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Relation between Magnesium Level and Cardiovascular Calcification in Chronic Hemodialysis Patients

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ABSTRACT

Background: Patients with chronic kidney disease (CKD) are susceptible to cardiovascular calcification because of a variety of factors. It is possible that magnesium (Mg) may play a role in the calcification of the arteries in several ways.
Objectives: The goal of this research was to examine the relationship between serum magnesium level and vascular stiffness & valvular calcification in hemodialysis patients.
Patients and methods: This prospective cross sectional case control study included a total of 100 prevalent hemodialysis patients who were maintained on thrice weekly hemodialysis sessions, attending at hemodialysis unit, Ain Shams university Hospitals. The included subjects were divided into two groups; Group I: consisted of 68 individuals with normal Mg levels, while group II: contained 32 patients with low Mg levels.
Results: No statistically significant differences were found as regards the laboratory and radiological investigations between both groups apart from hemoglobin (Hb) result. Mg level was positively correlated with Hb level.
Conclusion: It could be concluded that there is high prevalence of cardiovascular calcification among hemodialysis patients that may be related to age but without a statistically significant correlation to Mg level. Cardiac functions decrease with the progression of atherosclerosis and arterial stiffness.
Keywords: Chronic hemodialysis, vascular stiffness, Magnesium level, Aortic valve calcification.

INTRODUCTION

End-stage renal disease (ESRD) patients have a higher prevalence of vascular calcification, which develops earlier than in the general population and progresses more faster after chronic dialysis is started. A patient's risk of cardiovascular disease and mortality can be accurately predicted based on the presence and degree of calcification. CKD patients' vascular calcification pathophysiology is complex and multifactorial [(1)].

The inhibition of apatite production from amorphous Ca/P by Mg has been hypothesized as a possible mechanism for Mg's involvement in vascular calcification, serving as a mild calcium blocker to prevent Ca from entering the cell, influence on bone morphogenetic protein and matrix composition Reactions on calcium-sensory receptors by Gl protein limit calcification of smooth muscle cells [(2)]. Serum magnesium concentrations below 0.7 mmol/L have been shown to be an independent risk factor for cardiovascular disease, events, and death in the general population as well as those with chronic kidney disease [(3)].

The goal of this research was to examine the relationship between serum magnesium level and vascular stiffness& valvular calcification in hemodialysis patients.

PATIENTS AND METHODS

This prospective cross sectional case control study included a total of 100 prevalent hemodialysis patients who were maintained on thrice weekly hemodialysis sessions, attending at hemodialysis unit, Ain Shams university Hospitals.

The hemodialysis patients were maintained on thrice weekly hemodialysis sessions, four hours / session, with bicarbonate containing dialysate magnesium concentration in dialysate 0.5mmol/liter, and heparin-based anticoagulation.

The included subjects were divided into two groups; Group I: consisted of 68 individuals with normal Mg levels, while group II: contained 32 patients with low Mg levels.

Exclusion criteria:

Patients Older than 60 years old, patients with infection or Inflammation, malignancy, uncontrolled hypertension, and diabetes. Informed consent was obtained from each patient with full history focusing on the cause of ESRD and dialysis prescription.

Clinical and laboratory measurement:

Laboratory investigations included a complete blood picture, median magnesium level over three months (serum magnesium was assessed before the second session of the week and had been repeated every month for three months and the median level had been calculated). electrolytes, iPTH, lipid profile were done. Transthoracic echocardiography assessing the aortic pulse wave velocity of patients were done. The aortic pulse wave velocity serves as an indicator of the elasticity and stiffness of the aorta. Also, the patients were assessed for the existence of plaques in the carotid arteries, and measurement of the thickness of the carotid intima media.

Ethical Consideration:

The study was conducted in accordance with the principles outlined in the Helsinki Declaration. Ain Shams University's Faculty of Medicine's Ethics Committee approved the study. All patients who took part in this research gave their informed consent.

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Statistical method

For the purposes of this study, the statistical program for social sciences was used on a personal computer (IBM SPSS VERSION 20.0). This information was reported as mean and standard deviation (SD). Count and present data were used for qualitative data. T-test was used to compare two separate groups of people. Data from more than two groups were compared using the paired T-test. The Chi Square test was used to compare the qualitative data between various groups. It was used to measure the strength of a linear association between two quantitative variables, using the linear correlation coefficient.

