P

A STUDY ON INFLAMMATORY PROFILE IN ACUTE MYOCARDIAL INFARCTION

Submitted to

The Tamil Nadu Dr.M.G.R.Medical University

M.D. DEGREE EXAMINATION

BRANCH – I (GENERAL MEDICINE)

THE TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY

CHENNAI

MARCH 2009

BONAFIDE CERTIFICATE

This is to certify that **"INFLAMMATORY PROFILE IN ACUTE MYOCARDIAL INFARCTION"** is a bonafide work done by **Dr.T.KARTHIKEYAN,** post graduate student, Department of General Medicine, Kilpauk Medical College, Chennai-10, under my guidance and supervision in partial fulfillment of regulations of **The Tamilnadu Dr.M.G.R.Medical University** for the award of **M.D.Degree Branch I (General Medicine)** during the academic period from May 2006 to March 2009.

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ETHICAL COMMITTEE OF
GOVERNMENT KILPAUK MEDICAL COLLEGE HOSPITAL
KILPAUK, CHENNAI-10.
Venue: Dean Chamber, Date: 3.1.2008

Chair person
Prof. Dr. M. Dhanapal, M.D, D.M.
Director of Medical Education (OSD)
&
The Dean
Govt. Kilpauk Medical College & Hospital,
Chennai - 600010.

TO WHOMSOEVER IT MAY CONCERN

Dear Sir / Madam

Sub: Internal Medicine – MD PG's Dissertation Ethical Committee – Reg.

Ref: Requisition from H.O.D. Medicine.

This is in reference to the letter dated 2.1.2008 regarding Ethical committee meeting clearance with regard to the following topics

Sl.No	Name of the Post Graduate	Dissertation Topic
1	Dr. R.Ramprasad	A study on Prevalence and Risk Factors of Diabetic Nephropathy in Newly Detected Type 2 Diabetic Patients
2	Dr. V.Sakthivadivel	A study on Cardiac abnormalities in HIV infected individuals
3	Dr. K.S.Gopakumar	A study on Subclinical Hypothyroidism in females over 50 years of age
4	Dr. T.Karthikeyan	Inflammatory profile in Acute Myocardial Infarction

5	Dr. Maliyappa Vijay Kumar	A study on Prevalence of Microalbuminuria in HIV patients not on ART and Correlation with CD4 count
6	Dr. D.Radha	High sensitivity C - reactive protein as a determinant in the outcome of Acute ischemic stroke
7	Dr. Lakshmi Thampy M.S	A Study on the prevalence of increased LV mass & Proteinuria in newly diagnosed Hypertensive patients.
8	Dr. Manu Bhasker	A study on the effect of Intravenous Metoprolol along with Thrombolysis in Acute Myocardial infarction
9	Dr. P.Mohanraj	Evaluation of Lipid Profile in patients with non diabetic Chronic Kidney Disease Stage 3,4 and 5
10	Dr. P.Dhanalakshmi	A study On Metabolic Syndrome in Young Ischemic Stroke
11	Dr. V.Murugesan	A study on Electrocardiographic and Echocardiographic changes in Chronic Obstructive Airway Disease
12	Dr. M.Seetha	Effect of Right ventricular infarction on the immediate prognosis of Inferior wall Myocardial Infarction

We are glad to inform you that at the EC meeting held on 3.1.08 on the above topics were discussed and **Ethically approved**.

DEAN

Chair person
Prof. Dr. M. Dhanapal, M.D, D.M.
Director of Medical Education (OSD)
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The Dean,
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Chairman & Members of the Ethical Committee:

Chairman

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   & The Dean,
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   Nursing Superintendent

We confirm that no member of the study team is on the Ethics Committee and no member of the study team voted.

The trial will also follow the Ethics Guidelines for Bio-Medical Research On Human subjects issued by ICMR, New Delhi and will not involve any expense to the Government and will not be detrimental to the normal functioning of the Institution.

The study will also satisfy the revised order issued by the Government of Tamil Nadu, Health and Family Welfare Department G.O.MS.No:319, H & FW, Dept. dated 30.11.2001.

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CONTENTS

INTRODUCTION

Cardiovascular disease especially AMI accounts for approximately 12 million deaths annually and is the commonest cause of death globally. This problem is assuming epidemic propositions in the developing countries. The Asian Indians whether living in their own countries or elsewhere have much higher incidence of CAD as compared to all ethnic groups. CAD among Indians has been found to be severe, diffuse and associated with serious complications with increasing mortality at younger age. [1].

AMI is one of the most common diagnoses in hospitalized patients in industrialized countries as well. In the US approximately 650,000 patients experience a new AMI and 450,000 experience recurrent AMI every year. The early [30-day] mortality rate is approximately equal to 30%, with more than half of these deaths occur before the individual reaches hospital and 1 in 25 patients who survives first hospitalization dies in the first year after AMI. Mortality is four fold in elderly patients [over age 75] when compare with younger age groups.[2] That is the magnitude of the problem.

The current knowledge of pathophysiology of AMI started with autopsy description by Dr. James Herrick from Chicago in 1912 who concluded that the AMI results from thrombotic occlusion of coronary artery and recovery depends on restoration of blood flow. In 1972 when coronary angiography was performed during AMI revealed that in 85-90% patients cause of AMI was indeed thrombotic occlusion of infarct related artery.[3]

AMI and STEMI occur when coronary blood flow decreases abruptly after a thrombotic occlusion of a coronary artery previously affected by atherosclerosis. In most cases, AMI occurs when the atherosclerotic plaque becomes disrupted [plaqgue rupture], exposing the contends to blood and conditions [local and systemic] favor thrombogenesis.

Atherosclerosis is now proved as an inflammatory disease and inflammatory markers play a key role in plaque rupture and AMI. [5] An accumulation of clinical evidence shows markers of inflammation correlates with increased coronary risk. Inflammation in the vessel wall plays not only in the initiation and progression of atherosclerosis but also in the erosion or fissure of plaques and, eventually, in the rupture of plaques .Recent investigations have shown that various markers of systemic inflammation can predict future cardiovascular events including fatal and non fatal myocardial infarction, stroke, and the progression of

peripheral vascular disease in both men and women. A complex intravascular inflammatory response is the integral component of the disruption of the fibrous cap, which is the major pathophysiological event of the dynamic instability. [7]

In addition to hs-CRP other inflammatory markers like Total Leucocyte count, ESR, Free Fatty Acids were also found to be elevated during AMI. Vulnerable plaques have activated T cells that express proinflammatory cytokines such as Interferon Gamma [IFN-γ], Tumor necrosis factor Alpha [TNF-α], Interleukin 1 [IL-1], Interleukin 6 [IL-6]. During the inflammatory reaction, anti-inflammatory cytokines are also produced and tend to modulate the inflammatory process. IL-10 is an anti-inflammatory cytokine may greatly influence local inflammatory and thrombotic process with the atherosclerotic lesion.

In the present work a case control study was conducted highlighting the elevation of hs-CRP in the blood samples of patients with AMI [cases] when compared with that of volunteers with no apparent cardiac ailment who enrolled as controls. The other inflammatory markers like FFA, TC, ESR along with the risk factors-modifiable smoking, alcohol, HT, DM, nonmodifiable- age and gender are compared.

AIM

1. To analyze the levels of various Inflammatory markers including hs-CRP in Acute myocardial infarction.

2. To correlate the variations of these inflammatory markers with various ECG changes of Myocardial Infarction and controls.

3. To analyze the relationship between these markers and various cardiovascular risk factors

REVIEW OF LITERATURE

Understanding of the pathogenesis of cardiovascular disease has grown significantly over the past 15 years. Evidence of the role of atherosclerotic plaque instability and associated intravascular thrombosis has revolutionized the diagnosis and management of coronary and cerebrovascular disease. Atherosclerotic disease begins as early as the second decade of life with the development of fatty streaks on previously normal vascular endothelium. Disease progression leads to the formation of nonobstructive stable atherosclerotic plaques.

These may evolve to obstructive lesions that have the potential to produce symptoms such as angina, transient ischemic attacks (TIAs), or symptomatic peripheral vascular disease (claudication). Alternatively, transition of previously asymptomatic stable plaque to "vulnerable" plaque has the potential to result in plaque fissure or rupture, causing unstable angina, acute myocardial infarction, or stroke.[4] Substantial evidence indicates that inflammation plays a significant role in the transition from stable to vulnerable plaque and subsequently to plaque injury.[5] Identification of markers reflecting vascular inflammation has enhanced the ability to evaluate cardiovascular risk in both symptomatic and asymptomatic patients. C-reactive protein (CRP) is one of a number of markers of inflammation that has emerged a useful tool for assessing cardiovascular event risk.

Traditional Risk Factors for Coronary Artery Disease

Traditional risk factors for coronary artery disease (CAD)) have been used for many years to evaluate individual patient risk and have been incorporated into various diagnostic and therapeutic guidelines for primary and secondary prevention of cardiovascular disease. The Framingham Risk Score utilizes several traditional risk factors to determine cardiovascular risk in the National Cholesterol Education Program's Adult Treatment Panel III report (ATP III).[6]

In addition to traditional risk factors, ATP III identifies several nonlipid risk factors, including homocysteine; thrombogenic/hemostatic factors such as fibrinogen, protein C, and antithrombin III; and inflammatory markers including CRP, all of which have been shown to influence cardiovascular risk. ATP III suggests that these emerging risk factors may be used to adjust estimates of absolute risk obtained using standard risk factors. The report does not recommend routine monitoring of these additional risk factors, or alteration in lipid management strategies based on their presence.

Many models of atherosclerosis implicate inflammation in the process of plaque evolution, from initiation to growth and complication,

such as plaque rupture. Major risk factors for atherosclerosis, including hypertension, hyperlipidemia, cigarette smoking, and hyperglycemia, provoke a variety of noxious stimuli that elicit secretion of adhesion molecules from leukocytes, which facilitate the attachment of monocytes to endothelial cells on the vasculature.[7] Chemotactic factors stimulate the migration of monocytes into the subintimal space.

Monocytes are transformed into macrophages, which then take up cholesterol lipoproteins, becoming foam cells, and initiating the process of fatty streaking on the endothelial surface.[8] Continued exposure to factors that promote lesion growth leads to accumulation of macrophages, mast cells, and activated T-lymphocytes within the growing plaque. The condition of the fibrous cap of the developing plaque is critical to the stability of the vascular lesion.

