"A STUDY OF IN-HOSPITAL CLINICAL COURSE AND OUTCOME OF ACUTE MYOCARDIAL INFARCTION IN RELATION TO SERUM MAGNESIUM LEVELS"

By

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IN

GENERAL MEDICINE

Under the guidance of

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ABSTRACT

BACKGROUND : Magnesium has been implicated in the pathogenesis of acute myocardial infarction and its complication like arrhythmia.Magnesium improves myocardial metabolism, inhibits calcium accumulation and myocardial cell death. It improves vascular tone, peripheral vascular resistance, after load and cardiac output, reduces cardiac arrhythmias and improves lipid metabolism. Magnesium also reduces vulnerability to oxygen derived free radicals, improves endothelial function and inhibits platelet function including platelet aggregation and adhesion .

OBJECTIVES:

- To study in hospital morbidity and mortality of the patients during the clinical course of acute myocardial infarction.
- To correlate the total serum magnesium levels with obtained findings of mortality and morbidity

METHODS:

Fifty subjects aged between 18 and 65 years presenting with Acute myocardial infarction diagnosed by history, clinical examination, ECG findings(ST-segment elevation on the corresponding leads) and biochemical markers(CK-MB, troponin-T), who present to the casualty or who are admitted in Sri R. L. Jalappa Hospital & Research Centre and Narayana Hrudayalaya,kolar were taken up for the study

RESULTS: There is a significant difference in the magnesium levels in patients with complications and without complications.

CONCLUSION: In acute myocardial infarction, patients with low magnesium levels are more prone to get arrhythmias. So magnesium treatment can be considered in patients of acute myocardial infarction with low magnesium levels.

Key words: Magnesium; Myocardial infarction; Complications, Arrhythmias

LIST OF ABBREVIATIONS

AF	Atrial fibrillation
CVD	Coronary vascular disease
CAD	Coronary artery disease
ATP	Adenosine triphosphate
VT	Ventricular tachycardia
VF	Ventricular fibrillation
ECG	Electrocardiogram
IHD	Ischemic heart disease
CCF	Congestive cardiac failure
LVF	Left ventricular failure
JVP	Jugular venous pressure
$MgSO_4$	Magnesium sulphate
ACLS	Advanced cardiac life support
COPD	Chronic obstructive pulmonary disease

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INTRODUCTION

CREATE registry, the largest data from Indian patients with ACS has, based on its year 2003 population-based cross-sectional study, shown that 29.8 million Indians are affected by coronary heart disease.[1] It has been proved that inorganic salts have great importance in the normal growth and functioning of the biological forms. Magnesium, which is one of the most important inorganic salt in the human body plays an important role in neuromuscular excitability, in vital enzymatic reactions, in DNA/RNA synthesis and repair and is essential for maintenance of cardiac function.[2]

Magnesium has been implicated in the pathogenesis of acute myocardial infarction and its complications like arrhythmias. It plays a significant role in other cardiovascular diseases as well.

Magnesium ions are considered essential for the maintenance of the functional integrity of the myocardium as it was found to be low in patients with sudden death due to ischemic cardiac disease.[3] The process of re-storing blood flow to the ischemic myocardium, how- ever, can induce myocardial injury.[4]

This phenomenon, termed as a myocardial ischemia/reperfusion injury, draws more attentions of the cardiologists. It has been pointed out that magnesium has a cardio-protective effects on Myocardial infarction and reperfusion injury *in vivo* and *in vitro* role[4] in ventricular fibrillation, which causes sudden death in IHD.

These findings directly correlated with the resultant complications of myocardial infarction, such as arrhythmias to the magnesium levels.

It has been pointed out that magnesium has a vital role in ventricular fibrillation, which causes sudden death in IHD. The coronary vasospasm resulting from magnesium deficiency has been suggested as another important factor in the sudden

death of IHD. Although the total body magnesium content may not change with the onset of AMI, extracellular magnesium declines markedly, especially over the first 24 to 48 hours after the onset of AMI. Hypomagnesemia in the initial phase of post-AMI period is very critical, as ventricular tachyarrhythmias, sudden cardiac death and re-infarction are the usual outcomes. [5]

Magnesium deficiency was also postulated to have role in the genesis of atheromatous plaques in that it leads to hyperlipidemia.

As ischemic heart disease is one of the common causes of death in the world[6] at present where prognosis depends on multiple factor of which many still remain unexplained. This study is designed to know the relationship between serum magnesium levels and the in hospital clinical course of the patients presenting to the emergency ward of RLJ Hospital Narayana Hrudayalaya with acute myocardial infarction.

AIMS AND OBJECTIVES

- To study in hospital morbidity and mortality of the patients during the clinical course of acute myocardial infarction.
- To correlate the total serum magnesium levels with obtained findings of mortality and morbidity.

REVIEW OF LITERATURE

HISTORICAL REVIEW

At the time of Lavoisier (1743-1794) only 26 elements were known. Sodium, potassium, calcium and magnesium were shortly thereafter separated. It is primarily to Liebig (1803-1873) that we owe the appreciation of the importance of the minerals as normal constituents of plants and animal tissues. Although the inorganic constituents of the body are only small fraction of the total amount of the body tissue, they must not be considered un-important. They are in fact becoming recognized more and more as essential cogs in the human machine.

In 1936, Greenberg and associates described myocardial degeneration with fibrosis and polyplastic infiltration in rats that were fed on low magnesium diet from birth (Burch et al, 1977)[3]. The sequence of structural abnormalities suggested that interference with magnesium dependent enzymes involved in oxidative phosphorylation played an important role in pathogenesis of lesion observed.

The word 'magnesium' is derived from the name of ancient Gracian town of 'Magnesia'. In 1808, Sir Humphrey Devy investigated the alkaline earth metal and named the white magnesia stone by its modern name of magnesium.

Until middle of this century magnesium metabolism had been much neglected, though reasonably extensive literature regarding consequences of magnesium depletion in several lower species was available. There was some paucity notice in the field of magnesium metabolism in man during this period and the probably reason could be due to lack of uniformity and difficulty in estimation of magnesium.

The availability of more accurate uniform methods for estimation of serum magnesium in laboratory gave momentum to work on magnesium metabolism in man. Magnesium exists in three states: ionized magnesium (Free form), protein bound form, and a formed complexed to serum anions. Even though studies show the importance of measuring ionized calcium, most research shows that ionized magnesium can be inferred from total magnesium. Only 1% of total body magnesium is in the extra-cellular fluid and of this about 25% is in the plasma, rest is in the red cells. Around 50% of serum magnesium is free, 32% is protein bound and rest 13% is accounted for magnesium phosphate, citrate and other unidentified complexes.

Currently, the clinical role of measurement of ionized magnesium is unclear and measurement of ionized magnesium is not standard practice in the emergency medicine departments.[7]

Nevertheless, in contrast to complex balance studies on tissue determination, measurement of serum magnesium is the quickest, simplest, and most effective first approach to the evaluation of magnesium deficiency states. This procedure has wide spread success in the identification of clinical syndromes that have responded to replacement therapy with magnesium salts.

CORONARY CIRCULATION [8]

Anatomy of Coronary Arteries

The heart derives its blood supply from the right and left coronary arteries, which arise from anterior aortic and left posterior aortic sinus respectively. Right coronary artery after arising from the anterior sinus passes between the right auricular appendage and the infundibulum of the right ventricle.

Passing now vertically downwards in the atrio-ventricular groove the artery turns backwards at the inferior border of the heart and runs posteriorly. It gives off branches to both atria and ventricles as it passes vertically downwards.

At the inferior border, the marginal branch passes to the left along the right ventricle. On the diaphragmatic surface, the inferior inter-ventricular branch is given off. This large artery passes along the inter-ventricular groove to the apex of the heart.

The terminal part anastomoses with the terminal arterioles of the coronary artery at the lower part of the left atrium. The left coronary artery immediately after its origin divides into anterior descending artery and left circumflex artery. The anterior descending artery runs in the inter-ventricular groove to anastomose at the apex with the terminal branches of the inferior inter-ventricular artery.

The left circumflex gives off branches to the posterior wall of the left ventricle and runs on to anastomose with the termination of the right coronary artery, below the coronary sinus. Here in 40% of the individuals it gives off a sizable branch which running up over the posterior surface of the left atrium ends in the auricular appendage of the right atrium at the sino-atrial node.

Anastomoses Of Coronary Arteries

Anastomosis exists between the terminations of right and left coronary arteries in the atrio-ventricular groove and these surface anastomoses are insignificant. There are inter-coronary anastomoses freely at arteriolar level, between the inter-ventricular arteries. If the intra-ventricular arteries meet at the apex, this provides maximum anastomoses. If the meeting place of the intra-ventricular arteries falls short of the apex above or below, this diminishes the potential anastomotic area. In 10% of the individuals the inferior as well as the anterior inter-ventricular artery is a branch of the left coronary, in these cases there is no anastomoses between the coronaries.

Potential anastomoses exists between the coronary arteries and pericardial arteries, which are derived from the peri-cardiophrenic, the bronchial and the internal thoracic arteries. In very rare instances one of these may open to replace a coronary artery

Distribution Of The Coronaries

Right ventricle is supplied by the right coronary artery except at the upper margin of its anterior surface, where branches of anterior inter-ventricular arteries supply it.

Left ventricle is supplied by the left coronary artery except for a narrow strip of the diaphragmatic surface where it is supplied by the inferior inter-ventricular artery. The two inter-ventricular arteries share the supply of the inter-ventricular septum, usually about equally.

Left ventricle is supplied by the left coronary artery except for a narrow strip of the diaphragmatic surface where it is supplied by the inferior inter-ventricular artery. The two inter-ventricular arteries share the supply of the inter-ventricular septum, usually about equally.

SA Node: It is supplied by a branch of right coronary artery in 60% of cases and from left coronary artery in 40%. AV node and bundle of His are supplied by the inferior inter-ventricular artery, which arises in 90% of cases from the right coronary and in only 10% from the left coronary.

Dominant Arteries: In 67% of the cases right coronary is dominant, 15% of cases left coronary and in 18% of cases there is a balanced coronary arterial pattern.

Physiology of Coronary Circulation

Functionally, the right and left coronary arteries behave as end arteries, although anatomically there are numerous intercoronary anastomses in most of the normal hearts in the order of 40% microns in diameter.

Only the inner 75-100 microns of the endocardium can obtain significant amount of nutrition directly from the blood in the cardiac chamber

Normal Coronary Blood Flow

Resting coronary blood flow in human beings averages about 225 ml/min or 0.7-0.8 ml/G of heart muscle or 4.5 percent of the total cardiac output. Four to five fold increase can occur during exercise

Phasic Changes In Coronary Blood Flow

As a result of cardiac muscle compression blood flow decreases during systole and increases during diastole, in which left ventricle is more affected than the right because of its thickness.

The intra-myocardial pressures compress the sub-endocardial blood vessels more than the outer vessels, which throttle its blood supply and to compensate for this one, the sub-endocardial vessel are much larger than the nutrient arteries in the middle and outer layers of the heart, which increases the blood flow during diastole proportionately.

Control of Coronary Blood flow:

1. Local metabolism of myocardium - A prime controller
2. Nervous control

1. Local metabolism of myocardium: The rate of flow increases with the vigor of contraction and decreases with decrease in activity. The factors responsible are:

a) Oxygen Demand

I. Vasodilator Theory: Anoxia will liberate many vasodilator materials from myocardial cells, which increase the blood flow:

- Adenosine from the ATP
- Potassium ions
- Hydrogen ions
- Carbondioxide
- Bradykinin and possibly
- Prostaglindins

II. Arterial Smooth Muscle Relaxation Theory: Decrease in oxygen supply leads to anoxia of coronary arterial smooth muscle cells, which loses their tone thus getting the artery dilated. Factors that determine the oxygen consumption are:

a. Greater the work, greater the oxygen consumption, with in the

physiological limitations.

b. Oxygen consumption is proportionate to peak myocardial muscle tension.
    1. Increased arterial pressure, increases the workload and hence tension.
    2. Dilatation of the heart increases the tension development in myocardium to pump the blood according to Laplace law, which states that tension required to generate a given pressure increases in proportion to the diameter of the heart.
c. Other factors, which increase the oxygen consumption like stimulation of the heart by epinephrine and norepinephrine, thyroxine, digitalis, calcium ions, increased temperature of heart will increase the oxygen consumption.
d. Reactive hyperemia: Anoxia brings about increase flow because of the coronary dilatation after a brief period of coronary occlusion.

