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**Evaluation of serum magnesium levels in patients with acute myocardial infarction**

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**Abstract**---Aim: To evaluate the serum magnesium levels in patients with acute myocardial infarction. Material and method: The present prospective observational study was conducted in the department of Medicine among 50 patients with acute myocardial infarction. Patients who presented to the hospital within 24 hours of onset of symptoms and diagnosed with acute myocardial infarction were included in the study. Blood samples collection were taken within 24 hours of onset of symptoms. All patients were evaluated for their ECG and cardiac enzymes and serum magnesium level by taking 5 cc venous blood sample in a disposable syringe and sent to biochemistry laboratory for analysis in fluoride bulb and plain bulb respectively. Results: Smoking was reported in 82% of the subjects whereas hypertension and diabetes mellitus in 64% and 46% of the subjects respectively. Sixteen percent, 24% and 60% of the subject’s time of presentation was 3-6 hours, 6-12 hours and 12-18 hours respectively. On day 5, only six percent (3) of the subjects with arrhythmia were having serum magnesium level (mg/dL) <1.6 while 14% of the subjects with arrhythmia reported 1.7-2.4 serum magnesium level (mg/dL). There was an increase in serum magnesium from Day-1 to Day-5 with statistically significant difference. Conclusion: Serum Mg levels raised towards normal values by 5th day. So it can be concluded that measurement of serum magnesium levels is of prognostic significance in acute MI.

**Keywords**---MI, CAD, magnesium, acute myocardial infarction.
Introduction

Coronary heart disease is the most important form of heart disease and single most cause of death. By 2020, it is estimated that it will become the major cause of death in all regions of the world\(^1\). Acute myocardial infarction (AMI) is one of the most common diseases among the developing countries\(^2\). Indians are four time more prone to AMI as compared to the people of other countries due to a combination of the genetic and lifestyle factors that promote metabolic dysfunction\(^3\). The incidence of myocardial infarction in India is 64.37/1000 people\(^4\).

Magnesium is the fourth most common cation in the body, and the second most common intracellular cation after potassium. It is also involved in several processes including: hormone receptor binding; gating of calcium channels; transmembrane ion flux and regulation of adenylate cyclase; muscle contraction; neuronal activity; control of vasomotor tone; cardiac excitability; and neurotransmitter release. In many of its actions it has been likened to a physiological calcium antagonist\(^5\). In humans, less than 1% of total body magnesium is found in serum and red blood cells. It is distributed principally between bone (53%) and the intracellular compartments of muscle (27%) and soft tissues (19%)\(^6\).

Magnesium deficiency is common and is frequently multifactorial. Epidemiological studies trace the prevalence of cardiovascular disease and cardiac deaths to the degree of magnesium depletion induced by a diet and drinking water low in magnesium\(^7\). Magnesium deficiency has been demonstrated in 7–11% of hospitalized patients and is found to co-exist in up to 40% of patients with other electrolyte abnormalities, particularly hypokalaemia or hypophosphataemia and, to a lesser extent, hyponatraemia and hypocalcaemia\(^8\).

Studies from the general population have linked magnesium deficiency with endothelial dysfunction, insulin resistance, hyperaldosteronism and inflammation\(^9\), all of which are associated with vascular calcifications. On the other hand, hypomagnesaemia is associated with traditional Framingham cardiovascular risk factors, such as diabetes, lipid disorders, and hypertension\(^10\). 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\(^11\). Hypomagnesaemia induces an atherogenic lipid profile through activation of 3-hydroxy-3-methyl-glutaryl-CoA reductase (HMG-CoA reductase) next to a decrease of lecithin-cholesterol acetyltransferase and lipoprotein lipase activity\(^12\).

Hence it can be said that magnesium ions are considered essential for the maintenance of functional integrity of myocardium. The serum magnesium concentration was found to have great significance in acute MI. So, the present study was undertaken to evaluate the levels of serum magnesium in acute MI.
Material and Method

The present prospective observational study was conducted in the department of Medicine among 50 patients with acute myocardial infarction. Patients were enrolled in the study after obtaining written informed consent from parents and approval from Institutional Ethical Committee.

Inclusion criteria

1. Patients who presented to the hospital within 24 hours of onset of symptoms and diagnosed with acute myocardial infarction.