RESULTS

A total 100 prevalent hemodialysis patients from Ain Shams University Hospital dialysis units were included in our study, Aged 18-60 years with mean age of 40.640±14.5111 years. Male patients were 55 and the female patients were 45 with mean dialysis duration 7.530±5.914 years and the dialysis duration ranging from 1 to 28 years. About 94 patients had Arteriovenous fistula as their vascular access, while the remaining 6 had Permcath. Virology screening of the patients showed that about 72 patients were negative virology and the other 28 were Hepatitis C positive. There were no signs of cardiovascular problems in any of the patients who were all clinically stable. All studied population was kept on hemodialysis sessions thrice weekly, four hours per session with standard bicarbonate dialysis and magnesium concentration0.5mmol/liter in the dialysate used, Using a low flux polysulfone dialyzer with a membrane surface area of 1.3-1.6m₂. The patients' characteristics are described in table 1.

Table (1): This table shows the descriptive data of studied population including age, sex, and duration of hemodialysis, virology and vascular access.

Descriptive Statistics			
		Range	**Mean±SD**
Age (years)		17-60	40.640±14.511
Duration of HD (years)		1-28	7.530±5.914
		Number	**%**
Sex	**Males**	55	55
	Females	45	45
Virology (HCV)	**Negative**	72	72
	Positive	28	28
Vascular access	**AVF**	94	94
	Permicath	6	6

Abbreviations: HD : hemodialysis , AVF : arteriovenous fistula

Serum magnesium levels were used to split the study population into two groups:

Group I: patients with normal magnesium level (1.8 – 2.6), and Group II: patients with low magnesium level (less than 1.8). The difference in hemoglobin levels between groups I and II is statistically significant (p-value = 0.033*). There were no significant differences in the other laboratory data, Echocardiographic and carotid duplex findings, as indicated in Tables 2, 3 and 4.

Table (2): Comparison between group I and group II as regard age, duration of hemodialysis and laboratory data of the studied population:

		Mg level						T-Test	
		Group I			Group II			T	P-value
Age (years)	**Range**	18	-	60	17	-	60	-0.125	0.901
	Mean ±SD	40.515	±	14.583	40.906	±	14.585		
Duration of HD (years)	**Range**	1	-	28	1	-	25	-0.254	0.800
	Mean ±SD	7.426	±	5.946	7.750	±	5.935		
Ca (mg/dl)	**Mean ±SD**	8.618	±	0.919	8.447	±	0.843	0.890	0.376
Ca*ph product (mg2/dl 2)	**Mean ±SD**	39.482	±	4.543	35.573	±	4.469	1.256	0.212
Po4 (mg/dl)	**Mean ±SD**	4.607	±	1.701	4.216	±	1.589	1.096	0.276
PTH (pg/mL)	**Mean ±SD**	529.926	±	57.582	687.563	±	83.422	-1.470	0.145
Hb (g/dl)	**Mean ±SD**	10.090	±	1.645	9.363	±	1.387	2.164	0.033*
Na (mEq/L)	**Mean ±SD**	136.191	±	3.588	136.156	±	3.828	0.044	0.965
K (mEq/L)	**Mean ±SD**	5.174	±	0.777	5.238	±	0.754	-0.387	0.699
TGs (mg/dl)	**Mean ±SD**	118.662	±	7.718	117.750	±	9.668	0.111	0.912
LDL (mg/dl)	**Mean ±SD**	111.612	±	6.567	102.978	±	4.319	0.896	0.373
HDL (mg/dl)	**Mean ±SD**	43.762	±	4.642	42.875	±	1.586	0.301	0.764
Cholesterol (mg/dl)	**Mean ±SD**	180.412	±	4.451	171.625	±	4.149	0.937	0.351

Abbreviations: HD:hemodialysis,Ca:calcium,Po4:phosphorus,PTH:parathyroid hormone , Hb: hemoglobin level , Na: sodium , K: potassium, TG: triglycerides .

