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Hypomagnesemia as a Predictor of Cardiovascular Morbidity in Patients Undergoing Hemodialysis

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ABSTRACT

Background: Dialysis patients may be particularly vulnerable to the effects of magnesium deficiency, yet scant if any attention is being given to this cation in most dialysis centers, which should be rectified.

Objective: To find whether hypomagnesaemia represent an independent risk factor for increased cardiovascular morbidity in hemodialysis patient (HD) either with or without residual renal function (RRF).

Patients and methods: 60 prevalent hemodialysis patients were included and subdivided into 15 each; group 1a with normal serum magnesium and residual renal function, group 1b with low serum magnesium and residual renal function, group 2a with normal serum magnesium and no residual renal function and group 2b with low serum magnesium and no residual renal function. Patients were subjected to history taking, clinical examination, lab. tests, echo and ECG.

Results: Among 60 hemodialysis patients divided into 30 with RRF and 30 without, hypomagnesemia was found in 30% of whole patients. HD patients with RRF had lower mean serum magnesium level than those without. There was no statistical significant difference between the 2 groups regarding cardiovascular morbidities including diastolic dysfunction, pulmonary hypertension, and others, suggesting that RRF has no effect on cardiovascular morbidities in HD patients. There was no correlation between hypomagnesemia and diastolic dysfunction or pulmonary hypertension or hypertensive heart and left ventricular hypertrophy (LVH) or arrhythmias but we found significant correlation between hypomagnesemia and ischemic heart disease.

Conclusion: There is a close relationship between hypomagnesemia and risk factors for cardiovascular disease morbidity in hemodialysis patients.

Keywords: Hypomagnesemia, Residual Renal Function, Hemodialysis, Cardiovascular Disease Morbidity, Echo.

INTRODUCTION

Cardiovascular mortality in dialysis patients is 10-20 times greater compared to the general population [(1)]. There is increased prevalence of many traditional factors for cardiovascular risk. In addition, patients with chronic kidney disease (CKD) stage 5 have related risk factors such as anemia hyperhomocysteinemia, hyperparathyroidism, oxidative stress, prothrombotic factors, among others. Data suggest that uremic factor or factors related to renal replacement therapy (RRT)/dialysis may be implicated in the pathogenesis of heart disease in patients treated by dialysis, because cardiovascular survival improves after transplantation even in high risk patients. Conversely, aspects of the dialysis treatment itself may contribute to cardiovascular disease (CVD) [(2)].

Dysregulation in mineral and bone metabolism may contribute to the development of vascular calcification, cardiovascular disease and adverse clinical outcomes in patients with end-stage renal disease (ESRD) [(3)].

Studies from the general population have linked magnesium deficiency with endothelial dysfunction, insulin resistance, hyperaldosteronism and inflammation, all of which are associated with vascular calcifications [(4)]. In dialysis patients, losing the regulatory role of the kidneys can have significant effects on magnesium balance. It might appear that hypermagnesemia is the only possible outcome in such patient. However, dialysis patients in the modern era are usually normomagnesemic and sometime even hypomagnesemic [(5)].

Finally, increasing evidence points towards a link between magnesium and cardiovascular disease. The purpose of this work was to determine whether hypomagnesaemia is an independent risk factor for increased cardiovascular morbidity in end stage renal disease patients undergoing hemodialysis.

PATIENTS AND METHODS

This study was conducted on 60 prevalent hemodialysis patients who dialyze 3 times weekly, 4 hours for each session with low flux dialyzer, dialysate flow rate 500 mmHg, and blood flow rate 250 mmHg, for at least 6 months in El Sahel Teaching Hospital, Cairo, Egypt, including stable hemodialysis patients for 6 months aged from 21 to 50, with hemoglobin (Hb) more than 10g/dl, excluding those with thyroid illness, diabetes mellitus, active intercurrent infection, hyperkalemia or hypokalemia, hypercalcemia or hypocalcemia and severe metabolic acidosis or alkalosis.

