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STUDY OF SERUM MAGNESIUM LEVEL IN ACUTE KIDNEY INJURY AND CHRONIC KIDNEY DISEASE AND ITS CLINICAL MANIFESTATIONS AND CORRELATION WITH OTHER BIOCHEMICAL PARAMETERS

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HOW TO CITE THIS ARTICLE:

Amit Naik, Rakesh Singh Jagat, Pranay Dhurvey, Sachin Chittawar. "Study of Serum Magnesium Level in Acute Kidney Injury and Chronic Kidney Disease and Its Clinical manifestations and correlation with other Bio-Chemical Parameters". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 74, September 14; Page: 12928-12933, DOI: 10.14260/jemds/2015/1865

ABSTRACT OBJECTIVES: To study the serum magnesium level in AKI and CKD, and its correlation with clinical manifestations and other biochemical parameters. **DESIGN:** A hospital-based cross sectional study. **SETTING:** Tertiary care teaching hospital in central India. **SUBJECTS:** Study population comprised of 75 cases of renal failure (50 CKD and 25 AKI) and 25 healthy control cases. **METHODS:** Study populations included were subjected to a thorough history taking with special emphasis to exclude the presence of other diseases which are known to alter the magnesium levels in serum. Diagnosis of renal-failure was established by measuring raised clinical blood urea nitrogen and serum creatinine with clinical sign and symptoms of renal failure. Serum magnesium level is measured in "mg/dl" using metallochromic dye (Xylidyl) colorimetric assay. Relevant predefined clinical and biochemical parameters recorded from each subjects in all three groups. Data were computed and analyzed using SPSS statistical software. **RESULTS:** Hundred subjects were enrolled in the study, 75 cases of renal failure (50 CKD and 25 AKI) and 25 healthy control cases. Range of serum magnesium in controls was 1.32 to 2.4mg/dl with a mean 1.856($\pm$ 0.2959). Mean blood urea, serum creatinine, sodium, potassium, calcium and magnesium level were 127.65 mg/dl, 6.75mg/dl, 135.24 MEq/L, 4.86 MEq/L, 9.28mg/dl and 2.89mg/dl respectively in AKI cases, and 111.36mg/dl, 7.02 mEq/dl, 135.01 MEq/L, 4.93 MEq/L, 8.99mg/dl and 2.75mg/dl respectively in CKD cases. Eight (16%) CKD cases had central nervous system depression with their mean serum magnesium level of 3.61 mg/dl. Four (16%) AKI cases had central nervous system depression with mean serum magnesium level of 3.47mg/dl. **CONCLUSION:** Serum magnesium level has prognostic significance in severity in AKI and CKD and CNS symptoms. Baseline serum magnesium should be done in every case of CKD and AKI with other electrolytes and renal function tests. There is positive correlation between serum magnesium and blood urea, creatinine & potassium while negative correlation between serum magnesium and serum sodium & calcium levels both in AKI and CKD case.

KEYWORDS: Serum Magnesium, Acute Kidney Disease (AKI), Chronic Kidney Disease (CKD).

INTRODUCTION: Diseases of kidney are increasing day by day. This is due to increased incidence of various diseases causing CKD like hypertension, diabetes, and various causes of AKI like sepsis and diarrhea, hypovolumic shock. Electrolyte metabolism in kidney diseases and other diseases is a subject of modern physiology and medicine. Four major cations sodium, potassium, calcium and magnesium are macro minerals of body and essential for various functions at cellular level. Of these first three cations have been extensively studied but this is not so true in case of magnesium because of lack availability of easy and less time consuming laboratory methods. Importance of magnesium in health

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and diseases cannot be over emphasized. Magnesium is invariably present in all living tissues and is essential for life.

In the last four decades normal and abnormal magnesium metabolism has been widely studied and more than 40 diseases have been described in the literature where alteration in serum magnesium level has been demonstrated. Serum magnesium is of particular interest in kidney diseases, eclampsia, delirium tremens and myocardial infarction. There are conflicting reports in literature concerning serum magnesium in chronic renal diseases. Hirschfelder and Haury (1934), Martin et al (1952) found⁽¹⁾ hypomagnesaemia while Pradhan et al (1964)⁽²⁾ and numerous others workers found definite hypermagnesaemia in chronic renal disease. Pathophysiology of certain symptoms in uraemia remains a mystery. It is generally regarded that end products of metabolism accumulate and lead to depression of central nervous system.

If in cases of renal diseases without uraemia, magnesium is given which produces depression of central nervous system (Hirsch Felder, 1934)⁽³⁾ it suggests that increase in serum magnesium may explain the nervous depression in uraemia patients. Cantarow (1959)⁽⁴⁾ stated that rise in serum magnesium is associated with the depression of central nervous system. These workers and others who found hypermagnesaemia in chronic renal diseases have postulated that the central nervous system depression found in these cases may be at least in part due to excess of magnesium. Studies concerning serum levels of magnesium in kidney diseases are not much in the literature. Relationship between renal uraemia and serum magnesium has not been clearly established. In the present study an attempt has been made to find out the serum magnesium levels in various types of renal diseases and its relationship with central nervous system depression found in renal uraemia.