Exclusion criteria

It excludes patients with the following characteristics:

1) Patients having hypokalemia.
2) Patients on medicines which cause alteration in serum magnesium level e.g. Aminoglycosides, Amphotericin B, Cituximab, Cyclosporine, Digoxin, Diuretics (loop, thiazides, osmotic).
3) Patients receiving magnesium containing antacids.
4) Patients with history of chronic alcohol abuse.
5) Patients with malabsorption or chronic diarrhoea.
6) All pregnant women.

Criteria used to diagnose acute myocardial infarction

The following criteria have been used to diagnose acute myocardial infarction. The presence of any of the two criteria has been considered:

1. History of discomfort in the chest.
2. Changes in the ECG suggestive of acute myocardial infarction.
3. Rise of cardiac enzymes.

Blood samples collection

Samples were taken within 24 hours of onset of symptoms. All patients were evaluated for their ECG and cardiac enzymes and serum magnesium level by taking 5 cc venous blood sample in a disposable syringe and sent to biochemistry laboratory for analysis in fluoride bulb and plain bulb respectively.

Investigation

1. Serum magnesium level
2. Troponin T levels
3. CPK (Mb isoenzyme)
4. Serum sodium and potassium levels
5. Renal function test
6. Echocardiography
7. Serum Lipid profile
8. Twelve lead electro cardio gram

1. Serum magnesium level: Quantitative estimation of Serum magnesium by Calmagite dye method. Normal serum Magnesium level is ranging from 1.7 to 2.4 mg/dl. Serum magnesium level less than 1.7 mg/dl was considered as low magnesium level in this study.

2. Troponin T levels: Serum troponin T level was routinely measured at 12 h from the onset of symptoms in patients who were suspected of having ACS in accordance with a hospital-wide policy. Troponin T level was measured by the Elecsys troponin T electrochemiluminescence immunoassay ECLIA (4th generation) with the Roche Alecsys 2010 analyser (Hofman-La Roche Ltd, Basel, Switzerland). The Elecsys troponin T assay consists of two monoclonal antibodies specifically directed against human cardiac troponin T, and detects free cardiac troponin T, as well as its binary and ternary complexes. The lowest detection limit of troponin T concentration that can be distinguished from zero is 0.01 mg/l, and the lowest troponin T concentration that meets a 10% coefficient of variation requirement is 0.03 mg/l. Patients were separated into two groups according to their troponin T level: those with normal (<0.01 μg/l) and those with raised (>0.01 μg/l) troponin T levels.

3. CPK (Mb isoenzyme): The CPK-MB test is a cardiac marker used to assist diagnoses of an acute myocardial infarction. It measures the blood level of CK-MB (creatinine kinase-muscle/brain), the bound combination of two variants (isoenzymes CKM and CKB) of the enzyme phosphocreatine kinase. A significant concentration of CK-MB isoenzyme is found almost exclusively in the myocardium, and the appearance of elevated CK-MB levels in serum is highly specific and sensitive for myocardial cell wall injury. Normal reference values for serum CK-MB range from 3 to 5% (percentage of total CK) or 5 to 25 IU/L.

4. Serum sodium and potassium levels:
   a) Serum sodium: The normal serum sodium level is 135-145 mEq/L. Sodium below 135 mmol/l and above 145 mmol/l are defined as hyponatraemia and hypernatraemia respectively.
   b) Serum potassium: The normal potassium level in the blood is 3.5-5.0 milli Equivalents per liter (mEq/L). Potassium levels below 3.5 mmol/l and above 5.5 mmol/l were categorized as hypokalemia and hyperkalemia, respectively.

5. Serum Lipid profile: The lipid profile test is a combination of tests conducted together to check for any risks of coronary heart disease, or as a preventive measure to check any risks depending on factors like eating habits, diet, stress, exercise and life-style related. A typical lipid profile includes the following tests:
   a. High density lipoprotein cholesterol (HDL-C) - “good cholesterol”
   b. Low density lipoprotein cholesterol (LDL-C) -“bad cholesterol”
   c. LDL/HDL Ratio (calculated values)
   d. Triglycerides
   e. Very low density lipoprotein cholesterol (VLDL-C)

   The lipid profile normal values are as follows:
   a. LDL: 70 to 130 mg/dL (the lower, the better)
b. HDL: more than 40 to 60 mg/dL (the higher, the better)
c. Total cholesterol: less than 200 mg/dL (the lower, the better)
d. Triglycerides: 10 to 150 mg/dL (the lower, the better)

**Statistical analysis**

Data so collected was tabulated in an excel sheet, under the guidance of statistician. The means and standard deviations of the measurements per group were used for statistical analysis (SPSS 22.00 for windows; SPSS inc, Chicago, USA). Difference between two groups was determined using student t-test as well as chi square test and the level of significance was set at p<0.05.