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- **Group 1: included 30 hemodialysis patients that were subdivided into:**
- **Group 1a:** included hemodialysis patients with normal serum magnesium and residual renal function.
- **Group 1b** included hemodialysis patients with low serum magnesium and residual renal function.
- **Group 2: included 30 hemodialysis patients that were subdivided into:**
- **Group 2a:** that included hemodialysis patients with normal serum magnesium and no residual renal function.
- **Group 2b**: that included hemodialysis patients with low serum magnesium and no residual renal function.
- Residual renal function (RRF) was calculated by
  RRF = ID Urine Vol × Urine Urea Concentration / ID Period / Mean blood urea nitrogen (BUN)
  Mean BUN = (U1 + U2) / 2
  Notes:
  - U1 is the BUN just after the first dialysis session of the week.
  - U2 is the BUN just prior to the second dialysis session of the week.

ID: Interdialytic period.

Ethical approval

An informed written consent was taken from patients or guardians of patients who are invited to participate in the research and **Ain shams university ethical committee for human research approved the study protocol.**

Patients were subjected to history taking including past history of myocardial infarction, drug history, etiology of ESRD, hemodialysis vintage (year); clinical examination, intradialytic blood pressure measurement every 1 hour during the session; laboratory measures including blood urea nitrogen (BUN), serum corrected calcium (Ca), serum phosphorus (PO_4), serum albumin, intact parathyroid hormone (iPTH), CRP, HB, serum potassium and serum magnesium; and other investigations in the form of echocardiography and ECG for all patients.

Samples:

From each subjects, 5 ml venous blood samples were collected without anticoagulant. Samples were allowed to clot, then were centrifuged at 1000xg for 10 minutes within one hour after collecting. A part of the separated serum was aliquoted and stored frozen at –20ºC for subsequent determination of the other biochemical tests.

Data Management and Analysis:

The collected data was revised, coded, tabulated and introduced to a PC using Statistical Package for the Social Sciences (SPSS 20). Data were presented as mean, standard deviation (± SD) and range for numerical data, and as frequency and percentage for non-numerical data. Analytical statistics: Student t-test was used to assess the statistical significance of the difference between two means. Chi-square test was used to examine the relationship between two qualitative variables while Fisher's exact test was used to examine the relationship between two qualitative variables when the expected count is less than 5 in more than 20% of cells.

RESULTS

This study included sixty ESRD patients on hemodialysis, 30 of them with residual renal function and 30 with no residual renal function. Clinical characteristics and biochemical profiles of the 60 hemodialysis patients are reported in table 1.

Table (1): Demographic and laboratory results of the studied patients (N=60)

	Mean ± SD
Age (years)	42.60 ± 9.27
S. Mg (mg/dl)	2.01 ± 0.38
Corrected S. Ca (mg/dl)	8.34 ± 0.71
S. PO_4 (mg/dl)	6.14 ± 1.84
iPTH (pg/ml)	772.38 ± 23.69
S. albumin (g/dl)	3.69 ± 0.60
HB (g/dl)	10.65 ± 1.26
BUN (mg/dl)	53.40 ± 12.90
S. K (mmol/l)	4.27 ± 0.77
HDX duration (months)	59.30 ± 9.91
EEF (%)	61.65% ± 9.81%
Residual Renal function GFR (ml/min)	7.80 ± 1.60

There was no statistical significant difference between the 2 groups regarding age, serum calcium, serum phosphorus, serum potassium and hemoglobin level as clear in table 2.

