"MEAN PLATELET VOLUME IN PATIENTS OF ACUTE CORONARY SYNDROMES IN A TERTIARY CARE HOSPITAL."

By

REG NO.BG0113003

Dissertation

Submitted to the
KLE University, Belagavi, Karnataka

In Partial Fulfillment
of the requirements for the degree of

M. D.
in
GENERAL MEDICINE

DEPARTMENT OF MEDICINE,
JAWAHARLAL NEHRU MEDICAL COLLEGE,
BELAGAVI, KARNATAKA

APRIL - 2016

KLE UNIVERSITY, BELAGAVI, KARNATAKA

ENDORSEMENT

This is to certify that the dissertation entitled **"MEAN PLATELET VOLUME IN PATIENTS OF ACUTE CORONARY SYNDROMES IN A TERTIARY CARE HOSPITAL"** is a bonafide research work done by **REG NO.BG0113003.**

Dr. Rekha Patil $_{\text{MD}}$
Professor and Head,
Department of Medicine,
J. N. Medical College,
Nehru Nagar, Belagavi – 10

Date:
Place: Belagavi.

Dr. N. S. Mahantshetti $_{\text{MD}}$
Principal,
J. N. Medical College,
Nehru Nagar, Belagavi – 10

Date:
Place: Belagavi.

LIST OF ABBREVIATIONS USED

ACS	→	Acute Coronary Syndrome.
MI	→	Myocardial Infarction.
STEMI	→	ST segment Elevation Myocardial Infarction.
NSTEMI	→	Non ST segment Elevation Myocardial Infarction.
USA / UA	→	Unstable Angina.
MPV	→	Mean Platelet Volume.
cTnT	→	Troponin-T.
cTnI	→	Troponin- I.
CHD	→	Coronary Heart Disease.
CVD	→	Cardio Vascular Disease.
BMI	→	Body Mass Index.
CK-MB	→	Creatinine phosphokinase MB isoform.

ABSTRACT

Background and objectives

Platelet count and mean platelet volume being simple and reliable indicators of platelet size that correlates with platelet activation might be an emerging cardiovascular risk marker and potentially helpful in stratifying cardiovascular risk. Studying the correlation may help us to understand better and reduce the chance of myocardial infarction in the apparently healthy subjects

Methodology

The present one year cross-sectional study was done in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi. A total of 400 Acute Coronary Syndromes patients were included in the study. Patients were subjected to clinical examination, electrocardiogram, platelet count and mean platelet volume.

Results

Majority of the patients were males (75.5%). The male to female ratio was 3.08:1. ‘p’ value for platelet count when compared between male and female was statistically significant.(p=0.001).

In the present study majority of the patients were MI patients (75.75%). The MI patients to USA patients ratio was 3.123:1. The ‘p’ value for platelet count (p=0.99) and MPV(0.75) between the two groups was not significant.

In the present study majority of the patients were non hypertensives (60.5%). Hypertensives to non hypertensives ratio was 1.53:1. MPV and Platelet

counts were high in Hypertensives (8.927fl & 2.80 lacs) respectively. Hypertensives to non-hypertensives MPV and Platelet count ratio were 1.001 and 1.022 respectively which was not significant.

In the present study majority of the patients were diabetics (60.5%). Diabetics to non diabetics ratio was 1.77:1, MPV and Platelet counts were high in Diabetics (8.979fl & 2.764 lacs) respectively. Diabetics to non-diabetics MPV and Platelet counts ratio were 1.010 and 1.001 respectively which was also not significant.

In the present study majority of the patients were </=64 years(68.5%). Less than 65 years to more than 65 years ratio was 2.17:1. P value (p=0.011) was statistically significant for platelet count.

In the present study majority of the patients(89%) were not on anti platelet therapy before admission. Ratio of patients not on anti platelet therapy to patients on anti platelet therapy before admission was 8.09:1with ‘p’ value 0.70 and 0.05 for MPV and platelet count respectively which was not statistically significant for MPV but significant for platelet count.

In the present study majority of the patients were not thrombolysed (94.5%). Non thrombolysed to thrombolysed ratio was 17.18:1 with ‘p’ value of 0.13 and 0.19 for MPV and platelet count respectively.

Conclusion and interpretation

- The average values of MPV and platelet counts are **8.9+/-1.48 fl** and **2.7+/-0.88 lacs** in patients of acute coronary syndromes.

- MPV and Platelet counts were high in Hypertensives and diabetics but was not statistically significant as compared to Non-hypertensives and non diabetics, which shows that MPV is an independent risk factor.

- Platelet counts in patients of Acute Coronary Syndromes was higher in males as compared to that of females which was **statistically significant.**

- The platelet count was higher in patients aged < 64 years as compared to patients who are > 65 years which was **statistically significant.**

Keywords

Acute coronary syndromes, Mean platelet volume, STEMI, NSTEMI, Unstable angina.

CONTENTS

LIST OF TABLES

LIST OF GRAPHS

LIST OF FIGURES

INTRODUCTION

Acute coronary syndromes (ACS) encompass a spectrum of coronary artery disease, from unstable angina to transmural myocardial infarction.[1] Consensus guidelines on a universal definition of myocardial infarction have been issued recently by the International Federation of Clinical Biochemistry, European Society of Cardiology, the American College of Cardiology, and the American Heart Association and the World Heart Federation that recommend cardiac troponin I and cardiac troponin T (cTnT) measurements as the preferred biochemical cardiac biomarkers for diagnosing ACS[2].

Despite the developments regarding its diagnosis and treatment in recent years, acute coronary syndromes (ACS) keep its place of the most important reason of morbidity and mortality. Cardiac diseases have been known to be the number one cause of deaths since the beginning of twentieth century[3]. It has been observed that known cardiovascular risk factors such as smoking, diabetes mellitus, obesity and hypertension are associated with MPV[4][5]. Hence, MPV has a potential as a marker of platelet activation and may represent a risk factor for MI, dependent or independent of other cardiovascular risk factors.

The reasons for increased platelet size are not fully understood. It is possible that changes in the secretion and metabolism of biologically active substances during aging, increasing body fat, diabetic changes in metabolism, high blood pressure, exposure to tobacco-derived toxins and an acute coronary event, all may stimulate the bone marrow to produce large platelets[4]. Indeed, a recent study has shown that an increased fraction of immature platelets was associated with diabetes, active smoking and acute coronary syndromes, especially in patients with ST-segment elevation MI, suggesting an increased platelet turnover and perhaps an abnormal bone marrow stimulation [6].

A recent genome-wide association study has identified three polymorphisms in three different candidate genes that could modify the process of platelet formation and each is strongly associated with MPV [7]. Even if these three polymorphisms combined account for only 4–5% of the variation in MPV, it is reasonable to assume that genetic changes in MPV levels could contribute to risk of MI.

However, aspirin or similar drugs containing acetylsalicylic acid, which was used in a proportion of the included participants, did not modify the observed association between MPV and risk of MI. The effect of acetylsalicylic acid on MPV is not clarified, but the absence of an effect of interaction between MPV and anti-platelet therapy on the risk of MI in the present study indirectly suggests little if any effect of anti-platelet therapy on MPV, which is in accordance with previous findings(8)(9).

Platelets are heterogeneous in size, density, and activity (10). Alterations of these parameters may be associated with pulling the trigger of acute coronary syndrome and its spread (11). Large platelets are more adhesive and tend to aggregate more than smaller ones (12). Increase of platelet volume may contribute to increased pro-thrombotic tendency of atherosclerotic plaque in acute coronary syndrome and increased risk of intracoronary thrombus formation in AMI cases(13).

Patients with serious hepatic and renal disease, those previously detected to have malignancy, and subjects receiving an anticoagulant, anti-inflammatory or antiplatelet therapy were not included to the study. Since the fact that acetyl salicylic acid had no influence on platelet volume as revealed by earlier studies, ACS and stable AP patients receiving acetyl salicylic acid were not excluded from the study[14]. Platelets were heterogeneous cells in terms of size, density, and activity [10]. Platelet volume is an important indicator for platelet function and activation [15]. Larger platelets contain more secretory granules and mitochondria and are known to be more active than small platelets [16][17].

Activated platelets play an important role in the pathogenesis of coronary artery disease. The central mechanism is the formation of a platelet fibrin plug at the site of a ruptured atherosclerotic plaque, potentially leading to myocardial infarction.[55]Platelet count, mean platelet volume, a simple and reliable indicator of platelet size that correlates with platelet activation might be an emerging cardiovascular risk marker and potentially helpful in stratifying cardiovascular risk. Studying the correlation may help us to understand better and reduce the chance of myocardial infarction in the apparently healthy subjects.[19,20]

OBJECTIVES

Objectives of this study are:

To study mean platelet volume and platelet count as an independent risk factor in acute coronary syndromes.

REVIEW OF LITERATURE

Definition

Acute coronary syndromes refers to any group of clinical symptoms compatible with acute myocardial ischaemia and covers the spectrum of clinical conditions ranging from unstable angina (UA) to non ST segment elevation myocardial infarction (NSTEMI) to ST segment elevation myocardial infarction (STEMI).

Historical perspectives

Cardiovascular disease (CVD) is now the most common cause of death worldwide. Before 1900, infectious diseases and malnutrition were the leading causes and CVD was responsible for less than 10% of all deaths. Today, CVD constitutes for approximately 30% of deaths worldwide, including nearly 40% in high-income countries and about 28% in low- and middle-income countries.

Infants and childhood mortality rates have also declined, but deaths due to CVD increased to between 10% and 35% of all deaths. Rheumatic valvular disease, coronary heart disease, hypertension, and stroke are the predominant forms of CVD. Almost 40% of the world's population is currently in this stage.

The Age of Pestilence and Famine (before 1900):

At the end of the 1800s, the U.S. economy was still largely agrarian, with more than 60% of them being rural population. By 1900, average life expectancy had increased to about 50 years. However, tuberculosis, pneumonia, and other infectious diseases still constituted for more deaths than most other causes. CVD constituted for less than 10% of all deaths.

The Age of Receding Pandemics (1900–1930):

The shift of continuous population from a rural, agriculture-based economy to an urban, industrial economy had a number of consequences on risk behaviors and factors for CVD. Owing to a lack of refrigerated transport from farms to urban centers, usage of fresh fruits and vegetables declined and consumption of meat and grains increased, resulting in diets that were higher in animal fat and processed carbohydrates. In addition, the availability of factory made cigarettes has caused tobacco more accessible and affordable for the mass population. Age-adjusted CVD mortality rates increased from 300/100,000 population in 1900 to approximately 390/100,000 during 1930's, driven by rapidly rising CHD rates.

The Age of Degenerative and Human-Made Diseases (1930–1965):

During this period, deaths from infectious diseases fell to fewer than 50/100,000 per year and life expectancy increased from 50 to almost 70 years. At the same time, the countries are becoming increasingly urbanized and industrialized, precipitating a number of important lifestyle changes. By 1955, 55% of adult men were smokers, 40% of total calories accounted by fat consumption approximately. Lower activity levels, high-fat diets, and increased smoking increased CVD death rates to high levels.

The Age of Delayed Degenerative Diseases (1965–2000):

Substantial declines in age-adjusted CVD mortality rates began in the mid-1960s. In the 1970's and 1980's, age-adjusted CHD mortality rates fell down approximately 2% / year and stroke rates fell 3% / year. A main characteristic of this phase is the steadily rising age at which a first CVD event occurs. Two significant advances have been credited with the decline in CVD mortality rates: new therapeutic approaches and the implementation of prevention measures. Treatments once considered advanced, such as angioplasty, bypass surgery, and implantation of defibrillators, are now considered the standard of care. Treatments for hypertension and elevated cholesterol also contributed significantly to reducing deaths from CVD.

The decline in the age-adjusted CVD death rate of 3% per year through the 1970s and 1980s tapered off in the 1990s to 2%. However, CVD death rates declined by 3–5% per year during the first decade of the new millennium. In 2000, the age-adjusted CVD death rate was 341 per 100,000. By 2006, it had fallen to 263 per 100,000 in the U.S. population. On the one hand, the well-recognized increase in the prevalence of diabetes and obesity, a slowing in the rate of decline of smoking, and a leveling off in the rate of detection and treatment for hypertension are in the negative column. On the other hand, cholesterol levels continue to decline in the face of increased statin use along with the widespread use of aspirin have also contributed significantly to reducing deaths from CVD.

An epidemiologic transition much like that which occurred in the United States is occurring throughout the world, but unique regional features have modified aspects of the transition in various parts of the world.

High-Income Countries:

Approximately 940 million people live in high-income countries, where CHD is the dominant form of CVD, with rates that tend to be twofold to fivefold higher than stroke rates. The rates of CVD in Canada, New Zealand, Australia, and Western

Europe tend to be similar to those in the United States; however, among the countries of Western Europe, the absolute rates vary threefold with a clear north/south gradient.

The highest CVD death rates are in the northern countries, such as Finland, Ireland, and Scotland, and so are the lowest rates seen in the Mediterranean countries of France, Spain, and Italy.

Low- and Middle-Income Countries:

The World Bank groups the low and middle-income countries (gross national income per capita less than US $9200) into six geographic regions: East Asia and the Pacific, (Eastern) Europe and Central Asia, Latin America and the Caribbean, Middle East and North Africa, South Asia, and Sub-Saharan Africa. Although communicable diseases continue to be a major cause of death, CVD has emerged as a significant health concern in low- and middle-income countries. In most, an urban/rural gradient has emerged for CHD, stroke, and hypertension, with higher rates in urban centers.

Although CVD rates are rapidly rising, there are vast differences among the regions and countries and even within individual countries. Many factors contribute to this heterogeneity. First, the regions are in various stages of the epidemiologic transition. Second, vast differences in lifestyle and behavioral risk factors exist. Third, racial and ethnic differences may lead to altered susceptibilities to various forms of CVD. In addition, it should be noted that for most countries in these regions, accurate countrywide data on cause-specific mortality are not complete, as death certificate completion is not routine and most of those countries do not have a centralized registry for deaths (Figure below).

