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International Journal of Clinical Biochemistry and Research

Journal homepage: <https://www.ijcbr.in/>

Original Research Article

Serum magnesium and zinc levels- A predictor of cardiovascular risk in hemodialysis patients

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ARTICLE INFO

Article history:

Received 15-06-2021

Accepted 24-08-2021

Available online 08-10-2021

Keywords:

Cardiovascular disease

Dialysis patients

Framingham risk score

Magnesium

Zinc

ABSTRACT

Background: Cardiovascular disease is one of the leading causes of mortality in haemodialysis patients. Several studies have demonstrated the relation of zinc and magnesium in cardiovascular disease. In present study we aimed to measure serum zinc and magnesium levels and correlate with the Framingham score to calculate the cardiovascular risk.

Materials and Methods: Present study was prospective, cross sectional type, conducted in chronic kidney disease patients undergoing haemodialysis. Serum magnesium, zinc, cholesterol, urea, creatinine, HDL cholesterol, systolic BP are measured and Framingham score was calculated. And zinc and magnesium values were correlated with Framingham score.

Results: The study is conducted in 100 CKD patients undergoing hemodialysis. Out of 100 CKD patients undergoing hemodialysis, 59% had high risk, 28% had intermediate risk, and 13% had low risk of developing cardiovascular disease according to their Framingham risk score. In these patients, zinc and magnesium levels were found and correlated with Framingham risk score. Out of 100 patients undergoing hemodialysis, 37 patients were hypomagnesemic, 43 patients were normomagnesemic, 20 patients were hypermagnesemic. In this, a positive correlation was found between development of hypomagnesemia and duration of hemodialysis. Magnesium level was correlated with Framingham risk score. In this hypomagnesemic patients, 67% patients have low risk, 8% have intermediate risk, 24% patients have high risk of developing heart disease. Out of 100 patients, 86 patients have normal zinc level, 14 patients have increased zinc level. Zinc levels was not altered during dialysis. These patients already have risk of developing heart disease independent of zinc level.

Conclusion: In our study, magnesium level of haemodialysis patients was reduced and it is associated with duration of haemodialysis. Zinc levels were not altered in the patients.

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1. Introduction

Chronic kidney disease (CKD) is gradual loss of kidney function over a period of years associated with many other complications. CKD is defined as abnormalities of kidney structure and function present for more than 3 months with implications for health caused by Diabetes Mellitus

(31.5%), hypertension (27.4%), glomerulonephritis (13.5%), obstructive uropathy (5.4%), polycystic kidney disease (3.4%) and idiopathic (18%).¹ Complications CKD include electrolyte imbalances, abnormal bone mineral metabolism, cardiovascular abnormalities. Prevalence of CKD in India is 800 per million people. Each year 2 lakh patients develop CKD in India among which 1 lakh people are undergoing dialysis.² CKD is classified into

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five stages based on GFR and persistent albuminuria in which stage 4 and stage 5 patients require haemodialysis or kidney transplant. Criteria for initiating dialysis include the presence of uremic symptoms - the presence of hyperkalaemia, persistent extracellular volume expansion, acidosis, bleeding diathesis despite conservative measures and estimated GFR below 10ml/min/1.73m².

Patients undergoing long term haemodialysis have altered trace elements level may be due to decreased dietary intake, decreased absorption, altered dialysate concentration, increased excretion, etc.³ Zinc, an important trace mineral plays a significant role in immune function, metabolism of proteins, carbohydrates, nucleic acids, regulation of more than 300 enzyme activity and has antioxidant property which helps to protect cardiovascular disease.⁴⁻⁶ Magnesium, an abundant intracellular cation, is responsible for various metabolic process like protein synthesis cellular energy production and storage, cell growth, DNA and RNA synthesis and catalyses about 300 enzyme systems in our body.⁷⁻¹⁰ Magnesium homeostasis is maintained by bone, intestine and kidney.