III) NERVOUS CONTROL

INDIRECT:

Sympathetics increases the heart rate and contractility, through the local metabolic mechanisms, and hence increases the coronary flow.

Parasympathetics decrease the heart rate and depress the myocardium and hence bring about coronary constriction.

DIRECT EFFECT:

Parasympathetics: As the vagal supply to ventricles is negligible, except for slight dilatation which may occur, there is no effect of its stimulation.

Sympathetics: Epinephrine and norepinephrine through their receptors in coronary vessels usually bring about vasoconstriction or no change. When alpha effect dominates, severe constriction occurs which may bring about anginal attack.

EPIDEMIOLOGY OF CORONARY HEART DISEASE

The emergence of coronary heart disease epidemic in the south Asian countries during the last three to four decades has been a very concerning cause for the health providers in the recent years.

In fact it is a less recognized fact that the developing countries contribute a greater share to the global CVD burden than the industrialized countries. It has been estimated that 5.3 million deaths attributable to CVD occurred in the developing countries in 1990, whereas the corresponding figures from the developing countries ranged between 8 to 9 millions[9]. These facts are very alarming and need an in depth analysis of the causes which would help us in forming strategies to reduce the growing incidence. Accurate data regarding the prevalence of CAD in India are not available. Recently there are two studies addressing this issue.

Rajeev Gupta et al[10] have highlighted the persistent high prevalence of cardiovascular risk factors in the urban middle class in Jaipur, North Western part of India and have compared the risk factors with studies performed in similar locations in years 2002 to 2006. While the risk factors like smoking, obesity, hypertension and diabetes remain unchanged there is a clear trend of increasing levels of non-HDL cholesterol and triglycerides over the 8-year period

In another study from Guntur district in Andhra Pradesh murthy et al[11] have also pointed out to the high prevalence of coronary artery disease and a strikingly positive relationship with high levels of LDL cholesterol and triglycerides and impaired glucose tolerance.

The finding in both the studies point towards the nutritional transition with global availability of relatively cheap vegetable oils and fats and increasing buying power of the middle class income families which constitutes at least one third of the Indian population

In response to globalization of food, our population is showing a change in the dietary pattern with increase in energy rich foods poor in dietary fiber and several micronutrients.

Coronary artery disease occurs 5–10 years earlier in Indians than in other populations around the world and the major brunt of this phenomenon is borne by the productive age group (35–65 years) of the population.[13]

The developing countries like ours are grappling with the "double burden" of pre-transitional and post-transitional disease, and community awareness of the dangers of cardiovascular disease not being high.

PATHOPHYSIOLOGY OF ACUTE MYOCARDIAL INFARCTION[14]

Myocardial infarction generally occurs when there is an abrupt decrease in coronary blood flow following a thrombotic occlusion of a coronary artery previously narrowed by atherosclerotic plaque fissures, ruptures or ulcerates and when conditions favor thrombogenesis takes place, so that a mural thrombus forms at the site of rupture and leads to coronary artery occlusion. After an initial platelet monolayer forms at the site of the ruptured plaque, a variety of agonists (collagen, ADP, epinephrine, serotonin) promote platelet activation. Following agonist stimulation, there is production and release of thromboxane A_2, further platelet activation and potential resistance to thrombolysis.

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The coagulation cascade is activated on exposure of tissue factor in damaged endothelial cells at the site of the ruptured plaque. Factor VII and X are activated, ultimately leading to the conversion of prothrombin to thrombin which then converts fibrinogen to fibrin. The culprit coronary artery eventually becomes occluded by a thrombus containing platelet aggregates and fibrin strands.

Ultimately the amount of myocardial damage caused by coronary occlusion depends on the territory supplied by the affected vessel, whether or not the vessel becomes totally occluded, native factors that can produce early spontaneous lysis of the occlusive thrombus, the quantity of blood supplied by collateral vessels to the affected tissue, and the demand for oxygen of the myocardium whose blood supply has been suddenly limited.

CLINICAL FEATURES OF ACUTE MYOCARDIAL INFARCTION[14]

Acute myocardial infarction presents itself as a sudden catastrophic incident and its definite clinical picture may be established without warning. The clinical pictures can be classified as follows:

1) Cases dominated by chest pain

2) Cases dominated by shock

3) Cases dominated by pulmonary edema or other evidence of LV failure.

4) Cases characterized by the gradual development of CCF

5) Cases dominated by complication

6) Some cases may present with combination of any of the above.

1. Pain in the Chest:

In 80-85% of cases this is a presenting complaint. It is a deep visceral pain, involving the central portion of the chest and epigastrium, described as tightness, heaviness or constriction in the chest. In 25% of cases, pain radiates to the arms and commonly weakness, sweating, nausea , giddiness and anxiety often accompany it. It may occurs during exertion and emotional outbursts, not relieved with rest and makes the patient to move about in an attempt to find a comfortable position

2. Breathlessness :

Second most important symptom, breathlessness may be sudden in onset and intense or it may be exertional. It is common in those who had 'painless myocardial infarction' particularly diabetics and aged individuals, and those having complications like cardiogenic shock and pulmonary edema.

3. Sudden loss of consciousness:

A confusional state, a sense of profound weakness or unexplained fall in blood pressure with giddiness, syncope and/ or convulsions may be a presenting complaint.

4. Choking sensation in the neck may be the only presenting symptom.

5. Some patients present with gradual onset of breathlessness, paroxysmal nocturnal dyspnea and pain in abdomen with oliguria and swelling of lower limbs, a picture that of CCF.

6. In rare cases the infarct may go unrecognized until endocardial thrombosis resulting from its leads to systemic embolism.

PHYSICAL SIGNS

Patient may come with the hand on their pericardium indicating the site of maximum intensity of pain (Levine sign).

Often associated with perspiration and coolness of extremities, cyanosis may be there when the patient is having severe pulmonary edema or shock.

Pulse

May show bradycardia, normal sinus rhythm, tachycardia with or without irregularities, depending upon the presence or absence of arrhythmias and the type of arrhythmia.

Blood Pressure

Usually shows an initial rise because of pain, anxiety or the unfamiliarity of the environment, which will become normal within 3 or 4 days. Fall in the blood pressure may be due to cardiogenic shock or due to 'Bezold-Jarisch reflex', which is due to increased vagal tone that occurs in inferior wall infarction

Neck veins

Collapse of neck veins occurs when patient is in shock, cannon waves can be made out in complete heart block in which they are irregular

Precordium

The apical impulse may be difficult to palpate. In about one-fourth of the patients with anterior wall infarction, an abnormal systolic pulsation develops in the peri-apical area within the first few days of illness, which may resolve later, which represents a transient, palpable systolic bulging of the infarcted ventricle. Other physical signs of ventricular dysfunction that may be present are, muffled heart sounds, atrial (S4) and ventricular (S3) gallop sounds and paradoxical splitting of the 2^{nd} sound. A transient apical systolic murmur due to mitral regurgitation secondary to papillary muscle dysfunction during acute infarction may occur. A pericardial friction rub is audible if infarction is transmural in most of the cases.

Temperature elevations in the range of 37 to 38^{o}C are common during the first 3 to 4 days due to myocardial necrosis

Respiratory System

Tachypnea is common and crepitations are heard at the base or all over the lung fields depending upon the amount of pulmonary congestion

Gastrointestinal System

Enlarged tender liver will be present when patient is in CCF.

Central Nervous System

Anxiety, restlessness, stupor, coma, focal neurological deficit may occur when the patient is having fall in blood pressure and/ or thromboembolic phenomenon.

Renal System

Oliguria may be present if the patient is having fall in blood pressure.

MAGNESIUM METABOLISM

Magnesium (Mg) is the fourth-most abundant cation in the body and the second most prevalent intracellular cation, next to potassium[15]. The normal body content in the adult is approximately 2000 milli equivalent (mEq) or 24 grams. Magnesium is distributed unevenly, with greatest concentration in tissues having the higher metabolic activity such as brain, heart and kidney. Approximately 60% of the body magnesium is in the bone, one third of the skeletal magnesium has been shown to be exchangeable and this fraction may serve as a reservoir for maintaining a normal extracellular magnesium concentration.[16]

Extracellular magnesium accounts for only about 1% of total body magnesium content. The normal serum magnesium concentration is approximately 1.6 - 2.6 mgs/dl[17]. About 70-75% of the plasma magnesium is ultra filterable of which the major portion is ionized. The non-filterable portion is bound to plasma proteins, chiefly albumin. The remaining of the body magnesium is intracellular.

The concentration of total magnesium in cells varies with the tissues, but is of the order of 1-3 mmols/l.[18] In general, higher the metabolic activity of the cell, the higher the magnesium content. A low serum magnesium concentration usually implies magnesium deficiency. The serum magnesium however may not reflect intracellular magnesium.

Intracellular magnesium depletion may exist despite a normal serum magnesium concentration[9]. Because tissue and cellular assays are difficult to perform and not widely available, the serum magnesium determination is the method by which magnesium deficiency is identified in clinical practice.

Myocardial Magnesium

The adult human body contains between 21 and 28 gms of magnesium or about 3 mgm/kg of fat free tissue. Over half of it is present in bone. Cardiac muscle has a significant concentration of magnesium (17.4-19.8 mEq/l) higher concentration of magnesium is found in the ventricles then in the atria. There are no significant differences between magnesium concentration in the right and left ventricles or inter-ventricular septum (Burch et al, 1977)[3]. Magnesium has been shown to be involved in ATP hydrolysis by myofibrils, super-precipitation and sineresis of actinomycin gels, and binding and release of calcium ions by sacrotubule reactions, which are essential to the contraction of heart muscle. Magnesium also stimulates oxidative phosphorylation in heart mitochondria, and affects sodium potassium ATPase of heart membranes, and activates adenyl-cyclase and probably phosphorylase-kinase in the heart. Magnesium may have influence on muscle tone and conducting system, though the myocardium may be less sensitive to magnesium than nervous tissue (Wecker et al) [15]

Renal Magnesium Handling

The kidney is the principle organ involved in the regulation of magnesium homeostasis. Approximately 8 mEq is excreted into the urine each day. During magnesium - deprivation, magnesium is retained avidly by the kidneys and less than 1 mEq is excreted into the urine per 24 hours period. When dietary magnesium is plentiful or is administered parenterally so that filtered load exceeds the normal plasma concentration, the excess magnesium is excreted rapidly.[19] The renal handling of magnesium in humans is a filtration - reabsorption process. Micropuncture studies of the nephron have indicated that the proximal tubule and thick ascending limb of henle are the major sites of magnesium reabsorption.

20 to 30% filtered magnesium is reabsorbed passively in theproximal tubule where magnesium reabsorption follows change in salt and water reabsorption and is associated with the rate of fluid flow. Some 65% of filtered magnesium is reclaimed in thick ascending limb of henle by an active transport process. Aldosterone increases the renal excretion of magnesium, whereas parathormone reduces excretion. Parathyroid hormone regulates, in part, both calcium and magnesium excretion and metabolism. An increase in the blood magnesium cation reduces parathormone reaction and vice versa.[15] Patients with either primary hyperparathyrodism or hypoparathyrodism usually have normal serum magnesium concentration suggesting that PTH is not an important physiological regulator of magnesium heomeostasis.[19]

Intestinal magnesium absorption

The intestinal magnesium absorption is inversely proportional to the amount ingested[11]. The recommended minimum daily requirement is 300-500 mg. The estimated daily magnesium intake has ranges from 150-350 mg/day. About 30-50% of ingested magnesium is absorbed.[20] The major sources of magnesium are nuts, cereals, green leafy vegetables and meat.

Magnesium is absorbed along the entire intestinal tract, including the large and small bowels, but the site of maximum absorption appears to be in the ileum and jejunum. Magnesium is absorbed most efficiently in the chloride form in the alkaline environment of small intestine.[21] The existence of both an unsuitable passive transport system for magnesium absorption may account for the higher fractional absorption at low dietary magnesium intake.

