

# “A STUDY OF SERUM MAGNESIUM LEVELS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS, HYPERTENSION, DYSLIPIDEMIA, CORONARY ARTERY DISEASE AND CORRELATION WITH ASCVD RISK SCORE.

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**ABSTRACT-** There has been an association between serum Magnesium levels and presence of Diabetes Mellitus, Hypertension, Dyslipidemia, BMI and severity of coronary artery disease. In this study we measured the serum Magnesium levels in patients having Diabetes Mellitus, Hypertension, Dyslipidemia and angiographically proven coronary heart disease and studied the trend of Magnesium levels in these individuals. We observed that mean Magnesium levels were lower among the Diabetic group compared to non-diabetic; lower mean Magnesium levels in Hypertensive group compared to non-hypertensive group; lower mean Magnesium levels among the Coronary artery disease group compared to patients without coronary artery disease; higher mean Magnesium levels in the overweight people compared to normal BMI individuals. However, the severity of coronary artery disease i.e Single vessel/Double vessel/Triple vessel disease had no relationship with Magnesium levels.

**INDEX TERMS-** ASCVD risk, Coronary artery disease, Diabetes, Hypertension, Magnesium

## INTRODUCTION

As we all know that Magnesium is an abundant mineral in the human body. An average sized adult has around 25g of Magnesium.<sup>[1]</sup> Magnesium acts as a co-factor in numerous enzymes in the human body responsible for glycolysis, ATP production, Oxidative phosphorylation, synthesis of nuclear material, anti-oxidant action.<sup>[2]</sup> Mg is also responsible for Ca<sup>2+</sup> and K<sup>+</sup> ion transport across the cell membranes which is crucial for impulse conduction in nerves, muscle and cardiac contraction.<sup>[2]</sup> Rich sources of Magnesium are nuts, green leafy vegetables, whole wheat, brown rice, carrots, apple, banana, beef and chicken breast. <sup>[3]</sup> Magnesium deficiency has long been associated with Diabetes Mellitus and metabolic syndrome as Magnesium plays a role in glucose homeostasis. Certain clinical trials show role of magnesium supplementation in reducing the blood glucose values and hence reduce the risk of developing metabolic syndrome and its consequences. <sup>[4,5]</sup> Magnesium similarly has a role in hypertension. Magnesium relaxes the vascular Smooth muscle cells and hence reduces the blood pressure. The role of Magnesium in Coronary Artery Disease is still debatable as there are no enough studies establishing a causal relationship. As per a large systematic review and meta-analysis done by Grober U, people with low serum magnesium levels and low dietary intake of Magnesium containing foods had more risk of developing an Ischemic heart disease.<sup>[6]</sup> In this cross sectional study done in Kasturba Medical College & Hospital, Manipal; we have measured the serum Magnesium levels among the risk factors for Coronary artery disease like Diabetes, Hypertension, Dyslipidemia, Obesity and also studied the Magnesium levels in coronary artery disease and also compared with the severity of Coronary artery disease.

## Study Methodology

This is a cross sectional study done in Kasturba Medical College & Hospital, Manipal, Karnataka, India. The study was conducted only after obtaining an approval by the Institutional ethics committee and also the study was registered under the Clinical Trials Registry of India. The calculated sample size was 162. In our study we could obtain a total of 156 samples.

- Patient selection:** - Patients visiting our out-patient department and also in-patients admitted under the Department of Internal Medicine were selected for the study. Patients having Type 2 Diabetes Mellitus, Hypertension, Dyslipidemia and angiographically proven Coronary Heart Disease were included in the study. Patients who were having chronic kidney disease, chronic liver disease, endocrinopathy, rheumatologic diseases, magnesium supplements, antacids, diuretics and chronic alcoholic were excluded as these conditions can affect the serum magnesium levels and act as confounders. The patients were interviewed with a proforma and informed consent was taken after counseling. Questions related to Demographic details were taken; and history pertaining to whether Diabetic, Hypertensive or Dyslipidemia or suffering from Coronary artery disease were asked. Questions related to ASCVD risk score calculation like race, smoking history, whether on antihypertensive or statins were asked. Blood pressure was taken for all individuals included in the study. Height, weight, Waist circumference and Hip Circumference was measured. Blood samples were collected for measuring serum Magnesium levels by venepuncture. ASCVD risk score was calculated as per American college of cardiology ASCVD risk estimator.

### Statistical Analysis

We calculated that a sample size of 162 patients would be required for a 5% level of significance and 80% power considering moderate effect size. However, we obtained a total sample of 156 in the study. Data was entered and analyzed using the Statistical Package for the Social Sciences (SPSS), version 20.

The results obtained are tabulated as follows.