Table (3): Comparison between group I and group II as regard Echocardiography findings:

		Mg level		T-Test	
		Group I	Group II	T	P-value
EF%	Mean ±SD	61.724± 8.694	60.341± 6.010	0.812	0.419
Aortic wave pulse velocity (m/s)	Mean ±SD	1.384±0 .291	1.416±0 .211	-0.552	0.582
AV calcification	N	42	19	0.052	0.819
	%	61.76	59.38		
MV calcification	N	12	3	1.168	0.280
	%	17.65	9.38		

Mg: magnesium , EF: ejection fraction, AV: aortic valve, MV: mitral valve.

Table (4): Comparison between group I and group II as regard carotid duplex findings:

		Mg level		T-Test	
		Group I	Group II	T	P-value
IMT (mm)	Mean ±SD	4.612± 1.925	4.125± 1.932	1.178	0.242
Plaques	N	11	6	0.102	0.749
	%	16.18	18.75		

Mg: magnesium , IMT: intima media thickness.

Magnesium level in relation to demographic, laboratory and radiological findings:

Amongst hemodialysis patients, magnesium level correlated positively with hemoglobin level (p-value=0.009*) and LDL level (p-value =0.027*), while others didn't have any correlation with magnesium level as seen in table 5.

Table (5): Correlation between magnesium level and age, duration of hemodialysis, laboratory data, echocardiography and carotid duplex findings:

	Mg	
	R	P-value
Age (years)	0.068	0.501
Duration of HD (years)	-0.146	0.147
Ca (mg/dl)	0.102	0.310
Ca/ph product (mg2/dl 2)	0.145	0.150
Po4 (mg/dl)	0.118	0.242
PTH (pq/ml)	-0.048	0.634
Hb (g/dl)	0.259	0.009*
Na(mEq/L)	0.113	0.262
K (mEq/L)	-0.042	0.675
TGs (mg/dl)	0.037	0.711
LDL (mg/dl)	0.222	0.027*
HDL (mg/dl)	-0.107	0.289
Cholesterol (mg/dl)	0.179	0.074
EF%	0.173	0.086
Aortic wave pulse velocity (m/s)	0.045	0.658
IMT (mm)	0.099	0.327

HD: hemodialysis, Ca:calcium, Po4:phosphorus, PTH: parathyroid hormone , Hb: hemoglobin level , Na: sodium , K: potassium, TG: triglycerides , EF: ejection fraction ,IMT : intima media thickness.

Intimal media thickness in relation to demographic, laboratory and radiological findings:

Also, the intimal media thickness showed a positive correlation with age (p-value=0.022*), aortic wave pulse velocity (p-value=0.003*) and IMT and ejection fraction have a statistically significant negative relationship with (p-value =0.048*) as seen in table 6.

Table (6): Correlation between intimal medial thickness and age, duration of hemodialysis, laboratory data and echocardiographic findings:

	IMT (mm)	
	R	P-value
Age (years)	0.229	0.022*
Duration of HD (years)	0.035	0.730
Ca (mg/dl)	0.013	0.894
Ca/ph product (mg2/dl 2)	-0.017	0.870
Po4 (mg/dl)	-0.013	0.900
PTH (pg/ml)	0.041	0.688
Hb (g/dl)	0.111	0.273
Na (mEq/L)	0.013	0.896
K (mEq/L)	0.015	0.885
Mg (mg/dl)	0.099	0.327
TGs (mg/dl)	-0.169	0.092
LDL (mg/dl)	-0.043	0.667
HDL (mg/dl)	0.062	0.541
Cholesterol (mg/dl)	-0.055	0.586
EF%	-0.198	0.048*
Aortic wave pulse velocity (m/s)	0.297	0.003*

Abbreviations: : HD:hemodialysis,Ca:calcium,Po4:phosphorus,PTH:parathyroid hormone , Hb: hemoglobin level , Na: sodium , K: potassium, TG: triglycerides , EF: ejection fraction ,IMT : intima media thickness.

DISCUSSION

For patients with ESRD, cardiovascular illness is the major cause of death, and dialysis patients experience cardiovascular mortality ten to twenty times higher than the general population. [(4)]. There are many other variables contributing to the high mortality rate from cardiovascular disease outside atherosclerosis, such as volume overload and left ventricular hypertrophy. However, in dialysis patients, atherosclerosis is the leading cause of death and disability [(5)]. In general, atherosclerotic alterations in carotid arteries are thought to reflect the underlying pathophysiology of atherosclerosis in general. IMT is a well-established marker of atherosclerosis that has been linked to an elevated risk of cardiovascular disease in the general population using non-invasive ultrasonography measurements of the carotid intima media thickness (IMT) [(6)]. Vascular calcification in individuals with end-stage renal disease is largely mediated by hyperphosphatemia, hypercalcemia, and parathyroid hormone (PTH). Furthermore, there is considerable evidence that hypomagnesemia may play a significant impact in the general population's risk of cardiovascular disease [7].