MATERIAL & METHODS: The material for the present study comprised of 75 cases of renal failure (50 C.K.D. and 25 A.K.I.) and 25 healthy control cases. The cases were selected from different wards of Department of Medicine, Gandhi Medical College and Associated Hamidia Hospital, Bhopal. The subjects were divided in three groups healthy control (Group I). CKD (Group II) and AKI (Group III). Controls were selected from the resident staff medical students and members of the hospital staff. They were screened to exclude the presence of malnutrition, metabolic diseases, connective tissue diseases, malignancy, anaemia, myocardial ischemia renal disorder and leukemia. All patients were subjected to a thorough history taking with special emphasis to exclude the presence of other diseases which are known to alter the magnesium levels in serum. Diagnosis of renal-failure was established by measuring raised clinical blood urea. Nitrogen (BUN) and serum creatinine with clinical sign and symptoms of renal failure by taking basis of investigations the cases were divided in two irrespective of etiology.

The diagnosis of CKD is based on recognition of a constellation of signs and symptoms with or without urea nitrogen and creatinine concentration. The diagnosis of AKI was based on anuria or oliguria (Urine output less than 400ml/24 hours or falling urine output), however many patients with A. K. I. are not oliguric. Rising of BUN and/or serum creatinine concentration during biochemical monitoring of the seriously ill patient. All relevant predefined clinical parameters were recorded from enrolled cases. Enrolled cases were investigated for complete blood count with ESR, blood urea, serum creatinine, serum electrolytes (Na, K & Ca) and urine analysis. Plain X-ray abdomen (KUB region), intravenous pyelography, LE cell phenomenon, antinuclear antibodies and ultrasound were carried out as per indication in each patient. Serum magnesium level is measured in mg/dl using metallochromic dye (Xylidyl) colorimetric assay.

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STATISTICS: All data thus collected were computed and analyzed using SPSS software under the guidance of statistician. We summarized continuous variables using mean $\pm$ SD and categorical variables as frequencies and percentages. A Pearson's coefficient of correlation was calculated to find out significant correlation between various parameters and serum magnesium level. A probability of less than 5% (p value <0.05) is considered as significant in the study. The study was approved by the institute ethics committee and informed consent was obtained from subjects before enrollment.

RESULTS: Observations are based on 100 enrolled subjects in the study (25 controls, 50 CKD & 25 AKI). Among the 25 controls 14 were male, 11 were females. Mean age of control group was 30 (18-47) yrs. Range of serum magnesium in control cases was 1.32 to 2.4mg/dl with a mean 1.856($\pm$ 0.2959). Etiology of CKD (n=50) includes nephrotic syndrome in 10(20%), hypertensive encephalopathy in 20(40%), diabetics nephropathy in 19(38%). and obstructive uropathy in 1(2%) cases. Maximum 16 cases (32%) were from age group 51-60 years, while minimum i.e. 3 cases (6%) from Age group 10-20 years of age. 36 cases (72%) were males and 14 cases (28%) were females. Male to female ratio was 2.57:1. Of the 25 cases. of A.K.I. with highest 6 cases (24%) in 31-40 years consisting 3 males (12%) and 3 females (12%). Majority of cases CKD had fever, vomiting, oliguria and confusion. Presenting symptoms in AKI were oliguria (88%), fever (64%), odema (32%), diarrhea and vomiting (52%) encephalopathy (16%). Eight (16%) CKD cases had central nervous system depression with their mean serum magnesium level of 3.61 mg/dl. Four (16%) AKI cases had central nervous system depression with mean serum magnesium level of 3.47mg/dl. Mean blood urea, serum creatinine, sodium, potassium, calcium and magnesium level were 127.65 mg/dl, 6.75mg/dl, 135.24 MEq/L, 4.86 MEq/L, 9.28mg/dl and 2.89mg/dl respectively in AKI cases, and 111.36mg/dl, 7.02 mg/dl, 135.01 MEq/L, 4.93 MEq/L, 8.99mg/dl and 2.75 mg/dl respectively in CKD cases. A correlation between serum magnesium level with other biochemical parameters in AKI and CKD cases were shown in table I & table 11 respectively.

DISCUSSION: Electrolyte and metabolic, disturbances and their biochemical role in disease and its symptoms opened a new chapter in disease pathophysiology and treatment. Magnesium is gaining the important status now as other electrolytes have been extensively studied. This study is one of the few studies to evaluate the serum magnesium level in renal diseases and its correlation with clinical & other biochemical parameters. Serum magnesium level ranges from 1.3-2.4mg/dl with a mean of 1.85 ($\pm$ 0.29) in control without significant change in different age & sex groups.