**Table 1: Study Demographics**

| Characteristics                        | Value in % or Mean ± Standard deviation |
|----------------------------------------|-----------------------------------------|
| Age- yrs                               | 57.73 ± 9.925                           |
| Sex- Males(N)                          | 102 (65.38%)                            |
| Females(N)                             | 54 (34.62%)                             |
| Type 2 Diabetes Mellitus – Yes         | 98 (62.82%)                             |
| No                                     | 58 (37.18%)                             |
| Hypertension – Yes                     | 78 (50%)                                |
| No                                     | 78 (50%)                                |
| Dyslipidemia – Yes                     | 75 (48%)                                |
| No                                     | 81 (52%)                                |
| Coronary Artery Disease- Yes           | 95 (60.89%)                             |
| No                                     | 61 (39.11%)                             |
| Severity of Coronary Artery Disease    | (N=95)                                  |
| Single Vessel Disease                  | 40 (42.1%)                              |
| Double Vessel Disease                  | 38 (40%)                                |
| Triple Vessel Disease                  | 17 (17.9%)                              |
| Body Mass Index(BMI) kg/m <sup>2</sup> | (N=156)                                 |
| Normal(<22.9)                          | 49 (31.41%)                             |
| Overweight(23-24.99)                   | 36 (23%)                                |
| Pre-Obese(25-29.99)                    | 62 (39.7%)                              |
| Obese(>30)                             | 9 (5.89%)                               |
| Waist Hip Ratio(Mean)- Males           | 0.9845±0.054                            |
| Females                                | 0.9279±0.065                            |
| Total Cholesterol- Males               | 155±46.123                              |
| (mg/dl) Females                        | 178±56.108                              |

|                                   |               |
|-----------------------------------|---------------|
| Triglyceride – Males<br>(mg/dl)   | 153±98.5      |
| Females                           | 163±76.4      |
| LDL-Cholesterol- Males<br>(mg/dl) | 94± 38.4      |
| Females                           | 112±49.25     |
| HDL-Cholesterol- Males<br>(mg/dl) | 36±12.737     |
| Females                           | 39±13.823     |
| Magnesium Level- Males<br>(mg/dl) | 1.910±0.237   |
| Females                           | 1.894±0.212   |
| 10 yrs ASCVD Risk score (N=49)    | 12.130±10.614 |
| Optimal ASCVD risk score(N=53)    | 3.547±3.902   |

Plus-Minus Indicates Mean ± Standard Deviation

**Table2: Correlation between Serum Magnesium and Cardio-Vascular Risk Factors**

| Parameter                                                    | Serum Mg level<br>(Mean +/- S.D)                         | p-value      |
|--------------------------------------------------------------|----------------------------------------------------------|--------------|
| Sex<br>Male=102<br>Female= 54                                | 1.9107±0.237<br>1.8944±0.212                             | 0.673        |
| Diabetes<br>Yes=98<br>No=58                                  | 1.879±0.247<br>1.948±0.186                               | 0.070        |
| Hypertension<br>Yes=78<br>No=78                              | 1.896±0.258<br>1.914±0.196                               | 0.626        |
| Dyslipidemia<br>Yes=75<br>No=81                              | 1.906±0.231<br>1.903±0.025                               | 0.448        |
| Coronary artery<br>disease<br>Yes=95<br>No=61                | 1.898±0.235<br>1.914±0.219                               | 0.675        |
| SVD=40<br>DVD=38<br>TVD=17                                   | 1.9125±0.217<br>1.865±0.218<br>1.941±0.308               | 0.796        |
| BMI<br>Normal=49<br>Overweight=36<br>Pre-obese=62<br>Obese=9 | 1.869±0.221<br>2.019±0.237<br>1.8677±0.215<br>1.900±0.20 | <b>0.007</b> |

**Table3:**

| <b>Parameters</b>        | <b>p-value</b> |
|--------------------------|----------------|
| Age                      | 0.183          |
| Sex                      | 0.673          |
| Diabetes Mellitus        | 0.070          |
| Hypertension             | 0.626          |
| Dyslipidemia             | 0.448          |
| Body Mass Index          | 0.007          |
| Systolic Blood pressure  | 0.602          |
| Diastolic Blood pressure | 0.313          |
| WHR                      | 0.692          |
| Total cholesterol        | 0.379          |
| Triglycerides            | 0.289          |
| HDL-C                    | 0.256          |
| LDL-C                    | 0.140          |
| 10 yrs ASCVD             | 0.655          |
| Optimal ASCVD            | 0.119          |

**Correlation between Magnesium Levels and Cardiovascular risk factors**

An Independent samples T test was applied to compare the serum Magnesium levels with parameters viz. Age, Sex, Diabetes Mellitus, Hypertension, Dyslipidemia, Coronary Artery Disease. A one way Anova was used for comparing multiple groups viz. Severity of Coronary Artery Disease (Single vessel disease/Double Vessel Disease/ Triple Vessel Disease), Compare BMI groups (Normal/Overweight/Pre-Obese/Obesity). A Pearson correlation test was done to compare Serum Magnesium levels with Scalar variables like Systolic Blood pressure, Diastolic Blood Pressure, Waist-Hip Ratio, Total Cholesterol, Triglycerides, HDL-C, LDL-C and for ASCVD risk score.

**Results**

**Demographics and patient data**

The study population had a total of 102(65.3%) males and 54(34.7%) females among the 156 patients collected. Hence, males dominated the study population. This was similar to an Indian study done by Mahalle et al<sup>[7]</sup> which was male predominant. The age groups included were all above the age of 40 yrs for ASCVD risk estimation, except for 1 patient who was 36 yrs of age.

The study population comprised of 98(62.8%) diabetics and the rest 58(37.2%) were non-diabetics. The study had equal number of hypertensive and non-hypertensive patients. There were 75 people with dyslipidemia which constituted 48% of the study population and the rest 52% did not have dyslipidemia.

Out of the 156 patients, 95(60.8%) had angiographically proven coronary artery disease and the rest 39% did not have coronary artery disease. The frequency of severity of coronary artery disease were Single Vessel Disease > Double Vessel Disease > Triple Vessel Disease.

In this study only 31.4% of the individuals were in the normal BMI range, 23% of patients were overweight, 39.7% were in the pre-obese category and 5.7% were obese highlighting the high prevalence of overweight and obesity in the Asian population.

We also observed that total cholesterol, triglycerides, LDL cholesterol, HDL cholesterol were higher among the females than the males. This may be attributed to the age group recruited being more than 40 yrs, since postmenopausal women are at a higher risk of having dyslipidemia.

### **Magnesium and Cardiovascular risk factors**

In this study the mean Mg levels were slightly higher among the males than females however this was not statistically significant. This study showed that mean Mg levels were lower among the diabetics than non-diabetics which was consistent with the study done by Mahalle et al<sup>[7]</sup>, however our study did not show any statistical significance between the 2 groups. This study also showed that mean Mg levels were lower among the hypertensives than the non-hypertensives which was consistent with the study done by Mahalle et al<sup>[7]</sup>. However, our study did not show any statistical significance between the 2 groups. This may be explained by the fact that dietary patterns were not taken into consideration which can have a significant impact on the serum Mg levels. There may also be an element of selection bias as this was not an epidemiological study in the general population and the samples collected were hospitalized sick patients having co-morbidities.

This study did not show any difference between the Mg levels among the Dyslipidemia and non-dyslipidemia group. This was not consistent with the studies done by Mahalle et al<sup>[7]</sup> which showed a significant difference between the dyslipidemia and non-dyslipidemia group. The cause for this is multifactorial as most of the diabetics with ASCVD risk were already on a statin which would have reduced their cholesterol levels and also dietary habits were not taken into consideration. Hence, a matched comparison could not be made between the 2 groups due to confounders.

This study showed that patients having coronary artery disease had lower magnesium levels than those without a coronary artery disease. This was consistent with the studies done by Joachim M et al<sup>[8]</sup> which showed that serum magnesium levels were lower in patients with coronary artery disease than patients without CAD and the results were not statistically significant in both these studies. This may be attributed to the small range of serum Mg levels and also serum Mg level does not reflect the total body Magnesium. This study also showed that severity of Coronary artery disease had no statistical significance with serum Mg levels. However patients with DVD had a slightly lower Mg levels than patients with SVD, however this was not statistically significant.

In this study magnesium levels were found to be higher among the overweight and obese individuals compared to the normal BMI individuals and this correlation was statistically significant. This data was however not consistent with the studies done by Mahalle et al<sup>[7]</sup> and Gengiz et al<sup>[9]</sup> These conflicting results may again be explained as dietary history in this study has been omitted which is a major drawback. Other reason could possibly be that obese patients tend to eat more and may have a higher serum magnesium levels but at present this question may be debatable as currently there is not enough literature to support this.

In our study there was no correlation between waist-hip ratio and the serum Mg levels and this data was consistent with the studies done by Mahalle et al.<sup>[7]</sup>

In our study we could not establish any significant correlation with magnesium deficiency and lipid levels i.e Total cholesterol, triglycerides, LDL and HDL. This data was consistent with the study done by Joachim et al.<sup>[8]</sup>

All patients without having an ASCVD underwent an ASCVD risk assessment for 10yrs ASCVD risk and optimal ASCVD risk using an ASCVD risk estimator app by the American college of cardiology foundation. There was no statistically significant correlation between the serum magnesium levels and the 10 yrs ASCVD risk score and also the optimal ASCVD risk score. This is the 1<sup>st</sup> ever study in India comparing the ASCVD risk score with the magnesium levels. At present magnesium levels affecting the

future ASCVD risk need to be further assessed by larger epidemiological studies as this study data is insufficient to conclude the same.

## Conclusion

In this study we have observed that the mean Magnesium levels were lower among the Diabetics, Hypertensive, Coronary Artery Disease groups compared their counterparts. Dyslipidemia had no correlation with Magnesium levels; and also the Total Cholesterol, LDL, HDL and Triglycerides had no correlation with Magnesium levels. We also observed that higher BMI individuals had a higher serum Magnesium levels than the normal BMI individuals and the data was statistically significant, hence the possibility of obesity paradox can be bought in. However this is a very naïve concept and needs further understanding and research. The role of magnesium in metabolic syndrome and coronary artery disease needs further understanding and more studies in future to establish an association. The method of Magnesium estimation in the body also needs to be refined as current methods like serum assay and urinary magnesium excretion does not reflect the total magnesium level in the body which may hamper the magnesium estimation and hence the results.

## Appendix

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