A thick fibrous cap containing many smooth muscle cells, fibrin, and an intact endothelium covers stable atherosclerotic plaques. There are few inflammatory cells and the plaque core primarily contains free cholesterol esters within foam cells. Alternatively, the cap of vulnerable plaque contains eroded endothelium covering a thinner fibrous cap, which contains fewer smooth muscle cells and many inflammatory cells.

Data demonstrating that the surface temperature of vulnerable plaque is higher than that of stable plaque support the concept of inflammation.[9] In addition to foam cells, the core of vulnerable plaque contains activated macrophages, which secrete numerous inflammatory substances, such as matrix metalloproteinase, responsible for eroding the fibrous cap. The proposed pathologic mechanisms responsible for each stage in the process of plaque formation and injury involve cells associated with the inflammatory response.

Fissure or rupture of the fibrous cap exposes the plaque core to the bloodstream, instigating platelet activation, adhesion, and aggregation accompanied by thrombin formation leading to thrombus production and acute coronary or cerebrovascular events such as myocardial infarction or stroke. It is important to recognize that the majority of vulnerable plaques that produce acute coronary events such as myocardial infarction are not large enough to cause significant obstruction to blood flow with resultant exertional angina.

Methods to identify patients with few traditional risk factors who remain at high risk as a result of vulnerable plaque development may ultimately allow for more effective treatment strategies to reduce cardiovascular event risk.

Proinflammatory Risk Factors

Activation of the inflammatory process in both plaque development and in the transition to vulnerable plaque produces a number of molecules, which reflects ongoing inflammation. These include proinflammatory risk factors such as oxidized low-density lipoproteins; cytokines such as interleukin-1 and tumor necrosis factor alpha (TNF-alpha); adhesion molecules such as intracellular adhesion molecule-1; and inflammatory stimuli, which lead to the production of acute-phase reactants from the liver and other sources.[10]

CRP is an acute phase reactant produced by the liver and was initially understood to bind to complement to assist in the destruction of bacterial cell walls as part of the immune response to infection.[11] Hepatic production of CRP is thought to be a response to the presence of interleukin-6 and other products of the inflammatory cascade. Recently it has been shown that CRP may be produced locally in atherosclerotic plaques by macrophages.[12]

The role of CRP as more than a "marker" for vascular inflammation is supported by the knowledge that CRP within plaque induces the production of chemokines and adhesion molecules in a dose-dependent fashion, attracting additional monocytes and leading to a self-sustaining inflammatory reaction.[13]

Using CRP in Clinical Assessment of Risk

Many products of the inflammatory cascade, in addition to CRP, have been shown to be markers for cardiovascular events. These include white blood cell count, fibrinogen, interleukin-6, plasminogen activator, intracellular adhesion molecules, TNF-alpha, serum amyloid A, and others.[14] The advantages of utilizing CRP for clinical assessment of cardiovascular risk include assay reproducibility, standardization of measurement, long serum half-life, stability of basal levels over a long period of time, wide assay availability at reasonable cost (approximately $30), independence from established risk factors, and extensive data relative to its predictive value for future cardiovascular events.

Many prospective epidemiological studies have established a relationship between CRP and future cardiovascular events including coronary heart disease death, myocardial infarction, cardiovascular events, fatal and nonfatal stroke, peripheral arterial disease, and sudden cardiac death.[15-20] In many of these studies, CRP has been demonstrated to be independent of blood pressure, diabetes, smoking, age, or cholesterol levels.

Recently, Ridker et al demonstrated that CRP was a stronger predictor of cardiovascular events including myocardial infarction, ischemic stroke, coronary revascularization, or death from cardiovascular causes than low-density lipoprotein (LDL) cholesterol in approximately 28,000 healthy women followed for a mean of eight years.[21] CRP has been shown to be a stronger predictor of events than cholesterol to high-density lipoprotein (HDL) ratio, diabetes, heart failure, or smoking history.[22]

Among patients with known coronary artery disease, elevation of CRP has been associated with a 1.5-fold to twofold increase in cardiovascular events in patients with stable angina,[23] and a 1.5- to 16-fold increase in cardiovascular events in patients with unstable angina.[24,25] For patients who undergo percutaneous coronary intervention (PCI), elevated CRP levels have been shown to increase the risk of future restenosis and cardiovascular events twofold to 12-fold.[26-27]

As might be expected from an acute-phase reactant, a single measurement of CRP during acute myocardial infarction is not predictive of future events unless the sample is taken shortly after the onset of the event.[28]Similar to measurement of LDL cholesterol in the setting of acute myocardial infarction, several weeks are required for the serum

concentration to return to baseline. Comparable to the use of traditional risk factors in predicting risk of future cardiovascular events, CRP is most useful when added to traditional risk factors, as shown by its use with the Framingham Risk Score.[29]

Alternatively, CRP has not yet been demonstrated to be a reliable predictor of the extent of atherosclerotic disease when compared with other methods of evaluating this parameter, such as Doppler ultrasound scans of carotid arteries or electron beam computed tomography for coronary calcium.[30-32]

Atherosclerosis begins with accumulation of small lipoprotein molecules with arterial intima [51,53]. The particles coalesce together and are modified and then they induce localized endothelial inflammation, thereby attracting leucocytes. Scavenger receptors over the surface of monocytes bind to modified low density lipoprotein particles, which transform into foam cells that become a source for further inflammatory cytokines.

The level of inflammation is heightened in ruptured coronary plaques. Numerous inflammatory mediators such as C-RP, fibrinogen, IL- 18 and ICAM-1 have been proposed for risk stratification in ACS

patients.[58,64] Using a multivariate statistical technique called Factor analysis, three clusters were identified;

1. a "systemic inflammation" cluster with positive loadings of C-RP and fibrinogen.

2. a "local inflammation- endothelial dysfunction" cluster with positive loadings of IL- 8 and ICAM- 1

3. an "anti-inflammation"cluster comprising IL-10 and HDL Cholesterol [52, 55, 78].

Atheromatous plaque vulnerability is an important mechanism underlying acute coronary syndrome. Plaque destabilized by MMP- 9 and interferon gamma produced in response to inflammation participates in the mechanism of acute coronary syndrome.[67]

The composition of atheromatous plaque rather than the degree of stenosis is now recognized as a pivotal feature in determining the plaque vulnerability and hence the risk of acute coronary events.[36, 51, 69]

There is a current interest in the association of circulating inflammatory markers like C-RP, fibrinogen, white cell count, ESR, albumin, factor 8- VWF complex, tissue plasminogen activator:

plasminogen activator inhibitor type 1 complex and fibrin D-dimer not only with prognosis in ACS and acute stroke, but also in prediction of cardiovascular events.[73,77]

Activation of several neurohormonal systems occurs during AMI and is associated with short and long term outcomes. Renin and natriuretic cardiac peptides appeared to be strong predictors of outcome in patients with AMI. Recent research indicates that Albumin Excretion Rate is a powerful prediction of in-hospital and 3 year mortality in patients with AMI.[38]

Patients with unstable angina exhibit increased levels of inflammatory markers like IL- 6, SVCAM-1 and VWF but decreased levels of thrombotic markers like AT- III and protein- C whereas patients with AMI show higher levels of inflammatory as well as thrombotic/ fibrinolytic markers [39, 48, 76]

There exists a difference between inflammatory and thrombotic markers between UA and AMI. In acute phase and in a follow up of ACS, abnormal coagulation, inflammation and fibrinolytic markers have independent and direct relationship with cardiovascular adverse events.[49].

Other interesting finding -for its accessibility-in acute myocardial infarction under coronary percutaneous intervention is persistent ST elevation, leucocytes and fibrinogen predictive value.[61]

In consideration of the important role that inflammatory processes play in determining plaque stability, recent work has focused on whether plasma markers of inflammation may help improve risk stratification. Of these markers, C- RP has been the most widely studied. Even among patients with Troponin negative ACS, elevated levels of C-RP are predictors of future risk.[42]

C-RP formerly considered solely an excellent biomarker of inflammation , is now viewed as a direct contributor in atherosclerosis.[44] With the advent of high sensitive assays for determining C-RP , this protein has emerged as one of the most powerful independent predictors of cardiovascular events.

Levels of C-RP and IL-6 are elevated in patients with UA and myocardial infarction, with high levels predicting worse prognosis. [33, 37,63]

In people with ACS, hs-CRP measurement may be valuable. Elevated levels in the highest quartile seem to predict greater mortality

and poorer prognosis in patients with unstable angina and myocardial infarction.[62, 66.]

Research has focused on inflammatory, lipid and metabolic profile in ACS and correlated with hospital and post hospital events[21]. It is found that increased hs- CRP and altered glycemia are associated with a greater number of hospital events whereas age, previous AMI , AMI with or without ST elevation and altered glycemia are predictors of hospital mortality.

Recent evidences have emerged implicating C-RP directly in atherogenesis.[80, 82, 83] C-RP has been found in human atherosclerotic plaque and C-RP has been shown to cause endothelial cell dysfunction, oxidant stress and intimal hypertrophy in experimental models.

In severe acute coronary syndromes elevations of markers of inflammation and acute phase reactant like C-RP as well as release of troponins have been reported.[48, 81].

It must be stressed that C-RP, because of its analytical and biological properties and the large amount of available data, is the only inflammatory marker accepted for clinical use.[40, 54, 56]

The hs-CRP not only predicts future cardiovascular events but also can be used to target therapeutic interventions.[39,43,71] Levels of hs-CRP <1 ,1-3 and >3 mg/L correspond to lower, moderate and higher risk of cardiovascular events at all levels of Framingham Risk Score and at all levels of metabolic syndrome.[68,72].

Interventions that lower hs-CRP include diet, exercise, smoking cessation, statin therapy and improved glycemic control and when a PCI is necessary, provisional stenting.[79]

In the setting of AMI, elevated C-RP levels may reflect the inflammatory activity of a ruptured plaque.[34, 60, 75]

C-RP levels and neutrophil count are higher in angina patients with coronary stenoses. Compared to those without neutrophil count, but not C-RP levels, correlates with angiographic stenoses complexity.[35]

Experiments in rats have shown that a molecule called 1,6- bis (phosphocholine) –hexane inhibits C-RP and thereby limits the size of infarction. In addition, the availability of a C-RP inhibitor will facilitate experiments to determine the role of human C-RP in normal biological processes and disease states including atherogenesis, plaque instability, stroke, infection, inflammatory diseases and autoimmunity.[71]

C-REACTIVE PROTEIN

HISTORY AND NOMENCLATURE

C-RP was originally discovered by Tillett and Francis in 1930 as a substance in the serum of patients with acute inflammation that reacted with C-polysaccharide of pnuemococcus.