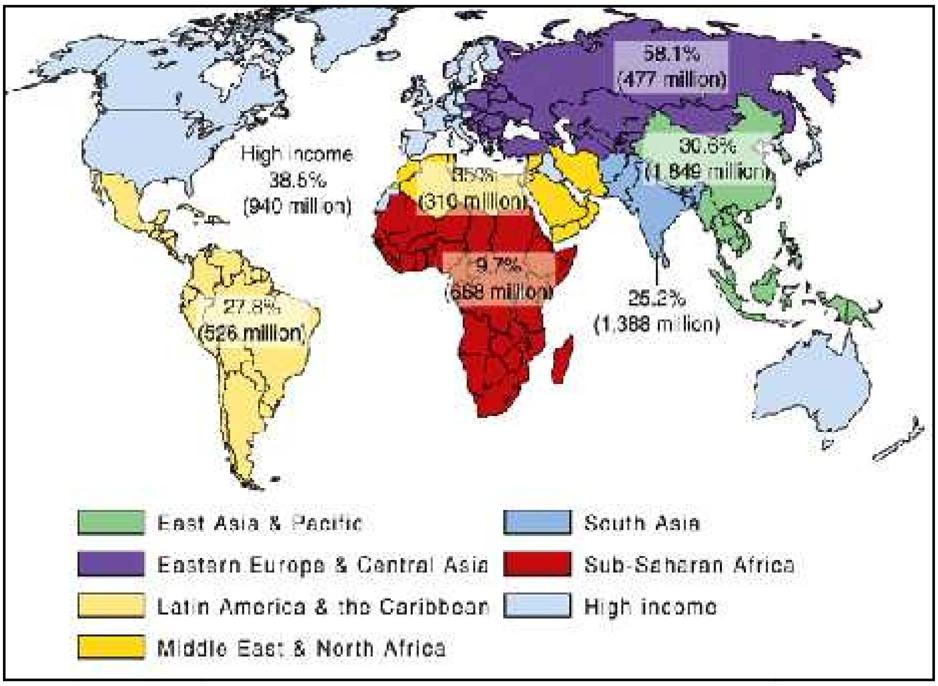


Figure 1. Cardio vascular deaths as a percentage of total deaths and total population in seven economic regions of the world defined by the World Bank(21).

Global Trends in Cardiovascular Disease:

In 1990, CVD accounted for 28% of the world's 50.4 million deaths and 9.7% of the 1.4 billion lost disability-adjusted life years (DALYs), and by 2001, CVD was responsible for 29% of all deaths and 14% of the 1.5 billion lost DALYs. By 2030, when the population is expected to reach 8.2 billion, 33% of all deaths will be the result of CVD (**Table A)**. Of these, 14.9% of deaths in men and 13.1% of deaths in women will be due to CHD. Stroke will be responsible for 10.4% of all male deaths and 11.8% of all female deaths.

According to OASIS registry, Indian patients are 7 to 8 years younger than western patients with mean age of 57 years as against 65 years in western population. Also, our patients are more often diabetic. A large registry- CREATE registry was done in 2008, involving 20,000 patients admitted in multiple centres in India. 33%

percent of these patients were less than 50 years of age. Patients of NSTEMI/STEMI reached hospital later as compared to the western patients. In young patients coming from poorer socio-economic strata, smoking was the risk factor in 50% of the patients. In older individuals from rich areas, diabetes and hypertension were more important risk factors. The mortality rate of NSTEMI in CREATE registry was 4% which is 1% more than in western registries(21).

Regional Trends in Risk Factors:

The global variation in CVD rates is related to temporal and regional variations in known risk behaviors and factors. Ecological analyses of major CVD risk factors and mortality demonstrate high correlations between expected and observed mortality rates for the three main risk factors—smoking, serum cholesterol, and hypertension—and suggest that many of the regional variations are based on differences in conventional risk factors(18).

Table A. Estimated Morbidity Related to Heart Disease: 2010-2030

Deaths	**By 2010**	**By 2030**
CVD deaths: annual number of all deaths	18.1 million	24.2 million
CVD deaths: percentage of all deaths	30.8%	32.5%
CHD deaths: percentage of all male deaths	13.1%	14.9%
CHD deaths: percentage of all female deaths	13.6%	13.1%
Stroke deaths: percentage of all male deaths	9.2%	10.4%
Stroke deaths: percentage of all female deaths	11.5%	11.8%

Behavioral Risk Factors:

1) **Tobacco→**

Every year, more than 5.5 trillion cigarettes are produced, enough to provide every person on the planet with 1,000 cigarettes. Worldwide, 1.3 billion people smoked in 2003, a number that is projected to increase to 1.6 billion by 2030. Tobacco currently causes about 5 million deaths—9% of all deaths—annually. Approximately 1.6 million are CVD-related. If current smoking patterns continue, by 2030 the global burden of disease attributable to tobacco will reach 10 million deaths annually. A unique feature of the low- and middle-income countries is easy access to smoking during the early stages of the epidemiologic transition due to the availability of relatively inexpensive tobacco products. In South Asia, the prominence of locally produced forms of tobacco other than manufactured cigarettes makes control of consumption more challenging.

2) **Diet→**

Total caloric intake per capita increases as countries develop. With regard to cardiovascular disease, a key element of dietary change is an increase in intake of saturated animal fats and hydrogenated vegetable fats, which contain atherogenic trans-fatty acids, along with a decrease in intake of plant-based foods and an increase in simple carbohydrates. Fat contributes less than 20% of calories in rural China and India, less than 30% in Japan, and well above 30% in the United States. Caloric contributions from fat appear to be falling in the high-income countries. In the United States, between 1971 and 2000, the percentage of calories derived from saturated fat decreased from 13% to 11%.

3) Physical Inactivity→

The increased mechanization that accompanies the economic transition leads to a shift from physically demanding agriculture-based work to largely sedentary industry- and office-based work. In the United States, approximately one-quarter of the population does not participate in any leisure-time physical activity and only 22% report engaging in sustained physical activity for at least 30 minutes on 5 or more days per week (the current recommendation). In contrast, in countries such as China, physical activity is still integral to everyday life. Approximately 90% of the urban population walks or rides a bicycle to work, shopping, or school daily.

Metabolic Risk Factors:

1) Lipid Levels→

Worldwide, high cholesterol levels are estimated to cause 56% of ischemic heart disease and 18% of strokes, amounting to 4.4 million deaths annually. As countries move through the epidemiologic transition, mean population plasma cholesterol levels tend to rise. Social and individual changes that accompany urbanization clearly play a role because plasma cholesterol levels tend to be higher among urban residents than among rural residents. This shift is driven largely by greater consumption of dietary fats—primarily from animal products and processed vegetable oils—and decreased physical activity. In the high-income countries, in general, mean population cholesterol levels are falling, whereas wide variation is seen in the low- and middle-income countries.

2) Hypertension→

Elevated blood pressure is an early indicator of the epidemiologic transition. Worldwide, approximately 62% of strokes and 49% of cases of ischemic heart disease are attributable to suboptimal (>115 mmHg systolic) blood pressure, which is believed to account for more than 7 million deaths annually. Remarkably, nearly half of this burden occurs among those with systolic blood pressure <140 mmHg, even as this level is used at the arbitrary threshold for defining hypertension in many national guidelines. Rising mean population blood pressure is apparent as populations industrialize and move from rural to urban settings. Among urban-dwelling men and women in India, for example, the prevalence of hypertension is 25.5% and 29.0%, respectively, whereas it is 14.0% and 10.8%, respectively, in rural communities. One major concern in low- and middle-income countries is the high rate of undetected, and therefore untreated, hypertension. This may explain, at least in part, the higher stroke rates in these countries in relation to CHD rates during the early stages of the transition. The high rates of hypertension, especially undiagnosed hypertension, throughout Asia probably contribute to the high prevalence of hemorrhagic stroke in the region.

3) Obesity→

Although clearly associated with increased risk of CHD, much of the risk posed by obesity may be mediated by other CVD risk factors, including hypertension, diabetes mellitus, and lipid profile imbalances. In the mid-1980s, the World Health Organization's MONICA Project sampled 48 populations for cardiovascular risk factors. In all but one male population (China) and in most of the female populations, between 50% and 75% of adults age 35–64 years were overweight or obese. In addition, the prevalence of extreme obesity (BMI >40 kg/m^2) more than tripled, increasing from 1.3% to 4.9%. In many of the low- and middle-income countries, obesity appears to coexist with under nutrition and malnutrition. Obesity is increasing throughout the world, particularly in developing countries, where the trajectories are steeper than those experienced in the developed countries. According to the latest World Health Organization (WHO) data, this is equivalent to about 1.3 billion overweight adults in the world. A survey undertaken in 1998 found that as many as 58% of African women living in South Africa might have been overweight or obese.

Diabetes Mellitus→

As a consequence of, or in addition to, increasing body mass index and decreasing levels of physical activity, worldwide rates of diabetes—predominantly Type 2 diabetes—are on the rise. In 2003, 194 million adults, or 5% of the world's population, had diabetes. By 2025, this number is predicted to increase 72 percent to 333 million. By 2025, the number of people with Type 2 diabetes is projected to double in three of the six low- and middle-income regions: Middle East and North Africa, South Asia, and Sub-Saharan Africa. There appear to be clear genetic susceptibilities to diabetes mellitus in various racial and ethnic groups. For example, migration studies suggest that South Asians and Indians tend to be at higher risk than are people of European ancestry[21][22][23].

Pathogenesis of atherosclerosis:

An integrated view of experimental results in animals and studies of human atherosclerosis suggests that the "fatty streak" represents the initial lesion of atherosclerosis. These early lesions most often seem to arise from focal increases in the content of lipoproteins within regions of the intima. This accumulation of lipoprotein particles may not result simply from increased permeability, or "leakiness," of the overlying endothelium. Rather, the lipoproteins may collect in the intima of arteries because they bind to constituents of the extracellular matrix, increasing the residence time of the lipid-rich particles within the arterial wall. Lipoproteins that accumulate in the extracellular space of the intima of arteries often associate with glycosaminoglycans of the arterial extracellular matrix, an interaction that may slow the egress of these lipid-rich particles from the intima.

Lipoprotein particles in the extracellular space of the intima, particularly those retained by binding to matrix macromolecules, may undergo oxidative modifications. Considerable evidence supports a pathogenic role for products of oxidized lipoproteins in atherogenesis. Lipoproteins sequestered from plasma antioxidants in the extracellular space of the intima become particularly susceptible to oxidative modification, giving rise to hydroperoxides, lysophospholipids, oxysterols, and aldehydic breakdown products of fatty acids and phospholipids. Modifications of the apoprotein moieties may include breaks in the peptide backbone as well as derivatization of certain amino acid residues. Local production of hypochlorous acid by myeloperoxidase associated with inflammatory cells within the plaque yields chlorinated species such as chlorotyrosyl moieties. High-density lipoprotein (HDL) particles modified by HOCl-mediated chlorination function poorly as cholesterol acceptors, a finding that links oxidative stress with impaired reverse cholesterol transport, which is one likely mechanism of the antiatherogenic action of HDL. Considerable evidence supports the presence of such oxidation products in atherosclerotic lesions. A particular member of the phospholipase family, lipoprotein-associated phospholipase A_2 (LpPL A_2), can generate proinflammatory lipids, including lysophosphatidyl choline-bearing oxidized lipid moieties from oxidized phospholipids found in oxidized low-density lipoproteins (LDLs). An inhibitor of this enzyme is in clinical development.

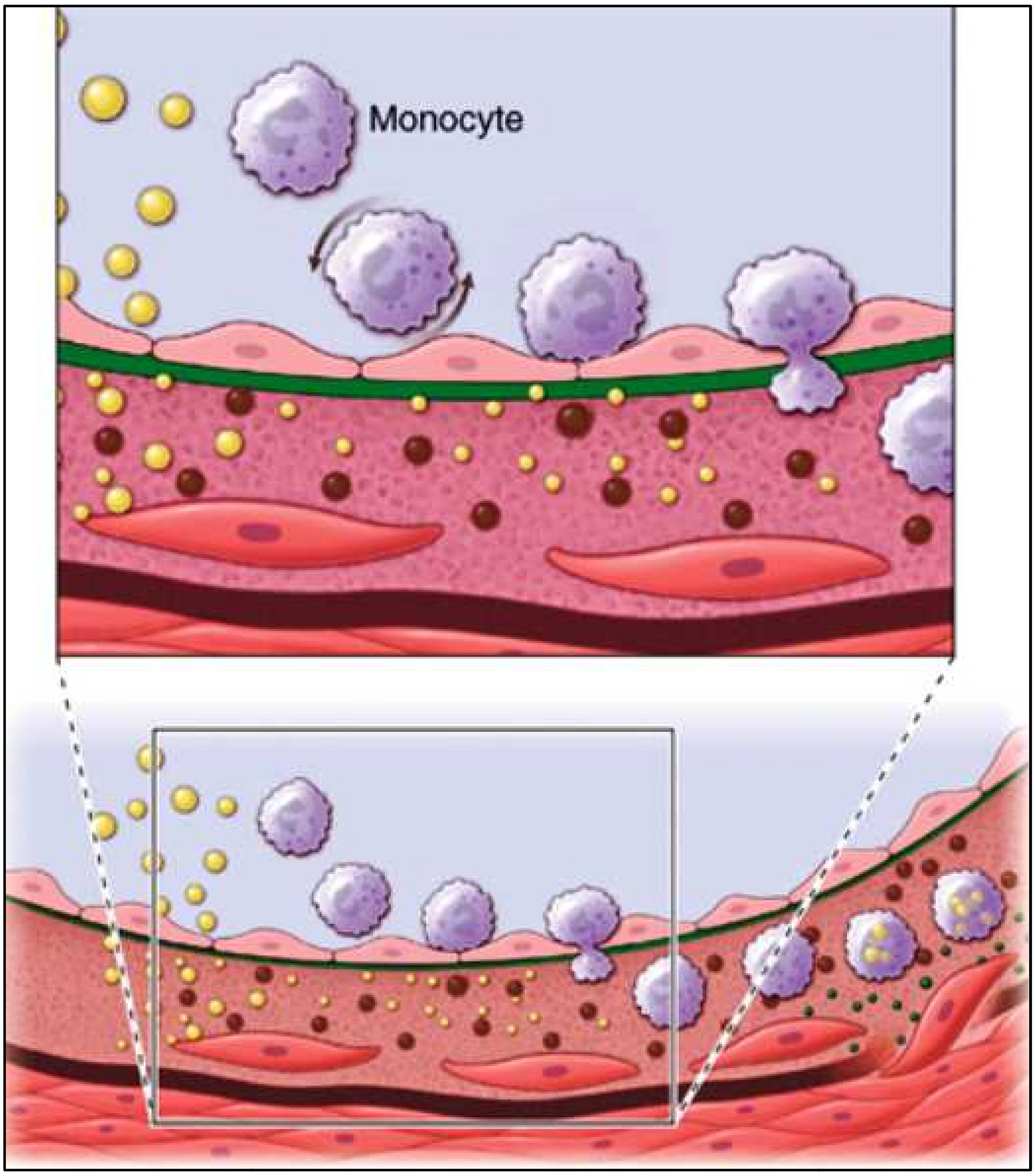


Figure-2: Figure showing an artery depicting steps in development of an atheroma.

Leukocyte Recruitment:

Accumulation of leukocytes characterizes the formation of early atherosclerotic lesions. Thus, from its very inception, atherogenesis involves elements of inflammation, a process that now provides a unifying theme in the pathogenesis of this disease. The inflammatory cell types typically found in the evolving atheroma include monocyte-derived macrophages and lymphocytes. A number of adhesion molecules or receptors for leukocytes expressed on the surface of the arterial endothelial cell probably participate in the recruitment of leukocytes to the nascent atheroma. Constituents of oxidatively modified low-density lipoprotein can augment the expression of leukocyte adhesion molecules. This example illustrates how the accumulation of lipoproteins in the arterial intima may link mechanistically with leukocyte recruitment, a key event in lesion formation.