A principle factor of hormone controlling intestinal magnesium transport has now been described. Vitamin-D and its metabolites, 25 hydroxy vitamin-D and 1,25 dihydroxy vitamin-D have been found to enhance magnesium absorption by the intestine[14]. Bioavailability of magnesium may also be a factor in magnesium intestinal absorption. The presence of excessive amounts of substances such as free fatty acids, phytates, oxalates, phosphate and fiber may bind magnesium and impair absorption[15].

Intracellular Magnesium

Magnesium is compartmentalized in the cell and is bound to proteins and negatively charged molecules. Significant amounts of magnesium are found in the nucleus, mitochondria and endoplasmic reticulum as well as cytoplasm[21]. 80% of magensium in the cytoplasm is complexed with adenosine triphosphate (ATP). The concentration of free ionized magnesium (mg^{2+}) is about 0.1 mmol/l to 1 mmol/l. It constitutes about 0.55 to 5% of the total cellular magnesium. The magnesium concentration in the cell cytoplasm appears to be maintained relatively constant.

The studies of magnesium transport suggests that the rate of magnesium exchange in the heart, liver and kidneys far exceeds that in skeletal muscle, red cells and brain. Increased cellular magnesium content has been reported for rapidly proliferating normal cells, indicating a possible relationship between the metabolic state of a cell and relative rates of magnesium transport into and out of cells. Absorbed magnesium is excreted through both the kidney and the stool over, two or three days being less than 1.4% of amount given.

In normal states the kidney filters approximately 2.5 gm of magnesium and retains 95%, excreting some 100 mg/day in the urine to maintain homeostasis. Under conditions of deprivation the kidneys conserve magnesium and hence excretion can

decrease to less than 12 mg/ day.

Aldosterone increases the renal excretion of magnesium, whereas parathormone reduces excretion. Also parathormone regulates in part, both calcium and magnesium excretion and metabolism. An increase in the blood magnesium cation reduces parathormone reaction and vice versa.[15]

PHYSIOLOGICAL ROLE OF MAGNESIUM

Magnesium plays a role in numerous enzymatic processes in the body.[15] It is essential for substrate formation and has direct role in the activation of enzymes such as phosphofructokinase, creatine kinase, adenylate cyclase and sodium-potassium ATPase. The effect of magnesium on these enzymes as well as on other important biological processes such as glycolysis, oxidative phosphorylation, nucleotide metabolism, protein biosynthesis signifies the importance of magnesium in cellular metabolism.

The compromised cell membrane cation pump causes loss of cellular potassium and accumulation of intracellular sodium. This effect is similar to that which occurs during digitalis therapy, and may explain, why magnesium deficiency enhances digitalis toxicity.

Impact of Magnesium on Vascular Tone

Magnesium is considered to be nature's physiologic calcium channel antagonist.[23] It reduces the release of calcium from and into the sarcoplasmic reticulum and protects the cell against calcium overload under conditions of ischemia.

Magnesium reduces systemic and pulmonary vascular resistance, with concomitant decrease in blood pressure and a slight increase in cardiac index.[24] Elevation of extracellular magnesium levels reduces arteriolar tone and tension in a wide variety of arteries and potentiates the dilatory action of some endogenous (adenosine, potassium and some prostaglandins) and exogenous (isoproternol and nitroprusside) vasodilators.[25]

As a result, magnesium has a mild inhibitory effect on systolic blood pressure may reduce after load and thus unload the ischemic ventricles. Kugiyama et al[26] demonstrated that exercise induced angina pectoris is suppressed by intravenous

magnesium in patients with variant angina, most probably as a result of improvement of regional myocardial blood flow by suppression of coronary artery spasm. Altura and Altura[27] found in an experimental vascular smooth muscle model that magnesium deficiency through potentiation of increased cellular calcium activity might be responsible for the arterial hypertension that accompanies toxemia of pregnancy. The proven effectiveness of parenteral magnesium therapy in toxemia of pregnancy is most likely the result of its calcium antagonist action.

Impact of Magnesium on Cardiac Rhythm

Magnesium deficiency is associated with intracellular hypo-potassemia, hypernatremia and augmentation of cell excitability. Magnesium has modest electrophysiologic effects: it prolongs the actual and corrected sinus node recovery time, prolongs the atrioventricular nodal function, relative and effective refractory periods, slightly increases the QRS duration during ventricular pacing at cycle lengths of 250 and 500 milliseconds, and increases the atrial-His interval and atrial paced-cycle length causing atrioventricular nodal Wenckebach conduction[28]. Zwillinger[31] in 1935 was the first to recognize that magnesium has an antiarrhythmic effect when used to convert paroxysmal tachycardia to sinus rhythm. Later on it was successfully used in patients with resistant ventricular tachycardias, ventricular arrhythmias induced by digitalis toxicity and in those with episodes of torsade de poites, a life threatening ventricular arrhythmia.

Magnesium was also found to be effective in the termination of episodes of supraventricular arrhythmia, such as multifocal atrial tachycardia and increased the susceptibility of atrial tachycardia to pharmacological conversion with digoxin

The American Heart Association has recently recommended magnesium as the third drug of choice (after amiodarone and lidocaine) in the resuscitation of patients with pulseless ventricular tachycardias or ventricular fibrillation.[29]

Impact of Magnesium on Lipid Metabolism

How magnesium plays a lipid regulation is interesting, although not yet fully understood. Magnesium is an important cofactor of two enzymes that are essential in lipid metabolism; lecithin-cholesterol acyltransferase (LACT) and lipoprotein lipase. In a rabbit model animals were fed a regular diet, or a high cholesterol diet supplemented with varying amounts of magnesium, and it was that the addition of supplemental magnesium achieved a dose-dependent reduction in both the area of the aortic lesions and the cholesterol content of the aorta.[30] Rats on the other hand, placed on diets severely deficient in magnesium developed adverse lipid changes. In another rat model, magnesium deficient diets led to the increased plasma levels of total cholesterol, low density lipoprotein-cholesterol and triglycerides, with a proportionate reduction in plasma levels of high density lipoproteins-cholesterol (HDL-C).[31]

Davis et al[32] demonstrated a significant improvement in the ratio of HDL-C and LDL-C plus VLDL-C by administering magnesium 18 mmol/day in a 4-month clinical trial. Rassmussen et al[33] gave magnesium 15 mmol/ day for 3 months and found a 27% reduction in plasma levels of triglycerides and very low-density lipoprotein-cholesterol (VLDL-C) and reduction in plasma levels of apoprotein B and elevation of plasma HDL-C levels.

Niemela et al[34] showed that in men, but not in women, platelet intracellular magnesium levels significantly inversely correlated with serum levels of total cholesterol ($r=-0.52$, $p<0.02$), LDL-C ($r=-0.54$, $p<0.009$) and apolipoprotein B($r=-0.42$, $p<0.04$).

The investigators also speculated that decreased platelet intracellular magnesium level is a possible marker for platelet membrane alterations that may affect platelet involvement in thrombosis and atherogenesis.

Anti-coagulant/ Anti-platelet Properties of Magnesium

In 1943 Greville and Lehmann[35] found that a small amount of magnesium added to fresh, unclotted human plasma prolonged the clotting time. During and shortly after World War II magnesium sulfate was widely used in Germany as a muscle relaxant, and it was observed that after such treatment the blood of patients examined postmortem was unclotted. In 1959 Anstall et al[36] demonstrated that magnesium inhibits human blood coagulation. Experimental studies have demonstrated the anti-platelet effects of magnesium, which may prevent the propagation of coronary artery thrombi or reocclusion of the infarct-related coronary artery after spontaneous or fibrinolysis-induced recanalization.[55,56]

Some studies have demonstrated that magnesium reduces platelet aggregation in healthy volunteers.[37,38] High plasma magnesium levels inhibit blood coagulation and thrombus formation in vivo, diminish platelet aggregation reduce synthesis of platelet agonist thromboxane $A_2$and inhibit thrombin-stimulated calcium influx. Platelet activation is a key element in acute vascular thrombosis, which is important in the pathogenesis of AMI and complications of coronary balloon angioplasty and stenting. Studies have demonstrated that magnesium can suppress platelet activation by either inhibiting platelet-stimulating factors, such as thromboxane A_2 or by stimulating synthesis of platelet inhibitory factors such as prostacyclin.[39,40]

Intravenous administration of magnesium to healthy volunteers, inhibited both ADP-induced platelet aggregation by 40% and the binding of fibrinogen or surface expression of glycoprotein IIb-IIIa complex GMP-140 by 30%.[40] Thus

pharmacological concentrations of magnesium effectively inhibit platelet function.

Gawaz[41] et al demonstrated that spontaneous (and ADP induced) P-selectin surface expression on platelets and platelet-leukocyte adhesion was increased in symptomatic patients with CAD compared with healthy controls.

However, intravenous magnesium administration significantly reduced both platelet surface expression of P-selectin and platelet leukocyte adhesion.

Impact of magnesium on endothelial function

In a canine model Pearson et al[42] demonstrated that hypomagnesemia selectively impaired the release of NO (nitric oxide) from coronary endothelium. Because NO is a potent endogenous vasodilator and inhibitor of platelet aggregation and adhesion, it has been hypothesized that hypomagnesemia may promote vasoconstriction and coronary thrombosis.

Impact of Magnesium on Infarct Size

Hypomagnesemia may increase coronary and systemic vasoconstriction and afterload. Administered soon after the onset of myocardial ischemia, magnesium infusion may limit the progression of ischemia, which in turn could reduce the risk of arrhythmias resulting from raised local catecholamine levels.[43]

Low concentrations of magnesium in laboratory animals seem to potentiate catecholamine-induced myocardial necrosis[43]. Magnesium deficiency may adversely influence the healing and re-endothelialization of vascular injuries, the healing of myocardial infarction and may also result in delayed or inadequate angiogenesis.[44]

Such effects could potentially lead to inadequate development of collaterals and infarct expansion. Magnesium reduces vulnerability to oxygen-derived free radicals, reperfusion injury and stunning of the myocardium.

MAGNESIUM DEFICIENCY

Magnesium deficiency is becoming more commonly recognized due to increased clinical awareness, and the greater frequency of assessment of magnesium status by a physician. Approximately 10% of the patients admitted to large city hospitals are hypomagnesemic. This incidence may increase to as high as 65% in an intensive care unit. Clinically apparent hypomagnesemia is usually due to losses of magnesium from either the gastrointestinal tract or the kidney. The causes of magnesium deficiency are as follows.

Gastrointestinal disorders

- Prolonged nasogastric suction
- Malabsorption syndrome
- Extensive bowel resection
- Acute and chronic diarrhea
- Protein calorie malnutrition
- Acute hemorrhagic pancreatitis
- Primary hypomagnesemia (neonatal).

Renal causes

— Chronic parenteral fluid therapy

— Osmotic diuresis

— Hypercalcemia

— Drugs like:

— Diuretics

— Frusemide, ethacrymic acid)

— Aminoglycosides

— Cisplastin

— Cyclosporin

— Amphotericin-B

Metabolic acidosis

— Starvation

— Ketoacidosis

Other Renal diseases like.

Chronic pyelonephritis, interstitial nephritis and glomerulonephritis

Diuretic phase of acute tubular necrosis

Post obstructive nephropathy

Renal tubular acidosis

Post renal transplantation.

Hypomagnesemia may be encountered in about 28% of patients with acute hemorrhagic or edematous pancreatitis. The low serum magnesium concentration may be due disorder predisposing to the pancreatitis.

Renal magnesium wasting

Magnesium loss into the urine underlies the basis of magnesium in many patients. Proximal tubular re-absorption of magnesium is proportional to tubular fluid flow and sodium reabsorption.[45] Therefore, chronic parenteral fluid therapy, particularly with sodium containing fluid may result in magnesium deficiency. Similarly osmotic diuresis due to diabetic mellitus result is urinary magnesium wasting.