GENETICS AND BIOCHEMISTRY

The C-RP gene is located on the first chromosome (1q21-q23). C-RP is a 224 residue protein with a monomer molar mass of 25106 Da and native cyclic pentamer mass of 125530**.**

FUNCTION

C-RP is a member of the class of acute phase reactants. It is thought to assist in complement binding to foreign and damaged cells and affect the humoral response to disease. It is also believed to play an important role in innate immunity, as an early defense system against infection.

DIAGNOSTIC USE

C-RP is used mainly as a marker of inflammation. Measuring and charting C-RP values can prove useful in determining disease processes or the effectiveness of treatment.

C-RP AND ATHEROSCLEROSIS

Accumulating data suggest that arterial tissue can produce C-RP,with C-RP and complement m-RNA being substantially up-regulated in atherosclerotic plaque [45]. Thus C-RP may serve as an endogenous activator of complement in atheroma.

DYNAMICS OF C-RP

The acute phase response comprises the non-specific physiological and biochemical responses of endothermic animals to most forms of tissue damage, infection, inflammation and neoplasia. In particular, the synthesis of a number of proteins is rapidly up-regulated principally in hepatocytes, under the control of a cascade of cytokines, including interleukins-1, tumour necrosis factor-alpha and interleukins-6, originating at the site of pathology.

C-RP levels rapidly rise after an inflammatory stimulus and depending on the intensity of the stimulus, even a several-hundred-fold increase in plasma levels may occur[41]. C-RP is not consumed to a significant extent in any process and its clearance is not influenced by any known condition. Therefore its concentration appears to be dependent only on the rates of production and excretion. The long half life of C-RP, approximately 19 hours, makes its detection in blood easy even several hours after acute stimulus. Because of all these characters. C-RP can be called as an "ideal marker of inflammation."

ERYTHROCYTE SEDIMENTATION RATE (ESR)

ESR is a non specific inflammatory marker discovered much before C-RP. It is primarily based on changes in aggregation (roulette formation or piling) tendency of red blood cells. ESR depends on concentration of positively charged serum proteins such as fibrinogen and immunoglobulins, with increased concentrations neutralizing the net negative charge (zeta potential) of red blood cells.

ESR is a complex phenomenon depending not only on the inflammatory condition but also on red cell density, plasma viscosity; red cell morphology and hemoglobin content.[57] Reference values for ESR

differ according to sex and age and are also influenced by pregnancy and obesity.

ESR rises in conditions of myocardial damage and necrosis in the order of 15-40 mm/hr Normal reference range:

Males- 0 to 17 mm/hr

Females – 1 to 25 mm/hr

LEUCOCYTE COUNT

Epidemiologic studies have demonstrated correlations between the white blood cell count and the risk of acute myocardial infarction and stroke. The risk of AMI is approximately four times greater in persons with WBC counts high in the normal range (>9,000/ml) than in persons with WBC counts low in the normal range (<6,000/ml). A high WBC count also predicts a greater risk of re-infarction and of in-hospital death. In the last decade it has become evident that the pathogenesis of atherosclerosis involves several complex mechanisms; these include the immune system, the inflammatory response, and the infectious etiologies. We would like to focus on the role of the white blood cell in atherogenesis, atherothrombosis, and the risk of developing AMI and its complications.[92]

Epidemiologic observations

In 1974, Friedman et al. reviewed 464 patients who had suffered a first AMI and whose WBC count had been measured in the preceding 2 years. These patients were compared with two control groups: one was matched for age, gender and race, and the other for these variables and for conventionally recognized risk factors for infarction. It was found that the WBC count was a strong predictor of infarction. The predictive value of the WBC count was similar to that of a serum total cholesterol measurement or a single determination of blood pressure.

The height of the WBC count correlated positively with tobacco smoking, but only about two-thirds of the predictive value of the WBC count could be explained on the basis of this observation. In another study 7,000 males were followed for an average of 6.5 years. Among smokers, the WBC count correlated strongly with the risk of AMI. Smokers with WBC counts exceeding 9,000/ml had an incidence of AMI four times higher than in smokers with a leukocyte count below 6,000/ml, a difference that was statistically significant.[93]

In the Hiroshima/Nagasaki survivors' surveillance, the WBC count correlated significantly with the incidence of coronary heart disease. That

is, a total WBC count in excess of 10,000/ml was associated with a risk that was approximately twice that seen when the WBC count was at or below 4,000/ml. This excess risk was independent of gender, smoking history, blood pressure, and cholesterol level.

Examination of differential cell counts showed the strongest association to be with the neutrophil count. It has been shown (also in the Hiroshima/Nagasaki survivors' surveillance) that total WBC count was correlated with the risk of thrombotic cerebral infarction; the 469 patients suffering thrombotic strokes had a statistically significantly higher antecedent WBC count than did members of the cohort not experiencing ischemic events.[94] [7].

Again, the examination of differential WBC counts showed a statistically significant predictive power only for neutrophils. A strong independent correlation was found in the Multiple Risk Factor Intervention Trial (MRFIT) between total WBC count and the risk of coronary heart disease.[95] Even when tobacco smoking was controlled/corrected for, the WBC count was found to predict coronary heart disease prevalence, risk of non-fatal MI, and risk of sudden cardiac death. Moreover, if the WBC count declined during the period of surveillance, so did the CHD risk: a decrement of 1,000 WBC/ml was

associated with a 14% decrement in risk of cardiac death, unexplainable by changes in other cardiac risk factors.

In the PARIS-1 study, 2,026 patients were examined 2±60 months after suffering a first AMI; the total WBC count obtained at that time was found to correlate strongly with risk of re-infarction. Men with WBC counts exceeding 9,000/ml had a relative risk of re-infarction of 3.5, when 1.0 was set equal to the risk for men with WBC counts at or below 5,000/ml. An elevated leucocyte count is an epidemiological marker for coronary heart diseases.

Acute myocardial infarction is usually accompanied by leucocytosis which is related to the magnitude of necrotic process, elevated glucocorticoid levels and possibly inflammation in coronary arteries. The magnitude of elevation of leucocyte count is associated with in-hospital mortality [47,68]Activation of neutrophils may produce important intermediaries such as LT-B4 and oxygen free radicals that have important micro circulatory effects. Neutrophilic leucocytosis in the order of 12000 to 15000 cells/cu.mm occurs in acute myocardial infarction.

Normal reference range: 4.5 to 11.0 X 10^3 Cells /cu.mm

HIGH SENSITIVE C-RP

C-RP molecule itself is not a harmful molecule in the body. The higher level of C-RP is simply a reflection of higher than normal inflammation. The measurement of C-RP does not reflect where the inflammation is. It may come from cells in the fatty deposits in arterial walls that reflects the process of atherosclerosis. It may come from other tissues.

The time honoured semi-quantitative immunoassay for serum C-RP employs a polyclonal antibody to detect gross elevations in acute inflammatory illness. This rise remains stable over a period of several days in vivo and the protein is resistant to in vitro degradation. Conventional flocculation assays used for C-RP measurement in acute or chronic inflammatory illness detect only gross elevations. This test is now being phased out.

The monoclonal antibody based hs-CRP enzyme immunoassay or its automatable rapid counterpart the monoclonal polystyrene microparticle assay, however may detect normal or slightly elevated serum C-RP concentrations. Consequently, hs-CRP is recommended as a

clinical tool to evaluate low level systemic inflammation and thus to predict cardiovascular diseses[30].

Normal reference range: 0.02 to 8.0 mg/L

FREE FATTY ACIDS

Serum concentrations of free fatty acids (FFA) have been shown to be raised in patients with acute myocardial infraction. In other studies several authors have suggested a positive relationship between serum FFA and complicating arrhythmias and death after myocardial infarction.[86, 88, 89] They were of the opinion that high circulating FFA levels, were associated with intracellular lipid disturbances which could in turn provoke the arrhythmias. Various authors considered that the lipid changes were merely coincidental and elevation of serum FFA may be due to other metabolic events such as increased catecholamine secretions or starvation. [90, 91]

Normal reference range: < 8-25mg/dl

MATERIALS AND METHODS

STUDY DESIGN:

A case control study conducted in Intensive Coronary Care Unit(ICCU) at Govt. Kilpauk Medical College, Chennai 600 010.

DURATION OF STUDY

January 2008 – August 2008

INCLUSION CRITERIA

CASES

Patients presenting with acute myocardial infarction (AMI) with acute ECG changes within 12 hrs of the onset of chest pain

CONTROLS

50 volunteers without any apparent cardiac ailment

EXCLUSION CRITERIA

1. Intercurrent inflammatory or neoplastic conditions likely to present with acute phase response by clinical evaluation.
2. Surgery, trauma in the preceding six months.
3. Presence of connective tissue disorders like SLE, Rheumatoid arthritis and other collagen vascular diseases
4. Inflammatory bowl disorders, pancreatitis
5. Hepatic failure
6. Renal failure
7. Heart failure 8. Cerebrovascular Accident

STUDY POPULATION

In our study a total of 100 patients were enrolled. Of which 50 patients presented with AMI and with acute changes in ECGs within 12 hrs of onset of chest pain were enrolled as cases. Patients were admitted to the intensive coronary care unit [ICCU] of Department of Cardiology Govt Kilpauk medical college Chennai-10. The age ranges from 30 to 85 and study included both sexes.

In the control group 50 healthy volunteers were included. They had no past history or evidence of cardiovascular diseases. None of the control subjects gave history of neoplastic, hepatic, infectious or autoimmune diseases or any surgical procedure in the preceding six months.

The study was approved by institutional ethics committee. Detailed history recorded from the patients with reference to the features of the chest pain, location, radiation, aggravating and reliving factors, increase autonomic activity and other clinical features suggestive of acute myocardial infarction (AMI). The diagnosis of myocardial infarction was based on clinical and electrographic evidence using the criteria recommended by W.H.O.[101]

The other conditions which are likely to induce acute phase reactants were carefully ruled out by detailed history taking and thorough clinical evaluation. The risk factors associated with, both modifiable like cigarette smoking, alcohol consumption, hypertension, diabetes mellitus and obesity (BMI) and non- modifiable like age, sex, family history were taken into consideration. Cases were grouped as per their age, BMI, sex and diagnosis and compared with controls.

