: Diabetic Nephropathy; GFR: Glomerular Filtration Rate; AD: Alzheimer's Disease; ADI: Alzheimer's Disease International; ESRD: End-Stage Renal Disease; HADS: Hospital Anxiety And Depression Scale; MMSE: Mini Mental State Examination; HD: Haemodialysis; CKD: Chronic Kidney Disease.

Introduction

Doubtless, developed countries have nowadays finally dealt with most of the diseases of the past, resulting in a significant increase of life expectancy of their citizens. At the same time, however, it has been noticed that developed countries are now suffering from so-called civilization diseases. Modern maladies include malignant neoplasms, respiratory and circulatory diseases, diabetes mellitus and dementia [1].

In recent years, the incidence of diabetes mellitus (DM) increases in almost all European countries, and more generally in the whole world [2]. The DM is considered to be one of the major chronic diseases for the 21st century with a pandemic character. According to the World Health Organization (WHO), the number of people with DM has reached 422 million, while in the age group for adults it is 8.5% (World Health Organization 2016). As far as Greece is concerned, according to the official figures of the International Federation of Diabetes, the incidence of DM is 7.04%. Especially for DM II, the incidence rate is between 6.9% to 8.7% and it is expected to rise to a higher rate in the following years.

Patients suffering for several years from DM may develop complications that affect the eyes, kidneys, nerves or large arteries. Large arteries in diabetic patients are affected by coronary artery disease, stroke and peripheral arterial disease. Specific pathognomonic complications that are present only in DM are diabetic retinopathy (DR), diabetic nephropathy (DN), diabetic neuropathy and certain skin manifestations that are considered to a large or minor extent to be complications of microangiopathy.

As mentioned above, a complication of DM is the DN. Kidneys play an important role in insulin metabolism, as 40% of insulin is metabolized by them. As glomerular filtration rate (GFR) decreases in the case of renal failure, insulin transfer also decreases in proximal glomerular cells, where it is metabolized. According to the Hellenic Nephrology Society the DN is divided into 5 stages. The basis for staging is the glomerular filtration rate (GFR) measured during creatinine clearance. The lower the GFR, the heavier the decline in renal function. In the fourth and fifth stage of renal failure, with GFR less than 10% of the normal value, end-stage uremia or renal disease occurs and nitrogen compounds (eg urea, creatinine, phenols) are added at toxic levels to the rest of the systems. At this stage, haemodialysis or kidney transplantation is necessary for patients' survival [3].

As mentioned above, dementia is one of the diseases that has become epidemic. It should be clarified that dementia is not a disease but is a set of symptoms that indicate the decline in cognitive function of the individual, such as memory, decision making and argumentation. Some of the forms of dementia are reversible. Those suffering from dementia may not be able to perform routine actions to deal with everyday life. The two most known cases of dementia are Alzheimer's disease (NA) and vascular dementia caused by disorders in the blood flow of the brain. Alzheimer's disease is the most common cause of dementia and is not reversible. It is defined according to the Alzheimer's disease and Related Disorders Association as the progressive neurodegenerative disorder with characteristic clinical and neuropathological findings with gradual disorganization of cognitive and functional abilities resulting in disruption of the professional and social obligations of the individual. There are individual differences in starting age, type of cognitive disorders and rate of disorganization. A prerequisite is that no other immune entity may be implicated that could cause dementia. The NA is today a real scourge in society, considering the medical costs and the social but also the purely human factor with the financial, physical and mental burden on the patients, their relatives and their environment.

Wimo, et al. [4] calculated the costs of AD comparing 2010 figures to those of 2015. According to the Alzheimer's Disease International (ADI) the disease costed US $ 604 billion in 2010, equivalent to 1% World Gross Product. The equivalent figure was raises to $ 818 billion in 2015, an increase of 35%, and it was estimated that in 2018 it would exceed S 1 trillion. Norton et al. [5] refer to a survey by Ferri, et al. (2005) for Europe which estimated that the number of people suffering from AD in Europe would rise from 7.7 million in 2001 to 15.9 in 2040, taking into account the aging population of the continent, but also generally advanced countries. Thus, today researchers are talking about a "burden" of the disease [6,7].

In our research we investigated the possible correlation of these three diseases with each other, ie the relationship of DM and dementia to patients with end-stage chronic renal insufficiency who undergo haemodialysis. Through haematological examinations and the depression scale, it was investigated whether or not DM leads these patients to dementia. For this purpose, biochemical and general blood tests as well as the HADS questionnaire measuring the rate of depression were related to the test MMSE that measures the presence of dementia.