Hypercalcemia is shown to decrease magnesium absorption in the proximal tubule and loop of henle and is perhaps the mechanism of renal magnesium wasting or the tendency towards hypomagnesemia in most hypercalcemia states.[46]

Gastrointestinal Disorder

The magnesium content of upper intestinal tract is approximately 1 mEq/l, therefore vomiting and nasogastric suction may contribute to magnesium depletion. The magnesium content of diarrheal fluid and fistulous drainage are much higher (up to 15 mEq/l) and consequently magnesium depletion is much common in acute and chronic diarrhea, regional enteritis, ulcerative colitis and intestinal and biliary fistulae[47] Malabsorption syndromes are due to non-tropical sprue, radiation injury resulting from therapy for disorders such as whipple disease and carcinoma of cervix may result in magnesium deficiency presumably due to an intestinal mucosal damage[48]. Steatorrhea may also cause or contribute to magnesium malabsorption through formation of non-absorbable magnesium lipid salts. Resection or bypass of small bowel for obesity, enteritis also results in magnesium deficiency.

The commonest cause of magnesium wasting is concurrent use of diuretics.[49] Diuretics acting on the proximal tubules, such as carbonic anhydrase inhibitors and osmotic agents may increase moderately magnesium excretion. Diuretics acting at the loop of henle such as frusemide and ethacrynic acid result in magnesium deficiency Aminoglycoside therapy initially with capreomycin, gentamycin and recently with tobramycin, amikacin has produced renal magnesium wasting. Amphotericin B therapy also has been reported to result in renal magnesium wasting.

Cisplastin is a chemo-therapeutic agent used in the treatment of epithelial neoplasms which leads to renal magnesium wasting resulting in hypomagnesemia in up to 100 of patients receiving the drug.

Endocrine and Metabolic Disorders

Certain endocrine and metabolic diseases are associated with magnesium depletion, usually through renal magnesium wasting. Diabetes mellitus is the most common disorder associated with magnesium deficiency[50]. The serum magnesium concentrates correlates inversely with the serum glucose concentration and degree of glucosuria. The mechanism of magnesium depletion is probably due to the glucosuria (osmotic diuresis).[51] In addition, insulin may cause a shift of magnesium into the cell.

Hypomagnesemia can be found in association with a number of other endocrine abnormalities. Phosphate depletion has been shown to result in urinary magnesium wasting and hypomagnesemia. That is hypophosphatemia is a contributing factor in the development of magnesium deficiency.

Other conditions leading to urinary magnesium wasting and hypomagnesemia are hyperthyrodism, thyrotoxicosis. The hypomagnesemia, which may be seen in primary hyperaldosteronism, has been related to plasma volume expansion and subsequent renal magnesium wasting.

Miscellaneous Causes

Total body magnesium depletion may occur via unusual routes of excretion. Excessive sweating may lead to clinically important degrees of magnesium losses.
Acute pancreatitis may result in hypomagnesemia but themechanism of this effect is unknown. Soft tissue deposition of magnesium fat complexus has been postulated. Redistribution of magnesium from extracellular to intracellular fluids or into bone is a frequent cause of reduced serum magnesium levels.

MAGNESIUM AND ACUTE MYOCARDIAL INFARCTION

Epidemiological studies have suggested that the incidence of myocardial infarction and of sudden death is higher in areas of soft water intake.[52] Cardiac magnesium content has been reported to be low in patients whose death was attributed to myocardial infarction.[53] It is unknown however, if the low cardiac content proceeds the myocardial infarction or is result of it. Cardiac magnesium exchanges quite rapidly with plasma magnesium and a number of clinical studies have shown a fall in the serum magnesium concentration within the first 24 to 48 hours after myocardial infarction.[54]

Infarcted myocardium has been repeatedly shown to reduce magnesium content. But the results regarding the study of serum magnesium values in first 24hours, following acute myocardial infarction has been variable. Some found no significant change of serum magnesium. It has, therefore been proposed that serum magnesium has an inverse relationship with coagulability of blood and serum cholesterol levels, following acute myocardial infarction.

Myocardial injury was established by histological examination of cardiac tissue. A significant rise in urinary magnesium excretion was observed during the first two hours after which the level declined but was still maintained above the control level. Magnesium content decreased significantly in infarcted myocardium.

Various authors have reported a decrease of serum magnesium following MI. Abraham S et al[54] from Israel checked serum magnesium levels of forty two patients of acute MI, nine patients of coronary insufficiency and fourteen patients of non-cardiac chest pain. Patients with acute myocardial infarction and those with acute coronary insufficiency had lower serum magnesium levels than eighty controls natural for age and sex, whereas there was no difference in patients with non-cardiac chest pain.

There was a significant fall of serum magnesium during the first five days and normal levels were reached by the 12th day.

Singh A et al[55] (1976) checked serum magnesium levels of twenty patients of acute MI on the first 7th and 12th day of admission. In all the cases, there was a significant fall of serum magnesium on the first day.

Babel S.Bhatnagar, HNS Bhatnagar[56] from Rajasthan tried to determine the prognostic significance of serum magnesium levels in acute MI. Twenty-five patients of acute myocardial infarction were studied. Serum magnesium was found to be significantly lowered on the first day and it gradually rose to normal value by the twenty first day.

But some studies have showed that magnesium depletion resulted in lowered intracellular magnesium and potassium, increased intracellular calcium and sodium, and focal cardiac necrosis.[57] Patients with coronary artery disease have been found to have decreased amount of exchangeable magnesium and patients sustaining an acute myocardial infarction were found to retain abnormally high amounts of magnesium during magnesium tolerance testing and to have lower skeletal muscle magnesium content suggesting the presence of magnesium deficiency.[58]

Magnesium depletion predisposes to vascular spasms, including coronary artery spasm and potentiates the contractile response to pressor agents such as angiotensin II and norepinephrine. Magnesium depletion potentially could worsen angina and precipitate acute myocardial infarction. The effectiveness of magnesium therapy in acute MI has been reported to decrease infarction size, decrease the incidence of cardiac arrhythmias and lower mortality rate.[59,60,61]

Mechanism of Tachydyrarrhythmias:

The exact mechanism behind the effect of magnesium on cardiac dysarrhythmias is unknown. Magnesium is essential for activation of ATP, which maintains the sodium-potassium pump. Therefore, it may have an important role in maintaining the resting membrane potential of electrocardiac cells, which depend on the intracellular potassium gradient. Magnesium deficiency is associated with loss of intracellular potassium, an increase in intracellular sodium, and an increase in cell excitability. One theory of magnesium and dysarrhythmias suggest failure of potassium to reenter the depolarized cell or a diastolic leak of potassium from already depolarized cells may promote aberrant condition, reentry phenomena and ventricular fibrillation.[62,63]

Another theory is that magnesium acts as a calcium blocking agent. The increased intracellular sodium linked with magnesium deficiency may be followed by a sodium-calcium exchange causing an increase in intracellular calcium. Phasic influx of intracellular calcium is linked with transient depolarization and repetitive dysarrhythmias, infusion of magnesium cause a clinical picture similar to that produced by infusion of a calcium blocking agent, peripheral vasodilatation, flushing, a decrease in blood pressure and a decrease in contractile strength of the heart.[64]

Lysophosphatidyl choline (LPC) is an endogenous lipid released from cell membranes during ischemia and has potent local effects on cardiac tissue. LPC causes membrane depolarization by decreasing potassium conductance of the inward rectified current and induces cardiac arrhythmias. LPC also triggers the accumulation of intracellular calcium in heart cells by inhibiting the sodium-potassium adenosine triphosphatase (ATPase) pump[65]. Increased systolic calcium can be detrimental to cells by activating calcium dependent phospholipases and proteases and by generating additional toxic fatty acids. Excess free intracellular calcium also potentates the

harmful effects of free radicals[66]. Because magnesium is a critical cofacors of myocardial ion pumps and antagonizes calcium influx. Antiarrhythmic effects of magnesium during ischemia were mediated by inhibition of increasing intracellular calcium induced by LPC.

Ventricular Tachydysarrhythmias and Magnesium

In 1935, Zwillinger[67] injected 15 ml of a 20% solution of magnesium sulfate ($MgSO_4$) as a bolus into left ventrice of a patient with ventricular fibrillation resistant to other therapy. The rhythm changed almost instantaneously to sinus rhythm.

In 1943, Boyd and Schesf[68] used 10-20 ml of IU 10% $MgSO_4$ to treat spontaneous dysarrhythmias with an approximately 50% success rate.

Rasmussen et al[69], experimental patients received approximately 1200 mg of magnesium chloride ($MgCl_2$) in the first 24 hours after AMI and approximately 300 mg in the second 24 hours. Results were compared with placebo control group. Those treated with $MgCl_2$ had significantly fewer incidence of dysarrhythmias requiring intervention (21% versus 47%) ($p<0.05$).

Ventricular dysarrhythmias induced by digitalis toxicity are extremely responsive to magnesium therapy. Hypomagnesemia is common during digitalis toxicity and even in the presence of normal serum magnesium, intracellular magnesium is frequently low. Magnesium counteracts the inhibitory effects of digitalis on sodium/ potassium ATP. During digitalis therapy, there is an increase in intracellular calcium leading to augmentation of ionotropism and excitability[70]. In a study in monkeys, low magnesium levels were associated with a decrease in tolerance to digitalis and the duration of digitalis toxicity was prolonged.

Holden et al[71] found a striking decrease in Mg^{2+} both during cardiovascular bypass surgery and 1-day postoperatively. Dysarrhythmias after cardiovascular surgery are believed to be partially caused by hypomagnesemia resulting from the use of anticoagulants during surgery i.e., anticoagulants bind Mg^{2+}. The use of Mg^{++} in the postoperative period has decreased the incidence of dysarrhythmias

Torsades de Pointes

Torsades de Pointes (TdP) is a life-threatening ventricular dysrhythmia. This repetitive polymorphic ventricular tachycardia occurs in the presence of QT prolongation. TdP is most commonly induced by type Ia antidysrhythmic drugs such as quinidine or disopyramide. Other QT prolonging drugs, such as amiodarone, have been reported to cause TdP. Hypokalemia and hypomagnesemia can potentiate the development of TdP and in rare cases can be the cause[72].

In a longitudinal study of 12 patients with TdP treated with intravenous $MgSO_4$, a single bolus of 2g of $MgSO_4$ completely abolished TdP within 1 to 5 minutes in nine patients[63]. In the other three patients, a second dose of $MgSO_4$ was given 5 to 15 minutes later completely corrected TdP. No side effects were associated with the treatment. Similar findings were reported by Perticone et al[73].

Atrial dysrhythmias :

Hypomagnesemia has been shown to make control of atrial fibrillation (AF) difficult[73]. In one study of 45 consecutive patients with symptomatic AF,20% had serum magnesium levels <1.5 mEq/L. In a blinded treatment protocol, hypomagnesemic patients required twice the amount of IV digoxin to control AF. This study suggests that monitoring and replacement of Mg^{++} may be beneficial in patients with symptomatic AF, especially when digoxin therapy is considered[74]

MANIFESTATIONS OF MAGNESIUM DEFICIENCY SIGNS AND SMPTOMS

Deprivation of dietary magnesium in otherwise nutritionally normal persons reach to a syndrome characterized by personality change, tremor, fasciculation, spontaneous carpo-pedal spasm and generalized spasticity. Restoration of dietary magnesium produces a prompt and complete remission of abnormal signs and symptoms.

Because magnesium deficiency is usually secondary to another disease process or to a therapeutic agent, the feature of the primary disease process may complicate or mask the magnesium deficiency. Manifestation of moderate to severe magnesium deficiency is shown in Table-1.

Manifestations of Moderate to Severe Magnesium Deficiency

Biochemical

- Hypokalemaia [70]
- Renal potassium wasting
- Decreased intracellular potassium
- Hypocalcemia
- Impaired PTH secretion
- Renal and skeletal resistance to PTH
- Resistance to vitamin D.

Neuromuscular

- Positive Chvostek's and Trausseau's sign
- Spontaneous carpo-pedal spasms
- Seizures
- Vertigo, ataxia, nystagmus, athetoid and choreiform movements.

- Muscular weaknes, tremor, fasciculation and wasting
- Psychiatric: Depression and psychosis.