At the onset standard 12 lead ECG was taken and blood sample was collected for routine investigations, and for acute phase reactants hs-CRP (highly sensitive C – reactive protein), FFA. Early morning blood sample was collected for ESR and Lipid Profile. The diagnosis is made by internationally accepted criteria recommended by WHO.

All the patients were thrombolysed and standard treatment guidelines were followed. The Inflammatory markers were studied for variations among 50 patients admitted in the ICCU of Govt Kilpauk Medical College with AMI and with acute ECG changes (cases) and 50 healthy volunteers with no apparent cardiac ailment who were enrolled as controls. The groups cases and controls were compared for Age distribution, Sex, BP,BMI and Lipid Profile to find out statistical significance.

The Inflammatory markers hs-CRP, TC, ESR, FFA in cases and controls were analyzed for statistical variance.

The risk factors smoking and alcohol were found out by careful history taking. The risk factors DM and HT were detected by past medical history and laboratory routine investigation and BP measurement. These risk factors were studied for statistical correlation

between cases and controls first. Then the Inflammatory markers were analyzed for statistical variations with risk factors smoking and alcohol followed by risk factors DM and HT. The statistical correlation between the Inflammatory Markers and the various changes of ECG in our study group was also studied.

MATERIALS

Questionnaire,

BMI calculation,

Blood pressure,

Blood Total WBC count

Erythrocyte Sedimentation Rate

Total Cholesterol,

Triglycerides,

HDL

LDL

hs-CRP

Free Fatty Acids.

BMI CALAULATION

Body mass index is calculated with height and weight of the subject using the following formula.

BMI= weight (kg) / height(m)^2

Normal 20- 25 kg/m^2

Over Weight > 25-30 kg/m^2

Obese > 30kg/m^2

BLOOD PRESSURE

Right upper arm blood pressure is taken in supine position by using sphygmomanometer under appropriate condition.

hs-CRP

Blood samples are collected from patients and tested in a private laboratory by Latex turbimetry method.

Total count

Blood samples are collected and estimated in Kilpauk Medical College Laboratory.

E S R

Calculated by Westegran's method.

Lipid Profile

Lipid profile is done for all the subjects in fasting blood sample. Blood samples were collected in early morning with over night fasting.

Total Cholesterol

Calculated by CHOD-PAP method.

Triglycerides

Calculated by GPO-pap method.

H D L

Calculated by HDLc-p precipitating method.

LDL

Calculated by Friedwald Formula

LDL cholesterol = Total cholesterol–[Triglyceride/5 – HDL cholesterol].

FFA

Calculated manually in a private laboratory.

STATISTICAL ANALYSIS:

Descriptive statistics mean and standard deviation was used to summarize normally distributed continuous variables. All statistical analysis was done using SPSS (Statistical Package for Social Sciences) v 1.5. A p value of less than 0.05 was considered statistically significant.

- Students two sample test was used to compare two variables.
- Chi square test was used to analyze descriptive variables.
- Anova test was used to compare multiple variables

RESULTS AND ANALYSIS

- A total of 50 patients admitted in the ICCU within 12 hrs of onset of chest pain and with acute ECG changes were enrolled as cases.

- A total of 50 volunteers with no cardiac abnormality were enrolled as controls.

- Mean age of cases was 53.30 ± 12.21 years.

- Mean age of controls was 48.7 ± 7 years.

- Statistically significant difference was noticed among cases and controls with regard to age. P value 0.027.

- Statistically significant difference was noticed among cases and controls with regard to sex. P value 0.000.

- In our study male gender predominance is observed with regard to AMI.

- Mean BMI of cases was 24.44 ± 4.49 kg/m².

- Mean BMI of controls was 26.996 ± 4.46 **kg**/m².

- Statistically significant difference was noticed among cases and controls with regard to BMI. P value 0.005.

- Statistically significant difference was noticed among cases and controls with regard to BP.

- Mean systolic BP for cases and controls were 135.76 ±28.31 and 124.4 ± 12.33. P value o.011

- Mean diastolic BP for cases and controls were 90.2 ± 16.84 and 82.72± 8.16. P value 0.006

- AMI had a significant correlation with high BP

- In Lipid profile TGI and HDL showed statistically significant difference. while Total Cholesterol and LDL did not show any significance

- P value for TGL was 0.000

- P value for HDL was 0.041

- Statistically significant difference was noticed among cases and controls with regard to risk factors smoking and alcohol. More occurrence of AMI among smokers and alcoholics in our study. P value 0.004.

  - The risk factors DM and Hypertension did not show any statistical significance.

  - Among the inflammatory markers studied only hs-CRP vary with statistical significance. P value 0.000.

  - TC, ESR, FFA values did not show any statistical significance.

  - The inflammatory profile did not show any statistical significance with regard to risk factors smoking and alcohol.

  - Except ESR no other inflammatory markers did show any statistical significance with regard to risk factors DM and HT.

  - P value for ESR when studied with risk factor DM and HT was 0.014

  - Among the Inflammatory profile markers studied on comparison with various ECG changes hs-CRP and ESR showed statistically significant variation while TC and FFA did not show any significance

    P value for hs-CRP was 0.000

    P value for ESR was 0.031.

TABLES AND VALUES

AGE DISTRIBUTION ANALYSIS

TABLE 1

GROUP	NO	MEAN AGE	STD DEVIATION
CASE	50	53.3	12.21
CONTROL	50	48.7	7.799

Mean age of cases was 53.30 ± 12.21 years.

Mean age of controls was 48.7 ± 7 years.

TABLE 2

AGE GROUP (Years)	CASE	CONTROL
30-35	8	9
36-40	9	10
41-45	4	11
46-50	8	9
51-55	8	9
>56	13	2

P = 0.027 SIGNIFICANT

Statistically significant difference was noticed among cases and controls with regard to age.

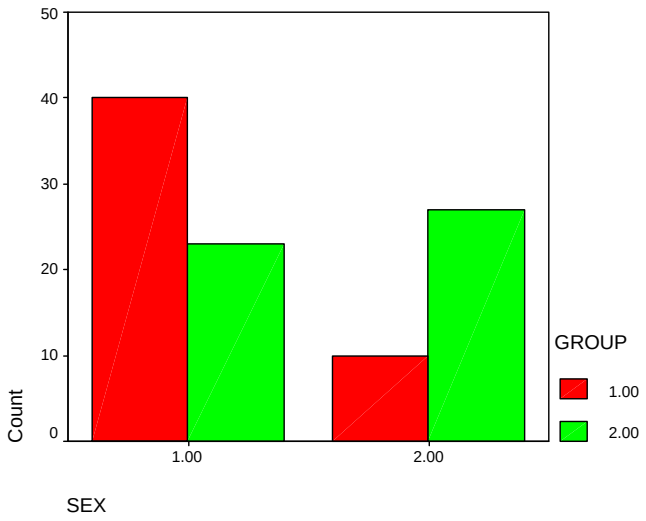
SEX DISTRIBUTION ANSLYSIS

TABLE 3

SEX	CASE	CONTROL
MALE	40	23
FEMALE	10	27

P VALUE 0.000 SIGNIFICANT

Statistically significant difference was noticed among cases and controls with regard to sex.



In our study male gender predominance is observed with regard to occurrence of AMI.

BMI

TABLE 4

GROUP	NO	MEAN	SD
CASE	50	24.44	4.49
CONTROL	50	26.996	4.46

Mean BMI of cases was 24.44 ± 4.49 kg/m².

Mean BMI of controls was 26.996 ± 4.46 **kg**/m².

TABLE 5

BMI GROUP	CASE	CONTROL
<25	28	19
25-30	13	18
>31	9	13

P = 0.005 SIGNIFICANT

Statistically significant difference was noticed among cases and controls with regard to BMI.

BLOOD PRESSURE

TABLE 6

BP	VALUES	CASE	CONTROL
SYSTOLE	MEAN ± SD	135.76 ± 28.31	124.40 ± 12.33
DIASTOLE	MAEN ± SD	90.20 ± 16.84	82.72 ± 8.16

P VALUE for SYSTOLIC BP was 0.011 SIGNIFICANT

P VALUE for DIASTOLIC BP was 0.006 SIGNIFICANT

Statistically significant difference was noticed among cases and controls with regard to BP.

LIPID PROFILE

TABLE 7

	NO	TGL	CHOLESTEROL	HDL	LDL
CASE	50	210 ± 58.74	192.4 ± 44.86	42.46 ± 7.1	110.64 ± 31.99
CONTROL	50	159 ± 77.23	184.02 ± 33.43	44.98 ± 4.87	107.4 ± 33.06

P VALUE for TGL was 0.000 SIGNIFICANT

P VALUE for HDL was 0.041 SIGNIFICANT

P VALUE for CHOLESTEROL was 0.292 NOT SIGNIFICANT

P VALUE for LDL was 0.62 NOT SIGNIFICANT

In Lipid profile TGI and HDL showed statistically significant difference while Total Cholesterol and LDL did not show any significance.

RISK FACTORS - SMOKING AND ALCOHOL

TABLE 8

SMOKING & ALCOHOL	CASES	CONTROLS
NIL	14	32
SMOKING	12	6
ALCOHOL	3	1
BOTH	21	11

P VALUE 0.004 SIGNIFICANT

Statistically significant difference was noticed among cases and controls with regard to risk factors smoking and alcohol. More occurrence of AMI among smokers and alcoholics in our study.

RISK FACTORS - DM AND HT

TABLE 9

DM & HT	CASE	CONTRTOL
NIL	14	20
DM	13	5
HTN	15	13
BOTH	8	12

P VALUE 0.135 NOT SIGNIFICANT

The risk factors DM and Hypertension did not show any statistical significance.