Numerous biological activities are dependent on magnesium, which is the fourth most abundant cation in the human body. The anti-atherosclerotic property of this mineral has led to its importance being acknowledged by scientists. Metabolic syndrome, cardiovascular disease (CVD), Hypertension as well as type 2 diabetes are all linked to decreased magnesium levels in the general population. Myocardial infarction, stroke, atrial fibrillation, and sudden cardiac death are all linked to lower magnesium consumption or its lower concentration in the body [8].

Multiple in vitro investigations have demonstrated that magnesium deficit induces vascular constriction, platelet accumulation, inflammation, and oxidative stress, ultimately leading to endothelial cell failure and vascular calcification [9].

The purpose of our study was to examine the levels of magnesium in the blood of hemodialysis patients and their relationship to the vascular stiffness of those patients. We correlated serum magnesium level of the studied population to various factors including echocardiographic parameters, laboratory parameters, vascular calcification observed by the carotid duplex. Our study population was subdivided into two groups according to serum magnesium level. Group I included 68 patients with normal serum magnesium level and group II included 32 patients with low Mg levels.

Most of the studied population were found to have normal and high normal levels of magnesium, this fact can be attributed to the use of bicarbonate dialysate with Mg concentration 0.5 mmol/L which went in line with the study of **Elsharkawy *et al.*** [10] in which serum magnesium (Mg) levels in the acetate group decreased significantly during the session, but in the bicarbonate group, there was no significant change in serum Mg levels from 0 to 2 hours, but a highly significant increase from 2 to 4 hours.

This imply to the importance of dialysis prescription, which can be used to adjust serum concentrations of magnesium according to the need and status of the hemodialysis patient. Moreover, our study revealed that when it came to hemoglobin levels, the two groups differed statistically, that was in consistence with **Selim *et al.*** [11] study, where HD patients with lower serum Mg levels had decreased hemoglobin levels (98.28 ± 14.31), in comparison to the Mg group of intermediate and higher (108.78 ± 10.25) and (108.43 ± 10.99) respectively. Magnesium levels were positively correlated with hemoglobin and LDL level in a statistically significant manner.

This result went in hands with **Ikee *et al.*** [12] study, which showed that Red blood cells, hemoglobin, and low-density lipoprotein cholesterol all showed a positive relationship with serum magnesium levels. Anemia and malnourishment in hypomagnesemia patients may be exacerbated by the presence of inflammation in these patients.

Multivariate regression analysis of the correlated data implies to that Hb level was the most important factor affecting Mg level.

When it came to aortic wave pulse velocity and plaque presence, the two groups were statistically indifferent.

Aortic wave pulse velocity and age were found to have a statistically significant positive connection with intimal medial thickness, which went in hand with **Akamatsu *et al.*** [13] study which showed that the mean IMT correlated positively with age while the mean IMT tended to be correlated with PWV, but did not reach statistical significance.

IMT and ejection fraction have a statistically significant negative relationship, which went in hand with **Rafieian-Kopaei *et al.*** [14] study, where the inverse relationship between cIMT and ejection % was discovered.

Limitations of the study: A small sample size was the main limitation factor in our study.

CONCLUSION

It could be concluded that there is high prevalence of cardiovascular calcification among hemodialysis patients that may be related to age but without a statistically significant correlation to Mg level. The cardiac function is inversely correlated to cardiovascular calcification. Hemoglobin may be negatively affected by magnesium level in hemodialysis patients.

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Authors' contributions:

All the authors were involved in the research's design. As a group, AHA, AK, and NAS worked together to analyze and interpret data. The initial draught was prepared by NAS. It was AHA, AK and MMZ's job to revise the first version. The final version of the manuscript was approved by all of the writers.

The authors have taken care to avoid any ethical difficulties (such as plagiarism, data manipulation, or multiple publications) at all costs.

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