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Study of serum HS-CRP and magnesium levels in acute myocardial infarction

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Abstract
Myocardial infarction (MI) is the leading cause of mortality and morbidity in present days. It is a common presentation of ischemic heart disease. Myocardial Ischemia is characterized by an imbalance between myocardial oxygen supply and demand. Unrelieved Ischemia produces cell death what is pathologically known as necrosis. Magnesium is the fourth most common cation found in the body and the second most common intracellular cation. C-reactive protein (CRP) is a hepatic acute phase reactant. The study group consisted of 120 subjects, of age groups 20-60 years and of both sexes. Of these, 40 were STEMI cases (Group 2), 40 were NSTEMI cases (Group 3) and 40 were healthy individuals as controls (Group 1). Serum hsCRP, Magnesium and Lipid profile were estimated in all the individuals. Results showed that the serum levels of hs CRP are increased in both Group 2 & Group 3 patients (Group 2 > Group 3) when compared to Group 1. Magnesium levels are decreased in both Group 2 & Group 3 patients (Group 2 > Group 3) when compared to Group 1. The changes in these parameters are extremely statistically significant in both groups when compared to controls ($p < 0.0001$). Hence they can be used as routine diagnostic tests along with other available biomarkers of MI.

Keywords: Myocardial infarction, hsCRP, Magnesium, STEMI, NSTEMI

1. Introduction
Myocardial infarction is the leading cause of mortality and morbidity in present days. Myocardial infarction is a common presentation of ischemic heart disease. The WHO estimated in 2002, that 12.6 percent of worldwide deaths were from ischemic heart disease with it being the leading cause of death in developed countries [1]. Myocardial Ischemia is characterized by an imbalance between myocardial oxygen supply and demand. Unrelieved Ischemia produces cell death what is pathologically known as necrosis. Severely ischemic myocardium undergoes necrosis first in the sub endocardium beginning as early as 15-20 minutes after coronary artery occlusion [2].

Patients with ischemic heart disease fall into two large groups: patients with stable angina secondary to chronic coronary artery disease and patients with acute coronary syndromes (ACS). The latter group, in turn, is composed of patients with acute myocardial infarction with ST-segment elevation (STEMI) on their presenting electrocardiogram and those with unstable angina (UA) and non-ST-segment elevation MI [3].

Almost all cases of myocardial infarction result from coronary atherosclerosis with superimposed coronary thrombus. Atherosclerosis is a chronic disease of elastic arteries and of large and medium sized muscular arteries. Intimal cells in the vessel wall interact with serum constituents to play a central role in forming cellular intimal lesions that ultimately become fibro fatty plaques [4]. An initial step of atherogenesis is thought to be an injury to the vessel wall resulting in endothelial dysfunction. This is followed by events involved in the atherosclerotic

plaque formation such as inflammatory responses, cell proliferation and remodelling of the vasculature and finally to vascular lesion formation, plaque rupture, thrombosis and tissue infarction [5].

Magnesium is the fourth most common cation found in the body and the second most common intracellular cation [6]. It is important to perform many physiological roles for different body functions like direct enzyme activation including many ATP generating reactions, membrane function, structural function which includes synthesis of RNA, DNA and protein, and acts as calcium antagonist in muscle contraction. Decreased of serum magnesium is known to promote thrombus formation, a key event in progression of atherosclerosis and ultimately leading to myocardial infarction [7].

C-reactive protein (CRP) is a hepatic acute phase reactant. Its synthesis is mainly controlled by IL-6, but IL-1 and TNF-α may also influence CRP levels. Initially it was suggested that CRP was a by-stander marker of inflammation, but subsequent works demonstrated that it was a risk marker in both ACS and in patients with myocardial ischemia [8, 9]. Tissue necrosis is a potent acute-phase stimulus, and following myocardial infarction, there is a major CRP response, the magnitude of which reflects the extent of myocardial necrosis [10].

Keeping this in view, the objective of the present study is to estimate the serum levels of high sensitivity C - reactive protein (hsCRP) and Magnesium in patients with acute myocardial infarction (both STEMI and NSTEMI) and compare them with that of controls.

2. Materials & methods
2.1. Study centre & Period
This research was conducted at Rangaraya Medical College between November 2015 and June 2016.

2.2. Subjects Selection
Patient selection was done by simple random sampling of individuals among the age group 20-60 years of both sexes, presenting to the O.P Department, Government General

Hospital, Kakinada. An informed consent was taken from the patients and controls before the collection of blood sample. The subjects were selected based on following inclusion and exclusion criteria.

2.3. Inclusion Criteria
- 40 diagnosed cases each of STEMI and NSTEMI.
- Controls were healthy individuals, age and sex matched without any major illness.

2.4. Exclusion Criteria
- Liver disorders.
- Renal diseases.
- Chronic inflammatory diseases.
- Pregnancy.
- Thyroid disorders.

2.5. Study Pattern
- Group 1: CONTROLS - 40 age and sex matched healthy individuals.
- Group 2: CASES – 40 patients with STEMI and
- Group 3: CASES - 40 patients with NSTEMI.

2.6. Assay of Markers
hs-C RP was measured by turbidimetric immunoassay. Magnesium by Calmagite method and assay of lipid profile parameters were carried out on Erba Chem 5 Semiautoanalyzer. The biochemical analysis was done within 24hrs.