Laminar shear forces such as those encountered in most regions of normal arteries also can suppress the expression of leukocyte adhesion molecules. Sites of predilection for atherosclerotic lesions (e.g., branch points) often have disturbed flow. Ordered, pulsatile laminar shear of normal blood flow augments the production of nitric oxide by endothelial cells. This molecule, in addition to its vasodilator properties, can act at the low levels constitutively produced by arterial endothelium as a local anti-inflammatory autacoid, e.g., limiting local adhesion molecule expression. Exposure of endothelial cells to laminar shear stress increases the transcription of Krüppel-like factor 2 (KLF2) and reduces the expression of a thioredoxin-interacting protein (Txnip) that inhibits the activity of the endogenous antioxidant thioredoxin. KLF2 augments the activity of endothelial nitric oxide synthase, and reduced Txnip levels boost the function of thioredoxin. Laminar shear stress also stimulates endothelial cells to produce superoxide dismutase, an antioxidant enzyme. These examples indicate how hemodynamic forces may influence the cellular events that underlie atherosclerotic lesion initiation and potentially explain the favored localization of atherosclerotic lesions at sites that experience disturbance to laminar shear stress.

Once captured on the surface of the arterial endothelial cell by adhesion receptors, the monocytes and lymphocytes penetrate the endothelial layer and take up residence in the intima. In addition to products of modified lipoproteins, cytokines (protein mediators of inflammation) can regulate the expression of adhesion molecules involved in leukocyte recruitment. For example, interleukin 1 (IL-1) or tumor necrosis factor (TNF-) induce or augment the expression of leukocyte adhesion molecules on endothelial cells. Because products of lipoprotein oxidation can induce cytokine release from vascular wall cells, this pathway may provide an additional link between arterial accumulation of lipoproteins and leukocyte recruitment. Chemoattractant cytokines such as monocyte chemoattractant protein 1 appear to direct the migration of leukocytes into the arterial wall.

Foam-Cell Formation:

Once resident within the intima, the mononuclear phagocytes mature into macrophages and become lipid-laden foam cells, a conversion that requires the uptake of lipoprotein particles by receptor-mediated endocytosis. One might suppose that the well-recognized "classic" receptor for LDL mediates this lipid uptake; however, humans or animals lacking effective LDL receptors due to genetic alterations (e.g., familial hypercholesterolemia) have abundant arterial lesions and extraarterial xanthomata rich in macrophage-derived foam cells. In addition, the exogenous cholesterol suppresses expression of the LDL receptor; thus, the level of this cell-surface receptor for LDL decreases under conditions of cholesterol excess. Candidates for alternative receptors that can mediate lipid loading of foam cells include a growing number of macrophage "scavenger" receptors, which preferentially endocytose modified lipoproteins, and other receptors for oxidized LDL or very low-density lipoprotein (VLDL). Monocyte attachment to the endothelium, migration into the intima, and maturation to form lipid-laden macrophages thus represent key steps in the formation of the fatty streak, the precursor of fully formed atherosclerotic plaques[(24)].

Unstable Angina:

UA is defined as angina pectoris or equivalent ischemic discomfort with at least one of three features: (1) it occurs at rest (or with minimal exertion), usually lasting >10 minutes; (2) it is severe and of new onset (i.e., within the prior 4–6 weeks); and/or (3) it occurs with a crescendo pattern (i.e., distinctly more severe, prolonged, or frequent than previously). The diagnosis of NSTEMI is established if a patient with the clinical features of UA develops evidence of myocardial necrosis, as reflected in elevated cardiac biomarkers[(24)].

Pathophysiology of UA/NSTEMI:

UA/NSTEMI is most commonly caused by a reduction in oxygen supply and/or by an increase in myocardial oxygen demand superimposed on a lesion that causes coronary arterial obstruction, usually an athero-thrombotic coronary plaque. Four pathophysiologic processes that may contribute to the development of UA/NSTEMI have been identified:

1. plaque rupture or erosion with a superimposed nonocclusive thrombus, believed to be the most common cause; in such patients, NSTEMI may occur with downstream embolization of platelet aggregates and/or atherosclerotic debris;
2. dynamic obstruction, e.g., coronary spasm, as in Prinzmetal's variant angina (PVA);
3. progressive mechanical obstruction [e.g., rapidly advancing coronary atherosclerosis or restenosis following percutaneous coronary intervention (PCI); and
4. UA secondary to increased myocardial oxygen demand and/or decreased supply (e.g., tachycardia, anemia). More than one of these processes may be involved.

Among patients with UA/NSTEMI studied at angiography, approximately 5% have stenosis of the left main coronary artery, 15% have three-vessel CAD, 30% have two-vessel disease, 40% have single-vessel disease, and 10% have no apparent critical epicardial coronary artery stenosis; some of the latter may have obstruction of the coronary microcirculation. The "culprit lesion" may show an eccentric stenosis with scalloped or overhanging edges and a narrow neck on angiography. Angioscopy has been reported to show "white" (platelet-rich) thrombi, as opposed to "red" (fibrin- and cell-rich) thrombi; the latter are more often seen in patients with acute STEMI. Patients with UA/NSTEMI frequently have multiple plaques at risk of disruption (vulnerable plaques)[24].

Pathophysiology of STEMI: (Role of acute plaque rupture)

STEMI usually occurs when coronary blood flow decreases abruptly after a thrombotic occlusion of a coronary artery previously affected by atherosclerosis. Slowly developing, high-grade coronary artery stenoses do not typically precipitate STEMI because of the development of a rich collateral network over time. Instead, STEMI occurs when a coronary artery thrombus develops rapidly at a site of vascular injury. This injury is produced or facilitated by factors such as cigarette smoking, hypertension, and lipid accumulation. In most cases, STEMI occurs when the surface of an atherosclerotic plaque becomes disrupted (exposing its contents to the blood) and conditions (local or systemic) favor thrombogenesis.

A mural thrombus forms at the site of plaque disruption, and the involved coronary artery becomes occluded. Histologic studies indicate that the coronary plaques prone to disruption are those with a rich lipid core and a thin fibrous cap. After an initial platelet monolayer forms at the site of the disrupted plaque, various agonists (collagen, ADP, epinephrine, serotonin) promote platelet activation. After agonist stimulation of platelets, thromboxane A_2 (a potent local vasoconstrictor) is released, further platelet activation occurs, and potential resistance to fibrinolysis develops [(24)].

In addition to the generation of thromboxane A_2, activation of platelets by agonists promotes a conformational change in the glycoprotein IIb/IIIa receptor. Once converted to its functional state, this receptor develops a high affinity for soluble adhesive proteins (i.e., integrins) such as fibrinogen. Since fibrinogen is a multivalent molecule, it can bind to two different platelets simultaneously, resulting in platelet cross-linking and aggregation.

The coagulation cascade is activated on exposure of tissue factor in damaged endothelial cells at the site of the disrupted plaque. Factors VII and X are activated, ultimately leading to the conversion of prothrombin to thrombin, which then converts fibrinogen to fibrin. Fluid-phase and clot-bound thrombin participate in an auto amplification reaction leading to further activation of the coagulation cascade. The culprit coronary artery eventually becomes occluded by a thrombus containing platelet aggregates and fibrin strands [(17)].

In some cases, STEMI may be rarely due to coronary artery occlusion caused by coronary emboli, congenital anomalies, coronary vasospasm, and a wide variety of systemic diseases —particularly inflammatory. The amount of myocardial damage caused by coronary occlusion depends on:

1. The territory that is supplied by the affected vessel,
2. Whether the vessel is totally occluded or not,
3. The time duration of coronary spasm/occlusion,
4. The amount of blood supplied to the affected myocardium by collateral vessels,
5. The demand of the myocardium whose blood supply has been suddenly limited for the oxygen supply,
6. Endogenous factors that counteract fast or spontaneous lysis of the occluded thrombus, and
7. The adequacy of myocardial perfusion in the infarcted zone when flow is restored in the occluded epicardial coronary artery[(24)(5)].

Patients at increased risk for developing STEMI are those with multiple risk factors and those with unstable angina. Less commonly the medical conditions underlying predispose patients to STEMI, which include hypercoagulable states, collagen vascular disease, cocaine abuse and intracardiac thrombi or masses that can produce coronary emboli.

There are major advances in the management of STEMI with recognition of the "chain of survival" involves a highly integrated system starting with prehospital care and extending to early hospital management so as to provide expeditious implementation of a reperfusion strategy[24].

Diagnosis:

Laboratory Findings:

Myocardial infarction (MI) progresses through the following temporal stages:

1. Acute (first few hours to7 days),
2. Healing (7–28 days), and
3. Healed (29 days). When evaluating the results of diagnostic tests for stemi, the temporal phase of the infarction must be considered.

The laboratory tests of value in confirming the diagnosis may be divided into four groups:

1. ECG,
2. serum cardiac biomarkers,
3. cardiac imaging, and
4. nonspecific indices of tissue necrosis and inflammation.

1) Electrocardiogram

During the initial stages, total occlusion of an epicardial coronary artery will produce ST-segment elevation and finally patients lands up in presenting with ST-segment elevation and evolved Q waves on the ECG. However, Q waves in the leads overlying the infarct zone may vary in magnitude/ amplitude and even appear only transiently, depending on the reperfusion status of the ischemic myocardium and restoration of trans-membrane potentials over time. A small percentage of patients who are presenting with ST-segment elevation will not develop Q waves when the obstructing thrombus is not totally occlusive or obstruction is transient or if a rich collaterals networks are present. Among patients presenting with ischemic discomfort but *without* ST-segment elevation, if serum cardiac biomarkers of necrosis are elevated, then diagnosis of NSTEMI is made ultimately. A minority of patients who present initially without ST-segment elevation may develop a Q-wave MI. Previously, it was thought that trans-mural MI is present if the ECG shows Q waves or poor progression of R waves and non trans-mural MI may be present if the ECG shows only transient ST-segment and T-wave changes. However, electrocardiographic-pathologic correlations are far pratically and terms such as *Q-wave MI*, *non-Q-wave MI*, *trans-mural MI*, and *non trans-mural MI*, have been replaced by STEMI and NSTEMI. Contemporary studies using MRI have suggested that the development of a Q wave on the ECG is more dependent on the volume of infarct tissue rather than the trans-mural infarction [(24)].

2) Serum Cardiac Biomarkers:

Certain serum proteins, also called serum cardiac biomarkers are released from necrosed cardiac tissue/muscle after STEMI/ NSTEMI. The rate of liberation of specific proteins differs depending on their intracellular location, their molecular weight, local perfusion and lymphatic flow. Cardiac biomarkers become detectable in the peripheral blood only when the threshold of the cardiac lymphatics to clear the interstitium of the infarct zone is exceeded and spill over into the venous circulation occurs. The temporal pattern of cardiac enzyme release is of diagnostic importance, but contemporary urgent reperfusion strategies necessitate in making a decision (based largely on a combination of clinical and ECG findings) before the results of cardiac enzymes have returned from the laboratory. Rapid whole-blood bedside assays for serum cardiac markers are now available and may facilitate management decisions, particularly in patients with nondiagnostic ECGs.

Cardiac-specific troponin T (cTnT) and *cardiac-specific troponin I* (cTnI) have amino-acid sequences different from those of the skeletal muscle forms of these proteins. These differences permitted the development of quantitative assays for cTnT and cTnI with highly specific monoclonal antibodies. Since cTnT and cTnI are not normally detectable in the blood of healthy individuals but may increase after STEMI to levels >20 times higher than the upper limit of normal (the highest value is seen in 99% of a reference population not suffering from MI), the measurement of cTnT or cTnI is of considerable diagnostic usefulness, and they are now the preferred biochemical markers for MI. The cardiac troponins are particularly valuable when there is clinical suspicion of either skeletal muscle injury or a small MI that may be below the detection limit for creatine phosphokinase (CK) and its MB isoenzyme (CKMB) measurements, and they are therefore, of particular value in distinguishing UA from NSTEMI. Levels of cTnI and cTnT may remain elevated for 7–10 days after STEMI.

CK rises within 4–8 hrs and generally returns to normal by 48–72 hrs. An important drawback of total CK measurement is its lack of specificity for STEMI, as CK may be elevated with skeletal muscle disease or trauma, including intramuscular injection. The MB isoenzyme of CK has the advantage over total CK that it is not present in significant concentrations in extracardiac tissue and, therefore, is considerably more specific. However, cardiac surgery, myocarditis, and electrical cardioversion often result in elevated serum levels of the MB isoenzyme. A ratio (relative index) of CKMB mass: CK activity 2.5 times suggests but is not diagnostic of a myocardial rather than a skeletal muscle source for the CKMB elevation.

Many hospitals are using cTnT or cTnI rather than CKMB as the routine serum cardiac marker for diagnosis of STEMI, although any of these analysis remain clinically acceptable. It is *not* cost-effective to measure both a cardiac-specific troponin-I or troponin-T and CKMB at all time points in every patient.

While it has long been recognized that the total quantity of protein released correlates with the size of the infarct, the peak protein concentration correlates only weakly with infarct size. Recanalization of a coronary artery occlusion (either spontaneously or by mechanical or pharmacologic means) in the early hours of STEMI causes earlier peaking of biomarker measurements because of a rapid washout from the interstitium of the infarct zone, quickly overwhelming lymphatic clearance of the proteins(24).

3) **Cardiac imaging:**

Abnormalities of wall motion on *two-dimensional echocardiography* are almost universally present. Although acute STEMI cannot be distinguished from an old myocardial scar or from acute severe ischemia by echocardiography, the ease and safety of the procedure make its use appealing as a screening tool in the Emergency Department setting. When the ECG is not diagnostic of STEMI, early detection of the presence or absence of wall motion abnormalities by echocardiography can aid in management decisions, such as whether the patient should receive reperfusion therapy [e.g., fibrinolysis or a percutaneous coronary intervention (PCI)]. Echocardiographic estimation of left ventricular (LV) function is useful prognostically; detection of reduced function serves as an indication for therapy with an inhibitor of the renin-angiotensin–aldosterone system. Echocardiography may also identify the presence of right ventricular (RV) infarction, ventricular aneurysm, pericardial effusion, and LV thrombus. In addition, Doppler echocardiography is useful in the detection and quantitation of a ventricular septal defect and mitral regurgitation, two serious complications of STEMI.