Cardiac Arrhythmias

- ECG - prolonged PR and QT interval and U-waves
- Atrial tachycardia, premature contractions and fibrillation
- Ventricular premature contractions
- Ventricular tachycardia and fibrillation
- Torsades de pointes
- Myocardial infarction
- Possible role of magnesium deficiency

Biochemical Abnormalities

Hypokalemia

A frequently encountered laboratory feature of magnesium deficiency is hypokalemia. During magnesium deficiency, there is loss of potassium from the cell with subsequent development of intracellular potassium depletion. In addition, there is an inability of the kidney to conserve potassium. Attempts to replace the potassium deficit with potassium therapy alone are not successful without simultaneous magnesium therapy. The reason for the disrupted potassium metabolism may be related to Mg^{2+} dependence of the Na^{+} K^{+} ATPase. During magnesium depletion intracellular sodium and calcium rise and magnesium and potassium fall.

Magnesium also appears to be important in the regulation of potassium channels in cardiac cells that are characterized by inward rectification.

Hypocalcemia

Magnesium deficiency is a recognized cause of hypocalcemia[76]. In hypocalcemia patients with hypomagnesemia, serum concentrations of PTH are usually inappropriately low.

Patients with magnesium deficiency are also resistant to the effect of vitamin-D. This may be due to impaired metabolism of vitamin-D as serum concentration of 1, 25 dihydroxy vitamin-D are low. It is important to recognize that calcium or vitamin D therapy for the hypocalcemia of magnesium deficiency is not usually effective in correcting the hypocalemia. Magnesium therapy is necessary for the restoration of a normal serum calcium concentration.

Neuromuscular

Neuromuscular hyper-excitability is commonly the presenting complaint of a patient with magnesium deficiency. Latent tetany, as dictated by positive Chvostek's and Trousseau's sign, or spontaneous carpo-pedal spasm may be present. Generalized seizures may also occur by positive Chvostek's and Trousseau's sign, or spontaneous carpo-pedal spasm may be present. Generalized seizures may also occur.

Other signs occasionally seen include vertigo, ataxia, nystagmus, athetoid and choreiform movements, muscular tremor, fasciculation, wasting and weakness also may be present.[15]

The various mechanisms responsible for neuromuscular problems in hypomagnesemia are:

1. Magnesium stabilizes the nerve axon. Lowering of the serum magnesium concentration decreases the threshold of axonal stimulation and increases nerve conduction velocity.

2. Magnesium influences the release of neuro-transmitters at the neuromuscular junction by competitively inhibiting the entry of calcium into the pre-synaptic nerve terminal[77]. A decrease of extracellular Mg^{2+} allows a greater influx of calcium into the pre- synaptic nerves and subsequent release of great quantity of neurotransmitters, resulting in hyperresponsive neuromuscular activity.
3. Another mechanism by which magnesium deficiency and a decrease in the intracellular magnesium could alter the neuromuscular excitability is by the effects that magnesium exerts on calcium handling by the muscle cell.

DIAGNOSIS OF MAGNESIUM DEFICIENCY

Serum Magnesium Concentration

Magnesium is principally an intracellular cation. Less than 1% of the body magnesium content is in the extracellular fluid compartments. The serum magnesium concentration may not reflect the intracellular magnesium content. The measurement of serum magnesium concentration is the most commonly employed test to assess magnesium status.

Exogenous and endogenous catecholamines have been shown to result in a slight fall in the serum magnesium concentration and increased catecholamine secretion could be a contributing cause of hypomagnesemia in acute illness and stress[54]. Volume contraction and rhabdomyolysis (cellular magnesium release) can cause an increase in the serum magnesium concentration and may mask an intracellular magnesium deficit.

Intracellular Magnesium Content

The magnesium content of the peripheral lymphocyte has been under recent investigation and it has found to correlate with skeletal and cardiac muscle magnesium content. It seems to be a more accurate indicator of magnesium status than the serum magnesium concentration.

Magnesium Tolerance Test

It is an accurate means of assessing magnesium status. Retention of a parenterally administered magnesium load is greater than normal in both hypomagnesemia patients and normo-magnesemia patients at risk for magnesium deficiency.

THE SUGGESTED PROTOCOL IS:

1. Collect baseline urine (spot and timed) for magnesium creatinine ratio.
2. Infuse 0.2 meq (2.4 mg) elemental magnesium per kg body weight in 50 ml 5% dextrose water over 4 hours.
3. Collect urine (starting with infusion) for magnesium for 24 hours.
4. Calculate percent of magnesium retained using the following formula.

$$\%\ \text{magnesium retained} = 1 - \frac{(\text{Post infusion 24 hours, urine magnesium}) - (\text{preinfusion urine magnesium/ creatinine}) \times (\text{post infusion creatinine})}{\text{Total elemental magnesium infused}} \times 100\%$$

5. Criteria for magnesium deficiency

   >50% retention at 24 hours = definite deficiency

   >25% retention at 24 hours = probable deficiency

Treatment of Magnesium Deficiency

Patients who present with signs and symptoms of magnesium deficiency and are at risk for magnesium depletion should be treated with magnesium

Most patients with hypomagnesemia can be treated by the institution of a normal diet. However, if ongoing renal or gastrointestinal losses occur, magnesium salt supplements are necessary. Renal function should be checked prior to the therapy. Even in severely magnesium deficient subjects, approximately 50% of an admissible dose is excreted in the urine so that renal failure dictates markedly reduced therapeutic doses. Symptomatic magnesium deficits are usually between 1 and 2 mEq/kg of body weight.

Symptomatic moderate tosevere magnesium deficiency should be treated by parenteral administration.

Administration of Parenteral Magnesium

Although a single dose of IV Mg^{++} may be effective, the kidney will excrete a arge amount of the dose delivered.

The American Society of Hospital Pharmacists recommends that the maximum loading dose of Mg^{++} be 150 mg/min[78]. In emergency situations of ventricular tachycardia or ventricular fibrillation, the adult ACLS regimen is 1 g diluted in 100 mL given over 1 to 2 minutes[79]. During this treatment, the electrocardiogram should be monitored continuously to avoid cardiac toxicity. Blood pressure should be monitored closely during IV replacement of Mg^{++}, with the infusion slowed if the patient becomes symptomatically hypotensive. Common side effects of rapid IV administration of Mg^{++} include cutaneous flushing, sweating, and sensation of heat, hypotension, decreased deep tendon reflexes, somnolence, hypocalcemia, tetany, respiratory insufficiency, paralysis, and cardiac arrest can occur.

These side effects can be alleviated by slowing the infusion. Patients also require monitoring of the serum magnesium level, neurologic status, respiratory status, and renal function. Patellar reflexes should be assessed before starting treatment and monitored carefully during treatment. Therapy should be stopped if the reflexes become suppressed.

If the patient has renal insufficiency, the magnesium dose is decreased by 25% to 50% to prevent hypermagnesemia. Replacement therapy is closely guided by the serum magnesium level to avoid toxicity. A potential

complication from $MgSO_4$ administration is hypocalcemia. The sulfate binds with calcium, forming sulfate and reducing ionized calcium. Zaloga and Charnow recommended IV magnesium chloride, rather than $MgSO_4$ to avoid calcium sulphate precipitation. Calcium gluconate should be kept available as an emergency treatment in the event of hypocalcemia, tetany or overdose apnea.

Administration of Oral Magnesium

For non-serious conditions oral forms of magnesium supplementation are available, although gastrointestinal absorption may vary. Large doses of oral magnesium salts often cause diarrhea. However, Mg^{++} in the Mg^{++} chloride salt form or in enteric-coated tablets is usually well tolerated. A course of three magnesium chloride tablets a day for 30 days will reduce the deficit for most patients.[80] For patients taking diuretics, the substitution or addition of a potassium/ magnesium-sparing diuretic is probably beneficial.

MATERIAL AND METHODS

Fifty subjects aged between 18 and 65 years presenting with Acute myocardial infarction diagnosed by history, clinical examination, ECG findings (ST-segment elevation on the corresponding leads) and biochemical markers (CK-MB, troponin-T), who present to the casualty or who are admitted in Sri R. L. Jalappa Hospital & Research Centre and Narayana Hrudayalaya,kolar were taken up for the study during the time period of Feb 2012 to July 2013

METHOD OF COLLECTION OF DATA

- Blood samples for estimation of serum total magnesium, CK-MB and troponin-T, serum sodium, potassium, hemoglobin, random blood sugar were taken at the time of admission to the hospital and repeated once after 48 hours.
- Serum Magnesium estimation was done by dry chemistry auto-analyzer
- Patients were under the continuous surveillance of a cardiac monitor to check for arrhythmias (supra-venticular and ventricular arrhythmias).
- The major risk factors for acute myocardial infarction like hypertension, diabetes, dyslipidemia and smoking were also documented.
- Morbid events documented were hypotension/cardiogenic shock, arrhythmias (supra-ventricular and ventricular), heart failure, renal failure and development of stroke, cardiac arrest.
- Other factors that affect the clinical course and the outcome of acute myocardial infarction such as serum Na^+, K^+, Ca^+ were documented
- Levels of serum total magnesium were correlated with the underlying risk factors (mentioned above), morbid complications (arrhythmias, cardiogenic shock, heart failure), mechanical ventilatory need of the patients

INCLUSION CRITERIA

Patients of Acute myocardial infarction of either sex aged between 18 and 65years diagnosed by history, clinical examination and 12 lead ECG(with ST- segment elevation,Q- wave,T-wave changes on their presenting ECG) and biochemical markers(CK-MB and troponin-T).

EXCLUSION CRITERIA

1. Patients with prior transfusion of magnesium or on magnesium oral supplementation.
2. Patients not belonging to the age group of 18-65years .

Magnesium Estimation

Serum magnesium levels were estimated on day-1 and after 48 hours of admission

Method of Serum Magnesium Estimation

Method: The VITROS Mg Slide method

Reagent:

Slide Ingredients

Reactive Ingredients per cm^2 1,2-bis(o-aminophenoxy)ethane-N,N,N',N'-tetraacetic acid (calcium chelator) 242 µg and 1,5-bis(2-hydroxy-3,5- dichlorophenyl)-3-cyanoformazan (dye) 38 µg.

Other Ingredients

Pigment, binders, buffer, dye solubilizer, surfactants, cross-linking agent and stabilizer.

Principle: The VITROS Mg Slide method is performed using the VITROS Mg Slides and the VITROS Chemistry Products Calibrator Kit 1 on VITROS 250/350/95/5,1 FS and 4600 Chemistry Systems and the VITROS 5600 Integrated System. The VITROS Mg Slide is a multilayered, analytical element coated on a polyester support.

A drop of patient sample is deposited on the slide and is evenly distributed by the spreading layer to the underlying layers. Magnesium (both free and protein-bound) from the sample then reacts with the formazan dye derivative in the reagent layer; the high magnesium affinity of the dye dissociates magnesium from binding proteins. The resulting magnesium-dye complex causes a shift in the dye absorption maximum. The amount of dye complex formed is proportional to the magnesium concentration present in the sample and is measured by reflection density.

Specimen

Non-hemolyzed serum or lithium heparin plasma may be analyzed since the magnesium concentration inside erythrocytes is 10 times greater than that in the ECF, hemolysis should be avoided and serum should be separated from the cell as soon as possible.

Reference range for magnesium

Serum magnesium: 1.6 - 2.6 mEq/l.