Patients with CKD have a high burden of cardiomyopathy, atherosclerosis and arteriosclerosis.^{11,12} There are various factors that increases the cardiovascular disease in haemodialysis patients such as hypertension, glucose intolerance, dyslipidaemia, high serum homocysteine levels, altered calcium-phosphorous metabolism and other contributing factors like altered zinc levels and altered magnesium levels increases cardiovascular risk.¹² Cardiovascular disease accounts for 50% of death among patients undergoing haemodialysis.¹³

Both zinc and magnesium levels are reduced in CKD patients undergoing haemodialysis. Reduced zinc levels lead to activation of many atherogenic factors such as increased production of reactive oxygen species and reduced magnesium levels leads to hypokalaemia causing cardiac arrhythmia, atrial fibrillation, ventricular fibrillation, both leading to cardiovascular disease.¹⁴

2. Materials and Methods

This Prospective cross-sectional study was conducted in CKD patients undergoing hemodialysis. The patients between the age 19 and 81 were included in the study. Patients with altered zinc (Wilson's disease, acrodermatitis, enteropathica) and magnesium (hypothyroidism, milk alkali syndrome, GI disease) levels were excluded from the study. The patient was enrolled in the study after obtaining written informed consent. The patients' detailed clinical history and examination is recorded. The Framingham risk score was calculated and the patient's serum zinc levels and magnesium levels were calculated using spectrophotometric method and calmagite method respectively. Statistical analysis was performed using student's t test and chi square test, p-values <0.05 were considered as statistically

significant.

3. Results

Totally about 100 patients undergoing haemodialysis were included in this study. Of these, 87 were males, 13 were females. Average years of age include 24 years to 76 years of age with standard deviation 49.34 ±12.1. 5ml of venous blood is collected post dialysis from which zinc, magnesium and HDL cholesterol, creatinine, urea, glucose values were calculated. And using these values Framingham score was calculated.

Table 1: Mean and Standard deviation of zinc and magnesium level

Serum Zinc Levels(Mean ± Standard deviation)	128.62 ± 12.23
Serum Magnesium Levels (Mean ± Standard deviation)	1.81 ± 0.81

3.1. Framingham risk score

Framingham risk score was calculated based on the parameters such as age, cholesterol, HDL cholesterol, systolic BP and smoking. And these patients were grouped into those with low, intermediate and high risk. Out of 100 patients, 59 patients have low risk, 28 patients have intermediate risk and 13 patients have high risk. In these patients, depletion of zinc and magnesium worsens the cardiovascular risk

3.2. Correlation of serum magnesium level and framingham risk score

The mean magnesium values were measured and patients were divided into below normal range, normal range and above normal range. The mean magnesium value measured was 1.81±0.81. Out of 100 patients, number of patients with normal range were 43, below normal range were 37 and above normal were 20.

Then correlation was made between serum magnesium level and Framingham risk score. In these patients, out of 37 patients with hypomagnesemia, 67% patients have low risk, 13% patients have intermediate risk, 24% patients have high risk.

3.3. Correlation of magnesium levels with duration of hemodialysis

Serum magnesium levels of the patients are correlated with the duration of dialysis undergone by the patients. In this, patients who undergone dialysis for long periods develop hypomagnesemia than patients who have undergone dialysis for short period. Out of 37 patients with hypomagnesemia, 48% patients are doing dialysis for more than 36 months,

Table 2: Correlation of magnesium levels with Framingham score

Risk Level	Correlation of magnesium levels with Framingham score (CAD risk score)			
	10 years CVD FRS Risk	Below Normal (<1.5 mEq/L)	Normal (1.5-2.5 mEq/L)	Above Normal (>2.5 mEq/L)
Low	<10%	25	18	12
Intermediate	10-19%	3	17	8
High	≥20%	9	8	3

Table 3: Correlation of magnesium level with the duration of haemodialysis

Duration	Below normal	Normal	Above normal
0-12 months	1(2%)	21(48%)	18(90%)
13-24 months	6(16%)	21(48%)	1(5%)
25-36 months	12(32%)	1(2%)	1(5%)
Above 36 months	18(48%)	-	-

32% patients are doing dialysis in the range of 25-36 months, 16% patients are doing dialysis in the range of 13-24 months, and 2% patients are in the range of 0-12 months. While patients with above normal and normal levels are more in the range of dialysis from 0-12 months. This indicates that patients who are undergoing long term haemodialysis are more prone to develop hypomagnesemia.

3.4. Correlation of serum zinc level and framingham risk score

Serum zinc values were measured and patients were grouped into normal and above normal. The mean value was 128.62 ± 12.23 . Out of 100 patients, 86 patients have normal values and 14 patients have above normal values.