Table (2): Comparison between the two studied groups regarding laboratory findings and hemodialysis duration

	Group 1 (N=30)		Group 2 (N=30)		T test	
	Mean	SD	Mean	SD	p value	sig.
Age (years)	41.93	9.91	43.27	8.69	0.582	NS
S. Mg (mg/dl)	1.92	0.36	2.10	0.38	0.069	NS
Corrected S. Ca (mg/dl)	8.22	0.71	8.46	0.71	0.209	NS
S. PO_4 (mg/dl)	4.99	1.54	7.29	9.48	0.195	NS
iPTH (pg/ml)	533.47	80.88	1011.30	64.86	0.002	S
S. albumin (g/dl)	3.56	0.59	3.81	0.60	0.115	NS
HB (g/dl)	10.34	1.41	10.95	1.04	0.061	NS
BUN (mg/dl)	48.89	12.21	57.90	12.15	0.006	S
S. K (mmol/l)	4.10	0.73	4.43	0.79	0.092	NS
HDX duration (months)	17.13	5.05	101.47	8.27	<0.001	S
EF (%)	60.73%	11.13%	62.57%	8.39%	0.474	NS

There was no statistical significant difference between the 2 studied groups regarding serum magnesium as shown in table 3.

Table (3): Comparison between the two studied groups regarding serum magnesium level

		Group 1 (N=30		Group 2 (N=30)		Chi square	
		N	%	N	%	p value	sig.
Mg	Normal (1.8-2.6mg/dl)	18	60.0%	24	80.0%	0.091	NS
	Hypomagnesemia (<1.8)	12	40.0%	6	20.0%		

There was no statistical significant difference between the 2 groups regarding cardiovascular morbidities including diastolic dysfunction, pulmonary hypertension, calcified valves, hypertensive heart, ischemic heart disease and arrhythmia as shown in table 4.

Table (4): Comparison between the two studied groups regarding cardiovascular morbidity

		Group 1 (N=30)		Group 2 (N=30)		Chi square	
		N	%	N	%	p value	sig.
EF	>50%	26	86.7%	28	93.3%	0.671*	NS
	<50%	4	13.3%	2	6.7%		
Diastolic dysfunction	Absent	16	53.3%	13	43.3%	0.438	NS
	Present	14	46.7%	17	56.7%		
Pulmonary hypertension	Absent	24	80.0%	22	73.3%	0.542	NS
	Present	6	20.0%	8	26.7%		
Calcified valves	Absent	26	86.7%	23	76.7%	0.317	NS
	Present	4	13.3%	7	23.3%		
Hypertensive heart (LVH)	Absent	18	60.0%	19	63.3%	0.791	NS
	Present	12	40.0%	11	36.7%		
Ischemic heart (hypokinesia)	Absent	24	80.0%	23	76.7%	0.754	NS
	Present	6	20.0%	7	23.3%		
ECG	Normal	26	86.7%	27	90.0%	1.000*	NS
	Arrhythmia	4	13.3%	3	10.0%		

*Fisher exact test

No significant correlation was found between low serum Mg and diastolic dysfunction in the 2 studied groups as in table 5.

Table (5) Comparison between those with negative and positive diastolic dysfunction regarding Mg and RRF

		Diastolic dysfunction				Chi square	
		Absent N=29		Present N=31			
		N	%	N	%	p value	sig.
Mg	Normal (1.8-2.6 mg/dl)	20	69.0%	22	71.0%	0.866	NS
	Hypomagnesemia (<1.8 mg/dl)	9	31.0%	9	29.0%		
RRF	No RRF	13	44.8%	17	54.8%	0.438	NS
	RRF	16	55.2%	14	45.2%		

There was significant correlation between older age and diastolic dysfunction, but there was no significant correlation between serum magnesium, corrected serum calcium, serum phosphorus, intact PTH, serum albumin and hemoglobin level and diastolic dysfunction in the study sample as shown in table 6.

