RELATION BETWEEN HOMOCYSTEINE LEVEL AND MACROANGIOPATHY IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Abstract: *Cardiovascular disease (CVD) is the leading cause of mortality in patients with chronic kidney disease. In the specialty literature, there are studies which support the existence of a direct relationship between chronic kidney disease, homocysteine (Hcy) level and the risk of cardiovascular complications. The purpose of this study is to demonstrate whether the presence of angiopathic changes is associated with elevated levels of homocysteine in pre-dialysis patients with chronic kidney disease. Objective: the study aims to identify a correlation between homocysteine level and the occurrence of macroangiopathy in patients with chronic renal disease. We have studied 40 patients with chronic kidney disease, who were in pre-dialysis. A carotid Doppler echography was performed on each patient, the homocysteine value was determined. The lot was divided into two groups according to the chronic kidney disease rank. The relationship between homocysteine and angiography was assessed by Statistical Package for the Social Sciences (SPSS). Most patients in the study have elevated Hcy levels. 94% in lot I and lot II. Women who represent 40% of patients have higher values than men, and they also have a high frequency of atherosclerotic plaques. Hcy may be considered a cardiovascular risk factor in patients with chronic kidney disease.*

INTRODUCTION

Homocysteine is an amino acid (contains thiol) formed in the process of converting methionine to cysteine. It can be converted to cysteine by trans-sulfation or back to methionine by remethylation.(1,2)

The deficiency of 5,10 methyltetrahydrofolate reductase (the enzyme involved in methionine remethylation, active form of folic acid) can lead to hyperhomocysteinemia There is no unique marker in appreciating the chronic kidney disease's evolution.

Hyperhomocysteinemia is considered an independent risk factor for thrombotic vascular disease and atherosclerosis. In patients with vitamin B_{12} deficiency and folate deficiency, increased homocysteine is explained by excessive excretion of tissues. Healthy kidneys are able to filter, reabsorb and metabolize homocysteine. Decreasing glomerular filtration rate (3,4) will also decrease the metabolism of homocysteine so that in the patients with chronic kidney disease, increased homocysteine levels are explained by decreasing renal clearance. There is an inverse relationship between homocysteine level and glomerular filtration rate (GFR).(5)

PURPOSE

The study aims to identify a correlation between homocysteine level and the occurrence of macroangiopathy in patients with chronic renal disease**.**

MATERIALS AND METHODS

A total of 40 patients with chronic kidney disease in stages 3 and 4 were studied. The lot was divided into two groups according to the chronic kidney disease stage. We excluded diabetes patients and smokers, for homocysteine level analysis and hypothyroid and cholesterol patients for the lipidic profile analysis.

The patients were divided in two groups: one group was made up of 30 patients in stage III of chronic kidney disease and the second group was made up of 10 patients with stage IV of chronic kidney disease.

In each patient, we determined the following: homocysteine, lipid profile, inflammatory profile, Vit. B_{12}, carotid Doppler angiography with Intimal Medial Thickness (IMT) determination. The homocysteine level was determined on an Abbott Architect machine.(6) We have identified other risk factors for cardiovascular disease such as hypertension, obesity, dyslipidemia. After performing carotid echography, we divided the groups into patients with no risk of atherosclerosis (ATS) and at risk of ATS. Considering the homocysteine values we divided the entire group into 3 groups: normal value <15 pg/l, moderately elevated between 15-30 pg/l, severe between 30-100 pg/l.

IMT is considered to have a high value above 0.9.

We followed if there is a significant correlation between:

- Filtration rate RFG and Homocysteine;
- Homocysteine and stages of chronic kidney disease;
- Homocysteine and IMT;
- IMT and atherosclerosys plaques;
- Cholesterol and atherosclerosys plaques;
- Cholesterol and homocysteine.

RESULTS

In both groups the percentage was 40% women and 60% man.

Group I

In the first group, cholesterol had high values in 22% of men and 58% of women. Obesity was present in 16% men and 16% women.

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HTA was present in 61% men and 75% women.

Homocysteine

In group I, 89% of men had high values, of whom 22% had values above 30pg / l. In women, 100% had increased values of whom16% over 30pg / l.

Group II

In group II, cholesterol was increased in 17% men and 50% women. Obesity was present in 2 males (30%) and 25% in females. HTA was present in 83% of men and 25% of women.