**Results**

In the present study, out of the 50 subjects, 80% were males and 20% were females. Mean age of the study subjects was 58.76±11.72 years. Thirty percent of the subjects belonged to 61-70 year age group. Subjects belonged to 51-60 year age group was 24%. Minimum subjects were found in 30-40 year age group (8%). 18% of the subjects were having age >70 years (table 1).

<table>
<thead>
<tr>
<th>Gender</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>40</td>
<td>80</td>
</tr>
<tr>
<td>Female</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age group (in years)</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-40</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>41-50</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>51-60</td>
<td>12</td>
<td>24</td>
</tr>
<tr>
<td>61-70</td>
<td>15</td>
<td>30</td>
</tr>
<tr>
<td>&gt;70</td>
<td>9</td>
<td>18</td>
</tr>
</tbody>
</table>

Smoking was reported in 82% of the subjects whereas hypertension and diabetes mellitus in 64% and 46% of the subjects respectively. Sixteen percent, 24% and 60% of the subject’s time of presentation was 3-6 hours, 6-12 hours and 12-18 hours respectively. Serum magnesium level (mg/dL) i.e. <1.6, 1.7-2.4 and >2.4 was found in 40%, 60% and 0% of the subjects respectively on day 1. On day 5, serum magnesium level (mg/dL) <1.6 was reported only in 8% of the subjects while >2.4 level was revealed in 46% of the subjects (table 2).

<table>
<thead>
<tr>
<th>Serum magnesium levels (mg/dL)</th>
<th>Day 1</th>
<th>Day 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1.6</td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>40%</td>
<td>8%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>58.76</td>
<td>11.72</td>
</tr>
</tbody>
</table>

Table 1: Gender and age distribution among the study subjects

Table 2: Serum magnesium levels among the study subjects
In the present study, arrhythmia was found in 10 (20%) subjects. Sixteen percent (8) of the subjects with arrhythmia were having serum magnesium level (mg/dL) <1.6 while only 4% of the subjects with arrhythmia reported 1.7-2.4 serum magnesium level (mg/dL) as shown in table 3.

Table 3: Serum magnesium levels distribution in relation to with and without arrhythmias at day 1

<table>
<thead>
<tr>
<th>Arrhythmias</th>
<th>Serum magnesium levels (mg/dL)</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;1.6</td>
<td>1.7-2.4</td>
<td>&gt;2.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>With</td>
<td>8</td>
<td>16</td>
<td>2</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Without</td>
<td>12</td>
<td>24</td>
<td>28</td>
<td>56</td>
<td>0</td>
</tr>
<tr>
<td>Chi square</td>
<td>8.33</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p value</td>
<td>0.004*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*: statistically significant

On day 5, only six percent (3) of the subjects with arrhythmia were having serum magnesium level (mg/dL) <1.6 while 14% of the subjects with arrhythmia reported 1.7-2.4 serum magnesium level (mg/dL). Seventy two percent of the subjects without arrhythmia reported 1.7-2.4 serum magnesium level (mg/dL). When subjects with and without arrhythmia were compared according to the serum magnesium level, it was found to be statistically significant as p<0.05 as shown in table 4.

Table 4: Serum magnesium levels distribution in relation to with and without arrhythmias at day 5

<table>
<thead>
<tr>
<th>Arrhythmias</th>
<th>Serum magnesium levels (mg/dL)</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;1.6</td>
<td>1.7-2.4</td>
<td>&gt;2.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>With</td>
<td>3</td>
<td>6</td>
<td>7</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>Without</td>
<td>1</td>
<td>2</td>
<td>36</td>
<td>72</td>
<td>3</td>
</tr>
<tr>
<td>Chi square</td>
<td>7.49</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p value</td>
<td>0.02*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*: statistically significant

There was an increase in serum magnesium from Day-1 to Day-5 with statistically significant difference. In the present study groups, the serum magnesium level on day-1 was significantly lower in patients with arrhythmias than those without arrhythmia (p<0.001). In the present study groups, the serum magnesium level on day-5 was significantly increased in patients with arrhythmias (1.99) as compared to the levels of day 1 (1.62). Serum magnesium level on day-5 was also significantly increased in patients without arrhythmias (2.55) as compared to the levels of day 1 (2.04). When mean serum magnesium level of day 1 and 5 was compared statistically among the subjects without
arrhythmias, it was found to be statistically significant as $p<0.05$ as shown in table 5.