Several *radionuclide imaging techniques* are available for evaluating patients with suspected STEMI. However, these imaging modalities are used less often than echocardiography because they are more cumbersome and lack sensitivity and specificity in many clinical circumstances. Myocardial perfusion imaging with [^{201}Tl] or [^{99m}Tc]-sestamibi, which are distributed in proportion to myocardial blood flow and concentrated by viable myocardium, reveal a defect ("cold spot") in most patients during the first few hours after development of a transmural infarct. Although perfusion scanning is extremely sensitive, it cannot distinguish acute infarcts from chronic scars and, thus, is not specific for the diagnosis of *acute* MI. Radionuclide ventriculography, carried out with [^{99m}Tc]-labeled red blood cells, frequently demonstrates wall motion disorders and reduction in the ventricular ejection fraction in patients with STEMI. While of value in assessing the hemodynamic consequences of infarction and in aiding in the diagnosis of RV infarction when the RV ejection fraction is depressed, this technique is nonspecific, as many cardiac abnormalities other than MI alter the radionuclide ventriculogram.

Myocardial infarction can be detected accurately with high-resolution cardiac MRI using a technique referred to as late enhancement. A standard imaging agent (gadolinium) is administered and images are obtained after a 10-min delay. Since little gadolinium enters normal myocardium, where there are tightly packed myocytes, but does percolate into the expanded intercellular region of the infarct zone, there is a bright signal in areas of infarction that appears in stark contrast to the dark areas of normal myocardium[(24)].

4) **Nonspecific reaction**s:

The nonspecific reactions to myocardial injury is associated with polymorphonuclear leukocytosis, which appears within a few hours after the onset of pain and persists for 3–7 days; the white blood cell count often reaches levels of 12,000–15,000/L. The erythrocyte sedimentation rate rises more slowly than the white blood cell count, peaking during the first week and sometimes remaining elevated for one or two weeks.

After erosion or rupture of atherosclerotic plaques in coronary arteries, platelet activation plays a crucial role in the prothrombotic events leading to MI. Increased platelet reactivity, as well as shortened bleeding time, is associated with increased platelet volume. Large platelets that contain more dense granules are metabolically and enzymatically more active than small platelets and they have higher thrombotic potential. They also express higher levels of procoagulatory surface proteins, such as

P-selectin and glycoprotein IIIa. An increased mean platelet volume (MPV) decreases the inhibitory effectiveness of prostacyclin (PGI2) on both platelet aggregation and the release reaction[(24)].

Previous studies have revealed an association between MPV and CAD, unstable angina pectoris (USAP), and the occurrence of acute MI[(27)(31)], while Halbmayer et al. observed no such effect[(59)]. The biological and prognostic value of increased MPV is still controversial. Platelet morphology and physiology are determined during fragmentation of the megakaryocyte. Although the mechanism is still unclear, megakaryocyte ploidy correlates with megakaryocyte and platelet volume[(17)].

Previous studies have shown for diagnosis of various illnesses that increased MPV or a decrease in platelet count might be useful[(28)(29)(32)]. They can be conjunct with other conventional biochemical cardiac markers understanding etiology for patients admitted with chest pain[(19)(31)(36)]. It has also been reported that MPV measurement at admission might be valuable in the prediction of the infarct-related artery patency[(38)] and is also a useful hematological marker for early and easy identification of patients with stable CAD who are at a higher risk of post percutaneous coronary intervention low reflow[(35)].

Finally, elevated MPV and resistance to aspirin have proven to be prognostic factors, for death, MI and the composite endpoint[(37)].

These valuable tests may also have some other advantages. High MPV may show adverse prognosis and therapeutic needs[(37)(40)(41)].

G. Slavka et al. showed that increased MPV, acting as a stand-alone risk factor, was associated with a high risk in patients experiencing an acute ischemic cardiovascular event. Patients within the highest quintile of MPV had a 1.5-fold higher hazard ratio for overall vascular mortality and an up to 1.8-fold higher risk in association with ischemic heart disease compared with patients within the lowest quintile(58).

Knowledge regarding the effects of various drugs on platelet size is weak. Previous in vitro studies found no effect of aspirin on platelet size(50). However, it is known that clopidogrel significantly inhibits the ADP-induced increase in MPV in vitro(51).

The best cut-off values for MPV when predicting AMI and SCAD in patients were 9.25 fl (sensitivity 56.4%; specificity 45.9%) and 9.15 fl (sensitivity 54.2%; specificity 42.23%), respectively(46).

The clinical implications of our findings are multiple. First, a multi-marker approach to the diagnosis of AMI, combining markers reflecting different pathophysiology, has been shown to be clinically helpful. Second, we have found that signs of platelet activation seem to occur as early as 6 hours after onset of chest pain in patients with AMI. MPV had been proven to be a prognostic factor for angiographic reperfusion and 6-month mortality in patients with AMI treated with primary percutaneous intervention(45).

Vitthal Khode et al.. showed like those of previous studies, demonstrated that MPV can be predictive of AMI, though it was not significant statistically for SCAD(46).

Patients with non-alcoholic fatty liver disease is associated with higher MPV compared with control individuals[47].

There are conflicting results about the effect of aspirin on MPV. Contrary to what has been assumed, aspirin has no effect on platelet size[48].

Azab et al found that the MPV/ platelet count ratio was superior to MPV alone in predicting long term mortality after non ST segment elevation myocardial infarction[56].

We think that it is difficult to attribute risk to a particular MPV value. In a review, Gasparyan et al illustrated that while high grade inflammatory disorders(e.g; active rheumatoid arthritis and ulcerative colitis) were associated with numerous small platelets, low grade inflammatory disorders(e.g; psoriasis and behcet’s disease) were associated with large MPV[57].

J. Klovaite et al.. showed increased MPV was associated with increased risk of MI. An interaction was observed between platelet count and MPV on risk of MI. In the group of individuals with low platelet count(< 248 · 109/L), risk of MI did not increase with increasing MPV after multifactorial adjustment (P values for trend among quintiles were 0.9). However, in individuals with medium (248–302 · 109/L) and high platelet count (> 302 · 109/L), increasing MPV was associated with increased risk of MI. After multifactorial adjustment, risk of MI was 34% (1–79%; P for trend, 0.005) and 63%(3–159%; P for trend, 0.004) in the upper vs. the lower quintile in the group of individuals with medium and high platelet count, respectively[55].

To investigate a possible modification of the observed association between MPV and risk of MI by use of antiplatelet therapy, we divided individuals into groups based on use of antiplatelet therapy, and within these groups, additionally, into tertiles of MPV. Increased risk of MI as a function of increased MPV was observed in both those with and without antiplatelet therapy; there was no evidence of an effect of interaction between antiplatelet therapy and MPV on risk of MI(55)(32)(34).

A recent genome-wide association study has identified three polymorphisms in three different candidate genes that could modify the process of platelet formation and each is strongly associated with MPV. Even if these three polymorphisms combined account for only 4–5% of the variation in MPV, it is reasonable to assume that genetic changes in MPV levels could contribute to risk of MI(7)(33).

However, aspirin or similar drugs containing acetylsalicylic acid, which was used in a proportion of the included participants, did not modify the observed association between MPV and risk of MI. The effect of acetylsalicylic acid on MPV is not clarified, but the absence of an effect of interaction between MPV and antiplatelet therapy on the risk of MI in the present study indirectly suggests little if any effect of antiplatelet therapy on MPV, which is in accordance with previous findings(8)(9).

Endler et al., in their study where they compared AMI patients to those with stable AP, found MPV to be increased. They also suggested that increased MPV was an indicator for larger and more active platelets and an independent risk factor for MI in coronary artery disease(27).

Kishk et al. compared AMI patients to stable angina pectoris and control groups and detected that the former group had lower platelet count and higher MPV.

They suggested that it was independent of smoking, area or diameter of infarct. They also claimed that increased MPV and decreased platelet count may be a major risk factor for AMI. In consistent with these findings, we found in our study that MPV was significantly higher and platelet count was lower in AMI group, compared to stable angina pectoris and control groups(14).

In the study consisting of 518 chronic hemodialysis patients with concurrent coronary artery disease, Hening et al. concluded that high MPV might be associated with coronary heart disease in hemodialysed patients(52).

Puzzili et al. found MPV to be higher in unstable angina pectoris patients, compared to stable angina and control groups(53).

Ridvan Mercan et al. detected that platelet counts were decreased and mean platelet volumes were increased in patients presenting with acute coronary syndrome. Based on these findings, we have concluded that larger platelet volumes may constitute a high risk for acute coronary syndrome and ischemic complications(54).

For this purpose, we think that MPV measurement, which is a non-invasive and easy-to-perform method, may be an important tool for the follow-up of these patients. Nonetheless, conflicting results of other studies make this issue controversial, which warrants this study.

Evaluation

The first goal is to determine the patient's cardiac stability and provide emergency stabilization if needed. If the patient is unstable because of hypotension, ongoing ischemia/ infarction; emergency thrombolysis or PCI is warranted. If the patient is clinically stable, the history, physical examination, and diagnostic testing should focus on potential causes, triggers, and comorbid conditions. Standard tests used to evaluate cardiac function and identify common comorbid conditions include electrocardiography, troponin-I, ck-mb, complete blood count, renal function test, chest radiography, and echocardiography.

METHODOLOGY

The present study was conducted in the Department of Medicine and cardiology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi from January 2014 to December 2014.

Study design and duration

The study design was a one year cross-sectional study.

Study period

The present study was carried out from January 2014 to December 2014.

Source of Data

Patients with complaints of chest pain and equivalents suggesting acute coronary syndrome above the age of 18 years attending Department of Cardiology and Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi were studied.

Sample size

A total of 400 patients with acute coronary syndromes were included in the study.

Sampling procedure

Based on this formula a sample size of 400 patients was considered.

Sample Size Calculation: $z\alpha^2 pq/d^2$

4pq/d2

where zα–1.96(constant),

p-sensitivity(50)-as obtained from previous studies , q-(100-p),

d-absolute error (05)

p=50%, q=50%, d=05.0,

sample size= 400.,

Selection criteria:

Inclusion Criteria:

Any patients admitted to cardio ward with STEMI, NSTEMI, Unstable angina in last six days.

Exclusion Criteria:

Patients with bleeding disorders, pre-eclampsia, sepsis, recent blood transfusion, patients who have underwent recent major operation or trauma, previous myocardial infarction in 6mts.

Ethical clearance

Prior to the beginning the study was approved by the Institutional Ethics Committee, Jawaharlal Nehru Medical College, Belagavi.

Informed consent

The patients who fulfilled the selection criteria were informed about the nature of study in detail and a written informed consent was obtained (Annexure→I).

Data collection

Patients were interviewed and demographic data, history of present illness, other comorbid conditions, personal and treatment history were obtained. Further these patients underwent clinical examination followed by systemic examination. These findings were noted on a predesigned and pretested proforma (Annexure-II).

Investigations

Patients were subjected to following investigations.

- Complete blood count
- Blood urea nitrogen
- Serum creatinine
- Random blood sugar
- 12 lead ECG
- Troponin-I, CK-MB. (whenever required)

Outcome variables

Based on clinical presentation, examination and investigations, patients were evaluated for;

- Symptom profile
- Risk factors (HTN, DM-2, Smoking, tobacco, etc..)

- Clinical Examination
- Haematological variations (including Mean Platelet Volume and Platelet count, Trop-I, CK-MB.)
- ECG, 2D- ECHO whenever necessary.

Statistical methods

The data obtained was coded and entered into the Microsoft Excel Spreadsheet (Annexure III). The categorical data was expressed in terms of rates, ratios and percentages and continuous data was expressed as mean ± standard deviation.

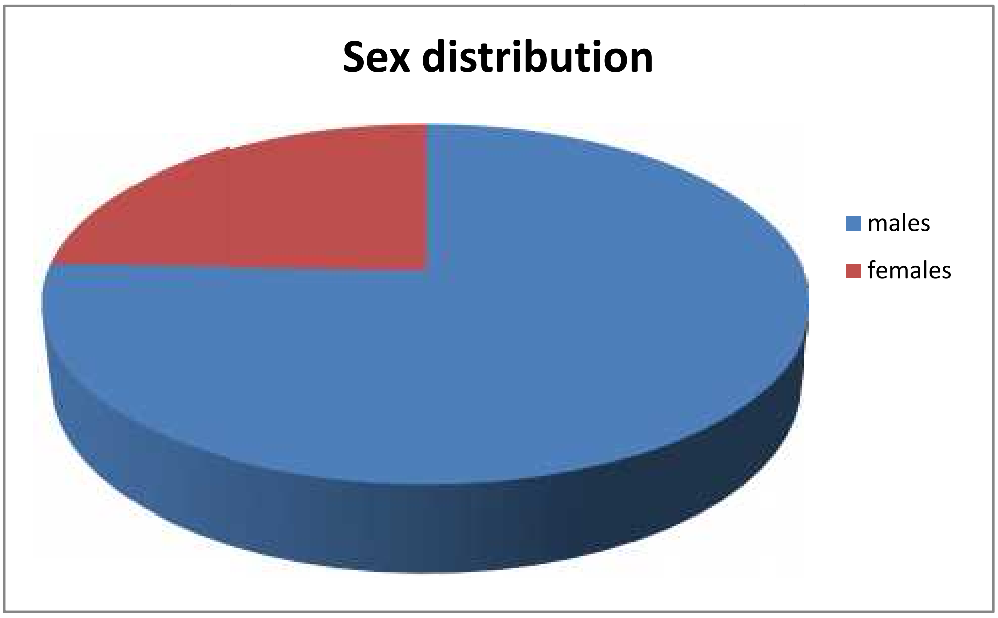
RESULTS

This one year cross-sectional study was done at Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi. A total of 400 acute coronary syndromes patients were included in the study.

The data obtained was coded and entered into the Microsoft Excel Spreadsheet (Annexure III). The data was analysed and the final results and observations were tabulated as follows:

Table 1. Sex distribution

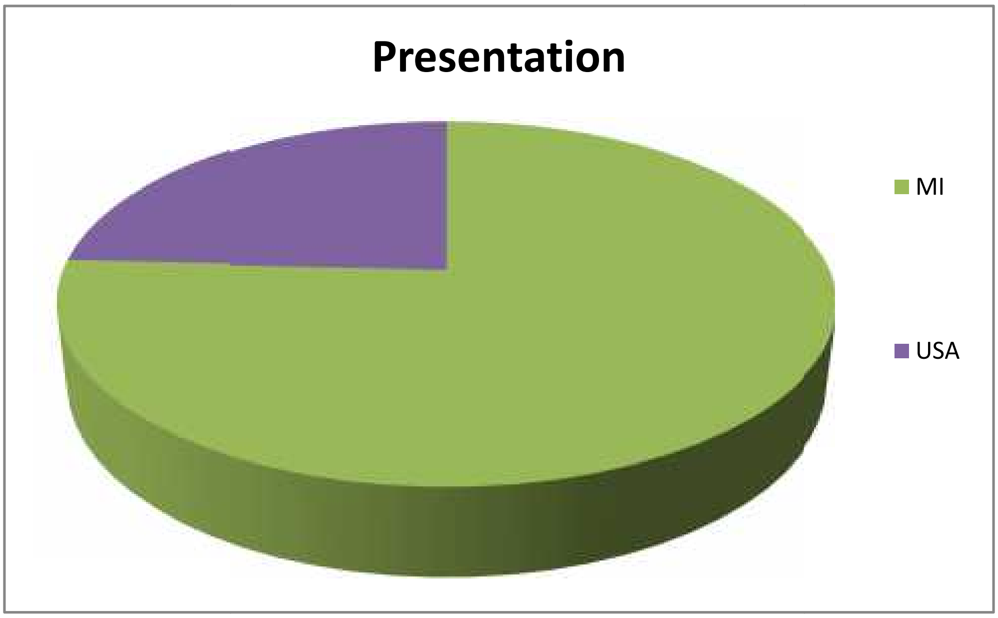
Sex	Distribution (n=400)	
	Number	Percentage
Male	302	75.50
Female	98	24.50
Total	**400**	**100.00**



In the present study majority of the patients were males (75.5%). The male to female ratio was 3.081:1.