Homocysteine

In the group II, 83% of men had high values, of whom 50% had values above 30pg / l. In women 75% had elevated values, of whom 33% over 30pg / l.

Echo Doppler gave us the following information:

In group I, 72% of IMT men had values above 0.9, of whom 56% had atherosclerosis plaques. In women, 75% had IMT above 0.9 and 100% had atherosclerosis plaques. In group II, 67% of IMT men had values above 0.9, of whom 84% had atherosclerosis plaques. In women, 25% had IMT above 0.9 and 50% had atherosclerosis plaques.

Figure no. 1. Correlation between eRFG and Homocysteine

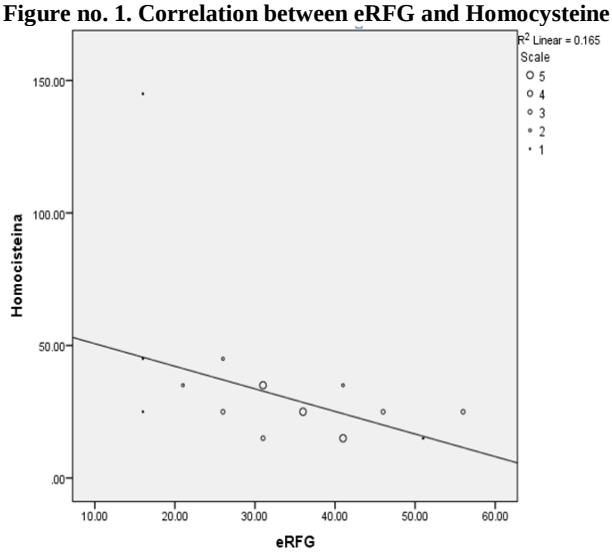


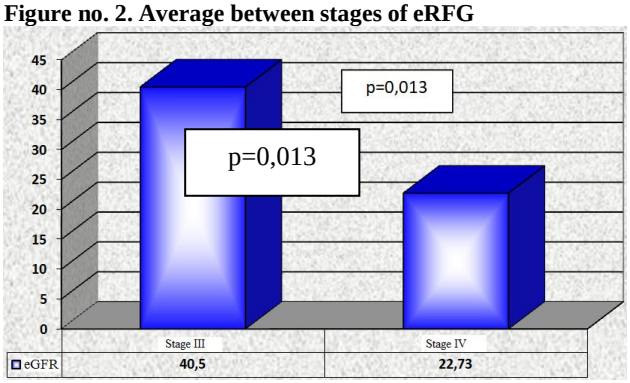
Table no. 1. Statistical analysis of the followed parameters

Homo		eGFR	Cholesterol	LDL	HDL	Homocysteine	B_{12}	Left ICA	Right ICA
<17	Frequency	6	6	6	6	6	6	6	6
	Mean	37.83	216.67	152.83	43.33	15.10	356.83	.91	1.05
	Standard deviation	5.64	58.37	70.013	7.99	1.81	145.38	.13	.36
15+30	Frequency	21	22	21	21	21	22	20	21
	Mean	37.48	193.29	121.51	46.03	22.57	311.55	.91	.90
	Standard deviation	11.69	36.13	29.87	9.06	3.49	172.10	.16	.10
>30	Frequency	10	10	9	9	10	10	10	10
	Mean	28.90	185.40	102.76	43.67	51.85	220.60	.95	.89
	Standard deviation	9.42	30.23	25.41	10.75	35.16	159.72	.19	.12
Total	Frequency	37	38	36	36	38	38	36	37
	Mean							.92	.92
	Standard deviation	35.21	194.90	122.04	44.99	29.10	294.76	.16	.17
t T test		.095	.295	.056	.732	.000	.228	.870	.151