Mean serum magnesium level was 2.75mg/dl in CKD cases with positive correlation between serum magnesium and blood urea, creatinine & potassium while negative correlation between serum magnesium and serum sodium & calcium- levels. Similar findings have been observed by various other authors. Hirschfelder and Haury (1934) (ref no.1) showed by animal experiments that injury to renal tubules is more important than injury to glomeruli for hypermagnesaemia of renal insufficiency. It is not possible to determine in the living human being whether tubules are more injured or glomeruli, but on the basis of above experiment it can be conjectured that renal tubules might be more injured than glomeruli in cases showing hypermagnesaemia.

The same mechanism could also explain the conflicting reports of high and low serum magnesium in chronic renal diseases on the basis that in some cases tubules might be more injured than glomeruli and vice versa. Robinson et al (1959) (ref no2) found that in renal disease cases when the glomerular filtration rate is less than 30c.c. per minute, there occurred definite hypermagnesaemia.

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Mean serum magnesium level was 2.89mg/dl in AKI cases with positive correlation between serum magnesium and blood urea, creatinine & potassium while negative correlation between serum magnesium and serum sodium & calcium levels.

Present findings are in close conformity with those of Hirschfelder and Haury (1993) (ref no. 1) who found hypermagnesaemia in 4 cases of acute nephritis. Our findings are also very close to those of Robinson et al (1959 (ref no. 2). Regarding the effect of hypermagnesaemia it is universally accepted that magnesium is central nervous system depressant. However the relationship between serum magnesium levels and various armies of central nervous system depression is not established. Cantarow (1959) (ref no. 3) stated that at 5 mg% of serum magnesium level sedation and mild hypnosis develops and at 15-20 mg% profound coma is produced and as the serum magnesium rises above normal drowsiness develops and at 10 mg% level the patient becomes comatose.

In the present series of 35 cases of chronic renal diseases hypermagnesaemia was present in 34 (97.14%) cases while only 12 cases (34.28%) had central nervous system depression of various grades.

Out of 12 cases of central nervous system depression, 9 had mental confusion and mean serum magnesium in these cases was 3.96mg%. Present study has shown that serum magnesium level is related with severity of ARF and CRF and CNS depression which can be treated with dialytic intervention. Basic cause of high serum magnesium is related with low glomerular filtration rate and passive back diffusion through damaged tubule cells. It is therefore concluded from the present study that all patients suffering from ARF or CRF should be advised low magnesium in diet similar restriction to potassium to prevent CNS depression & Cardiac arrhythmia. Serum magnesium level should also been routinely done in cases of CKI) and AKI and cases showing hyponatremia and hypocalcemia.

Table 1: Correlation between serum magnesium levels and blood urea, serum creatinine, potassium, sodium, calcium levels in AKI cases.

Sl. No.		Mean	Standard Deviation	Pearson Correlation	P value
1	Urea	127.65	49.31	0.158	0.451
2	Creatinine	6.75	2.25	0.190	0.362
3	Potassium	4.86	0.86	0.238	0.252
4	Sodium	135.24	6.78	-0.389	0.055
5	Calcium	9.28	0.91	-0.024	0.909

Table 1: Correlation between serum magnesium levels and blood urea, serum creatinine, potassium, sodium, calcium levels in AKI

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Table II: Correlation between serum magnesium levels and blood urea, serum creatinine, potassium, sodium, calcium levels in CKD cases.

Sl. No.		Mean	Standard Deviation	Pearson Correlation	P value
1	Urea	111.36	41.72	0.242	0.090
2	Creatinine	7.02	3.08	0.137	0.343
3	Potassium	4.93	0.64	0.336	0.017
4	Sodium	135.01	5.49	-0.167	0.246
5	Calcium	8.99	1.52	-0.619	0.00

Table 2: Correlation between serum magnesium levels and blood urea, serum creatinine, potassium, sodium, calcium levels in CKD cases

CONCLUSIONS: Serum magnesium level has prognostic significance in severity in AKI and CKD and CNS symptoms. A baseline serum magnesium should be done in every case of CKD and AKI with other electrolytes and renal function tests. There is positive correlation between serum magnesium and blood urea, creatinine & potassium while negative correlation between serum magnesium and serum sodium & calcium levels both in AKI and CKD cases. Hypermagnesaemia may be the cause of CNS depression in CKD and AKI patients so its level should be closely monitored in renal failure patient with CNS manifestations.

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Date of Submission: 26/08/2015.

Date of Peer Review: 27/08/2015.

Date of Acceptance: 08/09/2015.

Date of Publishing: 14/09/2015.