Table 2. Presentation distribution

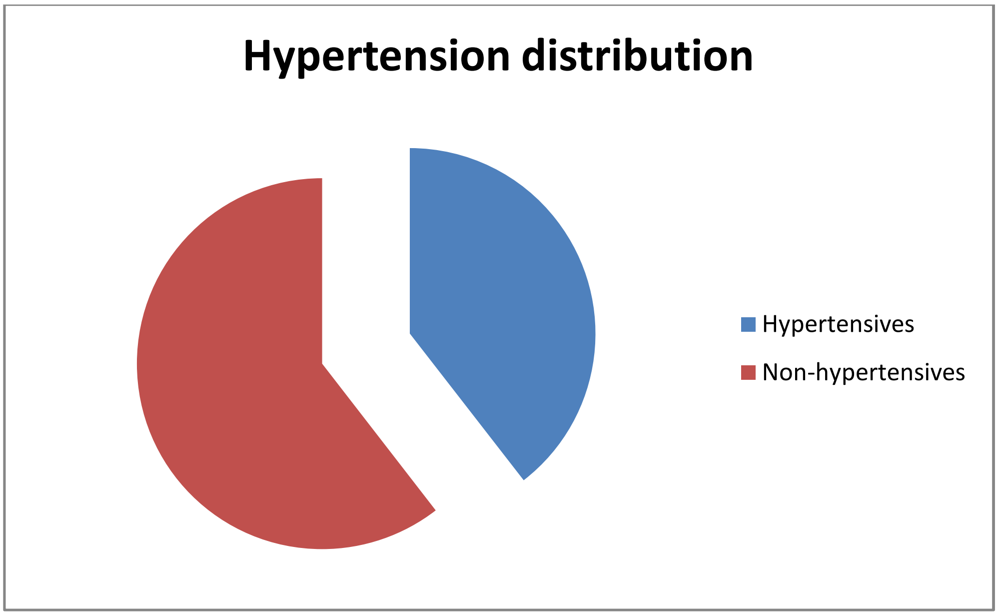
	Distribution (n=400)	
	Number	**Percentage**
Myocardial Infarction	303	75.75
Unstable Angina	97	24.25
Total	**400**	**100.00**



In the present study majority of the patients were MI patients (75.75%). The MI to USA ratio was 3.123:1.

Table 3. Hypertension distribution

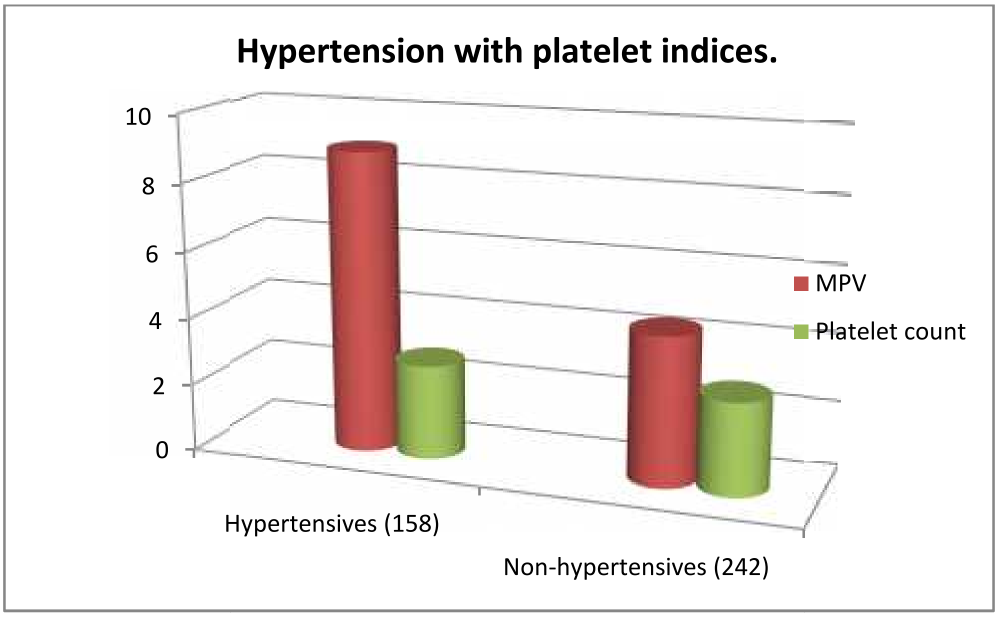
	Distribution (n=400)	
	Number	**Percentage**
Hypertensives	158	39.50
Non-Hypertensives	242	60.50
Total	**400**	**100.00**



In the present study majority of the patients were non hypertensives (60.5%). Hypertensives to non hypertensives ratio was 1.53:1.

Table 4. Hypertension with platelet indices.

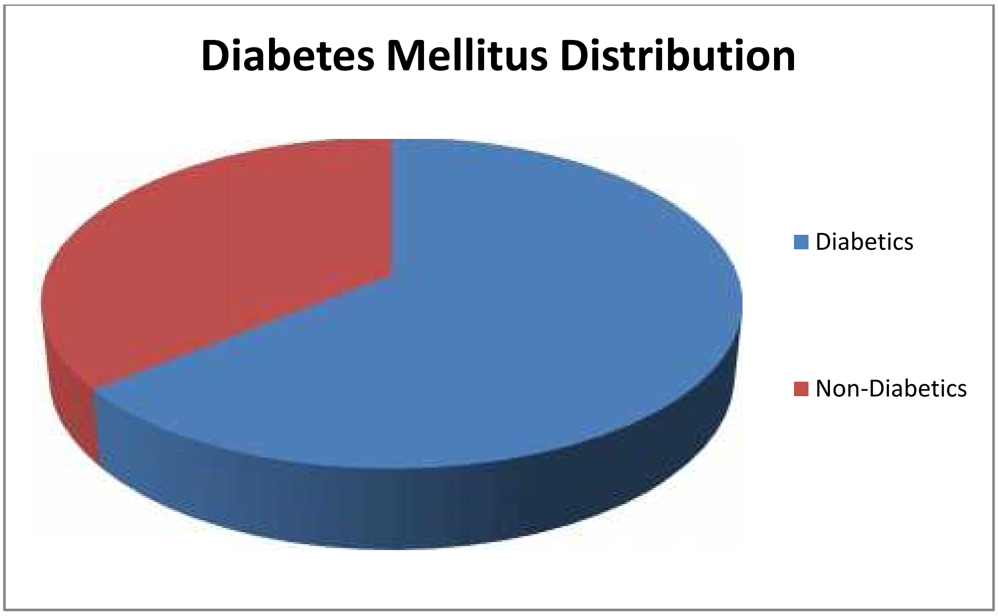
	Number	MPV(fl)	PLATELET COUNT(lac/dl)
Hypertensives	**158**	**8.927**	**2.800**
Non Hypertensives	**242**	**8.917**	**2.738**



In the present study MPV and Platelet counts were high in Hypertensives (8.927fl & 2.80 lacs) respectively. Hypertensives to non-hypertensives MPV and Platelet count ratio were 1.001 and 1.022 respectively.

Table 5. Diabetes Mellitus distribution

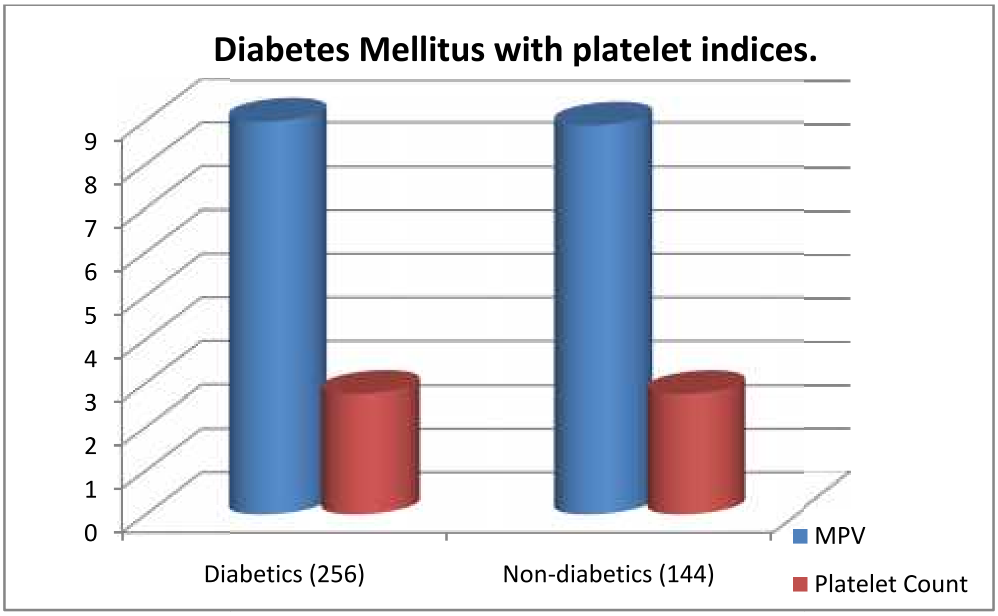
	Distribution (n=400)	
	Number	**Percentage**
Diabetics	256	64.00
Non-Diabetics	144	36.00
Total	**400**	**100.00**



In the present study majority of the patients were diabetics (60.5%). Diabetics to non diabetics ratio was 1.77:1.

Table 6. Diabetes Mellitus with platelet indices.

	Number	MPV(fl)	PLATELET COUNT(lac/dl)
Diabetics	**256**	**8.979**	**2.764**
Non Diabetics	**144**	**8.889**	**2.761**

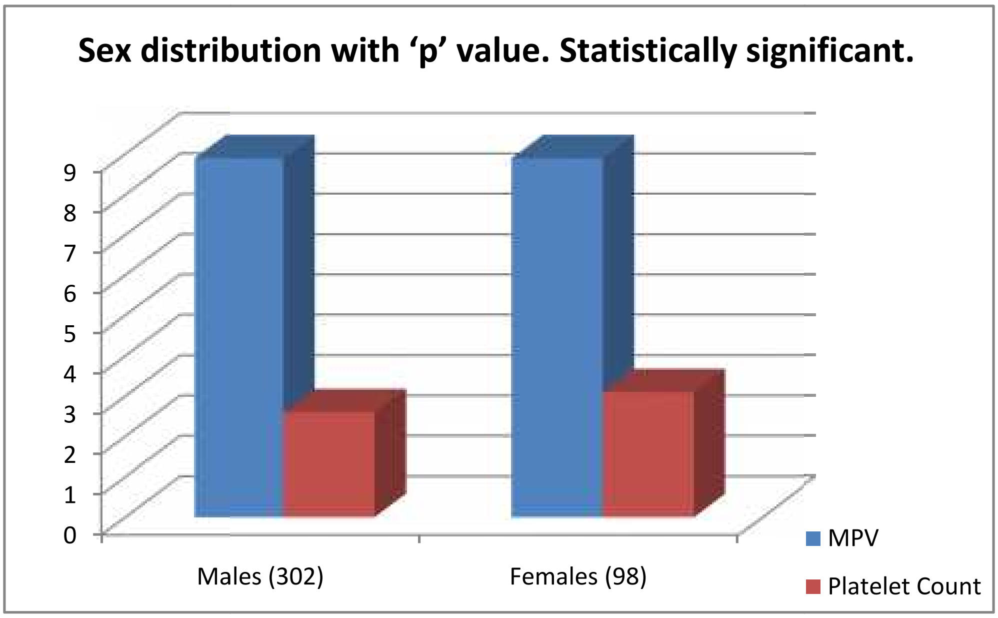


In the present study MPV and Platelet counts were high in Diabetics (8.979fl & 2.764 lacs) respectively. Diabetics to non-diabetics MPV and Platelet counts ratio were 1.010 and 1.001 respectively.

Table 7. Sex distribution with 'p' value. Statistically significant.

	Number	MPV(fl)	PLATELET COUNT(lac/dl)
MALES	302	8.9+/- 0.95	2.6+/- 0.86
FEMALES	98	8.9+/- 0.85	3.1+/- 0.91
'p'	--	0.856	0.001

Statistically significant.

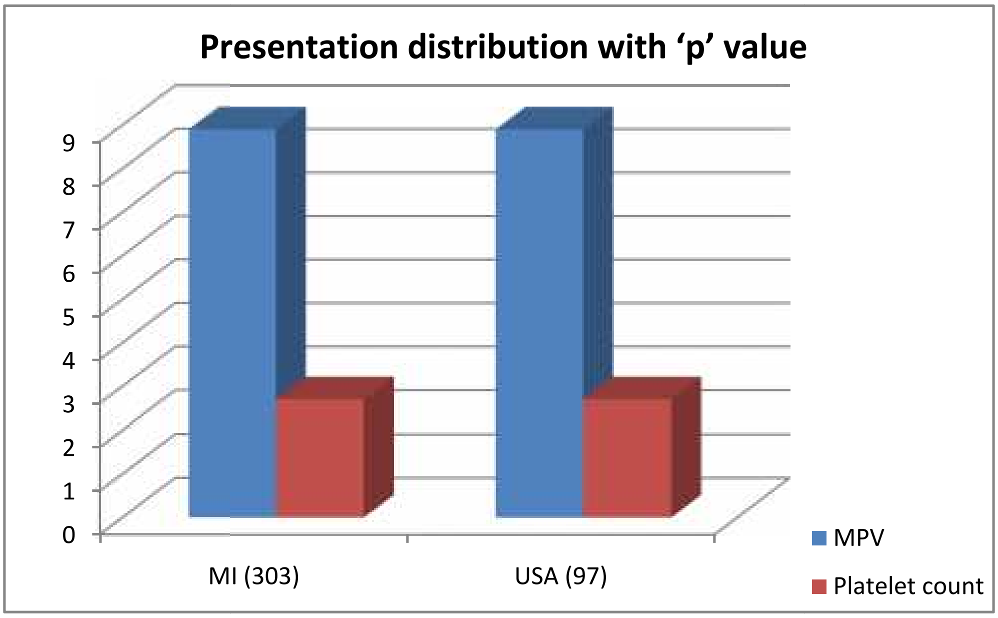


In the present study majority of the patients were males (75.5%). The male to female ratio was 3.081:1. p value between male to female platelet count was statistically significant and it was higher in case of females.