INFLAMMATORY PROFILE

TABLE 10

	NO	hs- CRP	TC	ESR	FFA
CASE	50	9.31 ± 2.36	10424 ± 2816.46	21.24 ± 21.97	3.34 ± 2.97
CONTROL	50	4.31 ± 4	9628 ± 894.19	18.36 ± 14.84	3.5 ± 3.09

P VALUE for hs- CRP was 0.000 SIGNIFICANT

P VALUE for TC was 0.134 NOT SIGNIFICANT

P VALUE for ESR was 0.444 NOT SIGNIFICANT

FFA P VALUE for FFA was 0.787 NOT SIGNIFICANT

Among the inflammatory markers studied only hs-CRP vary with statistical significance.

TC, ESR, FFA values did not show any statistical significance.

INFLAMMATORY PROFILE VS RISK FACTORS

SMOKING AND ALCOHOL

TABLE 11

RISK FACTOR	N0	hs-CRP	TC	ESR	FFA
NIL	46	5.9 ± 4.68	9682.6 ± 2253.6	17.57 ± 6.08	3.28 ± 2.88
SMOKING	18	7.18 ± 3.64	9427.8 ± 713.89	16.17 ± 16.60	3.92 ± 3.88
ALCOHOL	4	8.025 ± 4.69	1O575 ± 315.71	13 ± 3.46	4.225± 2.79
BOTH	32	7.706 ± 3.29	1O896.88 ± 2816.37	25.91 ± 23.04	3.24 ± 2.76

P VALUE for hs-CRP was 0.256 NOT SIGNIFICANT

P VALUE for TC was 0.093 NOT SIGNIFICANT

P VALUE for ESR was 0.152 NOT SIGNIFICANT

P VALUE for was FFA 0.803 NOT SIGNIFICANT

The inflammatory profile did not show any statistical significance with regard to risk factors smoking and alcohol

INFLAMMATORY PROFILE VS RISK FACTORS

DM AND HT

TABLE 12

RISK FACTOR	NO	hs-CRP	TC	ESR	FFA
NIL	34	5.57 ± 4.185	9417.65 ± 1521.46	12.53 ± 9.36	2.8 ± 2.45
DM	18	7.09 ± 4	10044.44 ± 2735.87	20.72 ± 20.61	3.5 ± 3.68
HTN	28	6.92 ± 3.68	10110.71 ± 2106.49	21.39 ± 18.5	3.996 ± 3.15
BOTH	20	8.5 ± 4.32	11100 ± 3391.16	29.1 ± 24.81	3.60 ± 3.08

P VALUE for ESR was 0.014 SIGNIFICANT

P VALUE for hs-CRP was 0.085 NOT SIGNIFICANT

P VALUE for TC was 0.104 NOT SIGNIFICANT

P VALUE for FFA was 0.471 NOT SIGNIFICANT

Except ESR no other inflammatory markers did show any statistical significance with regard to risk factors DM and HT.

INFLAMMATORY PROFILE VS ECG CHANGES

TABLE 13

ECG	NO	hs- CRP	TC	ESR	FFA
NORMAL	51	4.43 ± 4.05	9684.31±1877.698	18.16 ± 14.76	3.44 ± 3.089
AWMI	29	9.42 ± 2.58	9920.69 ± 2349.53	16.51±15.9	3.39 ± 3.41
IWMI	16	9.19 ± 2.29	11650 ± 3623.26	33.06 ± 29.48	3.39 ± 2.09
BOTH	1	8	9800	20	2.3
EXTENSIVE AWMI	3	9.43 ± 1.25	9433.33 ± 472.58	8.67 ± 2.3	8.67 ± 2.30

P VALUE FOR ECG CHANGES VS hs-CRP < 0.001

P VALUE FOR ECG CHANGES VS ESR 0.031

P VALUE FOR ECG CHANGES VS TC 0.072

P VALUE FOR ECG CHANGES VS FFA 0.0995

Among the Inflammatory profile markers studied on comparison with various ECG changes hs-CRP and ESR showed statistically significant variation while TC and FFA did not show any significance.

DISCUSSION

A case control study was carried out in our present study in which 50 patients with AMI with acute ECG changes were enrolled as cases and 50 volunteers with clinically no apparent cardiac aliment were enrolled as controls.

The inflammatory markers hs-CRP , TC, ESR and FFA levels n the cases were compared with that of controls along with modifiable risk factors like cigarette smoking, alcohol, HT, DM and non – modifiable risk factors like age and gender.

AGE

The mean age for the cases (Mean ± SD) was 53.3 ± 12.21 years and for controls (Mean ±SD) was 48.7 ± 7.799 years. A statistically significant difference with regard to age (P= 0.027) was observed.

This is inconsistent with the study conducted by Arunkumar[99] et al where the age (Mean ± SD) for cases and controls were 61.84± 3.80 vs 60.55± 3.98 with P=0.0037 respectively.

SEX

In our present study among the cases 80 % were males (40/50) and 20% (10/50) were females in controls 46% (23/50) were males and 54% (27/50) were females. As per this a statistically significant difference was present (P=0.000) with regard to sex and hence a male gender predominance.

This is in consistent with the study conducted by Arunkumar[99]et al, where among the 165 patients enrolled as cases 123 were males and 42 were females, while the controls and the same member of male and female volunteers, with statistically significant variation with regard to sex (P<0.05) and male gender predominance.

BMI

In the present study cases and controls were grouped into three categories according to BMI. 56% (28/50) were normal weight, 20% (13/50) were over weight and 18% (9/50) were obese in the cases. Among the control 38% (19/50) were of normal weight. 36% (18/50) were of over weight, 26% (13/50) were obese.

The mean BMI (Mean ± SD) for cases and controls were 24.43 ± 4.49 vs 26.996 ± 4.457 respectively. A statistically significant difference observed with regard to BMI in this study (P=0.005).

This is in consistent with the study conducted by Arunkumar[99] et al the BMI values (Mean ± SD) for cases and controls were 26.16 ± 1.45 vs 25.40 ± 1.20 respectively with P<0.01.

LIPID PROFILE

In our present study the lipid profile was compared between cases and controls. The values for TGL and HDL vary with statistical significance between the groups, while the values for total cholesterol and LDL did not show any significance. The values (Mean ± SD) for TGL for cases and controls were 210.16 ± 58.74 vs 159 ± 77.23, with P values 0.000.The values (Mean ± SD) for HDL were 42.46 ± 7.10 vs 44.98 ± 4.87 for cases and controls respectively with P values 0.041.

This is inconsistent with the study conducted by Arunkumar[99] et al where the TGL values (Mean ± SD) for cases and controls were 128.96 ± 12.19 vs 107.84 ± 11.51 with statistically significant difference (P< 0.001).

This is in contrast to the study conducted by Srikanth K. Sivaraman[96] et al where elevated levels of Total Cholesterol in patients with AMI (Mean ± SD) when compared with cases. The values were 199.76 ± 18.82 vs 168.75 ± 14.64 with statistical significance (P<0.001).While the values of TGL, HDL, LDL were not altered much when compared to controls.

In contrast to the present study, the study conducted by Arunkumar[99] et al showed statistical significance with regard to LDL. In our study the values for LDL (Mean ± SD) for cases and controls were 110.64± 31.995 vs 107.40 ± 33.062 respectively (P=0.62). The values in the study conducted by Arunkumar et al for cases and controls were 119.37 ± 14.05 vs 83.59 ± 11.95 with significant correlation with regard to LDL (P<0.001).

BLOOD PRESSURE

In the present study blood pressure systolic and diastolic found to show significant correlation between cases and controls.

The systolic BP values (Mean ± SD) for cases and controls were 135.76 ± 28.31 vs 124.40 ± 12.33 with P value 0.001, and diastolic BP values (Mean ± SD) for cases and controls were 90.20 ± 16.84 vs 82.72 ±

8.16 with the P values 0.006.So as per our study there was a correlation between high BP and AMI.

This is in consistent with the study conducted by Arunkumar [99]et al where the values for systolic BP (Mean ± SD) for cases and controls were 136 ± 23 vs 113 ± 8 with P < 0.02, and diastolic BP values (Mean ± SD) for cases and controls were 95 ± 10 vs 85 ± 7 with the P < 0.02.

RISK FACTORS

In our present study statistically significant correlation observed between AMI and risk factors smoking and alcohol (P=0.004). The risk factors DM and HT showed no significant correlation.

INFLAMMATORY PROFILE

Out of 50 patients in the cases, 43 were found to be with elevated hs-CRP. In the controls 7 volunteers without any apparent cardiac ailment were found with elevated hs-CRP. On comparing these two groups statistically significant difference was noted in hs-CRP levels. The values (Mean ± SD) for cases and controls were 9.308 ± 2.35 mg/L vs 4.31 ± 4.007 mg/L with highly significant P values (P=0.000). This is in consistent with various other studies.

A study conducted by Sreekanth L. Sivaraman [99]et al in 2004 CRP levels were elevated in AMI (40.8± 15.4 mg/L) when compare to controls with normal heart (12.6± 2.8 mg/L).There was a statistically significant difference between cases and controls with P values<0.001.

In a study conducted by A.L. Pasqui[102] et al in 2005 hs-CRP levels in AMI was 4.3 ± 2.8 and for controls was 1.2 ± 0.4. A statistically significant difference observed in this study (P<0.01).

In a study conducted by Dr.Arunkumar[99]et al (Pak.J.Med. Sci.) in 2002-2006 higher plasma levels of CRP was found in Pts with AMI when compare to control. The CRP levels for controls 1.12± 0.33 while for the patients with AMI it was 2.97 ± 1.11 .This was statistically significant with P= <0.001.

In a study conducted by YIP HK, [100] Wu CJ, Chang HW et al (CRP 3) Serum levels of hs-CRP was significantly higher in patients with an onset of MI <6 hrs when compared to healthy subjects. (2.7 ± 2.3 mg/L vs 1.0 ± 0.6 mg/L with P<0.0001).

In the present study TC was not found to be statistically significant. The values for TC (Mean ± SD) for cases and controls was (10424.00 ± 2816.46 vs 9698.00 ± 1894.19) with P values 0.134. The ESR was also not found to be varying significantly when AMI patients were compared with controls in our present study. The values for ESR (Mean ± SD) for cases and controls in our study were 21.24 ± 21.97 vs 18.36 ± 18.84 respectively.

This is in contrast to a study conducted by Srikanth K. Sivaraman[97] et al. There the values for total WBC count and ESR varied significantly with controls. The values for ESR in patients with MI compared with controls was 55.2 ± 28.0 vs 25.2 ± 10.3 ,and for total WBC count the values were 11480.8 ± 4345 vs 8949.6 ± 1853. The P values for both were <0.01.