		Correlations of Internal Carotid Arteries (ICA)								
		Age	eRFG	Cholesterol	LDL	HDL	Homocysteine	B12	Left ICA	Right ICA
Age	Pearson Correlation	1	-.196	.220	.278	.397	-.183	.417	.221	.276
	Sig. (2-tailed)		.483	.431	.316	.143	-513	.122	.428	.320
	N	15	15	15	15	15	15	15	15	15
eGFR	Pearson Correlation	-.196	1	.379	.686**	.130	-.314	-.443	-.613*	.129
	Sig. (2-tailed)	.483		.164	.005	.645	.254	.098	.015	.647
	N	15	15	15	15	15	15	15	15	15
Cholesterol	Pearson Correlation	.220	.379	1	.793**	.024	-.415	-.206	-.652**	.507
	Sig. (2-tailed)	.431	.164		.000	.934	.124	.460	.008	.054
	N	15	15	15	15	15	15	15	15	15
LDL	Pearson Correlation	.278	.686**	.793**	1	.121	-.581*	-.247	-.635*	.355
	Sig. (2-tailed)	.316	.005	.000		.667	.023	.347	.011	.195
	N	15	15	15	15	15	15	15	15	15
HDL	Pearson Correlation	.397	.130	.024	.121	1	-.175	.095	.247	-.306
	Sig. (2-tailed)	.143	.645	.934	.667		.533	.736	.376	.267
	N	15	15	15	15	15	15	15	15	15
Homocysteine	Pearson Correlation	-.183	-.314	-.415	-.581*	-.175	1	-.103	.282	-.188
	Sig. (2-tailed)	.513	.254	.124	.023	.533		.714	.309	.503
	N	15	15	15	15	15	15	15	15	15
B12	Pearson Correlation	.417	-.443	-.206	-.247	.095	-.103	1	.521*	.252
	Sig. (2-tailed)	.122	.098	.460	.374	.736	.714		.047	.364
	N	15	15	15	15	15	15	15	15	15
Left internal carotid artery	Pearson Correlation	.221	-6.13*	-.652**	-635*	.247	.282	.521*	1	-.246
	Sig. (2-tailed)	.428	.015	.008	.011	.376	.309	.047		.377
	N	15	15	15	15	15	15	15	15	15
Right internal carotid artery	Pearson Correlation	.276	.129	.507	.355	-.306	-.188	.252	-.252	1
	Sig. (2-tailed)	.320	.647	.054	.195	.267	.503	.364	.377	
	N	15	15	15	15	15	15	15	15	15

** Correlation is significant at the 0.01 level (2-tailed) * Correlation is significant at the 0.05 level (2-tailed)

Figure no. 2. Average between stages of eRFG



Homocysteine and stages of chronic kidney disease

Homocysteine was elevated in majority of patients with chronic kidney disease, in group I 94% and in group II 80%.

Homocysteine and IMT

Asignificant correlation regarding women in group I and IMT above 0.9 was present.

IMT and atherosclerosys plaques

There was no significant correlation between IMT and atherosclerosys plaques.

Cholesterol and atherosclerosys plaques

There was no significant correlation between cholesterol and atherosclerosys plaques.

Cholesterol and homocysteine

There was no significant correlation between cholesterol and homocysteine.

There was no growth of inflammatory markers in any of the groups.

Statistical analysis showed no significant correlation between Hy and IMT using the SPSS method.

DISCUSSIONS

Homocysteine and stages of chronic kidney disease

Homocysteine is elevated in majority of patients with chronic kidney disease, in group I 94% and in group II 80%.

We found that the proportion of those with increased Hcy is higher (94%) than those in group II, stage 4 chronic kidney disease (80%), in patients in group 1 and stage 3 of chronic kidney disease. Interestingly, the percentage is 100% for women in group I. Increases in Hcy in stage 3 versus stage 4 of chronic kidney disease may be explained by folate therapy.

Homocysteine and IMT

There is a significant correlation in women in group I and IMT above 0.9. However, the first group of patients who had Hcy 100% increased also had an increase by 75% regarding the IMT.

IMT and atherosclerosys plaques

There was no significant correlation between IMT and atherosclerosys plaques.

Cholesterol and atherosclerosys plaques

There was no significant correlation between cholesterol and atherosclerosys plaques.

Cholesterol and homocysteine

There was no significant correlation between cholesterol and homocysteine. There was no growth of inflammatory markers in any of the groups.

CONCLUSIONS

In patients with chronic kidney disease in pre-dialysis stages, elevated Hcy and macroangiopathy changes are present.

By comparing the Hcy and other risk factors for the atherosclerotic plaque in the two studied groups, we can conclude a significant correlation between the Hcy level and the macroangiopathy changes.

We have to acknowledge the limitations of the study due to the small number of patients included, which does not allow us to obtain high-precision conclusions. Continuing the study on larger comparative groups and including stage 5 of chronic kidney disease in pre-dialysis would probably allow for more significant correlations than in the current study.

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