Table (6): Comparison between those with negative and positive diastolic dysfunction regarding age, Lab results , EF and RRF

	Diastolic dysfunction				T test	
	Absent (29)		Present (31)		p value	sig.
	Mean	SD	Mean	SD		
Age (year)	40.07	9.98	44.97	8.00	0.040	S
S. Mg (mg/dl)	1.98	0.40	2.04	0.35	0.525	NS
Corrected S. Ca (mg/dl)	8.27	0.71	8.41	0.72	0.440	NS
S. PO_4(mg/dl)	5.54	1.59	6.70	9.43	0.516	NS
iPTH (pg/ml)	794.59	21.51	751.61	35.27	0.792	NS
S. albumin (g/dl)	3.57	0.69	3.80	0.50	0.151	NS
HB (g/dl)	10.66	0.94	10.64	1.52	0.952	NS
BUN (mg/dl)	52.31	14.04	54.41	11.88	0.533	NS
S.K (mmol/l)	4.11	0.78	4.41	0.75	0.135	NS
HDX duration (months)	54.62	3.19	63.68	7.36	0.563	NS
EF (%)	57.8%	11.9%	65.3%	5.4%	<0.003	S
Residual Renal function	7.29	1.75	8.39	2.46	0.414	NS

There was no significant correlation between serum magnesium and pulmonary hypertension as shown in table 7.

Table (7): Comparison between those with negative and positive pulmonary hypertension regarding Mg and RRF

		Pulmonary hypertension				Chi square	
		Absent N=46		Present N=14			
		N	%	N	%	p value	sig.
Mg	Normal(1.8-2.6 mg/dl)	33	71.7%	9	64.3%	0.594	NS
	Hypomagnesemia (<1.8 mg/dl)	13	28.3%	5	35.7%		
RRF	No RRF	22	47.8%	8	57.1%	0.542	NS
	RRF	24	52.2%	6	42.9%		

There was no significant correlation between serum magnesium level and pulmonary hypertension as shown in table 8.

Table (8): Comparison between those with negative and positive pulmonary hypertension regarding age, Lab results, EF and RRF

	Pulmonary hypertension				T test	
	Absent (46)		Present (14)		p value	sig.
	Mean	SD	Mean	SD		
Age (years)	43.67	9.02	39.07	9.53	0.104	NS
S. Mg (mg/dl)	2.04	0.39	1.91	0.32	0.274	NS
Corrected S. Ca (mg/dl)	8.34	0.71	8.34	0.74	0.980	NS
S. PO_4 (mg/dl)	5.09	1.27	9.56	2.78	0.247	NS
iPTH (pg/ml)	707.28	96.45	986.29	85.32	0.144	NS
S. albumin (g/dl)	3.62	0.65	3.91	0.38	0.119	NS
HB (g/dl)	10.65	1.34	10.66	1.02	0.977	NS
BUN (mg/dl)	52.89	14.03	55.05	8.40	0.588	NS
S. K (mmol/l)	4.24	0.81	4.36	0.67	0.615	NS
HDX duration (months)	54.93	9.33	73.64	1.74	0.310	NS
EF (%)	61.4%	10.4%	62.5%	7.8%	0.715	NS
Residual Renal function GFR (ml/min)	8.10	2.84	6.59	1.24	0.367	NS

There was no significant correlation between serum magnesium level and hypertensive heart disease. There was no significant correlation between residual renal function and hypertensive heart disease as shown in table 9.

Table (9): Comparison between those with negative and positive Hypertensive heart regarding Mg and RRF

		Hypertensive heart				Chi square	
		Absent N=37		Present N=23			
		N	%	N	%	p value	sig.
Mg	Normal(1.8-2.6mg/dl)	23	62.2%	19	82.6%	0.093	NS
	Hypomagnesemia(<1.8mg/dl)	14	37.8%	4	17.4%		
RRF	No RRF	19	51.4%	11	47.8%	0.791	NS
	RRF	18	48.6%	12	52.2%		

There was no significant correlation between serum magnesium and hypertensive heart disease as shown in table 10.