Methodology

Sample and Data Collection Process

Our population consisted of patients with end-stage renal disease (ESRD) with DM and no DM, who were enrolled in a haemodialysis program in a private unit of chronic haemodialysis (HD). The number of patients who were registered in the unit and followed the treatment schedule of HD in the investigation period (1-15 December 2016) was 65. Therefore, 65 questionnaires were administered and 52 were completed and returned (response rate 72%). Criteria for the participation of patients to the investigation were: 1) Over 18 years of age 2) Ability to communicate in the Greek language 3) Diagnosis of end-stage ESRD 4) Follow-up of haemodialysis program over 2 months 5) Session duration of HD over 2 hours 6) Not officially diagnosed Alzheimer's disease. The questionnaires were shared during the session, and the patients completed them at that time by themselves or they were read by the nurses of the unit who completed them according to the patients' answers.

Data Collection Tools

A self-completed questionnaire, consisting of 4 parts, was used to collect and record the necessary data. The first part included questions concerning socio-demographic, somatometric (height and dry Weight) and clinical characteristics (age, gender, marital status, level of education and occupational status). In the second part there were questions concerning a brief medical history of the patient. More specifically, there were questions about the patient's blood pressure, if they had orthostatic hypotension, if they had DM, and if so, for how many years and what the treatment is. There were also questions about their chronic kidney disease (CKD) and more particularly the length of treatment by the process of dialysis, the type of vascular access and of solution used, the total volume loss per session. Finally, the patient's medication was recorded and also the accompanying diseases and any existing mutilations. The third part of the questionnaire concerned haematological examinations, which were completed by the researcher one week after the patients completed the questionnaires. The fourth part of the questionnaire contained the questions of the two specific research measurement tools, HADS for hospital anxiety and depression, and MMSE for the cognitive status of patients.

Ethics and Ethics Issues

For the preparation of this study, approval was given by the Scientific and Management Board of the Unit in accordance with the procedure laid down in its rules of procedure. The questionnaires were completed by the participants on the basis of the principles of anonymity, confidentiality and protection of personal data. There are no foreseeable risks and other harmful consequences from the participation of this population in this survey.

Statistical Analysis

The statistical processing of the results was done with the statistical program SPSS 17.0. In descriptive statistics, continuous variables were expressed by average and standard deviation. Dichotomus and categorical variables were expressed as frequencies. The regularity of the variables was checked by the Kolmogorov-Smirnov test. Analytical statistics used the parametric t-test. The Pearson rhocorrelation coefficient was used to control the degree of correlation between two continuous variables. All cases were tested for a statistical significance level $p < 0.05$.

Results

Demographic Characteristics of the Sample

In the present study 52 questionnaires were collected, corresponding to 52 patients, of whom 38 were men (73% of the sample) and 14 women (26.9% of the sample). The average age of the patients was 69 years with a range of 24 to 93 years. As for the level of education, 25% of the sample had completed elementary school or some grades of it, 45% had middle school and high school education and 31% were graduates of tertiary education. Labor-related results are also characteristic, as 94% said they were retired. Only 6% of the sample said they were working in the private sector. Demographic characteristics of the sample are shown in Table 1.

Characteristics	Sample	Percentage of the Sample
Gender	man	70,3%
	woman	29,7%
Age	>65	68,5%
	20-65	31,4%
Education	Elementary school	25,45%
	Middle-high school	45,45%
	University	30,9%
occupational status	working	5,45%
	retired	94,54%

Table 1: Demographic Characteristics of the Sample.

Clinical Characteristics of the Patients

Regarding the clinical characteristics of patients in the sample (Table 2), it is worth noting that the most common

primary cause of nephropathy is DM with 49.09% followed by arterial hypertension with 17%, polycystic disease with 13% and glomerulonephritis with 11 %. In addition, various causes (9.91%) for nephropathy were reported due to incorrect medication and autoimmune diseases. Also, high rates of co-morbidity of ESRD with one or more diseases (83.63%) occur in the sample of patients. In particular, 49.09% suffer from DM, 17% from arterial hypertension, 3.63% from myocardial infarction, 16.4% from heart failure, 10.9% from stroke and 1.8% from amputation (Table 3).

Cause of CKD	Percentage of the Sample
DM	49,09%
Arterial hypertension	17%
Polycystic disease	13%
Glomerulonephritis	11%
Various causes	9,91%

Table 2: Percentage distribution of sample according to primary cause of CKD.

CKD and other disease	Percentage of comorbidity with other disease
DM	49,09%
Arterial Hypertension	17%
Myocardial Infection	3,63%
Heart failure	16,4%
Stroke	10,9%
Amputation	1,8%

Table 3: Percentage of comorbidity with other diseases.

According to the results of the laboratory tests, the average values of iron levels was 65.5 μg/ dl, the glycosylated hemoglobin was 5.67%, sugar level was 132 mg/ dl, clearance was 0.96, cholesterol was 41.41 mg / dl, CRP was 11.59 and finally sodium value before dialysis was 140.05 meq/ L.

Finally, according to the responses given by patients for the depression scale and the dementia scale, the average was 7.45 (negative for depression) and 15 respectively (moderate cognitive impairment).