In our present study the inflammatory markers FFA levels in AMI patients was compared with that of controls. No significant difference observed in this study. The values for cases and controls (Mean ± SD) were 3.34 ± 2.97 vs 3.50 ± 3.09 with P values of 0.181. This was in contrast to the study conducted by V.S. Singh [98] S.Kirti et al. Where serum FFA have been shown to be raised with AMI with statistical significance.

INFLAMMATORY PROFILE VERSUS RISK FACTORS

In the present study the inflammatory markers hs-CRP, Total count, ESR and FFA were compared with various risk factors. The levels of these markers were not found to vary significantly in smokers and alcoholic when compared with patients with nonsmokers/nonalcoholic. This is in contrast with the study conducted by Moghbeli[66] N et al, where smokers with Acute coronary syndrome had higher CRP levels than non-smokers ($P<0.001$).While comparing these inflammatory markers with DM and HTN only ESR found to be vary statistically significant manner ($P=0.014$).

INFLAMMATORY PROFILE VERSUS ECG CHANGES

In our present study the inflammatory markers were compared with various types of ECG changes between cases and controls. In these both hs-CRP and ESR were found to be vary significantly among the various ECG changes, hs-CRP with the P values <0.001 and for ESR with P values 0.031. This is in consistent with the study conducted by Srikanth .K. Sivaraman [96]et al.

SUMMARY

- There was significant correlation between AMI and Age, Sex, BP and BMI.

- There was a significant correlation between AMI and the risk factors smoking and alcohol.

- In the lipid profile TGL and HDL showed significant correlation with AMI while Total cholesterol and LDL did not show any statistical significance.

- The values of hs-CRP were found to have highly significant correlation with AMI.

- The other inflammations markers TC, ESR and FFA did not vary with statistical significance.

- ESR and hs-CRP were found to have statistically significant correlation with various types of ECG changes.

- There was no statistically significant correlation of inflammatory markers with regards to DM and HTN except ESR.

- The risk factors smoking and alcohol did not alter inflammatory profile significantly.

- Elevation of hs-CRP can be used as adjuncts in the diagnosis of AMI.

LIMITATIONS:

- Only selected inflammatory markers were studied

- Coronary artery disease not confirmed by angiogram.

- Complications and follow up were not included in this study.

- Cardiac enzymes could not be studied due to financial constraints.

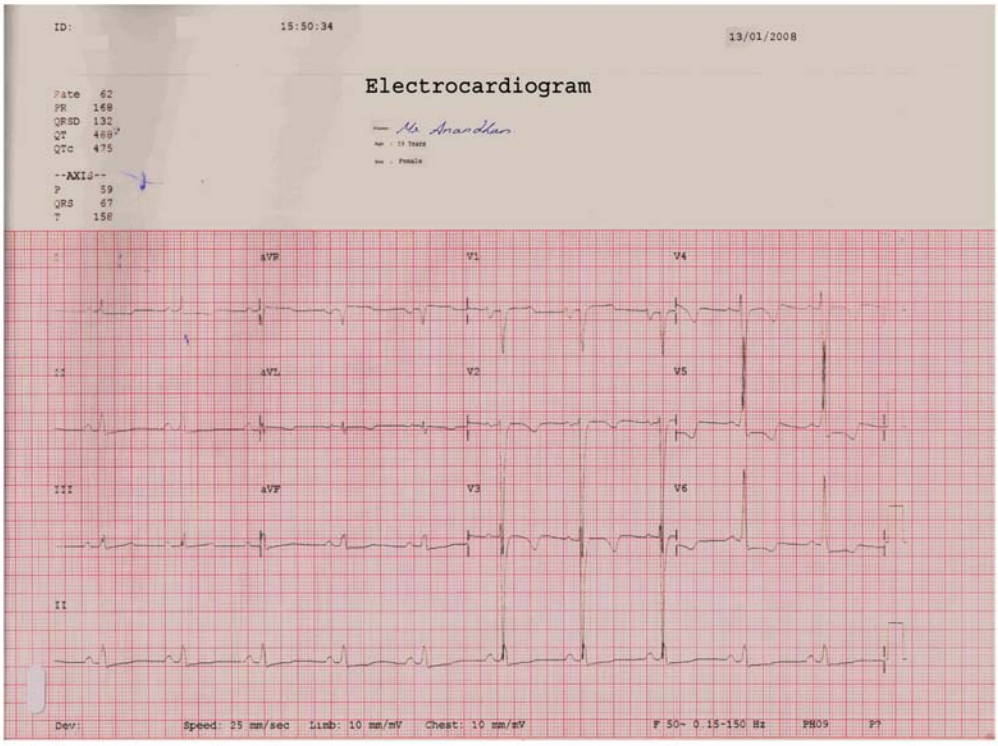
CONCLUSIONS

Our study clearly indicated that hs-CRP is elevated in most of the cases of AMI and supporting the view that inflammation in the coronary vessels plays a very important role in the pathogenesis of AMI and other cardiac events. But AMI is not an overt inflammatory disease but events leading to AMI are every much influenced by the inflammatory process especially the plaque rupture.

The hs-CRP measured by high sensitive assay is capable of detecting the ongoing inflammation in the coronary arteries. By considering hs-CRP as a diagnostic and therapeutic marker, added with the clear understanding of vascular biology, atherosclerosis and inflammation, our diagnostic and therapeutic methods will move in to new level in the management of CAD and AMI.

The knowledge that atherosclerosis is an inflammatory disease, offers new opportunities for the prevention and management of CAD and AMI. However further evaluation and studies are required to clarify the exact roles played by these various inflammatory markers in the disease causation, progression and the therapeutic interventions.

