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ASSOCIATION OF CARNITINE DEFICIENCY IN INDIAN CONTINUOUS AMBULATORY PERITONEAL DIALYSIS PATIENTS WITH ANEMIA, ERYTHROPOIETIN USE, RESIDUAL RENAL FUNCTION, AND DIABETES MELLITUS

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♦♦ ***Objective:*** **In the present study, we aimed to determine levels of free carnitine in hemodialysis (HD) and peritoneal dialysis (PD) patients in India and to correlate carnitine deficiency with various clinical parameters.**

♦♦ ***Methods:*** **Patients on HD and PD at two tertiary care centers were selected for the study. Baseline data were obtained, and a free carnitine analysis was performed. Carnitine deficiency was defined as a free carnitine level of less than 40 μmol/L.**

♦♦ ***Results:*** **The total number of study patients was 96 (77 on HD, 19 on PD). In the PD group, the mean age was 56 years, with 26.3% of the patients being vegan, 47.4% having diabetes, and 57.9% having a daily urine output of <500 mL. The mean carnitine level in that group was 38.9 μmol/L, and 68.4% of the patients had a carnitine deficiency. A Pearson correlation test failed to show any association of carnitine level with parameters such as anemia, use of erythropoietin, non-vegetarian diet, diabetes, and hypertension. In the HD group, the mean age was 45 years, with 22% of the patients being vegan, 23% having diabetes, and 45.5% having a daily urine output of <500 mL. The mean carnitine level in the group was 38.2 μmol/L, and 64.3% of the patients had a carnitine deficiency. Residual renal function and duration of dialysis were different in HD patients with and without carnitine deficiency. Carnitine levels in the HD group correlated positively and statistically significantly with the presence of diabetes and hypertension.**

♦♦ ***Conclusion:*** **This study is the first demonstration that Indian dialysis patients have carnitine deficiency.**

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KEY WORDS: Carnitine deficiency; CAPD; hemodialysis; anemia; residual renal function.

Carnitine is a water-soluble molecule that is present in almost all animal species. It is an important intermediary in fat metabolism. Patients on dialysis and those with chronic renal failure appear to have abnormal renal handling of carnitine, leading to symptoms of lethargy, muscular weakness, cardiac dysfunction, and recurrent cramps. This symptom constellation has been termed "dialysis-related carnitine deficiency" and occurs because of the disparity between carnitine availability and metabolic need. The aim of the present study was to demonstrate carnitine levels in hemodialysis (HD) and peritoneal dialysis (PD) patients, and to correlate carnitine deficiency with various clinical parameters.

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PATIENTS AND METHODS

Study patients with stage V chronic kidney disease on maintenance dialysis (HD and PD) were selected from two tertiary care centers. Baseline characteristics such as age, dialysis duration, type of diet, underlying renal disease, residual renal function (RRF), serum total protein, serum albumin, hemoglobin, and use of erythropoietin (EPO) were collected.

BIOCHEMICAL ANALYSIS

We collected 3 mL fasting whole blood samples in standard sample tubes treated with ethylenediaminetetraacetic acid. In patients on HD, blood was collected before a HD session. Samples were centrifuged at 3000*g* for 10 minutes, and the plasma was separated. The plasma was then deproteinized by centrifugation for 20 – 40 minutes with Amicon Centricon filters (Millipore, Billerica, MA, U.S.A.) having a molecular weight cut-off of 2000 – 5000.

A commercial kit and the modified method of Marquis and Fritz (1) was then used to analyze the resulting filtrate for level of free carnitine. Spectrometric enzyme analysis was performed on a random-access, fully-automated chemical analyzer. Carnitine deficiency was defined as a free carnitine level of less than 40 μmol/L.

STATISTICAL ANALYSIS

Descriptive statistics (mean and standard deviation) are used to present patient data. Comparisons between patient groups (with and without carnitine deficiency) used the *t*-test analysis. The Pearson correlation coefficient and the chi-square test were used to look for associations between carnitine level and various independent variables.

RESULTS

The total number of study patients was 96 (77 on HD, 19 on PD). Table 1 describes the PD and HD groups.

In the PD group, the mean carnitine level was 38.87 ± 13.66 μmol/L (range: 21 – 70 μmol/L), and in the HD group, it was 38.25 ± 11.91 μmol/L (range: 19.6 – 82 μmol/L, Table 2). In the PD and HD groups respectively, 68.42% and 64.93% of patients were carnitine-deficient (Table 3).

In the PD group, a comparison of the patients with and without carnitine deficiency revealed no differences in age, hemoglobin, total protein, serum albumin, RRF, or dialysis duration. We then tested correlations between serum carnitine level and other clinical parameters. No statistically significant associations were observed in the PD group with regard to the various parameters tested (Table 4).

In the HD group, patients with and without carnitine deficiency showed a statistically significant difference in RRF (<500 mL daily, $p = 0.000$) and in dialysis duration ($p = 0.007$). In addition, carnitine levels in this group correlated positively with the presence of diabetes and hypertension. No associations with the other tested parameters (diet, anemia, EPO use) were observed (Table 5).