2.7. Statistical Analysis
All results were expressed as Mean ± S.D. The data obtained were analyzed using Student's t-test for p-value, where $p<0.001$ was considered as highly significant.

3. Results & observations
The results obtained for various parameters are tabulated as follows

Table 1

Value	Group 1 (N=40)	Group 2 (N=40)	Group 3 (N=40)
hs-CRP (mg/L)	1.57 ± 0.64	7.42 ± 2.35	5.57 ± 1.84
Magnesium mg/dl)	2.26 ± 0.52	1.52 ± 0.34	1.71 ± 0.53
Total Cholesterol	168.82 ± 6.38	248.0 ± 18.24	236.7 ± 17.12
Triglycerides (mg/dl)	140.70 ±10.74	221.4 ± 28.36	210.4 ± 26.42
HDL (mg/dl)	38.35 ± 4.53	31.75 ± 5.90	33.83 ± 4.98
LDL (mg/dl)	103.33 ±18.15	192.56 ±21.43	183.85 ± 9.27

The values of serum Magnesium are decreased in Group 2 and Group 3 (cases: Group 2 > Group 3) when compared to Group 1 (controls). On the other hand, the values of hs-CRP, TC, TGL, LDL are increased in Group 2 and Group 3 (cases: Group 2 > Group 3) when compared to Group1.

Table 2

	p value (Gr.2/ Gr.1)	p value (Gr.3/ Gr.1)	p value (Gr.3/ Gr.2)
hs-CRP (mg/L)	<0.0001*	<0.0001*	<0.0001*
Magnesium (mg/dl)	<0.0001*	<0.0001*	0.0600ns
Total Cholesterol	<0.0001*	<0.0001*	0.0620ns
Triglycerides (mg/dl)	<0.0001*	<0.0001*	0.0765ns
HDL (mg/dl)	<0.0001*	<0.0001*	0.0924ns
LDL (mg/dl)	<0.0001*	<0.0001*	0.0596ns

Extremely statistically significant, ns not statistically ignificant.

4. Discussion
Several qualitative inferences can be drawn on the basis of the results in our present study. Hypomagnesemia is present in acute myocardial infarction (AMI) as shift of magnesium from extra cellular to intracellular compartments occur as it is taken up by adipocytes after catecholamine induced lipolysis and combined with soaps formed by free fatty acids [11].

Flink *et al.* [12] presented a study of the relation between free fatty acids (FFA) and Mg^{+2} in patients with AMI. They demonstrated a rise in FFA and a concomitant decrease in Mg^{+2} levels. These results were interpreted as a binding of Mg^{+2} to FFA, which will yield an insoluble complex. One may speculate whether the rise in catecholamines in AMI activates the enzyme adenyl cyclase, which brings about an increased synthesis of c-AMP, c-AMP then induces lipolysis, thus increasing FFA which according to Flink *et al.* could chelate Mg^{+2} and thus gives a lowered serum Mg^{+2} level.

The cardiovascular consequences of magnesium deficiency in animal and clinical studies have been summarized by Seelig [13] and include multifocal necrosis with calcium accumulation in mitochondria in a pattern reminiscent of myocardial ischemia and catecholamine induced cardiomyopathy, atherogenesis, a heightened tendency to platelet aggregation, increased coronary and peripheral vascular resistances.The findings of present study correlate well with findings of previous studies of A K Ibrahem *et al.* (2012), P Kiranmai *et al.* (2013), M H Jaffery *et al.* (2014), Sugunakar *et al.* (2014), Saira Baloch *et al.* (2015), N Tanuja *et al.* (2015), Lamia FA Marzog *et al.* (2016).

CRP it is an exquisitely sensitive systemic marker of inflammation and tissue damage. The presence of CRP within most atherosclerotic plaques and all acute myocardial infarction lesions, coupled with binding of CRP to lipoproteins and its capacity for pro-inflammatory complement activation,

suggests that CRP may contribute to the pathogenesis and complications of cardiovascular disease [8].

Elevated hs-CRP levels during STEMI than NSTEMI seems to be linked to the extension of myocardial damage, rather than to the pre-existing inflammation. The intracardiac inflammatory response in ACS can be attributed to the evolution of myocardial necrosis indicated by higher hs-CRP, TNFα, IL-6 and troponin T levels in patients with major adverse cardiac events. Severe myocardial infarction causes greater ventricular remodelling & lowers ejection fraction worsening the cardiac failure [14, 15, 16].

Tissue necrosis is a potent acute-phase stimulus, and following myocardial infarction, there is a major CRP response, the magnitude of which reflects the extent of myocardial necrosis [17, 18]. The findings of present study correlate well with findings of previous studies of Krintus *et al.* (2012), Kavita S *et al.* (2012), Sheikh *et al.* (2013), Srikrishna R *et al.* (2015), Basha S J *et al.* (2016).

5. Conclusion

The results of the present research provide valuable information and association between serum hs-CRP, Magnesium levels and myocardial infarction. The findings showed that there was significant increase in the levels of hs-CRP and a significant decrease in levels of magnesium. Hence we suggest that these parameters can be used as routine diagnostic tests along with other available biomarkers for MI.

6. References

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