Statistical Methods:

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data are made, Assumptions:1.Dependent variables should be normally distributed, 2.Samples drawn from the population should be random, Cases of the samples should be independent

Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups Inter group analysis) on metric parameters. Leven1s test for homogeneity of variance has been performed to assess the homogeneity of variance. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

Significant figures

+ Suggestive significance (P value: $0.05<P<0.10$)

* Moderately significant (P value:$0.01<P \leq 0.05$)

** Strongly significant (P value : $P \leq 0.01$)

Statistical software: The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1 ,Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

RESULTS

Age and Sex Distribution of the Study group

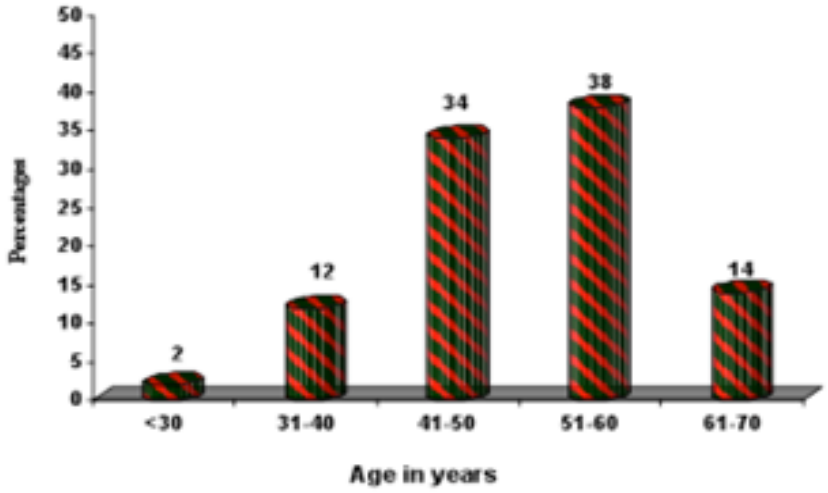
Table-1

Age in years	No. of patients	%
<30	1	2.0
31-40	6	12.0
41-50	17	34.0
51-60	19	38.0
61-70	7	14.0
Total	50	100.0

Table 2:

Gender	No. of patients	%
Female	3	6.0
Male	47	94.0
Total	50	100.0

Graph 1 : Age distribution of the study group



In this study group of 50 cases, 47 were males and 3 were female patients with a male-female ratio of 15.6:1. The maximum incidence of acute myocardial infarction was seen in the 5th decade, immediately followed by 4th decade. 34% of patients belong to 40-50 years age group, which is a weight bearing age group of Indian economy. Mean ± SD for age in this study is 51.94±9.02

Risk Factors

Table-3

Risk factors	No. of patients	%
Absent	17	34.0
Present	33	66.0
Smokers	18	36.0
T2DM	15	30.0
HTN	9	18.0
CentralObesity	4	8.0
HIV positive	1	2.0

Smoking

In the study, smoking is the most common risk factor found in the patients with acute myocardial infarction. Cigarette smoking accelerates coronary atherosclerosis in both sexes and at all ages and increases the risk of thrombosis, plaque instability and myocardial infarction. In addition, by increasing myocardial oxygen needs and reducing oxygen supply, it aggravates angina.

It is alarming to find out through our study that 34% of the patients did not have any known cardiac risk factors prior to the myocardial infarction

Diabetes Mellitus

In the present study, of the 50 patients,15(30%) patients were found to be diabetics .

Hypertension

In the present study, of 50 patients 15 (30%) patients were found to be hypertensive.

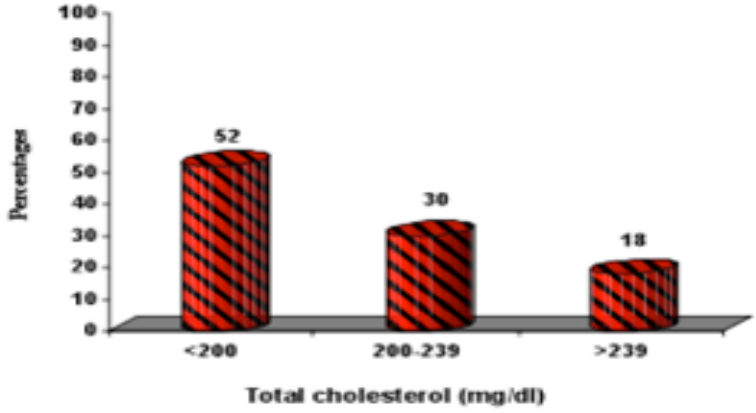
Central Obesity and Lipid Profile

In the present study, out of 50 patients, 12 (24%) were found to have central obesity. Waist circumference was measured in all patients, men whose waist circumference is more than 102 cm and females whose waist circumference is more than 88cms were considered to be obese. The mean standard deviations of the lipid profile parameters have been mention in table 4.

Table 4 : Lipid Profiles

Lipid profile	**No. of patients (n=50)**	**%**	**Mean ± SD**
Total cholesterol (mg/dl)			
• <200	26	52.0	206.92±30.24
• 200-239	15	30.0	
• >239	9	18.0	
TGL(mg/dl)			
• <150	22	44.0	145.94±37.09
• 150-199	27	54.0	
• >199	1	2.0	
HDL (mg/dl)			
• <35	13	26.0	43.66±13.16
• 35-45	20	40.0	
• >45	17	34.0	
LDL (mg/dl)			
• <130	3	6.0	171.10±27.75
• 130-159	13	26.0	
• >159	34	68.0	

Graph 2 : Profile of total Cholesterol in the study group



In this study 48% of the patients had raise serum total cholesterol and the standard mean standard deviation for the serum total cholesterol is 206.92±30.24.

Presentation to the Hospital

Chest pain was the commonest symptom and was present in 92% of the cases in the present study. In this study other associated symptoms are sweating in 20 (40%) patients, breathlessness in 3 (6%) , palpitations in 4 (8%) of the patients, Giddiness in 1(2%) of the patients and vomiting in 3 (6%) of the patients

Table 5:

Symptoms	**No. of patients (n=50)**	**%**
Chest pain	46	92.0
Sweating	20	40.0
Dyspnea	3	6.0
Giddiness	1	2.0
Palpitating	4	8.0
Vomiting	3	6.0

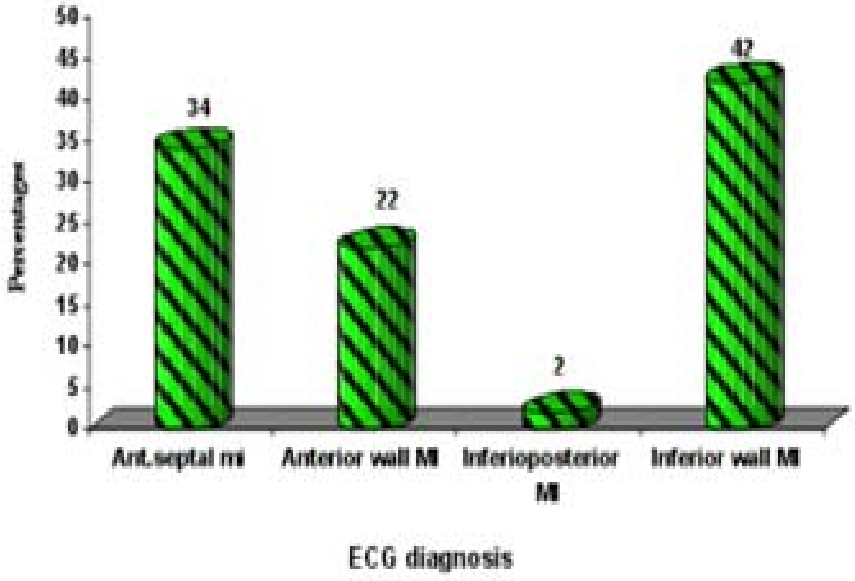
Variation in type of Myocardial Infarction

In the present study of 50 patients, 21 (42%) patients had inferior wall MI, 17 (34%) patients had anterior septal wall MI and 11 (22%) patients had Anterior wall MI , 1 (2%) patients had anterolateral MI and 1(2%) had inferio posterior wall MI .

Table 6

ECG diagnosis	No. of patients	%
Ant.septal mi	17	34.0
Anterior wall MI	11	22.0
Inferioposterior MI	1	2.0
Inferior wall MI	21	42.0
Total	**50**	**100.0**

Graph 3: Variation in type of Myocardial Infarction



Documented values of Serum electrolytes (Na^+,K^+,Ca^{+2}) in Acute Myocardial Infarction

Table 7

Electrolyte values	**No. of patients (n=50)**	**%**	**Mean ± SD**
Na^+			
• <135	9	18.0	**137.86±4.12**
• 135-145	41	82.0	
• >145	0	0.0	
Ca^{+2}			
• <8.5	3	6.0	**9.26±0.52**
• 8.5-10.3	47	94.0	
• >10.3	0	0.0	
K^+			
• <3.5	6	12.0	**3.98±0.51**
• 3.5-5.5	44	88.0	
• >5.5	0	0.0	

In this study of 50 patients, the mean serum Na^+ is 137.86±4.12, the mean serum K^+ values is 3.98±0.51 and the mean serum Ca^{+2} is 9.26±0.52.

Serum Magnesium levels in Acute Myocardial Infarction

Table 8

Serum Magnesium	**Serum Magnesium at the time MI presentation (n=50)**	**Serum Magnesium after 48 hours of MI presentation (n=47)**	**% change**
<1.6 mEq\L	16(32.0%)	0	+32.0%
1.6-2.6 mEq\L	34(68.0%)	46(97.8%)	-29.8%
>2.6 mEq\L	0	1(2.1%)	+2.1%
Mean ±SD	**1.71±0.23**	**2.43±2.47**	**-**

The above table show the serum Magnesium values of patients at the time of presentation , after 48 hours of presentation and their mean standard deviations.In this study we have noted 16 patients with serum Magnesium values <1.6 mEq\L. and no patients with hypomagnesimia after 48 hours of presentation.

Difference of serum magnesium levels are significantly higher after 48 hours of MI with difference of 0.72(p=0.055)

Complications studied in the patients of Acute myocardial infarctions

Table 9:

Complications	**No. of patients (n=50)**	**%**
• VPC	16	32.0
• Cardiogenic Shock	7	14.0
• ARF	5	10.0
• Ventilator support	3	6.0
• VT	3	6.0
• LBBB	1	2.0
• Complete Heart block	1	2.0

In this study we have documented 35 patients with the above mentioned complications and the above table depicts the number of patients with the mentioned complication and the percentage of complications found in this study. Ventricular premature complex (VPCs) was the most common complication we found in this study with the incidence of 32% followed by cardiogenic shock found in 7 patients (14%)

Correlation of clinical variables with hypomagnesemia

Table 10

Clinical variables	**hypomagnesemia**	
	Yes (n=16)	**No (n=34)**
Age in years		
• <30	0(0%)	1(2.9%)
• 31-40	2(12.5%)	4(11.8%)
• 41-50	6(37.5%)	11(32.4%)
• 51-60	6(37.5%)	13(38.2%)
• 61-70	2(12.5%)	5(14.7%)
Gender		
• Female	1(6.3%)	2(5.9%)
• Male	15(93.8%)	32(94.1%)
Symptoms		
• Chest pain	15(93.8%)	31(91.2%)
• Dyspnea	1(6.3%)	2(5.9%)
• Giddiness	0(0%)	1(2.9%)

In this study 16 patients were found to be hypomagnesimic and the above table correlates the mentioned clinical variables in patients with hypomagnesimia and without hypomagnesimia. Patients in their 4^{th} and 5^{th} decades of their life are found have highest incidence of hypomagnesimia.