Table (10): Comparison between those with negative and positive hypertensive heart regarding age, Lab results, EF and RRF

	Hypertensive heart				T test	
	Absent (37)		Present (23)		p value	sig.
	Mean	SD	Mean	SD		
Age (years)	43.30	9.28	41.48	9.34	0.464	NS
S. Mg (mg/dl)	1.99	0.36	2.04	0.41	0.611	NS
Corrected S. Ca (mg/dl)	8.21	0.61	8.55	0.83	0.076	NS
S. PO_4 (mg/dl)	6.58	8.63	5.43	1.57	0.533	NS
iPTH (pg/ml)	738.97	16.16	826.13	45.79	0.603	NS
S. albumin (g/dl)	3.75	0.59	3.58	0.63	0.297	NS
HB (g/dl)	10.67	1.05	10.61	1.58	0.850	NS
BUN (mg/dl)	54.61	12.55	51.44	13.49	0.359	NS
S. K (mmol/l)	4.24	0.80	4.30	0.75	0.785	NS
HDX duration (months)	64.35	3.62	51.17	3.76	0.412	NS
EF (%)	60.4%	10.5%	63.7%	8.5%	0.216	NS
Residual Renal function GFR (ml/min)	8.46	2.04	6.82	1.68	0.227	NS

Low serum magnesium was correlated to ischemic heart disease and it was highly significant and there was no significant correlation between residual renal function and ischemic heart disease as shown in table 11.

Table (11): Comparison between those with negative and positive ischemic heart regarding Mg and RRF

		Ischemic heart				Chi square	
		Absent N=47		Present N=13			
		N	%	N	%	p value	sig.
Mg	Normal (1.8-2.6mg/dl)	38	80.9%	4	30.8%	0.001*	S
	Hypomagnesemia (<1.8mg/dl)	9	19.1%	9	69.2%		
CRP	<6	20	42.6%	4	30.8%	0.443	NS
	>6	27	57.4%	9	69.2%		
Etiology	Others	21	44.7%	6	46.2%	0.925	NS
	HTN	26	55.3%	7	53.8%		
EF	Normal	47	100.0%	7	53.8%	<0.001*	S
	Low EF	0	0.0%	6	46.2%		
RRF	No RRF	23	48.9%	7	53.8%	0.754	NS
	RRF	24	51.1%	6	46.2%		

*Fisher exact test

There was inverse relation between serum magnesium level and ischemic heart disease but it was statistically non-significant as shown in table 12.

Table (12): Comparison between those with negative and positive Ischemic heart regarding age, Lab results, EF and RRF

	Ischemic heart				T test	
	Absent (47)		Present (13)		p value	sig.
	Mean	SD	Mean	SD		
Age (years)	41.89	9.48	45.15	8.28	0.265	NS
S. Mg (mg/dl)	2.05	0.36	1.88	0.31	0.172	NS
Corrected S. Ca (mg/dl)	8.33	0.73	8.36	0.67	0.904	NS
S. PO_4 (mg/dl)	6.47	1.69	4.95	0.93	0.483	NS
iPTH (pg/ml)	804.83	37.26	655.08	80.29	0.448	NS
S. albumin (g/dl)	3.75	0.61	3.45	0.56	0.117	NS
HB (g/dl)	10.65	1.25	10.63	1.37	0.955	NS
BUN (mg/dl)	53.11	12.54	54.42	14.62	0.749	NS
S. K (mmol/l)	4.31	0.73	4.09	0.93	0.368	NS
HDX duration (months)	59.89	6.19	57.15	6.23	0.885	NS
EF (%)	64.7%	6.2%	50.8%	12.8%	<0.001	S
Residual Renal function GFR (ml/min)	7.40	1.20	9.41	2.93	0.227	NS

There was no significant correlation between serum magnesium level and arrhythmia. There was no significant correlation between residual renal function and arrhythmia as shown in table 13.