DISCUSSION

Treatment of carnitine deficiency in the dialysis population is gaining in popularity because the condition is easily recognized and L-carnitine supplements are easily available. Carnitine supplementation may also be useful in treating severe symptoms that might otherwise be labeled uremic.

Carnitine is crucial for energy production in cardiac and skeletal muscles. It plays an indispensable role in the metabolism of fatty acids, where it is involved in the transport of activated fatty acids between various cellular compartments (2). Reactions of carnitine with

TABLE 1
Characteristics of the Patients in the Hemodialysis (HD) and Peritoneal Dialysis (PD) Groups

	PD	HD
Patients (*n*)	19	77
Age (years)	56.00±15.25	45.19±11.39
Range	19–78	21–71
Vegan (%)	26.3	22.1
Diabetes (%)	47.4	23.4
Duration of dialysis (months)	22.62±18.75	26.66±30.01
Range	3–72 (*n*=16)	2–144 (*n*=54)
Daily urine output <500 mL (%)	57.9	45.5
Total protein (g/dL)	6.60±0.90	6.63±0.64
Range	4.8–8.2 (*n*=11)	4.5–8.2 (*n*=66)
Serum albumin (g/dL)	3.45±0.62	3.71±0.49
Range	2.1–4.0 (*n*=12)	2.3–4.9 (*n*=69)
Hemoglobin (g/dL)	9.75±0.85 (*n*=11)	8.42±1.64 (*n*=61)
Use of erythropoietin (%)	73.7 (*n*=17)	32.5 (*n*=26)

TABLE 2
Mean Carnitine Values in the Hemodialysis (HD) and Peritoneal Dialysis (PD) Groups

	PD	HD
Mean serum carnitine (μmol/L)	38.87±13.66	38.25±11.91

TABLE 3
Carnitine Deficiency in the Hemodialysis (HD) and Peritoneal Dialysis (PD) Groups

	PD	HD
Carnitine <40 μmol/L (%)	68.42	64.93

TABLE 4
Association of Carnitine with Clinical Parameters in the Peritoneal Dialysis (PD) Group

	PD	*p* Value[a]
Non-vegetarian	0.655	0.418
Anemia	0.244	0.621
Use of erythropoietin	0.027	0.87
Diabetes mellitus	0.148	0.70
Hypertension	0.012	0.91

[a] All values nonsignificant.

TABLE 5
Association of Carnitine with Clinical Parameters in the Hemodialysis (HD) Group

	HD	*p* Value
Non-vegetarian	0.177	0.674
Anemia	1.244	0.269
Use of erythropoietin	0.650	0.420
Diabetes mellitus	4.126	0.042[a]
Hypertension	4.133	0.043[a]

[a] Significant.

activated fatty acids are catalyzed by carnitine acyltransferases:

$$\text{acyl CoA} + \text{carnitine} \rightarrow \text{acylcarnitine} + \text{CoASH}$$

Carnitine is derived from red meat and dairy products and biosynthesized in liver, kidney, and brain. Free carnitine is filtered at the glomerulus, with more than 90% undergoing tubular reabsorption. In the dialysis population, free carnitine is lower and acylcarnitine is higher than in the general population. This shift may be attributable to loss of renal parenchyma, poor clearances, and poor dietary intake (3). Carnitine deficiency leads to multiple comorbidities such as poor exercise tolerance, anemia, and cardiac dysfunction.

The present study is the first in India that assesses free carnitine levels in the Indian dialysis population. In our PD and HD groups alike, more than half of the patients showed carnitine deficiency. Average carnitine values were similar in both groups.

In the HD group, RRF was significantly different in the patients with and without carnitine deficiency. That finding emphasizes the vital role that the kidneys play in maintaining carnitine balance. No association of carnitine level with RRF was found in the PD group, a result that could be a result of the small sample size.

Although carnitine comes mainly from animal fats, we found no correlation between carnitine and a vegan or non-vegan diet. However, even the South Indian non-vegetarian diet contains little in the way of meat products, such products usually being consumed only once or twice weekly—which may explain the lack of an association.

Available data indicate that the free carnitine levels are typically normal in PD patients, but our data show carnitine deficiency in these patients. The reduction in plasma L-carnitine levels occurred within the first few months of dialysis, and muscle levels continued to decline even after 1 year (4); however, our study found no association between carnitine level and dialysis duration.

Serum albumin is a marker of nutrition status, and serum albumin levels in our patients were not significantly associated with carnitine levels. Supplementary L-carnitine has been used as an adjunct treatment in dialysis patients with EPO-resistant anemia, but its possible mechanism of action is unknown. Carnitine has been shown to increase the erythroid colony–forming units in mouse bone marrow (5). We found no association between anemia, EPO use, and free carnitine levels in the present study.

Chronic conditions such as diabetes and heart failure also have been reported to cause carnitine deficiency (6). We found positive correlations between carnitine deficiency and diabetes and hypertension in our HD patients.

CONCLUSIONS

The present study demonstrates that HD and PD patients in the Indian dialysis population can both have carnitine deficiency. The causes are likely multifactorial and connected to dietary practices. We found an association between serum carnitine level and RRF in HD patients, and all possible means should be used to preserve RRF. Understanding carnitine deficiency and treating it may improve quality of life in our dialysis patients.

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