Comparison of Serum electrolytes with incidence of Hypomagnesimia at the time Myocardial Infacrtion

Table 11

Serum electrolyse	Hypomagnesimia	
	Yes (n=16)	**No (n=34)**
Na^{+}	137.38±4.86	138.09±3.78
Ca^{+2}	9.33±0.53	9.23±0.52
K^{+}	4.1±0.62	3.92±0.44

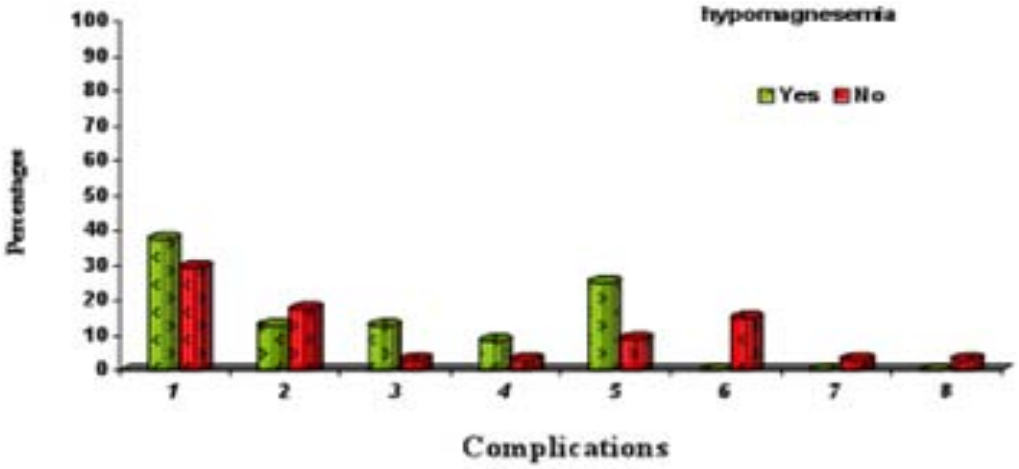
In this study hypomagnesimia is not associated with any documented electrolytic abnormality

Comparison of Complications with incidence of Hypomagnesimia at the time of presentation

Table 12

Complications	Hypomagnesimia	
	Yes (n=16)	**No (n=34)**
1)VPC	6(37.5%)	10(29.4%)
2)Death	2(12.5%)	6(17.6%)
3)Ventilator support	2(12.5%)	1(2.9%)
4)VT	1(8.3%)	1(2.9%)
5)Cardiogenic Shock	4(25.0%)	3(8.8%)
6)ARF	0	5(14.7%)
7)LBBB	0	1(2.9%)
8)Complete Heart block	0	1(2.9%)

Graph 4: Comparison of Complications with incidence of Hypomagnesimia



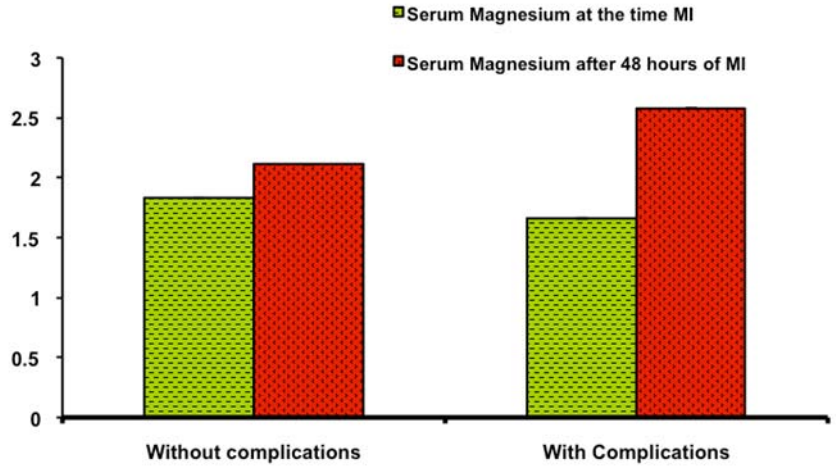
In this study 37% of hypomagnesimic patients are associated with ventricular premature complexes and 25% patients are associated with cardiogenic shock.

Comparison of Mean ± SD Serum magnesium levels of patients at the time of MI ,after 48 Hours with complications and without complications

Table 13

	Serum Magnesium at the time MI (n=50)	**Serum Magnesium after 48 hours of MI (n=47)**	**Difference**
Without complications	1.83±0.24	2.11±0.15	0.28
With Complications	1.66±0.21	2.58±3.01	0.93
p value	0.015*	0.549	0.074*

Graph 5: Comparison of Mean ± SD Serum magnesium levels of patients at the time of MI ,after 48 Hours with complications and without complications



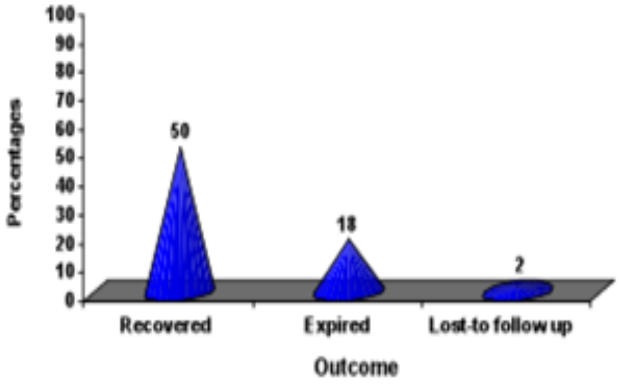
The difference between the serum magnesium levels in patients with complications and without complications is statically significant on both the day of presentation and after 48 hours with a p value of 0.074+

Mortality:

Table 14 : Outcome

Outcome	No. of patients (n=50)	%
• Recovered	41	50.0
• Expired	8	18.0
• Lost-to follow up	1	2.0

Graph 6: Outcome



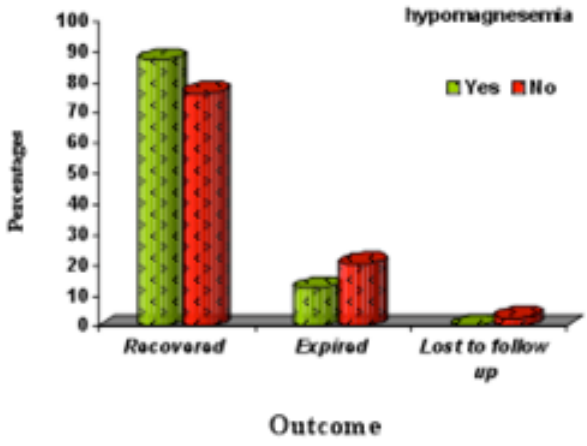
In the above study of 50 patients, 8 patients died during their in-hospital clinical course. 5 patients were died of cardiogenic shock , 1 patients were died of complete heart block and 2 patients died of ventricular arrhythmias. Mortality percentage was 18%.

Correlation of outcome with hypomagnesemia

Table 15:

Outcome	hypomagnesemia	
	Yes (n=16)	**No (n=34)**
Recovered	14(87.5%)	26(76.4%)
Expired	2(12.5%)	7(20.6%)
Lost to follow up	0	1(2.9%)

Graph 7: Correlation of outcome with hypomagnesemia



Death is not statistically associated with Hypomagnesimia with P=0.698

DISCUSSION

Magnesium ion has emerged as a premier cardiovascular cation during the decade. It has been implicated in the pathogenesis of acute myocardial infarction and complication like arrhythmias. Magnesium is essential for activation of ATP, which maintains the sodium-potassium pump and also because of calcium blocking action magnesium has been implicated in relation to arrhythmias after acute myocardial infarction.

In the study group of 50 patients, 47 were males and 3 were females with a male-female ratio of 15.6:1. The maximum incidence of acute myocardial infarction was seen in the 5^{th} decade, followed by 4^{th} decade which is working age group of the country.

In the present study of 50 patients, the mean serum magnesium level on the day of presentation in all 50 patients was 1.71±0.23 and the mean serum magnesium level after 48 hours of presentation was 2.43±2.47

Abraham et al[81] reviewed magnesium level of 65 consecutive patients with an admission diagnosis of acute myocardial infarction. Serum magnesium concentration were low in patient who had AMI (mean 1.70 mg/dl, $p<0.001$) or acute coronary insufficiency (mean 1.61 mg/dl, $p<0.01$), but not in the control group or patients with non-cardiac chest pain (mean 1.91 mg/dl).

Dimtruk[82] in his series of 67 patients of ischemic heart disease showed a distinct reduction of plasma magnesium during the first 3 days following onset of disease, the level normalized by 15-25 days from onset of the disease.

Sachdev et al[83] in 30 patients of myocardial infarction determine the magnesium levels within 24 hours, 5th and 8th day and reported as1.83±0.087 mg%,1.91±0.149 and 1.97±0.089 as against control of 2.44±0.162 mg%. The values were statistically lower on all the three days showing a progressive rise.

In the present study, the serum magnesium level on day of presentation was significant lower in patients with complications (35) in the course of their hospital stay than those without any complications ($p<0.015$). There was an increase in serum magnesium from the day of presentation to 48 hours after presentation in both those patients with complications and without complications

Ceremuzynski et al[84] assigned 48 patients with acute myocardial infarction over 24 hours infusion of magnesium or placebo. The incidence of ventricular tachycardia (3 or more consecutive premature ventricular contraction at a rate faster than 120/ min) recorded by Holter monitoring was significantly reduced ($p<0.001$), but the incidence of other ventricular arrhythmias was not statistically different.

Raismusen et al[85] randomized 273 patiens with suspected acute myocardial infarction to intravenous magnesium or placebo. There is a significant decrease in the ventricular arrhythmia in the magnesium group compared to placebo ($p<0.05$).

Dyckner T et al[7] during their 1Ω years, 905 admission, 342 with acute myocardial infarction, 563 other diagnoses ere treated in the CCU on admission both acute myocardial infarction and non AMI group had significantly lower serum magnesium level than as reference group. The incidence of serious ventricular premature beats, ventricular tachycardia and ventricular fibrillation on admission was significantly higher in the hypomagnesemic patients with acute myocardial infarction.

CONCLUSION

This study was carried out in 50 patients of acute myocardial infarction who are admitted to the ICCU of Sri RLJ hospital and research center and Narayana Hrudayalaya cardiac center, Kolar.

1. The male to female ratio in the study group was 15.6:1 and the
   Maximum incidence of acute myocardial infarction was seen in 5^{th} decade and the Mean ± SD for age in this study is 51.94±9.02
2. In the study 46 patients (92%) presented with chest pain which is the most common presenting symptom, which was associated with sweating in 20 patients ,breathlessness in 3 (6%) , palpitations in 4 (8%) of the patients, Giddiness in 1(2%) of the patients and vomiting 3 (6%) of the patients
3. In the study, the most common risk factor found was smoking (36%) followed by diabetes and hypertension
4. In this study inferior wall myocardial infarction is the most common variant with the incidence in 42% of the total study group
5. In the study group mean serum magnesium level in 50 patients on the day of presentation is 1.71±0.23 and after 48hours of admission is 2.43±2.47
6. In the study group mean serum magnesium level in 35 patients with complications is 1.66±0.21 on day-1 and 2.58±3.01 after 48hours of admission.
7. In the study group, mean serum magnesium level in patients with out complications is 1.83±0.24 on day-1 and 2.11±0.15 after 48hours of admission.
8. The difference between the serum magnesium levels in patients with complications and without complications is statically significant on both the day of presentation and after 48 hours with a p value of 0.074+
9. Unlike complications, death is not statistically associated with Hypomagnesimia with p value 0.698

SUMMARY

Coronary artery disease is a major cause of morbidity and mortality throughout the world. Major cause of death in coronary artery disease is due to complications like arrhythmias and cardiogenic shock.

In the present study, patients with acute myocardial infarction with low magnesium level are more prone to develop complications are ventricular arrhythmias , cardiogenic shock compared to those who are having normal serum magnesium levels .It is equally important to note that majority of the patients with complications, who are listed under normo-magnesimic category on the day of presentation with MI had their magnesium values at the lower limit of the normal reference range.

So Magnesium replacement therapy in patients with acute myocardial infarction who is having low serum magnesium level may reduce the incidence of complications.