Among the various inflammatory markers hs-CRP found to be highly significant and it can very well suggested to be a reliable diagnostic marker of inflammatory process in AMI, after excluding other condition which can produce elevation of hs-CRP.P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QRSD 132
QT 468
QTc 475
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QRS 67
T 158
I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II
Dev
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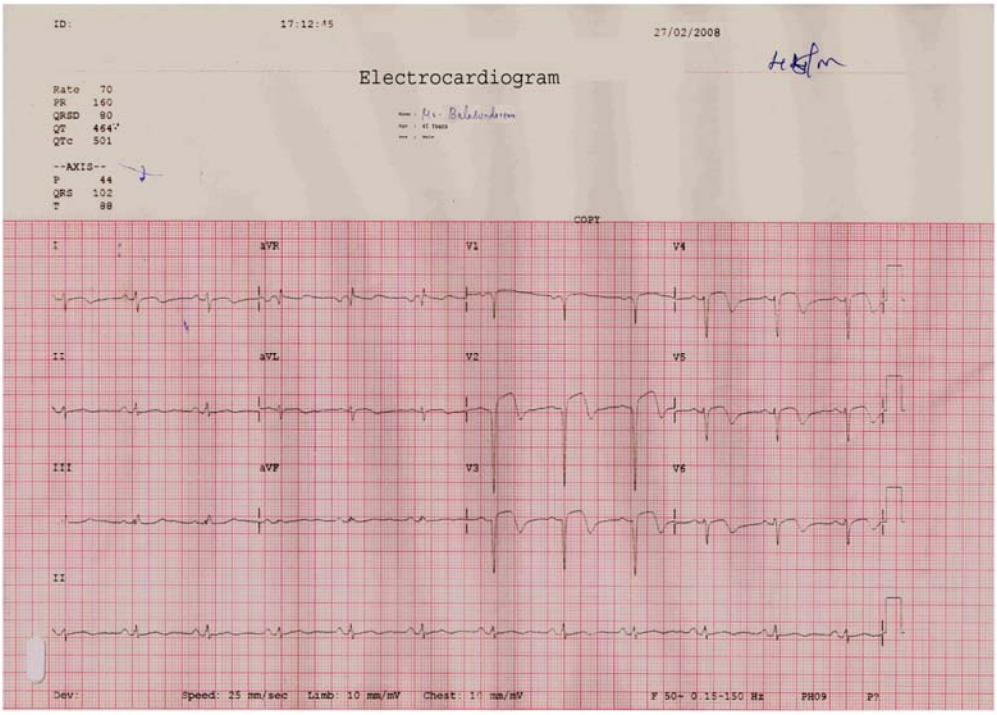
Limb: 10 mm/mV
Chest: 10 mm/mV
F 50- 0.15-150 Hz
PH09
P?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T 88
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V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II
Dev
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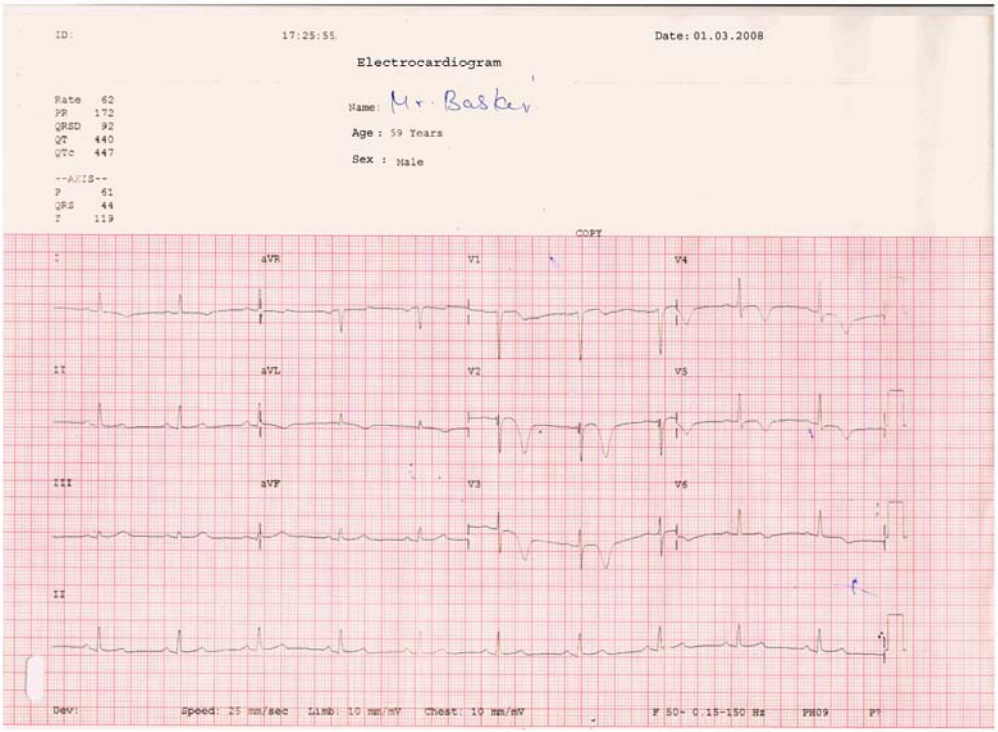
Limb: 10 mm/mV
F 50- 0.15-150 Hz
PH09
P?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Age : 59 Years
Sex : Male
COPY
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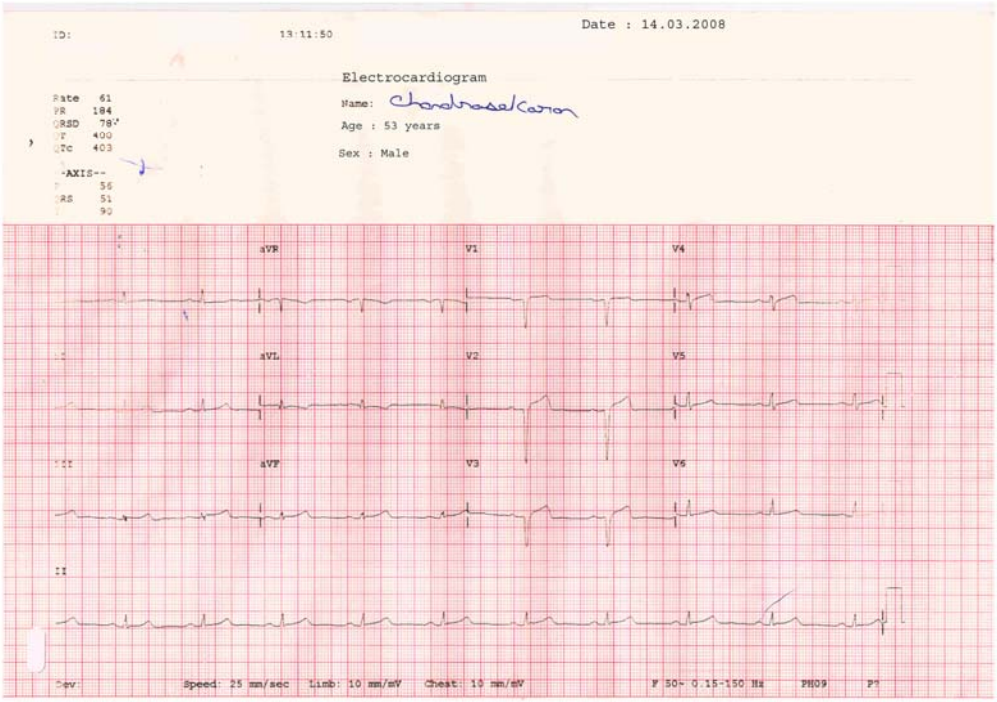
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II
Dev
Speed: 25 mm/sec
Limb: 10 mm/mV
Chest: 10 mm/mV
F 50- 0.15-150 Hz
PH09
P?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QT 400
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RS 51
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Age : 53 years
Sex : Male
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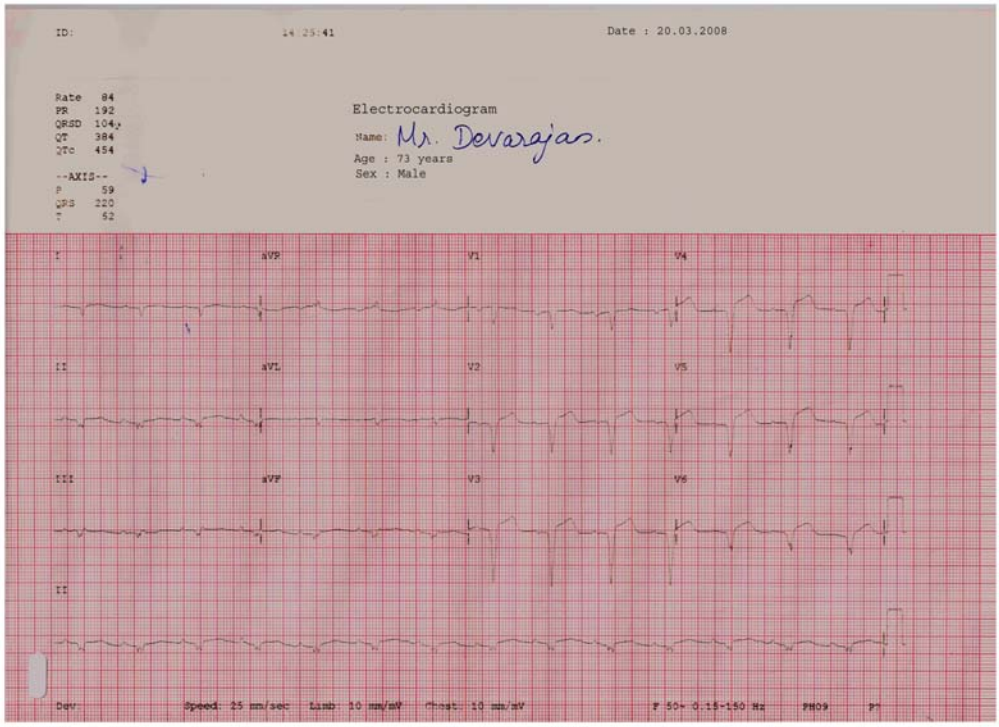
V1
V4
aVL
V2
V5
aVF
V3
V6
II
Dev
Speed: 25 mm/sec
Limb: 10 mm/mV
Chest: 10 mm/mV
F 50- 0.15-150 Hz
PH09
P?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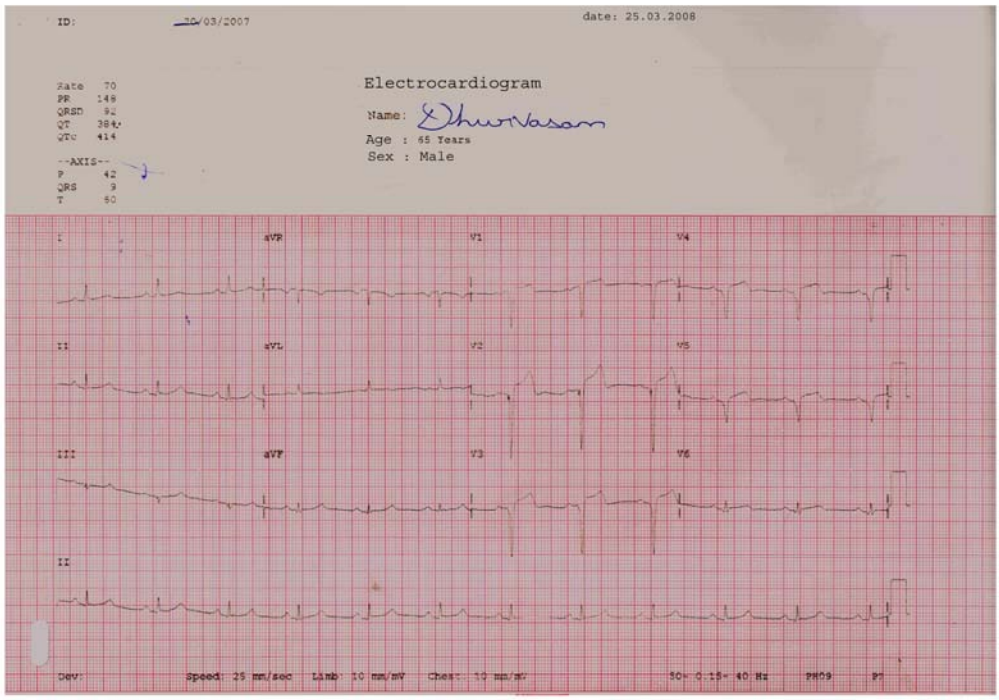
QRS 220
T 52
Electrocardiogram
Name: Mr. Devarajan.
Age : 73 years
Sex : Male
I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II
Dev
Speed: 25 mm/sec
Limb: 10 mm/mV
Chest: 10 mm/mV
F 50- 0.15-150 Hz
PH09
P?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V1
V4
II
aVL
V2
V5
III
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Dev
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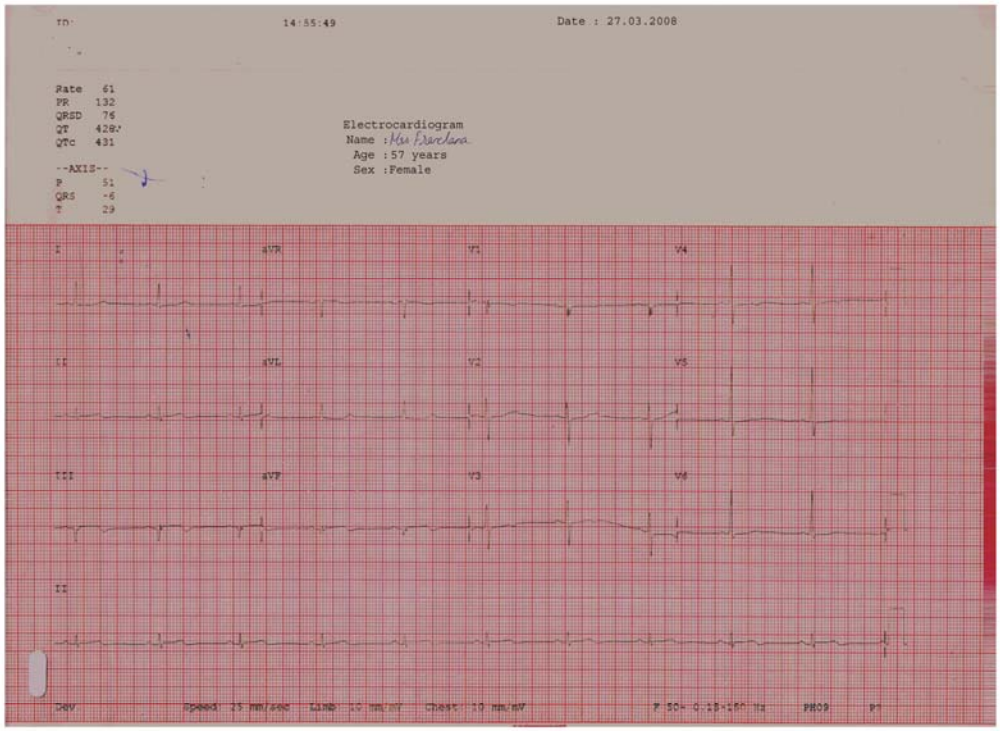
P?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V1
V4
II
aVL
V2
V5
III
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V6
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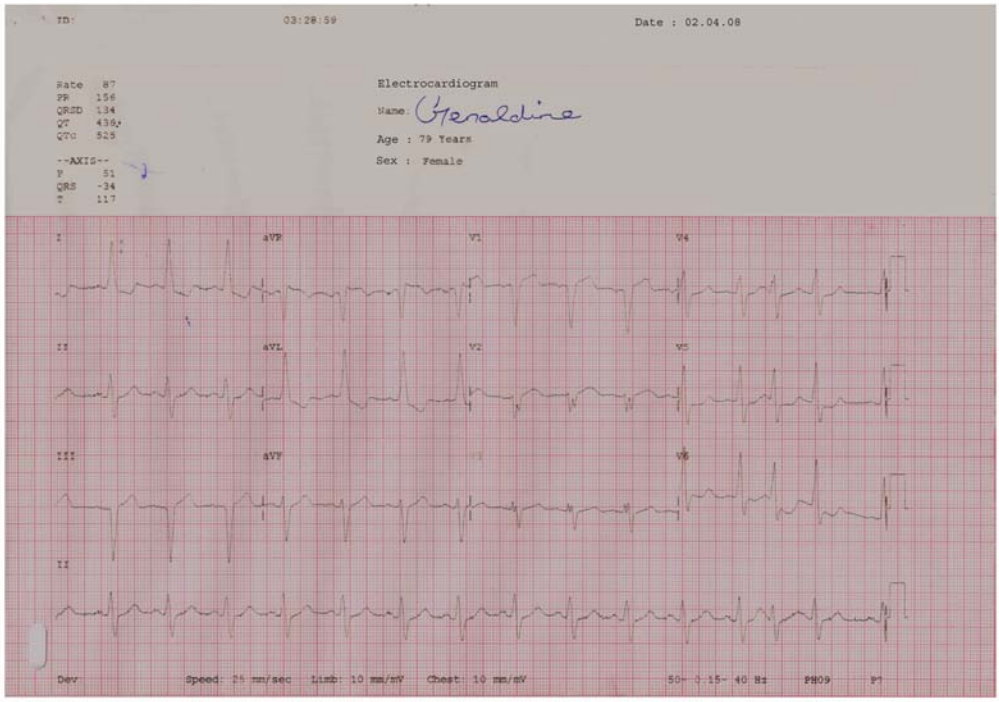
PH09
P1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Age : 79 Years
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V1
V4
II
aVL
V2
V5
III
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V6
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PH09
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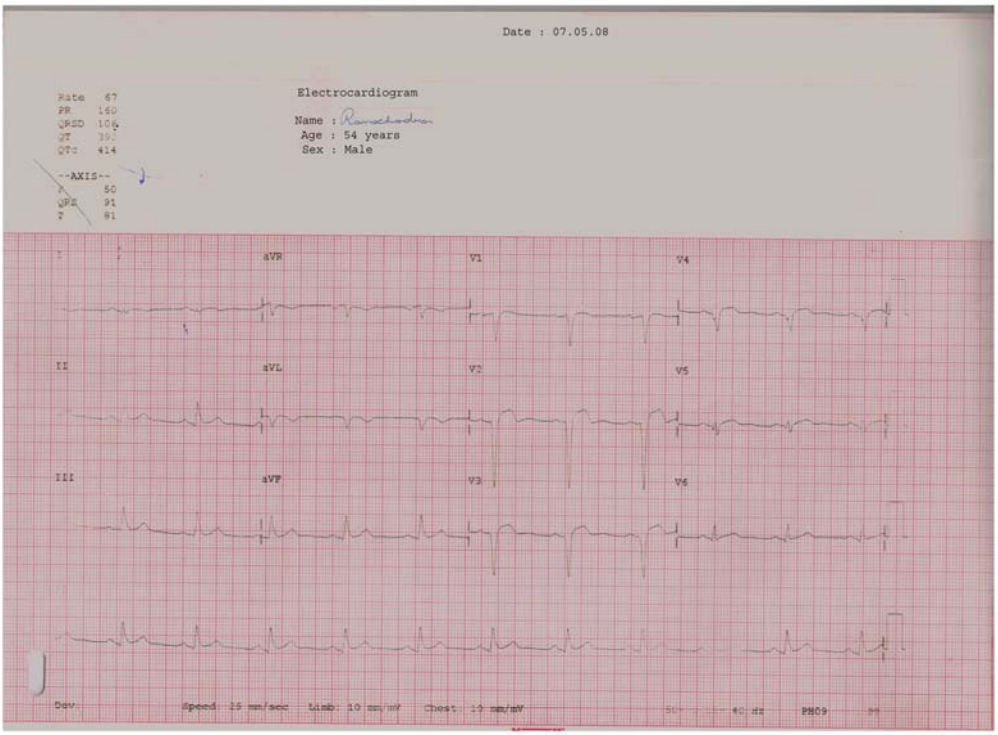
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Age : 54 years
Sex : Male
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aVR
V1
V4
II
aVL
V2
V5
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V6
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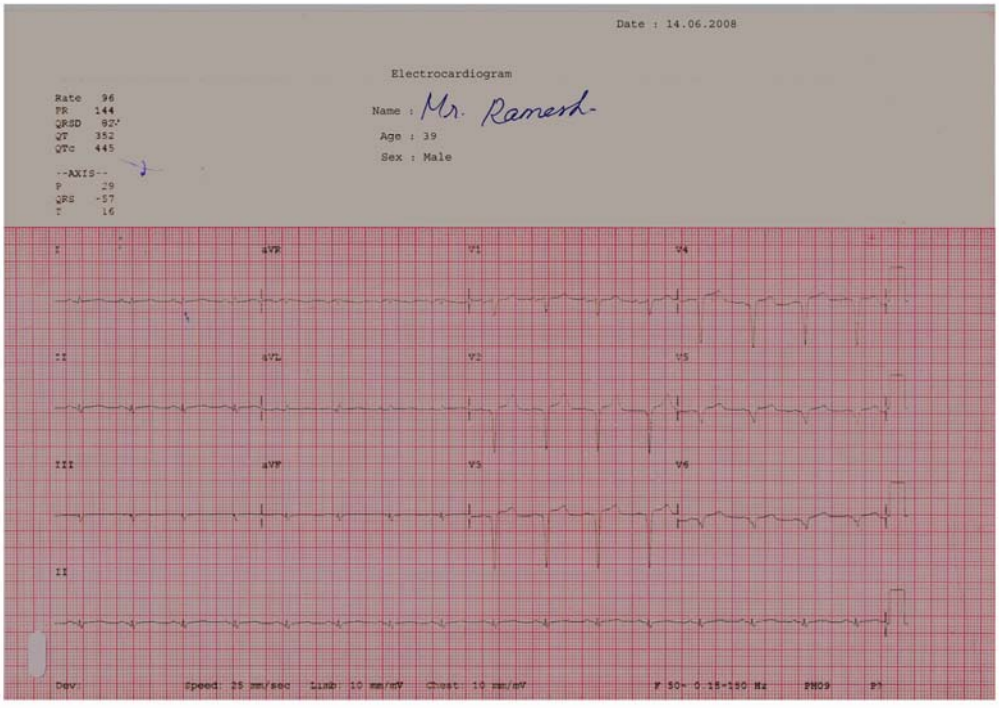
40 Hz
PH09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V4
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V5
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V3
V6
II
Dev
Speed: 25 mm/sec Limb: 10 mm/mV Chest: 10 mm/mV
F 50- 0.15-150 Hz
PH09