Table 5: Serum magnesium level among the subjects with and without arrhythmias

<table>
<thead>
<tr>
<th>Magnesium level</th>
<th>Arrhythmias</th>
<th>Without Arrhythmias</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 1</td>
<td>Day 5</td>
</tr>
<tr>
<td>Mean</td>
<td>1.62</td>
<td>1.99</td>
</tr>
<tr>
<td>SD</td>
<td>0.36</td>
<td>0.40</td>
</tr>
<tr>
<td>t test</td>
<td>2.73</td>
<td></td>
</tr>
<tr>
<td>p value</td>
<td>0.03*</td>
<td></td>
</tr>
</tbody>
</table>

*: statistically significant

Discussion

The magnesium ion is becoming a major cardiovascular cation during these decades. It has been implicated in the pathogenesis of acute myocardial infarction and complication like arrhythmias. Magnesium inhibits the accumulation of calcium ion, improves the myocardial metabolism and reduces the myocardial cell death. It also helps in the activation of ATP which maintains the sodium potassium pump and also because of its calcium blocking action, it is implicated in relation to arrhythmias after an acute myocardial infarction\textsuperscript{14}. Hence it can be said that magnesium ions are considered essential for the maintenance of functional integrity of myocardium. The serum magnesium concentration was found to have great significance in acute MI. So, the present study was undertaken to evaluate the levels of serum magnesium in acute MI.

In the present study, out of the 50 subjects, 80% were males and 20% were females (male: female; 4:1). Similar male dominancy was revealed by M. Arun karki et al\textsuperscript{14}, Stamler J et al\textsuperscript{15} and Kedarnath et al\textsuperscript{16} in their study. Mean age of the study subjects was 58.76±11.72 years. Thirty percent of the subjects belonged to 61-70 year age group. Subjects belonged to 51-60 year age group was 24%. Minimum subjects were found in 30-40 year age group (8%). 18% of the subjects were having age >70 years in the present study. Little dissimilar findings were reported by Subramanyam NT et al\textsuperscript{17} who revealed maximum number of patients were seen in the age group of 51-60 years forming 38% of all cases of acute MI.

Serum magnesium level (mg/dL) i.e. <1.6, 1.7-2.4 and >2.4 was found in 40%, 60% and 0% of the subjects respectively on day 1. On day 5, serum magnesium level (mg/dL) <1.6 was reported only in 8% of the subjects while >2.4 level was revealed in 46% of the subjects in the present study. In the present study groups, the serum magnesium level on day-1 was 1.83 whereas on day, the same was 2.27. There was an increase in serum magnesium from Day-1 to Day-5 with statistically significant difference. M.Arun karki et al\textsuperscript{14} reported serum magnesium <1.6 in 20% of the subjects on day 1 and on day the same was among 4% of the subjects. The overall mean magnesium level was 1.86 and 2.26 on day 1 and 5 respectively.
Dissimilar results were reported by Henryk Kafka et al\textsuperscript{18} who found incidence of 6% hypomagnesemia in the patients with acute myocardial infarction 6%, much lower than the 46% reported by Dyckner\textsuperscript{19} as well as compared to the present study. Part of this difference can be explained on the basis of the accepted reference range for serum magnesium levels. Seelig\textsuperscript{20} has commented on the variability of normal values and exhorts each laboratory to "obtain its own mean for a healthy control population."

In the present study groups, the serum magnesium level on day-1 was significantly lower in patients with arrhythmias (1.62) than those without arrhythmia (2.04). Serum magnesium level on day-5 was significantly lower in patients with arrhythmias (1.99) than those without arrhythmia (2.55). Serum magnesium level on day-5 was significantly increased in patients with arrhythmias (1.99) as compared to the levels of day 1 (1.62). When mean serum magnesium level of day 1 and 5 was compared statistically among the arrhythmias subjects, it was found to be statistically significant. The serum magnesium level on day-5 was significantly increased in patients without arrhythmias (2.55) as compared to the levels of day 1 (2.04). When mean serum magnesium level of day 1 and 5 was compared statistically among the subjects without arrhythmias, it was found to be statistically significant.