Table (13): Comparison between those with negative and positive Arrhythmia regarding Mg, and RRF

		ECG				Fisher exact test	
		Normal N=53		Arrhythmias N=7			
		N	%	N	%	p value	sig.
Mg	Normal (1.8-2.6mg/dl)	38	71.7%	4	57.1%	0.419	NS
	Hypomagnesemia(<1.8mg/dl)	15	28.3%	3	42.9%		
RRF	No RRF	27	50.9%	3	42.9%	1.000	NS
	RRF	26	49.1%	4	57.1%		

There was no significant correlation between serum magnesium level and arrhythmia as seen in table 14.

Table (14): Comparison between those with negative and positive ECG regarding age, Lab results, EF and RRF

	ECG				T test	
	Normal (53)		Arrhythmias (7)		p value	sig.
	Mean	SD	Mean	SD		
Age (years)	42.15	9.46	46.00	7.28	0.306	NS
S. Mg (mg/dl)	2.03	0.39	1.86	0.29	0.252	NS
Corrected S. Ca(mg/dl)	8.30	0.71	8.64	0.75	0.236	NS
S. PO_4 (mg/dl)	5.39	1.48	11.81	1.95	0.427	NS
iPTH (pg/ml)	809.40	35.69	492.14	68.05	0.209	NS
S. albumin (g/dl)	3.74	0.58	3.27	0.69	0.052	NS
HB (g/dl)	10.61	1.26	10.94	1.33	0.517	NS
BUN (mg/dl)	53.76	13.53	50.67	6.32	0.556	NS
S. K (mmol/l)	4.28	0.78	4.14	0.77	0.660	NS
HDX duration (months)	59.66	6.16	56.57	6.53	0.899	NS
EF (%)	61.7%	9.5%	61.4%	12.9%	0.950	NS
Residual Renal function GFR(ml/min)	7.57	1.33	9.28	1.43	0.386	NS

DISCUSSION

Based on observational studies in hemodialysis (HD) patients, it was suggested that low serum magnesium levels are associated with cardiovascular (CV) morbidity (e.g., mitral annular calcification, peripheral arterial calcification, and increased carotid intima-media thickness [cIMT]). Moreover, magnesium may have a myocardial protective role [(6)].

To the best of our knowledge, this is the first study to make a comparison between ESRD patients on regular hemodialysis with RRF and those without RRF regarding serum magnesium level.

In our study we found that group 1 had lower mean serum magnesium level than group 2 but with no significant difference, while **Cunningham *et al.*** [(7)] found that as renal function further deteriorates to CKD Stages 4 and 5, the quantitative excretion of magnesium tends to decrease and cannot be compensated any longer by an increased fractional excretion of magnesium.

Our study revealed also that group 2 had significantly higher mean serum intact parathyroid hormone than group 1 similar to **Okada *et al.*** [(8)], who studied patients on continuous ambulatory peritoneal dialysis patients demonstrating that the increase in intact PTH correlates significantly with decline in RRF after adjustment in other variables such as serum Ca, phosphate, and creatinine.

We didn't find any statistical significant difference between the 2 groups regarding cardiovascular morbidities including diastolic dysfunction, pulmonary hypertension, calcified valves, hypertensive heart, ischemic heart disease and arrhythmia opposite to **Wang *et al.*** [(9)], who found that RRF associates with better overall survival, cardiovascular outcomes, and quality of life.

Our study also found No significant correlation between low serum Mg and diastolic dysfunction in the 2 studied groups contradictory to **Angkananard *et al.*** [(10)] mentioning that, in heart failure (HF) patients, hypermagnesemia with serum Mg≥1.05 mmol/L was associated with an increased risk of CV mortality but this was not observed for hypomagnesemia. This finding was limited to the elderly patients with chronic HF who had reduced LV systolic function.