Table 8. Presentation distribution with 'p' value

	Number	MPV(fl)	PLATELET COUNT(lac/dl)
MI	**303**	**8.9+/- 0.89**	**2.7+/- 0.91**
USA	**97**	**8.9+/- 1.04**	**2.7+/- 0.86**
'p'	**--**	**0.751**	**0.992**

Statistically not significant.

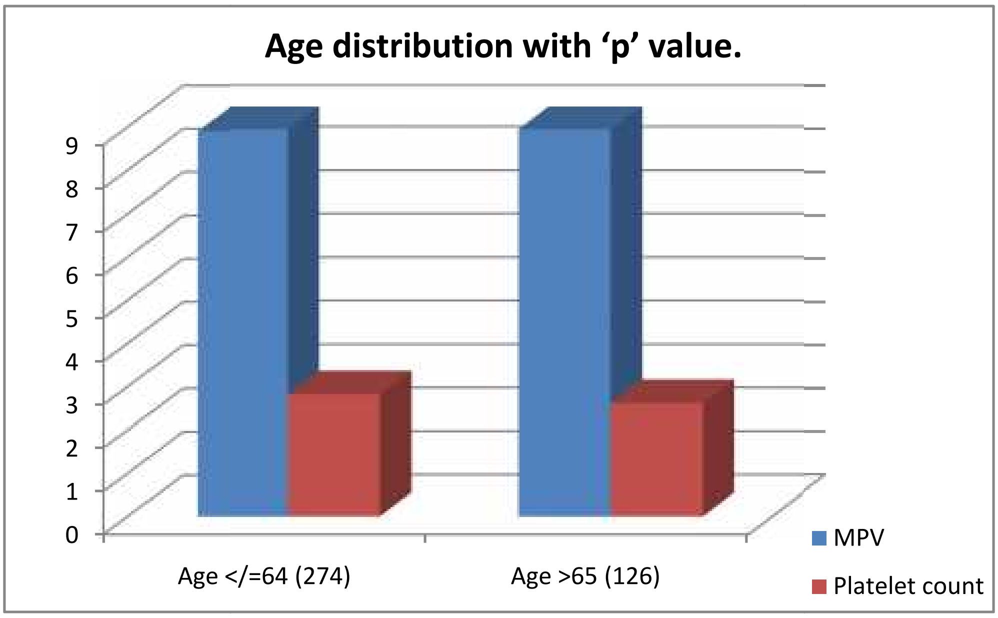


In the present study majority of the patients were MI patients (75.75%). The MI to USA ratio was 3.123:1.

Table 9. Age distribution with 'p' value.

AGE (in Years)	Number	MPV(fl)	PLATELET COUNT(lac/dl)
</= 64	274	8.9+/- 0.95	2.8+/- 0.94
>65	126	8.9+/- 0.88	2.6+/- 0.75
'p'	--	0.674	0.011

Statistically significant.

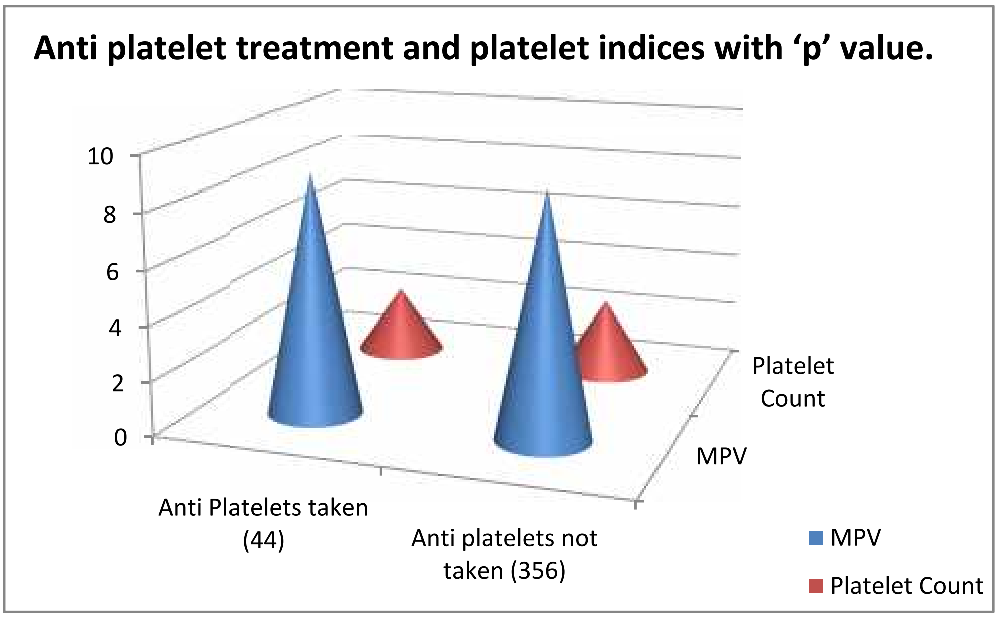


In the present study majority of the patients were </=64 years(68.5%). Less than 65 years to more than 65 years ratio was 2.17:1 and platelet count was higher in <64 years. 'p' value was significant for platelet count in patients of < 64 years.

Table 10. Anti platelet treatment and platelet indices with 'p' value.

Anti platelet treatment taken before hospital admission	Number	MPV(fl)	PLATELET COUNT(lac/dl)
YES	44	8.9+/- 0.82	2.5+/- 0.85
NO	356	8.9+/- 0.94	2.8+/- 0.89
'p'	--	0.707	0.054

Statistically significant.

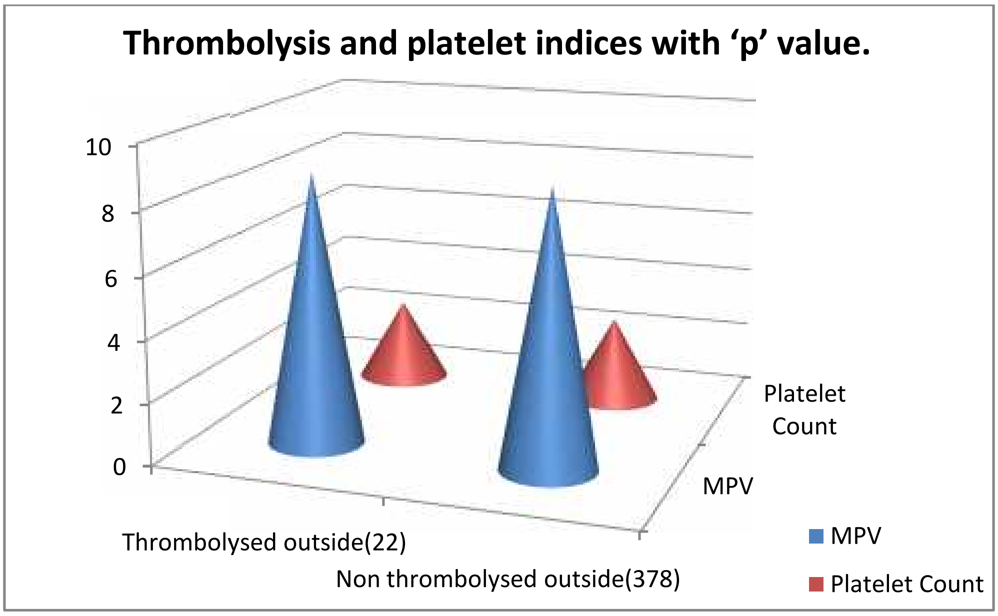


In the present study majority of the patients were not taken anti platelet therapy before hospital admission(89%). Not taken anti platelet therapy to taken anti platelet therapy ratio was 8.09:1. 'p' value was statistically significant for platelet count and platelet count was higher in patients who had not taken anti-platelet therapy.

Table 11. Thrombolysis and platelet indices with 'p' value.

Thrombolysed outside before hospital admission	Number	MPV(fl)	PLATELET COUNT(lac/dl)
YES	**22**	**9.2+/- 0.90**	**2.5+/- 0.70**
NO	**378**	**8.9+/- 0.93**	**2.7+/- 0.91**
'p'	**--**	**0.139**	**0.191**

Statistically not significant.

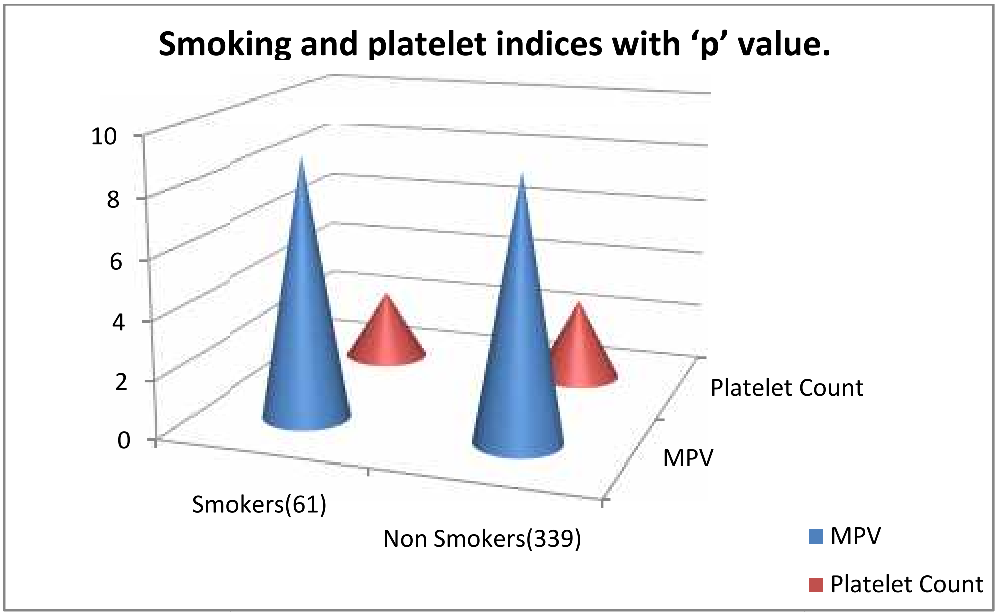


In the present study majority of the patients were not thrombolysed (94.5%). Non thrombolysed to thrombolysed ratio was 17.18:1.

Table 12. Smoking and platelet indices with 'p' value.

Smoking	Number	MPV(fl)	PLATELET COUNT(lac/dl)
YES	61	8.9+/- 0.89	2.4+/- 0.68
NO	339	8.9+/- 0.92	2.8+/- 0.89
'p'	--	0.15	0.14

Statistically not significant.

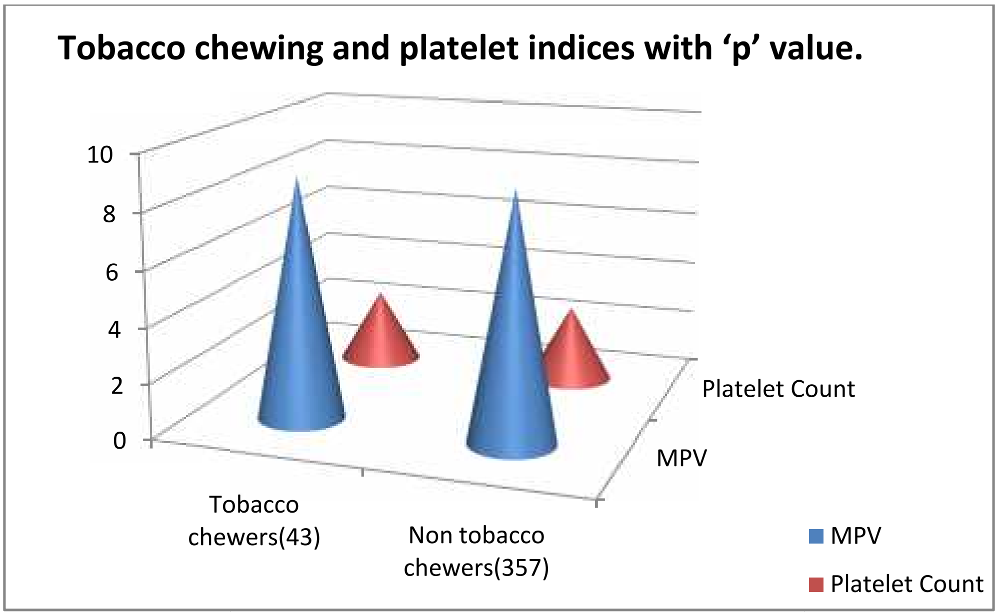


In the present study majority of the patients were non smokers (84.75%). Non smokers to smokers ratio was 5.55:1.

Table 13. Tobacco chewing and platelet indices with 'p' value.

Tobacco chewing	Number	MPV(fl)	PLATELET COUNT(lac/dl)
YES	43	8.8+/- 0.51	2.7+/- 0.68
NO	357	8.9+/- 0.28	2.8+/- 0.54
'p'	--	0.17	0.16

Statistically not significant.



In the present study majority of the patients were non tobacco chewers (89.25%). Non tobacco chewers to tobacco chewers ratio was 8.3:1.

DISCUSSION

Activated platelets play an important role in the pathogenesis of coronary artery disease. The central mechanism is the formation of a platelet fibrin plug at the site of a ruptured atherosclerotic plaque, potentially leading to myocardial infarction.[55]

Platelet count, mean platelet volume, a simple and reliable indicators of platelet size that correlates with platelet activation might be emerging cardiovascular risk markers and potentially helpful in stratifying cardiovascular risk. Studying the correlation may help us to understand better and reduce the chance of myocardial infarction in the apparently healthy subjects.[19][20]

Despite the developments regarding its diagnosis and treatment in recent years, acute coronary syndromes (ACS) keeps its place of the most important reason of morbidity and mortality. Cardiac diseases have been known to be the number one cause of deaths since the beginning of twentieth century[3]. It has been observed that known cardiovascular risk factors such as smoking, diabetes mellitus, obesity and hypertension are associated with MPV[4][5]. Hence, MPV has a potential as a marker of platelet activation and may represent a risk factor for MI, dependent or independent of other cardiovascular risk factors.

The reasons for increased platelet size are not fully understood. It is possible that changes in the secretion and metabolism of biologically active substances during aging, increasing body fat, diabetic changes in metabolism, high blood pressure, exposure to tobacco-derived toxins and an acute coronary event, all may stimulate the bone marrow to produce large platelets[4]. Indeed, a recent study has shown that an increased fraction of immature platelets was associated with diabetes, active smoking and acute coronary syndromes, especially in patients with ST-segment elevation MI, suggesting an increased platelet turnover and perhaps an abnormal bone marrow stimulation [6].