ABBREVIATIONS

ACS	Acute Coronary Syndrome
AMI	Acute Myocardial Infarction
AT-III	Anti-Thrombin III
ATP-III	Adult Treatment Panel III
AWMI	Anterior Wall MI
BMI	Body Mass Index
BP	Blood Pressure
CAD	Coronary Artery Disease
CRP	C- Reactive Protein
DM	Diabetes Mellitus
ECG	Electrocardiogram
ECHO	Echocardiography
ESR	Erythrocyte Sedimentation Rate
HDL	High density Lipoprotein
hs-CRP	high sensitive C -Reactive Protein
HT	Hypertension
ICAM	Intercellular Adhesion Molecule
ICCU	Intensive Coronary Care Unit
IL	Interleukin
IWMI	Inferior Wall MI
LDL	Low Density Lipoprotein
LT	Leukotriene
LV	Left ventricle
MI	Myocardial Infarction
MMP-9	Matrix Metallo Proteinase-9

MRFIT	Multiple Risk Factor Intervention Trial
NSTEMI	Non ST Elevation Myocardial Infarction
PCI	Percutaneous Coronary Intervention
P value	Probability value
PR	Pulse Rate
STEMI	ST Elevation Myocardial Infarction
SVCAM	Soluble Vascular Cell Adhesion Molecule
TC	Total Count
UA	Unstable Angina
VLDL	Very LOW density Lipoprotein
vWF	von Willebrand Factor
WBC	White Blood Cell
WHO	World Health Organization

MASTER CHART ABBREVIATIONS

F	Female
M	Male
Risk F	Smoking and Alcohol
Risk G	Diabetes and Hypertension
BP	Blood pressure

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PROFORMA

Name of the patient :

AID no :

Age :

Sex :

Address :

Symptomatology

Chest pain yes/no:

Dyspnoea yes/no:

Palpitations yes /no:

Syncope yes /no :

Sweating yes /no :

Risk factors

H/O smoking :

H/O alcohol consumption :

H/O hypertension :

H/O diabetes :

Height :

Weight :

BMI :

Vitals

Temperature :

Pulse rate :

Blood pressure :

Lipid profile :

TGL :

LDL :

HDL :

Inflammatory profile :

Hs CRP :

Total count :

Free fatty acid :

E S R :

Obesity :

Family history :

Previous H/o angina :

ECG :

Chest X ray :

Types of AMI :

Acute AWMI :

Acute IWMI :

Both AWMI and IWMI :

Extensive AWMI :

Echocardiogram :