In our study there was significant correlation between older age and diastolic dysfunction similar to **Evelien *et al.*** [(11)] who found that in community-dwelling people aged ≥60 years, diastolic left ventricular dysfunction is very common, with a median prevalence of 36.0% (range 15.8–52.8%), and systolic dysfunction is less common with a median of 5.5% (range 3.3–9.2%).

Also we found no significant correlation between serum magnesium and pulmonary hypertension. Another opinion states that pulmonary hypertension in ESRD patients may be induced and/or aggravated by left ventricular disorders and risk factors including arteriovenous fistula, volume overload, vascular calcification and stiffening and severe anemia. However, evidence from **Yigla *et al.*** [(12)] does not support the role of pulmonary calcification in the pathogenesis of pulmonary hypertension, and as mentioned by **Gonzalez *et al.*** (4) there is a link between Mg deficiency and vascular calcification, therefore there could be an indirect relation between Mg level and pulmonary hypertension but as a matter of fact this conclusion needs further studies.

In our study there was no significant correlation between serum magnesium level and hypertensive heart disease. **Cunha *et al.*** [(13)] found that hypertensive patients generally have reduced intracellular concentrations of magnesium, while the contents of sodium and calcium are often increased compared to normotensive subjects.

Rodríguez-Moran and Guerrero-Romero [(14)] suggested that low serum magnesium levels could play an important role in the pathophysiology of prehypertension in otherwise healthy subjects.

Low serum magnesium was also a strong predictor of an increase in left ventricular mass in a large German cohort of patients, even after adjustment for many covariates including hypertension [(15)].

According to **Matias *et al.*** [(16)] results, from a large prevalent HD population, low magnesium levels are a good cardiovascular risk marker, associated with higher pulse pressure, left ventricular mass index and vascular calcifications, and a good predictor of all-cause and cardiovascular mortality.

One possible explanation for this association is the relationship between hypomagnesaemia and high aldosterone levels, responsible for the development of left ventricular hypertrophy and myocardial fibrosis. Moreover, hypermagnesemia inhibits parathyroid hormone (PTH) secretion, which is considered an independent risk factor for vascular calcification, left ventricular hypertrophy and mortality in CKD patients [(16)].

There was no significant correlation between residual renal function and hypertensive heart disease. This study is in direct contrast to the retrospective study by **Wang *et al.*** [(9)], where loss of RRF was associated with more severe LVH. Similar results was described by **Menon *et al.*** [(17)] showing that blood pressure control worsened with time on peritoneal dialysis as RRF declines

In our study we also found that Low serum magnesium was highly significantly correlated

to ischemic heart disease. However, in **Matias *et al.*** [16] study, patients with coronary artery disease did not present lower magnesium concentrations. **Sakaguchi *et al.*** [18] found a significant inverse association between the coronary artery calcification density and serum magnesium levels. This association was maintained after extensive adjustment for clinical factors related to MIA syndrome and MBD including FGF23. **Sugunakar *et al.*** [19] found that serum Mg levels, independent of other risk factors, are inversely related to the incidence of acute myocardial infarction.

We also found that there was no significant correlation between serum magnesium level and arrhythmia. In nondialysis patients, there are anecdotal reports of monomorphic ventricular tachycardia, torsades de pointes, and ventricular fibrillation associated with hypomagnesemia that responded to magnesium repletion [5]. Magnesium deficiency is known to predispose to the evolution of cardiac arrhythmias even with normal serum potassium concentration. Magnesium deficiency interferes with the function of membrane ATPase and thus, the pumping of sodium out from the cells and potassium into the cells is impaired. This disequilibrium of potassium between intra and extra cellular spaces may result in changes in resting membrane as well as disturbance in the repolarization phase and results in cardiac arrhythmias [19].

Severe hypermagnesemia is known to cause cardiac conduction defects, including bradyarrhythmias complete heart block. However, these findings are rarely seen unless plasma magnesium concentration is elevated (>4-5 mg/dL), which is now very uncommon in HD patients [5].

Conflict of interest: nil

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