Comparisons between the MMSE Scale and Individual Factors Across the Survey Population

Table 4 presents the comparisons between the MMSE scale and the individual haematological and socio-demographic factors across the population. Interesting is the relationship between the MMSE scale and age, HbA1c, CRP, and HADS, namely: age (r = 0.342, p = 0.012), HbA1c (r = -.302, p = 0.028 pearson test), CRP (r = -.268, p = 0.042) and HADS (r = 0.534, p = 0.000 pearson test), where the respective relationships are statistically significant but the relationship between them is weak.

	Pearson r	P
Age	0.342	0.012
bmi	-.084	0.552
HbA1c	-.302	0.028
Fe	0.017	0.902
Kt/v	0.075	0.594
CRP	-.268	0.042
HADS	0.534	0.000

Table 4: Comparisons between the MMSE scale and the individual factors across the population.

Apart from the general set, we also wanted to study the correlation of the MMSE scale with the other factors in the two subgroups of our population, ie those who suffered from DM and those who did not have DM. Table 5 shows the results of the comparison in the population suffering from DM. In Table 5 interesting are the relationships between MMSE and age, sodium, and cholesterol, particularly age (r = -.387 p = 0.046) and sodium (r = -.360 p = 0.055). The respective relationships are here statistically significant, but the relationship between them is weak.

	Pearson r	P
Age	-.387	0.046
BMI	-.134	0.507
Fe	0.038	0.852
HbA1c	-.168	.401
Kt/v	-.041	0.838
na	-.360	0.055
Hads	-.225	0.259

Table 5: Correlations between the MMSE scale and the individual factors by patients suffering from DM.

Also, Table 6 presents the comparisons between the MMSE scale and the individual factors in the population that do not suffer from DM. Table 6 shows the comparisons between MMSE, sodium and HADS scale. In particular, sodium (r = -.380 p = 0.055) and HADS (r = -.533 p = 0.003) where the respective relationships are statistically significant, but the relationship between them is weak.

	Pearson r	P
BMI	.100	0.633
Age	-.364	0.054
Fe	-.148	0.471
HbA1c	-.044	0.832
Kt/v	.148	0.471
crp	-.300	0.137
na	-.380	0.055
hads	-.533	0.003

Table 6: Correlations between the MMSE scale and the individual factors by patients not suffering from DM.

Discussion

Survival and quality of life depend on the periodic correction of biological parameters with the appropriate technical assistance, such as the haemodialysis method for patients with end-stage RD. which were studied in this research. It has been found that some social, demographic and haematological factors play an important role in the lives of haemodialysis patients and some of them will suffer from Alzheimer's disease. For haemodialysis patients, according to the present study, age, glycosylated hemoglobin, CRP and depression seem to be of great importance in the appearance of dementia. After separating the patients into two groups, those suffering from DM and those who did not suffer from DM (since we saw that DM is one of the main causes of CKD), significant associations were found by patients suffering from DM among dementia and age, cholesterol and depression, whereas by individuals who did not have DM a relationship was found only between dementia and sodium levels. According to Bugnicourt, et al. [8], it has been estimated that 30% - 60% of patients undergoing haemodialysis have cognitive impairment. In the present study, 100% of patients had cognitive impairment, either mild or moderate or severe. Mild and moderate cognitive impairment was about 87.2% consistent with Murray, et al. [6] which state that the actual prevalence of mild to severe attenuation in haemodialysis patients was very high at the level of 87%.

Furthermore, according to Terawaki, et al. [9], nephrogenic agents for dementia are anemia and hyponatremia, but in the present study there was no similar finding. With regard to obesity as a risk factor for Alzheimer's disease, the study by Qiu, et al. [10] agrees with the above. In our research, 30.9% of our sample was obese (BMI> 30 kg / m^2), but according to the statistical analysis the body mass index is not correlated with NA.

According to Sajjadi, et al. [11], haemodialysis patients suffer from depression, which is another risk factor for developing AD. Our findings agree with this view, but if we observe the two groups, we will see that patients suffering from DM have a higher level of depression than those without DM. This is likely to happen because these people have to deal with two very serious and difficult diseases to deal with that put them in more constraints than patients who only had to deal with nephropathy.

Accardi, et al. [12] argued that people with MD have a higher incidence of cognitive decline and then NA. The present study concluded that the level of DM regulation is a risk factor for NA since HbA1c is related to NA. Lastly, the CRP was considered and we are in agreement with Papagalanis [13] who states that the price of CRP is a non-traditional risk factor for dementia.

Conclusions - Proposals

The prospects arising from this research would be of interest from both the medical and the nursing side. Longitudinal research into the cognitive status of these patients over a reasonable period of time would probably reveal interesting parameters. Blood counts, which in both groups differ statistically, would also require more detailed examinations. From the nursing side, attention to appropriate patient medication and its effects on slowing down dementia factors could be explored. Also, the human factor that appeared to play such a big role along with more detailed research on depression could perhaps be investigated, because increasing evidence has shown that the mental factor affects physical health as well.

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