Then correlation was made between serum zinc level and Framingham risk score. Out of 86 patients with normal range, 44 patients have low risk, 25 patients have intermediate risk and 17 patients have high risk of cardiovascular risk.

In our study there was no alteration in zinc level in patients undergoing dialysis. This indicates that there was no association between zinc level and duration of dialysis.

4. Discussion

We included 100 patients undergoing haemodialysis in our study and their serum zinc and magnesium levels were measured and Framingham score was calculated to estimate the cardiovascular risk. Out of 100 patients, 59 patients have low risk, 28 patients have intermediate risk and 13 patients have high risk of developing cardiac disease. In addition to this, patients with low zinc and magnesium levels have increased risk of developing cardiovascular disease.

The mean value of serum magnesium was 1.81 ± 0.81 . In 100 patients, 37 patients were hypomagnesemic, 43 patients with normal range and 20 were hypermagnesemic. This indicates that patients who are undergoing dialysis may be prone to develop hypomagnesemia. Delmar J Mahler et al⁶

established that differences in dialysis concentration and dietary intake leads to changes in magnesium concentration. Hypomagnesemia is correlated with Framingham risk score to calculate 10-year cardiovascular risk. Of these, 67% patients have low risk, 13% patients have intermediate risk and 24% patients have high risk of developing heart disease. Hypomagnesemia causes alteration in $\text{Na}^+\text{-k}^+\text{-ATPase}$ pump, increase in serum levels of inflammatory cytokines, IL-1, IL-6, TNF, increases endothelial cell secretion of IL-8, PDGF-BB and MMP-2, MMP-9 and tissue inhibitor of metalloproteinases, and decreased production of SOD and catalase, which leads to increased production of ROS. All these changes lead to increased cardiovascular stress and leads to cardiovascular disease. In 2007 Eiji Ishimura et al¹⁵ described the role of magnesium in its protective effects against cardiovascular disease, neoplasia, inflammation and infectious diseases and stated its deficiency increases cardiovascular risk. Haigney et al¹⁴ described decreased magnesium levels is associated with increased cardiovascular risk. In our study, level of decrease of magnesium levels in dialysis patients corresponds to the duration of dialysis. The patients who were undergoing haemodialysis for long periods develops hypomagnesemia than patients who were undergoing haemodialysis for short period. Cardiovascular disease accounts for increased mortality in CKD patients rather than the kidney failure. Mark. J. Sarnak et al.,¹⁶ William. G. Goodman et al¹⁷ and many authors suggests that cardiovascular events lead to increased mortality in chronic kidney disease patients. The 1998 report of NSK task force on cardiovascular disease in chronic renal failure recommended that patients with CKD are considered to be in the highest risk of developing subsequent cardiac events. These conclusions were confirmed by 2003 statement from American council on kidney in cardiovascular disease, high BP research, clinical cardiology, epidemiology and prevention.

Other patients with normal and above normal range have risk of developing cardiac disease which is attributed by the parameters used to calculate Framingham score.

Table 4: Correlation of zinc levels with Framingham score

Risk Level	Correlation of Zinc levels with Framingham score (CAD risk score)		
	10 years CVD FRS Risk	Normal (70-140 micrograms)	Above Normal (>140 micrograms)
Low	<10%	44	10
Intermediate	10-19%	25	2
High	≥20%	17	2

And in our study, the mean value of serum zinc was 128.62 ± 12.23 . In our study, serum zinc levels were not altered during dialysis treatment. There was no correlation found between serum zinc level and cardiovascular disease.

5. Conclusion

This study shows the increased prevalence of hypomagnesemia among patients who are undergoing long term haemodialysis. And also, that patients with low magnesium levels are at increased risk of developing heart disease than patients with normal magnesium levels. And in this study, zinc level was not altered during dialysis treatment. Therefore, we conclude that magnesium levels are altered during dialysis treatment. So, monitoring of magnesium levels and maintaining normal magnesium levels by oral supplementation and altering dialysate concentration prevent increased risk of developing cardiovascular disease.

6. Conflict of Interest

The authors declare no conflict of interest.

7. Acknowledgement

Indian Council of Medical Research – Short Term Studentship 2018.

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Cite this article: Muruganantham B, Ganesan H, Gunavathi G, Devi M. Serum magnesium and zinc levels- A predictor of cardiovascular risk in hemodialysis patients. *Int J Clin Biochem Res* 2021;8(3):186-189.