Similar results were reported by M. Arun karki et al\textsuperscript{14}. Nambakam Tanuja Subramanyam et al\textsuperscript{17} observed significant lower serum Mg concentration of 1.62±0.27 mg/dl at onset in comparison to control mean of 2.49±0.35 mg/dl. Serum Mg gradually raised to normal value by 7th day with mean value of 2.0±0.12 mg/dl. Further, mean serum Mg in this study on the 1st day in complicated cases was 1.38±0.03 mg/dl and in uncomplicated cases was 1.73±0.29 mg/dl and 7th day, in complicated cases 2±0.1 mg/dl and uncomplicated cases was 2.06±0.12 mg/dl.

Wannasilp N et al\textsuperscript{21} 2001 demonstrated that CAD patients may be associated with Mg deficiency and contribute to the pathogenesis of CAD. Mean value of serum Mg level in 100 CAD patients was 2.14±0.39 mg/dl (p=0.052) with 100 healthy controls (mean value 2.24±0.3 mg/dl) in the study. The prevalence of Mg deficiency did not differ significantly between the study groups, however it tended to be higher in CAD patients. GQ Khan et al\textsuperscript{22} 2002 reported statistically significant (p<0.001) fall of serum Mg in 50 cases of acute MI with mean serum Mg in controls being 2.2±0.24 mg/dl. Further, the serum Mg level was found comparatively lower in the patients getting cardiac arrhythmias. They concluded that, the fall in serum Mg in acute MI can be taken as sensitive diagnostic index, especially in early hours of postinfarction period when cardiac enzymes and ECG may not be significant. Simmkharb et al\textsuperscript{23} 1999 demonstrated mean serum Mg levels in 22 acute MI to be 1.27±0.57 mg/dl (p<0.001) compared to mean value in 15 controls to be 2.41±0.54 mg/dl. They concluded that Mg deficiency in MI patients can potentiate oxidative injury to post ischemic myocardium.

Govind Mohan et al\textsuperscript{24} demonstrated mean serum Mg levels in 53 acute MI cases to be statistically significant of 1.38±0.21 mg/dl (p<0.001) on 1st day and 2.35±0.23 mg/dl on 10th day compared to mean value of 2.51±0.16 mg/dl% in 30 controls. Further, they reported even lower serum Mg levels of 1.26±0.19 mg/dl
on 1st day in 42 cases of acute MI with complications compared to 1.41±0.13 mg/dl in all 11 cases of acute MI without complications and by 10th day, mean serum Mg level in acute MI with complications raised to 2.36±0.12 mg/dl compared to mean serum Mg values in acute MI without complications of 2.29±0.16 mg%. It was observed that serum Mg were lowest in patients who died due to major arrhythmias and cardiogenic shock followed by pump failure.

Magnesium probably functions as an inorganic calcium channel blocker and there are several plausible mechanisms for a beneficial effect in acute myocardial infarction (Woods 1991)\textsuperscript{25}. Research on animals and humans has shown that magnesium is a peripheral and coronary vasodilator. It can increase the threshold for depolarization of cardiac myocytes, thereby reducing the likelihood of cardiac arrhythmia caused by injury currents near ischemic or infarcted tissue. Magnesium decreases reperfusion injury by preventing or lessening mitochondrial calcium overload in ischemic myocardial cells during the first few minutes of reperfusion (namely, the restoration of blood flow to an organ or tissue) and preserving intracellular Adenosine Triphosphate (ATP) and creatine phosphate, and inhibits platelet function, perhaps indirectly by release of prostacyclin. Thus, magnesium-infusion started early after the onset of myocardial ischemia might limit infarct size, prevent serious arrhythmias, and reduce mortality.

Low serum magnesium has been implicated in cardiovascular mortality, but results are conflicting. Total body magnesium depends on dietary intake and recent studies showed that vast majority of elderly do not consume the average dietary requirement for magnesium\textsuperscript{26}. The prevalence of magnesium in the general population is estimated at 2\%\textsuperscript{27}, but it may be as high as 53\% in specific high risk group such as patients with chronic heart failure\textsuperscript{28}. Although hypomagnesemia may have acute and chronic complications, serum magnesium is still measured relatively in frequently.

**Conclusion**

Serum magnesium levels on admission were significantly low in patients of arrhythmia as compared with without arrhythmia. Serum Mg levels were found to be lower in acute MI cases at presentation within 24 hours as compared to matched controls. Serum magnesium levels were lower in acute MI with complication, when compared with acute MI without complication. Serum Mg levels raised towards normal values by 5\textsuperscript{th} day. So it can be concluded that measurement of serum magnesium levels is of prognostic significance in acute MI.

**References**