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ANNEXURE

PROFORMA

CASE HISTORY OF THE PATIENTS

Case No:

Name: Mr/Mrs OP No:

Age: IP No:

Gender: Ward:

Date: Occupation:

Weight:

Address:

CHIEF COMPLAINTS:

HISTORY OF PRESENTING ILLNESS:

PAST HISTORY:

Hypertension : yes/no if yes, duration:

Diabetes : yes/no if yes, duration:

Congestive Heart Failure : yes/no if yes, duration:

Chronic Renal Failure : yes/no if yes, duration:

Valvular Heart Disease : yes/no if yes, duration:

Atrial Fibrillation : yes/no

Thyroid disorders:

Parathyroid Disorders:

Others:

FAMILY HISTORY:

OCCUPATIONAL HISTORY:

PERSONAL HISTORY:

Economic status: Below poverty level/Above poverty level

Diet: Vegetarian / mixed/non-vegetarian

Smoking: yes/no if yes, duration: Alcohol: yes/no if yes, duration:

MENSTRUAL HISTORY: Regular/irregular/not applicable/other abnormalities

GENERAL PHYSICAL EXAMINATION:

Ht: Wt: BMI:

Waist hip ratio: Abdominal girth:

Built : normal / below normal / well built / obese/athletic Nourishment: well / poor nourished

PICKLE:

Blood pressure: Pulse rate:

SYSTEMIC EXAMINATION :

CVS :

RS :

CNS :

PER ABDOMEN :

ECG:

Troponin	
CK MB	

CLINICAL DIAGNOSIS:

2 D Echo (if affordable by the patient and with his consent) :

Thrombolysis:

CAG:

PCI:

Days 1:

Days after 48 hours:

Final Outcome :

INVESTIGATIONS:

BLOOD:

PLASMA FBS: mg/dl

PLASMA PPBS: mg/dl

LIPID PROFILE

- → SERUM TOTAL CHOLESTEROL: mg/dl
- → SERUM TRIGLYCERIDES: mg/dl
- → SERUM HDLc: mg/dl
- → SERUM LDL (calculated): mg/dl
- → NON HDLc (calculated): mg/dl

HEMOGLOBIN : g/dl

PERIPHERAL BLOOD SMEAR:

Serum Na^{+}:

Serum K^{+}:

Serum Ca^{+2}:

Serum Mg^{+2}: on Day 1: After 48 hours:

URINE examinantion (Spot) :

Blood Urea :

Serum creatinine :

OTHERS /COMPLICATIONS:

Comments:

INFORMED CONSENT

I understand that I remain free to withdraw from this study at any time.

I have read or had read to me and understand the purpose of this study and the confidential nature of the information that will be collected and disclosed during the study.

I have had the opportunity to ask my questions regarding the various aspects of this study and my questions have been answered to my satisfaction.

I, the undersigned agree to participate in this study and authorize the collection and disclosure of my personal information as outlined in this consent form.

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Participant's Name & signature	Date
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Signature of the witness	Date
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Signature of the principal investigator	Date

MASTER CHART

SL.no	Patient's name	IP number	Age	Sex	Presnting symptoms	HR/min	BP in mmHg	Risk Factors	T.chol	TGL	HDL	LDL	ECG Diagnosis	S. Na+	S.Ca+2	S.K+	Serum Mg^{2}+ 1st Sample	Seum Mg^{2}+ 2nd Sample	Complications/Special considerations
1	Lokesh	877196	42	M	chest pain	76	140/90	smoker	254	55	30	177	Ant.Septal MI	138	8.2	3.5	1.5	2	recovered
2	Gnanasoundaryam	877222	60	M	chest pain	44	90/60	T2Dm,HTN	210	110	55	179	inferior wall MI	140	9.2	3.8	1.5	2.2	ventilatory support,recoverd
3	Narayana swami	877474	45	M	chest pain,sweating	95	110/70	smoker,obesity	246	112	38	159	Ant.Septal MI	139	8.5	4.2	1.7	2	Discharged after 48 Hrs
4	Selva Kumar	875911	60	M	chest pain,sweating	86	140/70	HIV positive	187	68	39	165	inferior wall MI	139	8.9	4.6	1.8	2.2	Occasional VPCs ,recovered
5	Venkatamma	876498	60	F	chest pain,sweating	76	140/90	-	194	113	30	187	inferior wall MI	141	9	3.9	1.4	1.6	Cardiogenic shock and expired
6	Hanumesh	875850	58	M	chest pain,sweating	70	110/60	T2DM	206	118	43	138	inferior wall MI	137	9.5	5.3	1.5	1.9	recovered
7	Ravikumar	875858	49	M	chest pain,sweating	80	120/70	obesity,T2DM,H	245	98	47	174	Anterior wall MI	140	8.4	4.8	1.6	2.2	Occasional VPCs ,recovered
8	Narayana chari	875860	60	M	chestpain ,palpitations	84	140/90	smoker,HTN	202	115	46	168	Ant.Septal MI	138	8.6	3.9	2	2.2	ARF,Recovered
9	Murthy MD	875864	50	M	chest pain,sweating	72	130/80	Obesity,HTN	232	156	47	189	Anterior wall MI	132	8.9	4.1	1.5	2.4	Occasional VPCs ,recovered
10	RameGowda	875582	60	M	chest pain	85	100/70	smoker	190	175	49	205	inferior wall MI	140	9.1	3.5	1.4	2	Occasional VPCs ,recovered
11	Velan	878297	36	M	chest pain	86	140/90	Smoker ,T2DM	298	129	43	195	Anterior wall MI	126	8.6	3.8	1.7	1.8	Occasional VPCs ,recovered
12	Mr.Syed nazeer	880045	62	M	chest pain,sweating	106	150/110	T2DM,HTN,Smo	189	138	28	188	Ant.Septal MI	139	8.9	4.4	1.8	2.2	Occasional VPCs ,recovered
13	Mr.Venkataramanappa	879896	50	M	chestapain,sweating,von	70	120/70	-	210	178	28	208	Ant.Lateral MI	142	9.8	3.8	1.6	2.2	LBBB,Recovered
14	Mr.Ravikumar	875858	49	M	chest pain	60	170/100	HTN	178	183	48	180	Anterior wall MI	137	9.5	3.2	1.6	2	vent.support,cardiogenic shock,expired
15	Mr.Gunashelan	886968	48	M	dyspnea	84	160/110	smoker	188	195	67	178	inferior wall MI	140	9.4	4.2	2	2.2	ARF,Recovered
16	Mr.Suresh babu	886987	29	M	chestpain ,palpitations	40	100/70	smoker	182	79	55	199	Ant.Septal MI	142	9.5	4.3	1.6	2	Complete heart block,expired
17	Mr.Mukthiyaar	875848	43	M	chest pain	90	140/80	smoker	250	197	45	146	Anterior wall MI	133	9.6	3.5	1.9	2.3	recovered
18	Mrs.Zaibunnisa	880677	60	F	chest pain	84	120/70	-	202	165	56	189	inferior wall MI	142	9.8	3.8	2.1	2.2	recovered
19	Mr.M.Asadulla	880938	55	M	chest pain	90	100/60	-	178	163	43	178	inferior wall MI	122	10	5.5	1.3	2	cardiogenic shock,recovered
20	Mr.Ameenulla	881460	40	M	chest pain	84	110/70	smoker,obesity	244	174	49	198	Ant.Septal MI	134	9.5	4.1	1.4	19	vent.suppot,VT,recovered
21	Mr.Ramaiah	882158	60	M	chest pain,sweating	86	150/100	-	200	98	42	187	Ant.Septal MI	138	9.9	4.4	1.5	2	Occasional VPCs ,recovered
22	Mr.Subbaramayya	880568	55	M	chestapain,sweating,von	90	70/40	-	179	155	40	165	Anterior wall MI	136	9.7	3.5	1.6	2.1	VT ,Expired
23	Mr.Aejar Pasha	883093	40	M	chest pain	60	120/80	-	185	159	32	212	inferior wall MI	140	10.2	3.6	1.4	1.9	Occasional VPCs ,recovered
24	Mr.Nagaraj B	881299	50	M	dyspnea	70	160/100	smoker	252	170	28	155	inferior wall MI	141	8.8	3.3	1.5	1.8	RBBB,recovered
25	Mr.Timmaya	883487	60	M	chest pain	72	180/110	-	224	185	34	128	Ant.Septal MI	136	9	3.2	1.8	2.2	ARF,occasional VPCs,Recovered
26	Mr.Nagaraj MR	882315	56	M	chest pain	86	110/70	-	189	120	34	198	inferior wall MI	134	9	3.8	1.6	1.9	Occasional VPCs ,recovered
27	Mr.Ramesh babu	883439	35	M	chest pain	78	160/90	smoker	187	202	38	189	Ant.Septal MI	140	9.6	3.2	2	2.2	Occasional VPCs ,recovered
28	Mr.Srinivas	883485	45	M	chest pain,sweating	81	150/90	T2DM	236	112	35	134	inferior wall MI	138	9.5	4.2	1.5	1.9	recovered
29	Mr.Channarayappa	884654	60	M	chestpain ,palpitations	62	130/70	Smoker ,T2DM	192	102	39	148	inferior wall MI	134	10.1	3.8	1.6	2.3	ARF,Recovered
30	Mr.M.Noorulla	883883	60	M	chest pain,sweating	120	100/60	Smoker ,T2DM	212	176	38	148	Ant.Septal MI	135	10	3.9	2	2.3	recovered
31	Mr.Channarayappa	884654	62	M	chestpain ,palpitations	70	130/70	-	183	156	86	189	inferior wall MI	140	8.8	4	1.5	2	Occasional VPCs ,recovered
32	Mr.Anjayareddy	883170	55	M	dyspnea	76	130/70	-	263	155	84	165	Ant.Lateral MI	130	10.2	4.2	2	2.2	recovered
33	Mr.Ashwathappa	884233	62	M	chest pain	63	140/90	T2DM	186	189	44	164	inferior wall MI	141	9.6	5	1.8	2.1	Occasional VPCs ,recovered
34	Mrs.Raziya begum	885653	63	F	chest pain	69	120/80	T2DM	209	195	42	178	inferior wall MI	138	8.9	4.3	1.7	1.9	recovered
35	Mr.Venkatappa	886746	45	M	chest pain,sweating	82	150/90	-	182	156	62	175	Ant.Septal MI	141	9.5	4.2	1.5	1.6	Cardiogenic shock and expired
36	Mr.Kumar reddy	885152	60	M	chest pain	89	160/90	-	168	178	42	198	Ant.Septal MI	136	9.5	3.9	2	2.1	recovered
37	Mr.Venkatachalapathi	885038	43	M	chest pain,sweating	80	120/80	-	202	190	34	150	inferior wall MI	140	9.3	3.6	1.5	1.9	cardiogenic shock,occasional VPCs recovered
38	Mr.Venkatachalapathi	885840	38	M	chest pain	72	130/80	-	232	187	41	137	inferioposterior I	143	9	4.2	1.8	2.1	recovered
39	Mr.Venkatesh Kc	884376	53	M	chest pain,sweating	80	120/70	-	183	120	35	208	inferior wall MI	140	8.9	4	2.1	2	Occasional VPCs ,recovered
40	Mr.Jayaram R	886028	63	M	giddiness	86	110/70	T2DM	172	98	52	200	Ant.Septal MI	138	10	3.3	2	2.3	recovered
41	Mr.Govindappa	885965	50	M	chest pain,sweating	72	130/80	T2DM	189	178	25	210	Anterior wall MI	142	8.6	3.3	1.7	2.4	RBBB,recovered
42	Mr.NagarajBN	885377	50	M	chest pain	40	150/100	Smoker ,T2DM	286	167	42	165	Ant.Septal MI	138	9	4.1	2.2	2.3	recovered
43	Mr.NarayanaGowde	884364	64	M	chestapain,sweating,von	120	100/80	T2Dm,HTN	176	188	24	135	Anterior wall MI	136	9.9	4.6	1.5	2	recovered
44	Mr.Shankar Reddy	885967	45	M	chest pain	100	150/80	smoker	210	156	52	154	inferior wall MI	141	9.4	4.3	1.8	1.9	Occasional VPCs ,recovered
45	Mrs.Gowramma	886069	62	M	chest pain	68	170/100	HTN	216	149	56	158	Ant.Lateral MI	139	9.4	3.8	1.9	2	recovered
46	Mr.Shaik Ismail	877944	38	M	chest pain,sweating	88	110/60	-	189	115	65	194	inferior wall MI	134	8.8	3.6	1.7	-	frequent VPCs noted,Expired
47	Mr.Nataraj B	886764	55	M	chest pain,sweating	80	150/100	smoker	178	125	45	79	inferior wall MI	143	9.2	3.8	2.1	2.2	ARF,Recovered
48	Mr.Kumar Swami	875307	60	M	chest pain	130	100/70	T2DM	196	154	44	176	Anterior wall MI	141	8.4	3.9	1.7	-	Cardiogenic shock and expired
49	Mr.Javed Pasha	888299	47	M	chest pain,sweating	112	150/100	HTN	198	113	34	104	Anterior wall MI	138	9.6	4.2	1.9	-	Expired
50	Mr.Wazeer Khan	888367	45	M	chest pain	75	130/80	smoker	187	128	28	152	Anterior wall MI	141	8.5	3.6	1.9	2.2	recovered