In Klovaite J et al, 39531 acute coronary syndrome subjects were investigated from 2003-2007 from the CGPS (45% participation rate) on all of whom MPV measuring was done(55).

In Slavka G et al, 206554 patients of acute coronary syndromes were studied between Jan 1996 to July 2003 and showed that individuals with lower MPV (_8.7 fL), hazard ratios for overall vascular mortality gradually increased to 1.5 in the highest category (_11.01 fL). The relationship of MPV to ischemic heart disease was even stronger and increased from 1.2 (8.71 to 9.60 fL category) to 1.8 in the highest category (_11.01 fL)(58).

In Lippi G et al, overall 2304 patients were enrolled and 456 acute coronary syndrome patients were studied and concluded that MPV is a simple and inexpensive laboratory measurement which might be considered a useful rule-out test along with other conventional cardiac biomarkers for the risk stratification of ACS patients admitted to the emergency departments(19).

The present one year cross-sectional study was done from January 2014 to December 2014 at Department of Medicine and Cardiology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi. A total of 400 acute coronary syndrome patients who presented to the hospital during the study period were included. Patients underwent clinical, haematological, biochemical examination. Electrocardiograph, platelet count and mean platelet volume were also done.

Age, sex distribution and platelet indices:

In this study the mean age group out of 400 acute coronary syndrome patients was 57.81 years with lowest being 26 years and highest being 87 years. Amongst 97 females, the mean age group was 59.48 years and the lowest being 30 years and highest being 86 years. Amongst 303 males mean age group was 57.26 years and the highest age group was 87 years and the lowest age group was 26 years. Males were 74.5% and females were 24.5%, which was seen in accordance with Klovaite et al(55) where in males were 46% and females were 54% but in contrast to other study Slavka G et al(58) where in males were less,i.e; 43% and females(43.4%) respectively.

In our study we also showed that there was statistically significant difference between the platelet count of male (2.6 lac) and female sub group(3.1 lac) of acute coronary syndrome which was much higher in female sub group but we didn't find any such correlation for mean platelet volume amongst the two sub groups.

In our study we also showed that patients of age less than or equal to 64 years were more in number and constituting of about 68.5% as compared to patients of age more than 65 years (31.5%), and also the platelet counts were high in patients of less than 64 years which was statistically significant.

Hypertension, Diabetes mellitus distribution and platelet indices:

In our present study 40% of the patients were hypertensives and 60% were non hypertensives with mean platelet volume of 8.92fl and 8.91fl respectively and platelet count of 2.80 lac and 2.73 lac respectively with no statistical difference amongst the two group and it is in accordance with Klovaite et al, where in they showed 58% of hypertensives and 42% were non hypertensives.

In our study there were 64% diabetics and 36% non diabetics with mean platelet volume of 8.97fl and 8.88fl respectively and platelet count of 2.76 lac and 2.76 lac respectively with no statistical difference amongst the two group.

Klovaite et al, showed that a strong association of increased MPV with geriatric age, high BMI, diabetes mellitus, hypertension and smoking, but after adjustment for these factors, the association of MPV with risk of MI still persisted, showing that MPV was independently associated irrespective of these risk factors with risk of MI(55).

Lippi G et al, suggests that MPV may be a risk factor for recurrent myocardial infarction independent of such established risk factors as hypertension, dyslipidemia, increased fibrinogen, white blood cell count, or plasma viscosity(19).

Myocardial Infarction, Unstable angina distribution and platelet indices:

In our study among 400 acute coronary syndrome patients, 303 were myocardial infarction patients and 97 were unstable angina patients. In comparison of platelet count and mean platelet volume amongst the two sub groups where the ‘p’ value was 0.9 and 0.7 respectively, there was no statistically significant difference between the two sub groups as seen in concordance with Mercan R et al. where the ‘p’ value for platelet count was 0.7 and for mean platelet volume was 0.9 respectively amongst the unstable angina and myocardial infarction sub groups.

Anti-platelets and platelet indices:

To determine the effect of anti-platelet therapy on platelet count and mean platelet volume our study divided them into anti platelet therapy taken outside, i.e; after the onset of chest pain but before admission to hospital (anti-platelet therapy taken -YES) group and anti platelet therapy taken after coming to the hospital(anti-platelet therapy taken-NO) group.

We had 44(11%) patients who had taken anti-platelet therapy outside before admission and 356(89%) patients who had not taken anti platelet therapy outside and on comparison of platelet count and MPV between these two groups, ‘p’ value was 0.05 and 0.7 for platelet count and MPV respectively which was statistically significant for platelet count but not for MPV between these two groups, hence showing that platelet count is dependent on anti platelet therapy but MPV is an independent risk factor.

Klovaite et al, investigated a probable modification of the observed association between MPV and risk of MI by use of antiplatelet therapy by dividing individuals into different groups based on use of antiplatelets and within these groups, in turn dividing into tertiles of MPV. Increased risk of MI as a result of increased MPV was observed in both those with and without antiplatelets and there was no evidence of an effect of interaction between MPV and antiplatelets on risk of MI[55].

Thrombolysis with platelet indices:

To determine the effect of thrombolysis on platelet count and mean platelet volume our study divided them into thrombolysed outside before coming to our hospital (thrombolysed outside -YES) group and not thrombolysed before drawing blood sample after coming to the hospital for platelet indices (thrombolysed outside-NO) group.

We had 22 patients who were thrombolysed outside as compared to the 378 patients who were not thrombolysed and on comparison of platelet count and mean platelet volume between these two sub groups 'p' value for platelet count and mean platelet volume were 0.19 and 0.13 respectively, which were not statistically significant, showing that platelet indices are independent risk factors.

Smoking and platelet indices:

To determine the effect of smoking on platelet count and mean platelet volume, our study divided all patients into two groups; i.e; smokers and non smokers.

We had 61 patients who were smokers and 339 patients who were non smokers and on comparison of platelet count and mean platelet volume between these two groups 'p' value for platelet count and mean platelet volume were 0.14 and 0.15 respectively, which were not statistically significant, showing that platelet indices are not dependent on smoking and are independent risk factors.

Tobacco and platelet indices:

To determine the effect of tobacco on platelet count and mean platelet volume, our study divided all patients into two groups; i.e; tobacco chewers and non tobacco chewers.

We had 43 patients who were tobacco chewers and 357 patients who were non tobacco chewers and on comparison of platelet count and mean platelet volume between these two groups 'p' value for platelet count and mean platelet volume were 0.16 and 0.17 respectively, which were not statistically significant, showing that platelet indices are not dependent on tobacco cheweing and are independent risk factors.

Average platelet count and Mean Platelet volume:

In our study, the mean values of MPV and platelet counts are 8.9+/-1.48 fl and 2.7+/-0.88 lacs in patients of acute coronary syndromes.

The risk of MI associated with MPV was most pronounced in individuals with a platelet count above 248 * 10^9 /L. In prospective, multifactorially adjusted analyses, risk of MI increased by 38% (8–75%) in individuals with MPV =/>7.4 vs. < 7.4 fL[(55)].

Patients with diagnosed ACS, all of whom had cTnT values of 0.03 ng/mL or greater, showed significantly higher MPVs than non-ACS patients (n _ 1848; median, 8.0 fL [5th to 95th percentiles, 6.7–10.0 fL] versus median, 7.4 fL [5th to 95th percentiles, 6.5–9.5 fL]; *P* =0.001)[(19)].

Results show that patients with an increased MPV (11.01 fL) are at higher risk of expiry due to ischemic heart disease, with hazard ratios as comparable to those reported for obesity and/or smoking[(58)].

Average platelet count in MI patient was 228.5+/= 74.1 * 10^9 /L and in that of unstable angina was 239.6+/= 59.2 * 10^9 /L respectively, and for that of mean platelet volume in MI patients was 8.9+/-0.8 fl and in unstable angina was 9.0+/- 1.0 fl respectively[(54)].

The cut-off values for Mean Platelet Volume when predicting AMI and CAD in patients were 9.25 fl (sensitivity 56.4%; specificity 45.9%) and 9.15 fl (sensitivity 54.2%; specificity 42.23%), respectively[(46)].

Compared to our study results to other studies, our results are in concordance with other studies.

CONCLUSION

Based on the findings of the present study the prominent features are;

- Males are more commonly affected compared to females.
- The commonest presentation are chest pain alone(151), chest pain with breathlessness(153), atypical presentations(78) like syncope, epigastric pain/ burning sensation/etc.
- The average values of MPV and platelet counts are **8.9+/-1.48 fl** and **2.7+/-0.88 lacs** in patients of acute coronary syndromes.
- Cases of MI were more as compared to that of Unstable Angina in spectrum of Acute Coronary Syndromes.
- There is no statistically significant increase in MPV and platelet counts as compared between MI and unstable angina group.
- Patients of Non-Hypertensives and Diabetics were more as compared to hypertensives and non-diabetics.
- MPV and Platelet counts were high in Hypertensives but was not statistically significant as compared to Non-hypertensives, which shows that MPV is an independent risk factor.
- MPV and Platelet counts were high in Diabetics but was not statistically significant as compared to Non-diabetics, which shows that MPV is an independent risk factor.

- Platelet counts in patients of Acute Coronary Syndromes was higher in male sub group as compared to that of female sub group which was **statistically significant.**

- The platelet count was higher in patients aged less than or equal to 64 years as compared to patients who are more than or equal to 65 years which was **statistically significant.**

- There was **statistically significant** difference in platelet counts of patients of acute coronary syndromes who took and who didn't take anti platelet therapy outside, showing that platelet count is dependent on anti platelet therapy.

  In contrast, there was no statistically difference in MPV of patients of acute coronary syndromes who took and who didn't take anti platelet therapy outside, showing that MPV is an independent risk factor unlike platelet count.

- There was no statistically significant difference in MPV and platelet counts of patients of acute coronary syndromes who were thrombolysed and who weren't thrombolysed outside, showing that MPV is independent of thrombolysis therapy.

- There was no statistically significant difference in MPV and platelet counts of patients of acute coronary syndromes who were smokers as compared to that of non smokers, showing that platelet count and MPV are independent risk factors.

- There was no statistically significant difference in MPV and platelet counts of patients of acute coronary syndromes who were tobacco chewers as compared to that of non tobacco chewers, showing that platelet count and MPV are independent risk factors.

- Overall, this study has thrown light on the Mean Platelet Volume(MPV) and Platelet count in comparison with different sub groups of acute coronary syndromes and also found out the average values of MPV and platelet count in patients of acute coronary syndromes.

SUMMARY

The frequency of ACS is increasing as the population ages, and therefore, knowledge of knowing who are at high risk is essential. This study was aimed at exploring the Mean Platelet Volume and Platelet Count of acute coronary syndrome (STEMI, NSTEMI, Unstable Angina) patients.

The present one year cross-sectional study was done in the Department of Medicine and Cardiology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi. A total of 400 patients of age more than 18 years who presented with Acute Coronary Syndromes were included in the study. Patients were subjected to clinical examination, necessary investigations including Complete Haemogram, platelet count, electrocardiogram and Mean Platelet Volume and Troponin-I/ck-mb the following observations were made.

Majority of the patients were males (75.5%). The male to female ratio was 3.08:1. ‘p’ value for platelet count when compared between male and female was statistically significant.(p,0.001).

In the present study majority of the patients were MI patients (75.75%). The MI patients to USA patients ratio was 3.123:1. The ‘p’ value for platelet count (p=0.99) and MPV(0.75) between the two groups was not significant.

In the present study majority of the patients were non hypertensives (60.5%). Hypertensives to non hypertensives ratio was 1.53:1. MPV and Platelet counts were high in Hypertensives (8.927fl & 2.80 lacs) respectively. Hypertensives to non-hypertensives MPV and Platelet count ratio were 1.001 and 1.022 respectively which was not significant.

In the present study majority of the patients were diabetics (60.5%). Diabetics to non diabetics ratio was 1.77:1, MPV and Platelet counts were high in Diabetics (8.979fl & 2.764 lacs) respectively. Diabetics to non-diabetics MPV and Platelet counts ratio were 1.010 and 1.001 respectively which was also not significant.

In the present study majority of the patients were males (75.5%). The male to female ratio was 3.081:1. ‘p’ value (p=0.001) between male to female platelet count was statistically significant.

In the present study majority of the patients were </=64 years(68.5%). Age less than 65 years to more than 65 years patients ratio was 2.17:1. ‘p’ value (p=0.011) was statistically significant for platelet count.

In the present study majority of the patients were not taken anti platelet therapy outside(89%). Non taken anti platelet therapy to taken anti platelet therapy ratio was 8.09:1with ‘p’ value 0.70 and 0.05 for MPV and platelet count respectively which was not statistically significant for MPV but statistically significant for Platelet count.

In the present study majority of the patients were not thrombolysed (94.5%). Non thrombolysed to thrombolysed ratio was 17.18:1 with ‘p’ value of 0.13 and 0.19 for MPV and platelet count respectively.

In the present study majority of the patients were non smokers (84.75%). Non smokers to smokers ratio was 5.55:1 with ‘p’ value of 0.15 and 0.14 for MPV and platelet count respectively.

In the present study majority of the patients were non tobacco chewers (89.25%). Non tobacco chewers to tobacco chewers ratio was 8.3:1 with ‘p’ value of 0.17 and 0.16 for MPV and platelet count respectively.

The average values of MPV and platelet counts are 8.9+/-1.48 fl and 2.7+/-0.88 lacs in patients of acute coronary syndrome in our study population.

BIBLIOGRAPHY

1. Ross R. Atherosclerosis: an inflammatory disease. *N Engl J Med.* 1999;340: 115–126.
2. Lippi G, Montagnana M, Salvagno GL, Guidi GC. Potential value for new diagnostic markers in the early recognition of acute coronary syndromes. *CJEM.*2006;8:27–31.
3. Van de Werf F, Ardissino D, Betriu A, Cokkinos DV, Falk E, Fox KA, et al. Management of acute myocardial infarction in patients presenting with ST-segment elevation. The Task Force on the Management of Acute Myocardial Infarction of the European Society of Cardiology. Eur Heart J 2003; 24(1):28-66.
4. Boos CJ, Lip GY. Assessment of mean platelet volume in coronary artery disease – what does it mean? Thromb Res 2007; 120: 11–3.
5. Muscari A, De Pascalis S, Cenni A, Ludovico C, Castaldini N, Antonelli S, Determinants of mean platelet volume (MPV) in an elderly population: relevance of body fat, blood glucose and ischaemic electrocardiographic changes. Thromb Haemost 2008; 99: 1079–84.
6. Grove EL, Hvas AM, Kristensen SD. Immature platelets in patients with acute coronary syndromes. Thromb Haemost 2009; 101: 151–6.
7. Meisinger C, Prokisch H, Gieger C, Soranzo N, Mehta D, Rosskop D et al. A genome-wide association study identifies three loci associated with mean platelet volume. Am J Hum Genet 2009; 84: 66–71.
8. Erhart S, Beer JH, ReinhartWH. Influence of aspirin on platelet count and volume in humans. Acta Haematol 1999; 101: 140–4.

