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Inflammatory Cytokines and Malnutrition as Related to Risk for Coronary Heart Disease in Hemodialysis Patients

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Malnutrition and inflammation are associated with end-stage renal disease (ESRD). Interleukin (IL)-6 and tumor necrosis factor-alfa (TNF-α) powerfully predict death from cardiovascular disease in dialysis patients as well as progression of vascular injury.The total concentration of serum non-esterified fatty acids (NEFA) plays an important role in the pathogenesis of cardiovascular disease (CVD).Individual circulating NEFA have achieved less scientific focus in relation to atherosclerosis compared to total NEFA.A strong link exists between chronic inflammation and nutritional markers in hemodialysis (HD) patients.Biological effects of n-3 fatty acids have been shown in studies of animals and humans in which anti-inflammatory and antithrombotic effects could be of relevance in HD patients.

Aim of our study was to establish association between markers of inflammation and parameters of malnutrition in hemodialysis patients.

The study population consisted of 42 hemodialysis patients with different parameters of malnutrition and mean age 55±8 with dialysis duration 6,25±2.Patients were divided according to tertiles of lean body mass(LBM) was assessed by bioelectrical impedance(BIA) and with the following intertertiles ranges: 1st tertile (LBM-37kg), 2nd (LBM 38-50kg) and 3rd (LBM ≥51kg). For nutritional assessment simple parameters were used: triceps skinfold (TSF), midarm muscle circumference (MAMC), body mass index (BMI), and serum albumin concentration as representative of body fat, muscle protein and visceral protein respectively.Blood samples were taken after an overnight fast and plasma lipid profiles were measured: total cholesterol, LDL cholesterol, high-density lipoprotein (HDL) cholesterol, and tryglicerides, using conventional enzymatic methods.Serum urea and creatinine levels were also measured by the routine procedures of our laboratory.The fatty acid pattern of plasma and erytrocytes were examined by gas chromatography. Inflammatory cytokines, IL-6 and TNF-α, was measured by photometric enzyme-linked immunosorbent assay (ELISA).

We used standard Doppler echo examinations to determine of left ventricular mass index (LVMI).

The main results of the patients of each tertile are shown in the table below (table 1).

Table 1. Comparison between groups

	1st tertile	**3rd tertile**	**p**
Number:	14	16	
BMIkg/m²	22±3.4	24±1.97	0.04
MAMCcm	23.9±4.7	25.7±3.1	0.04
Albuming/L	31±3.01	33±3.21	<0.05
Transferin pg/ml	1.42±0.29	1.75±0.32	NS
TNF-α pg/ml	207.73±165	195.41±153	NS
IL-6 pg/ml	450.14±419	341.27±339	.03
Carotid plaques %	62	39	<0.05
CVD %	89	72	<0.05

The patients of the 3rd tertile, representing 30% of the whole group, presented LBM levels indicative of an well nourished group. These patients presented BMI and other nutritional parameters, significantly higher than that of the patients in the 1st tertile.IL-6 and TNF-α were lower than that found in the patients in the 1st tertile and these differences were significantly (table 2).

Table 2. Correlation coefficient (r) between TNF-α and LDL/HDL-cholesterol concentration

	LDL/HDL-cholesterol			
	1st tertile		**3rd tertile**	
TNF-α	r = 0.33	p < 0.05	r = 0.32	p< 0.05

Patients with a lower LBM values had decreased BMI,TSF, MAMC, serum creatinine, serum albumin, serum cholesterol and dietary protein intake values than those in the higher tertile.

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Malnourished patients had significantly increased cardiovascular disease and carotid plaques. Significant positive relations between TNF-α and LDL/HDL cholesterol was found in the groups ($p< 0.05$) and positive correlation between IL-6 and LVMI ($p<0.05$). Plasma PUFA decreased whereas palmitic and monounsatirated acids increased in plasma and erythrocyte membranes of HD patients compared to healthy subjects.The fatty acid profile of HD patients is abnormal and results confirmed on essential fatty acid (EFA) deficiency.Plasma phospholipids fatty acids profile of HD patients indicated lower 18:2n-6 (25.89±2.8 vs 26.40±2.7% of total), 18:3n-3(0.42±0.2 vs 0.48±0.3% 0f total) and 22:6n-3 (2.93±0.9 vs 3.63±1.1), the latest two, significantly.The main findings of this study was that PUFA, namely 18:3n-3 and 22:6n-3 were dwcreased in phospholipids and membrane erytrocytes and the decreased was related to the degree of malnutrition. There was correlation between serum albumin and docosahexaaenoic acid-DHA (r 0.415 p 0.05) and correlation between serum albumin and arachidonic acid – AA, r 0.643 , p 0.002) Table 3.

Table 3. Correlation between serum albumin level and PUFA

Parameters	p	r
DHA er 22:6 (n-3)	0.05	0.415
AA er 20:4 (n-6)	0.002	0.643

There was correlation between diastolic blood pressure and PUFA (Table 4).

Table 4. Correlation between diastolic blood pressure and PUFA

Parameters	p	r
DHA er 22:6 (n-3)	0.05	-0.409
AA er 20:4 (n-6)	0.06	-0.411

In summary, this study has demonstrated high prevalence of malnutrition, inflammation, carotid plaques and cardiovascular disease. Malnourished dialysis patients are more often with cardiovaslcular disease and carotid plaques and have elevated inflammatory cytokines which all may increase the risk of atherosclerotic vascular disease.
This results suggest that nutritional intervention strategies may improve the nutritional status of malnourished HD patients and thus possibly help to lower mortality rates.

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Key words: inflammatory cytokines, lean body mass, cardiovascular disease, hemodialysis

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