9. Guthikonda S, Alviar CL, Vaduganathan M, Arikan M, Tellez A, DeLao T, et al. Role of reticulated platelets and platelet size heterogeneity on platelet activity after dual antiplatelet therapy with aspirin and clopidogrel in patients with stable coronary artery disease. J Am Coll Cardiol 2008; 52: 743–9.

10. Karpatkin S. Heterogeneity of human platelets. II. Functional evidence suggestive of young and old platelets. J Clin Invest 1969; 48:1083-1087.

11. Martin JF, Bath PM, Burr ML. Influence of platelet size on outcome after myocardial infarction. Lancet 1991; 338:1409-1411.

12. Schoene NW. Design Criteria: tests used to assess platelet function. Am J Clin Nutr.1997; 65(Sup):1665-1685.

13. Davies MJ, Thomas AC. Thrombosis and acute coronary artery lesions in sudden cardiac ischemic death. N Engl J Med 1984; 310:1137-1140.

14. Kishk YT, Trowbridge EA, Martin JF. Platelet volume subpopulations in acute myocardial infarction: an investigation of their homogeneity for smoking, infarct size and site. Clin Sci 1985; 68:419-425.

15. Bath PM, Butterworth RJ. Platelet size: measurement, physiology and vascular disease. Blood Coagul Fibrinolysis 1996; 7: 157-161.

16. Thompson CB, Jakubowski JA, Quinn PG, Deykin D, Valeri CR. Platelet size as a determinant of platelet function. J Lab Clin Med 1983; 101:205-213.

17. Martin JF, Trowbridge EA, Salmon GL, Plumb J. The biological significance of platelet volume: its relationship to bleeding time, platelet thromboxane B2 production and megakaryocyte nuclear DNA concentration. Thromb Res 1983; 32:443-460.

18. Gaziano T, Gaziano JM: Global burden of cardiovascular disease, in Heart Disease: A Textbook of Cardiovascular Medicine, 9th ed, E Braunwald (ed). Philadelphia, Elsevier Saunders, 2009.

19. Lippi G, Filippozzi L, Salvagno GL, Montagnana M, Franchini M, Guidi GC, et al. Increased mean platelet volume in patients with acute coronary syndromes. Arch Pathol Lab Med 2009 Sep; 133(9):1441-3.

20. Abdullah S A et al: Diagnostic importance of platelet parameters in patients with acute coronary syndromes admitted to a tertiary care hospital in southwest region. J Saudi Heart Assoc 2012- January; 24(1):17-2.

21. Lopez AD et al (eds): Global Burden of Disease and Risk Factors. Washington, DC, Oxford University Press, 2006.

22. Lawes CM et al: Global burden of blood-pressure-related disease, 2001. Lancet 371:1513, 2008[PMID: 18456100].

23. Jamison DT et al (eds): Disease Control Priorities in Developing Countries, 2nd ed. Washington, DC, Oxford University Press, 2006.

24. Braunwald E, Antman EM: ST-Elevation Myocardial Infarction: Pathology, Pathophysiology, and Clinical Features in P Libby, RO Bonow, DL Mann, DP Zipes (eds) *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*, 8th ed, Philadelphia, Saunders Elsevier, 2008, pp 1207–1232.

25. Chu H, Chen WL, Huang CC, Chang HY, Kuo HY, Gau CM, et al. Diagnostic performance of mean platelet volume for patients with acute coronary syndrome visiting an emergency department with acute chest pain: the Chinese scenario. Emerg Med J 2011 Jul; 28(7):569-74.

26. Kilicli-Camur N, Demirtunc R, Konuralp C, Eskiser A, Basaran Y. Could mean platelet volume be a predictive marker for acute myocardial infarction? Med Sci Monit 2005 Aug; 11(8):387-92.

27. Endler G, Klimesch A, Sunder-Plassmann H, Schillinger M, Exner M, Mannhalter C, et al, Mean platelet volume is an independent risk factor for myocardial infarction but not for coronary artery disease. Br J Haematol 2002 May; 117(2):399-404.

28. Sequist TD, Bates DW, Cook EF, Lampert S, Schaefer M, Wright J, et al. Prediction of missed myocardial infarction among symptomatic outpatients without coronary heart disease. Am Heart J 2005 Jan; 149(1):74-81.

29. Yilmaz MB, Cihan G, Guray Y, Guray U, Kisacik HL, Sasmaz H, et al. Role of mean platelet volume in triagging acute coronary syndromes. J Thromb Thrombolysis 2008 Aug; 26(1):49-54.

30. Alan H. B. Wu. Cardiac markers, 2nd ed. Totowa**,** New Jersey**:** Humana Press; 2003.pp.344-350.

31. Mathur A, Robinson MS, Cotton J, Martin JF, Erusalimsky JD. Platelet reactivity in acute coronary syndromes: evidence for differences in platelet behavior between unstable angina and myocardial infarction. Thromb Haemost 2001 Jun; 85(6):989-94.

32. Khandekar MM, Khurana AS, Deshmukh SD, Kakrani AL, Katdare AD, Inamdar AK. Platelet volume indices in patients with coronary artery disease and acute myocardial infarction: an Indian scenario. J Clin Pathol 2006 Feb; 59(2):146-9.

33. Huczek Z, Filipiak KJ, Kochman J, Michalak M, Roik M, Piatkowski R, et al. Baseline platelet size is increased in patients with acute coronary syndromes developing early stent thrombosis and predicts future residual platelet reactivity, A case-control study. Thromb Res 2010 May;125(5):406-12.

34. Cemin R, Donazzan L, Lippi G, Clari F, Daves M. Blood cells characteristics as determinants of acute myocardial infarction. Clin Chem Lab Med 2011 Jul; 49(7):1231-6.

35. Duygu H, Turkoglu C, Kirilmaz B, Turk U. Effect of mean platelet volume on postintervention coronary blood flow in patients with chronic stable angina pectoris. J Invasive Cardiol 2008 Mar; 20(3):120-4.

36. Avramakis G, Papadimitraki E, Papakonstandinou D, Liakou K, Zidianakis M, Dermitzakis A, et al. Platelets and white blood cell subpopulations among patients with myocardial infarction and unstable angina. Platelets 2007 Feb;18(1):16-23.

37. Aksu H, Ozer O, Unal H, Hobikoglu G, Norgaz T, Buturak A, et al. Significance of mean platelet volume on prognosis of patients with and without aspirin resistance in settings of non-ST segment elevated acute coronary syndromes. Blood Coagul Fibrinolysis 2009 Dec; 20(8):686-93.

38. Maden O, Kacmaz F, Selcuk MT, Selcuk H, Metin F, Tufekcioglu O, et al. Relationship of admission haematological indices with infarct-related artery patency in patients with acute ST-segment elevation myocardial infarction treated with primary angioplasty. Coron Artery Dis 2007 Dec; 18(8):639-44.

39. Yetkin, E. Mean platelet volume not so far from being a routine diagnostic and prognostic measurement. Thromb Haemost 2008 Jul; 100(1):3–4.

40. Goncalves SC, Labinaz M, Le May M, Glover C, Froeschl M, Marquis JF, et al. Usefulness of mean platelet volume as a biomarker for long-term outcomes after percutaneous coronary intervention. Am J Cardiol 2011 Jan; 107(2):204-9.

41. Yang A, Pizzulli L, Lüderitz B. Mean platelet volume as marker of restenosis after percutaneous transluminal coronary angioplasty in patients with stable and unstable angina pectoris. Thromb Res 2006; 117(4):371-7.

42. Ranjith MP, Divya R, Mehta VK, Krishnan MG, KamalRaj R, Kavishwar A. Significance of platelet volume indices and platelet count in ischaemic heart disease. J Clin Pathol 2009;62:830-3.

43. Coban E, Ozdogan M, Yazicioglu G, Akcit H. The mean platelet volume in patients with obesity. Int J Clin Pract 2005;59:981-2.

44. Yilmaz MB, Cihan G, Guray Y, Guray U, Kisacik HL, Sasmaz H, *et al*. Role of mean platelet volume in triaging acute coronary syndromes. J Thromb Thrombolysis 2008;26:49-54.

45. Huczek Z, Kochman J, Filipiak KJ, Horszczaruk GJ, Grabowski M, Piatkowski R, *et al*. Mean platelet volume on admission predicts impaired reperfusion and long-term mortality in acute myocardial infarction treated with primary percutaneous coronary intervention. J Am Coll Cardiol 2005;46:284-90.

46. Khode V, Sindhur J, Kanbur D, Ruikar K, Nallulwar S. Mean platelet volume and other platelet volume indices in patients with stable coronary artery disease and acute myocardial infarction: A case control study. J Cardiovasc Dis Res 2012;3:272-5.

47. Ozhan H, Aydin M, Yazici M, et al. Mean platelet volume in patients with non-alcoholic fatty liver disease. *Platelets*. 2010; 21(1):29-32.

48. De Luca G, Santagostino M, Secco GG, et al. Mean platelet volume and the extent of coronary artery disease: results from a large prospective study. Atherosclerosis. 2009; 101(5):911-15.

49. Smyth DW, Martin JF, Michalis L, Bucknall CA, Jewitt DE. Influence of platelet size before coronary angioplasty on subsequent restenosis. *Eur J Clin Invest*. 1993;23:361–367.

50. Sharpe PC, Desai ZR, Morris TC. Increase in mean platelet volume in patients with chronic renal failure treated with erythropoietin. *J Clin Pathol*. 1994;47:159 –161.

51. Jagroop IA, Tsiara S, Mikhailidis DP. Mean platelet volume as an indicator of platelet activation: methodological issues. *Platelets*. 2003;14: 335–336.

52. Henning BF, Zidek W, Linder B, Tepel M. Mean platelet volume and coronary heart disease in hemodialysis patients. Kidney Blood Press Res 2002; 25:103-108.

53. Pizzulli L, Yang A, Martin JF, Luderitz B. Changes in platelet size and count in unstable angina compared to stable angina or non cardiac chest pain. Eur Heart J 1998; 19:80-84.

54. Ridvan M, Cengiz D, Imdat D, Muntecep A, Murat A. Mean platelet volume in acute coronary syndrome. Van Tıp Dergisi: 17 (3): 89-95, 2010.

55. Klovaite J, Benn.M, Yazdanyar.S, Nordestgaard.B.G. High platelet volume and increased risk of myocardial infarction: 39 531 participants from the general population. Journal of Thrombosis and Haemostasis, 9: 49–56.

56. Azab.B, Torbey E, Singh J et al. Mean platelet volume/platelet count ratio as a predictor of longterm mortality after non ST elevation myocardial infarction. J Platelets. 2011; 22(8);557-566.

57. Gasparyan A Y, Ayvazyan L, MiKhailidis D P, Kitas G D. Mean platelet volume: a link between thrombosis and inflammation? Curr Pharm Des. 2011:17(1):47-58.

58. Slavka G, Perkmann T, Haslacher H, Greisenegger S, Marsik C, Oswald F et al. Mean Platelet Volume May Represent a Predictive Parameter for Overall Vascular Mortality and Ischemic Heart Disease. *Arterioscler Thromb Vasc Biol.* 2011;31:1215-1218.

59. Halbmayer WM, Haushofer A, Radek J et al: Platelet size, fibrinogen and lipoprotein(a) in coronary heart disease. Coron Artery Dis, 1995;6: 397–402.

ANNEXURE I – CONSENT FORM

Title Of Research Study:

"MEAN PLATELET VOLUME IN PATIENTS OF ACUTE CORONARY SYNDROMES IN A TERTIARY CARE HOSPITAL"

Principal Investigator:-

Introduction and Purpose:-

The study is to determine the correlation between mean platelet volume in acute coronary syndromes, as it could be attributed as an independent risk factor for myocardial infarction.

Procedure:

If you agree to be part of the research study, you will be asked the history of any chest pain, associated with sweating, radiating to left shoulder/neck and will be subjected to relevant examination and investigations like platelet count and mean platelet volume. You will also have to give blood and urine samples for the necessary investigations.

Risk and Benefits:

The only risk and possible discomfort you might get is while taking blood from your arm for the investigations. It may cause swelling, pain, redness, bruising or infection (rarely happens) at the site from where the blood is drawn.

The benefit is that it helps in risk stratification of acute coronary syndromes.

Alternatives:

Taking part in this study is voluntary. You may choose not to take part in this study, or if you decide to take part you can later change your mind and withdraw from the study. Your decision will not change the present or future health care or other services that you receive. The study doctor or sponsor may stop your participation in this study at any time. If you choose not to take part in the study, you will receive the standard treatment for patients with your condition.

Privacy and Confidentiality:

All information collected about you during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify you in this research record. Information from this study may be published but your identity will be confidential in any publication.

Institution / Sponsor's policy / compensation:

In case of any injury related to the study, treatment will be made available at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi. There is no compensation or payment for such medical treatment by law.

Financial incentives for participation:

You will not be paid / offered any gifts /incentives for participating in the study.

Authorization to publish the results:

The results of the study would be forwarded to the KLE University, Belagavi as part of requirement towards the completion of MD degree, review and publishing.

Questions: During study/ in future you may contact following persons for any questions.

1. Dr. GANGA S PILLI,
Chairman,
J.N.M.C Ethical Committee for Human Research.
ph.no-9480275601.

Consent Statement:

“MEAN PLATELET VOLUME IN PATIENTS OF ACUTE CORONARY SYNDROMES IN A TERTIARY CARE HOSPITAL.”

I voluntarily agree to take part in this study by signing below. I may withdraw at any time. I am not giving up any of my legal rights by signing this form. My signature below indicates that I have read, or it has been read to me, this entire consent form, and have had all my questions answered.

Name of the Participant: ____________ Signature /Thumb print: _______________

Name of the Witness: _______________ Signature/ Thumb print: _____________

Investigator Name: ______________________ Signature :____________________

Date: Place:

ANNEXURE II – PROFORMA

Case No:

NAME: **AGE/SEX:**

IP No. **ADDRESS:**

OCCUPATION

COMPLAINTS AT PRESENTATION: **YES** **NO**

PAST HISTORY:

TREATMENT HISTORY:

PHYSICAL EXAMINATION:

GENERAL CONDITION:

Pallor: Yes/No

Icterus: Yes/No

Lymphadenopathy: Yes/No

Cyanosis: Yes/No

Clubbing: Yes/No

Edema: Yes/No

VITALS:

Temperature:

Pulse:

Respiratory rate:

Blood pressure:

SYSTEMIC EXAMINATION:

R. S.:

C.V.S.:

P.A.:

C.N.S.:

Investigations:

Haemogram

Hb%	:				
TC	:				
DC	:	N -	M -	E -	B –

Renal profile

Serum Urea

Serum Creatinine

E.C.G:

Others: