DISSERTATION TITLED

"HIGH SENSITIVITY C REACTIVE PROTIEN (HSCRP) LEVELS & CORRELATION WITH LIPID PROFILE IN HYPERTENSION"

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CERTIFICATE

This is to certify that the dissertation entitled **"HIGH SENSITIVITY C REACTIVE PROTIEN (HsCRP) LEVELS & CORRELATION WITH LIPID PROFILE IN HYPERTENSION"** is a bonafide work done by **Dr.DEVANAND KUMAR.G,** Post Graduate Student, Institute of Internal Medicine, Madras Medical College, Chennai-3, during March 2015 to August 2015 in partial fulfillment of the University Rules and Regulations for the award of MD Branch – I General Medicine, under our guidance and supervision, during the academic year 2013 - 2016.

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I solemnly declare that the dissertation entitled "**HIGH SENSITIVITY C REACTIVE PROTIEN (HsCRP) LEVELS & CORRELATION WITH LIPID PROFILE IN HYPERTENSION**" is done by me at Madras Medical College, Chennai-3 during March 2015 TO August 2015 under the guidance and supervision of **Prof.K.S.CHENTHIL, M.D.,** to be submitted to The Tamilnadu Dr.M.G.R Medical University towards the partial fulfillment of requirements for the award of M.D. DEGREE IN GENERAL MEDICINE BRANCH-I.

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ABBREVATIONS

ACE	Angiotensin-Converting Enzyme
ACC	American College of Cardiology
ACS	Acute Coronary Syndrome
AMI	Acute Myocardial Infarction
CABG	Coronary Artery Bypass Grafting
CAD	Coronary Artery Disease
CCS	Canadian Cardiovascular Society
CK-MB	Creatine Kinase MB
CRP	C-Reactive Protein
CV	Cardiovascular
ECG	Electrocardiographic, Electrocardiography
ESC	European Society Of Cardiology
FDA US	Food And Drug Administration
GP	Glycoprotein
HSCRP	High sensitive C-Reactive protein
LBBB	Left Bundle Branch Block
MI	Myocardial Infarction

NSTEMI	Non–ST-segment elevation myocardial Infarction
PCI	Percutaneous Coronary Intervention
SCD	Sudden Cardiac Death
STEMI	ST-Segment Elevation Myocardial Infarction
Apo	Apolipoprotein
CETP	Cholesteryl ester transfer protein
CK	Creatine kinase
HDL	High-density lipoproteins
HMG-CoA	3-Hydroxy-3-methylglutaryl-coenzyme A
IDL	Intermediate-density lipoproteins
LCAT	Lecithin:cholesterol acyltransferase
LDL	Low-density lipoproteins
Lp(a)	Lipoprotein(a)
LPL	Lipoprotein lipase
PPAR	Peroxisome proliferator-activated receptor
VLDL	Very-low-density lipoproteins

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INTRODUCTION

CRP is secreted as a acute phase reactant that is primarily produced in the liver in response to elevations of cytokines in the blood, like IL-6 and TNF-alpha.

The developing atherosclerotic lesion is of a inflammatory nature which provides a link between production of activating cytokines in the atheroma and the generation of CRP which is hepatically produced. Evidence suggests that CRP may play a direct role in worsening atherosclerosis and raising the risk of cardiovascular events .

A large ammount of epidemiologic evidence supports CRP as an independent prognostic indicator of future CV events irrespective of male or female. CRP has also been used as a prognostic indicator in patients with both acute coronary syndromes and stable, chronic coronary disease.

In the landmark JUPITER study of healthy normocholesterolemic persons (LDL cholesterol <130 mg/dL) and higher levels of highly sensitive CRP >2.0 mg/L), treatment with a potent statin that lowers CRP caused a reduction in CV events 2 times that which would be expected from the reduction in LDL

cholesterol alone. Similar results have been found in studies of statin therapy in patients with coronary disease.

Those with the greatest CRP reductions have the best cardiovascular outcomes, independent lowering of LDL.

The mechanisms by which hypertension increases the risks of ischemic coronary events may include impairment of endothelial function, increased oxidative stress, increased endothelial lipid permeability, as well as hemodynamic stress. Randomized trials have demonstrated that lowering blood pressure (BP) can rapidly reduce cardiovascular risk, with a sustained drop of 10mm Hg leading up to a 40-50% reduction in risk.

Treatment of elevated lipid levels reduces cardiovascular morbidity and mortality,improving quality of life and extending life expectancy.

The comprehensive cardiovascular risk assessment for patients with a lipid disorder begins with measuring lipid levels and those identified by the Framingham Risk Score. These include hypertension, smoking, diabetes, family history of premature CAD, age, sex, and presence of established CAD or other atherosclerotic disease (e.g.,peripheral arterial insufficiency, symptomatic carotid disease).

AIM AND OBJECTIVES

- To evaluate HsCRP levels and correlate it with the lipid profile in hypertension.

- To correlate the above biochemical parameters in identifying patients who are at higher risk of developing coronary artery disease (CAD) and for providing primary prevention treatment in such patients.

REVEIW OF LITERATURE

HIGHLY SENSITIVE C REACTIVE PROTEIN (HSCRP)

INTRODUCTION

Highly Sensitive C Reactive Protein (hsCRP) known as ultra sensitive CRP also called as cardiac CRP. It measures low levels of CRP using nephelometry or immuno turbidimetry technique. Since the method has high sensitivity, even small quantity (1–10 ng/dL) can be measured accurately.

CRP levels increase in the blood with onset of inflammation. Even a low level of persistent inflammation contributes to a important role in development of atherosclerosis.

The High sensitivity CRP (hs CRP) test measures accurately very low levels of CRP and detects very low levels of inflammation which in turn can predict a individual's risk of developing CAD.

Highly sensitive CRP is a useful test for determining risk of .It is a marker of at risk for atherosclerosis process and is used as a predictor for future myocardial infarction within the next 120 months. More than fifty percent of cardiovascular events and CVAs happen in those who do not have dyslipidemia, measuring hsCRP

levels can help to identify patients who are at risk and may need primary preventive treatment.

The hs CRP test clearly adds to the predictive value. The best method to predict risk of CAD is to combine a surrogate and sensitive marker of inflammation, like hsCRP, with the lipid levels.

HISTORY

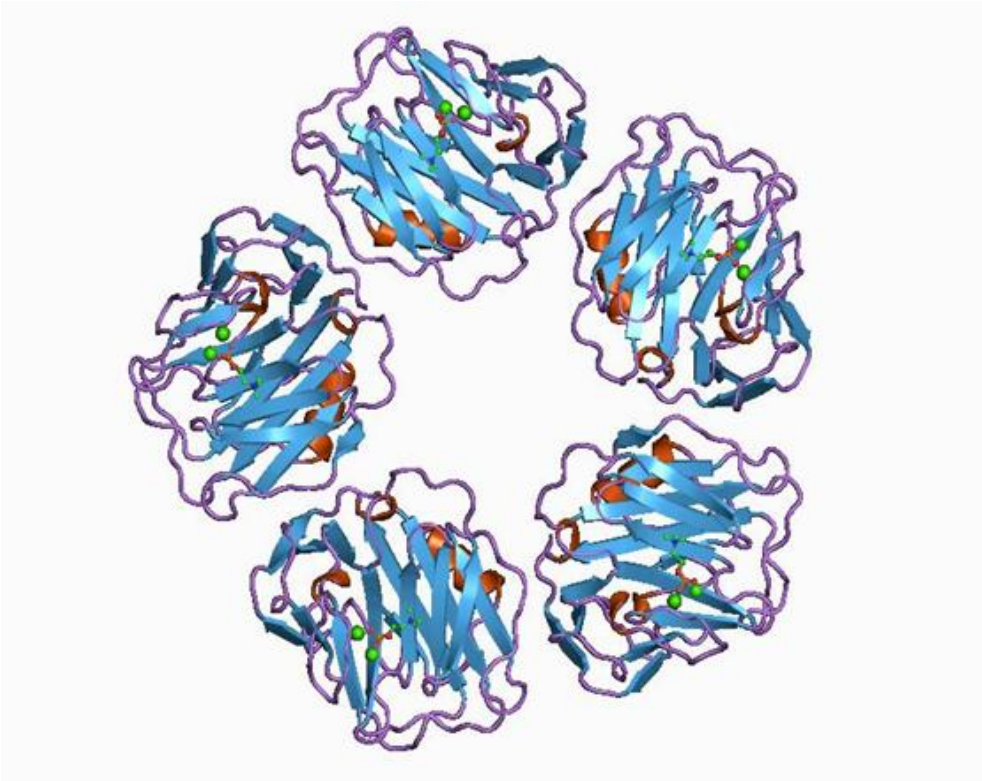
CRP was first described by Tillet and Francis in 930. Experiments revealed serum of patients suffering from acute bacterial infection showed precipitation with the C polysaccharide pneumococcus extract. This reaction causing protein was called C-reactive protein (CRP).

The discovery of CRP was in the sera of a patient with pneumonia caused by S. pneumonia infection. CRP was present in very high concentrations in the acute phase sera of the patient and caused precipitation of pneumococcal cell wall extracts but only in the presence of calcium ions.

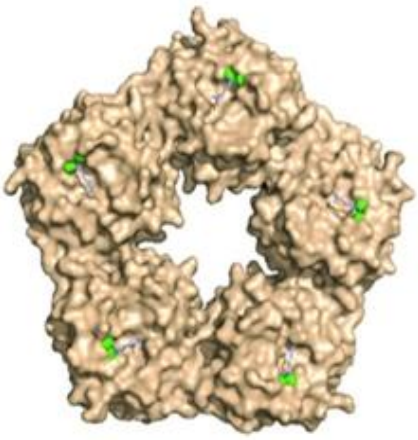
Most of the acute inflammatory processes and some malignancies, cause a rise in CRPlevels as a non specific mechanism.

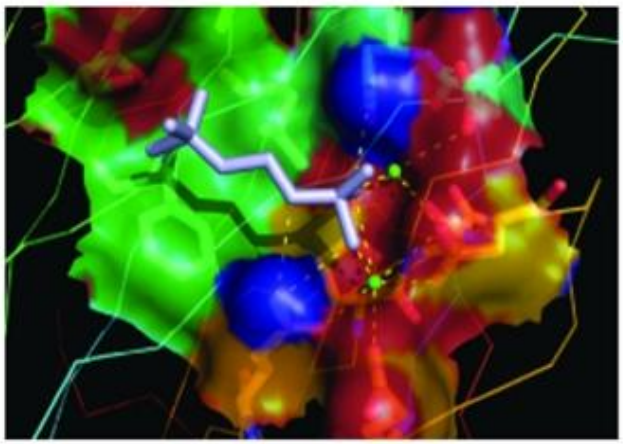
STRUCTURE OF CRP

CRP has a unique pentraxin configuration,. In humans one of the two members of this family are CRP .



Structure of C-reactive protein (CRP),Pentraxin model





Structure of CRP

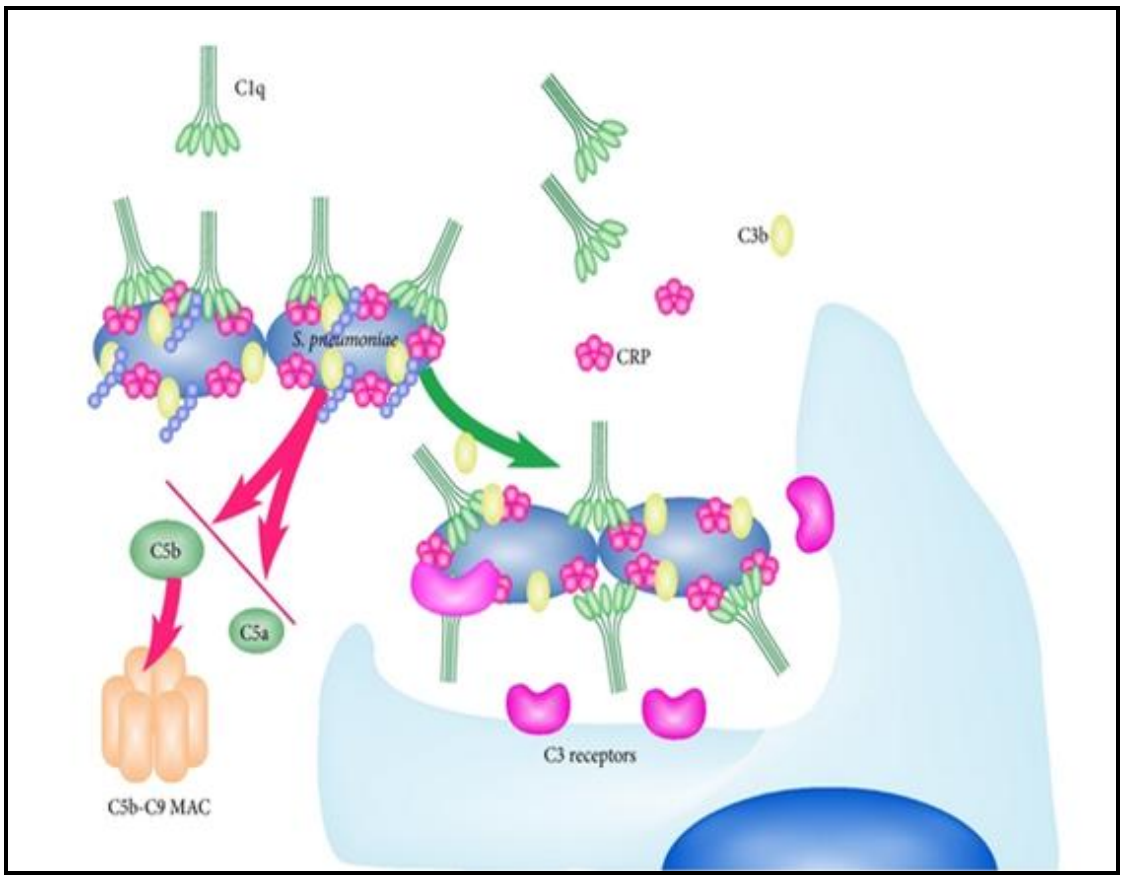
	C-reactive protein (CRP)	Serum amyloid P (SAP)
Fc receptor binding	Yes	Yes
Calcium-dependent ligand binding	Yes	Yes
Complement activation through C1q	Yes	Yes
Ligands	Phosphocholine snRNP (Sm, RNP) Histones Apoptotic cells Oxidized LDL	Phosphoethanolamine DNA, chromatin Heparin Apoptotic cells Amyloid fibrils
Major synthetic site	Liver	Liver
Inducers	IL-6 (acute phase reactant)	Constitutive
Structure	Cyclic pentamer 115,135 Da Each subunit 23,027 Da 206 amino acids	Cyclic pentamer 127,310 Da Each subunit 25,462 Da 204 amino acids
Glycosylation	No	Yes
Chromosomal location	1q23.2	1q23.2

COMPARISON OF THE PROPERTIES BETWEEN CRP AND SERUM AMYLOID P (SAP)

Production of CRP in hepatocytes is mediated by cytokines. Interleukins 1, 6 and TNF .The CRP molecule is arranged in a doughnut shaped polymer.

PATHOPHYSIOLOGY OF CRP

Genes for CRP lie on chromosome 1q23.2 in man .CRP is secreted as an acute phase reactant protein.It has a plasma half life of 19 hours,it also functions as opsonins for pathogenic bacterial micro organisms through activation of the complement pathway and through binding to Fc gamma receptors.



CRP complexes

CRP is produced in the liver and in the smooth muscle cells of an atherosclerotic plaque.Among the various markers, significant importance has been given to circulating levels of CRP as a risk indicator.

The CRP levels in blood can be measured accurately and reproducible to very low levels by latest advanced high sensitivity assays. It is a stable molecule with a long half life of 19 hours approximately and does not show circadian variation.

The general population have stable CRP levels characteristic for each individual except occasional increases associated with minor or subclinical infections, trauma, or inflammation. The levels of CRP may also be regulated by genetic variations.

Twin studies show a highly significant genetic basis for CRP levels which is independent of age and body mass index.

C-REACTIVE PROTEIN AND PATHOGENESIS OF ATHEROTHROMBOSIS

It has been demonstrated that cellular effects of CRP may directly cause atherothrombosis thus acting as a risk factor in addition to being a risk marker. Recent datas show that CRP may also be produced by vascular wall cells where it has proinflammatory effects and stimulate macrophage uptake of LDL, thereby contributing to the pathogenesis of atherothrombosis.

CRP which is immunoreactive has been identified in atheromatous plaques. aggregated fraction of CRP binds to LDL, whereas native fraction CRP binds to oxidized and aggregated LDL which leads to complement activation . Complement activation,experimentally has shown to be involved in atherogenesis, could be one significant mechanism by which CRP could contribute to atherogenesis.

Recent datas, have changed the view that the liver exclusively produces CRP where transcriptional PCR data suggest that endothelial cells ,smooth muscle cells and macrophages are also capable of producing CRP.

Other than cells themselves, CRP is also produced in atherosclerotic plaques where, according to many independent studies, it is involved in atherothrombosis and plaque vulnerability by mediating the secretion of vascular adhesion molecules, inducing production of NO, alteration of innate complement functions, uptake of oxidized LDL, matrix degradation, and inhibition of intrinsic fibrinolysis.

CRP directly involves in the atherosclerotic process initiating the innate inflammatory response, stopping production of endothelial nitric oxide synthase, by activation of PAI-1, all of which have a direct effect on arterial thrombosis.

The free radicals oxidize PUFA present in LDL,this modified LDL is not recognized by the hepatocytes in liver, so it is taken up by macrophage scavenger receptors present on macrophages resulting in formation of foam cells, thus starting the atherosclerotic process .

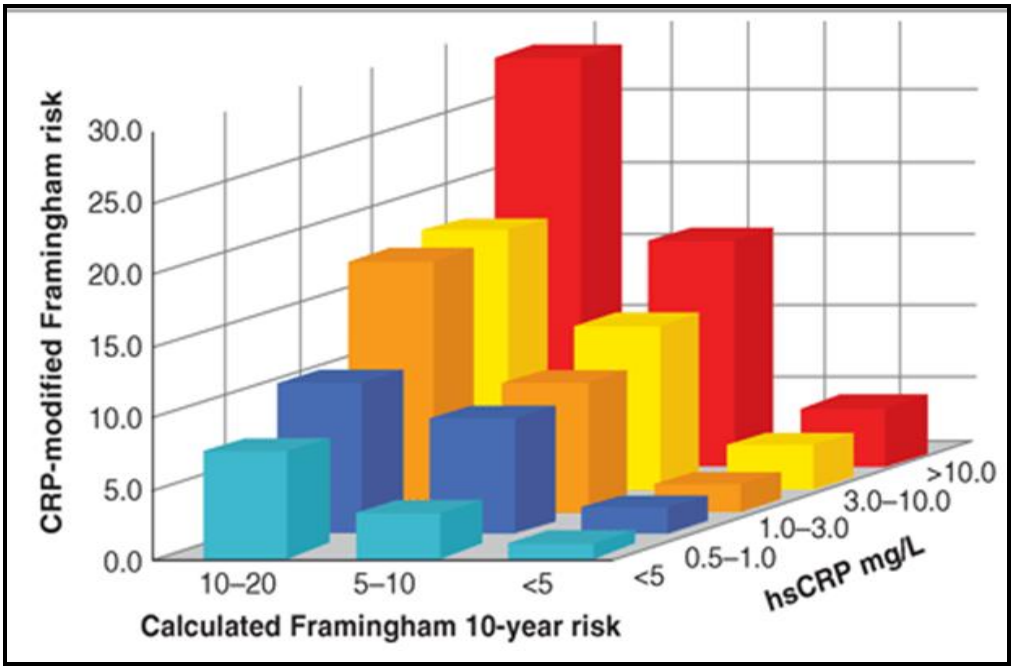
The exact mechanisms of CRP elevation in vascular disease are not well understood and several mechanisms have been proposed Amplified release of cytokines IL-1and IL-6 from inflammatory focus within the atherosclerotic plaque leading to hepatic overproduction of CRP.

Intimal smooth muscle myocyte damage from acute vascular occlusion causing an acute phase response.

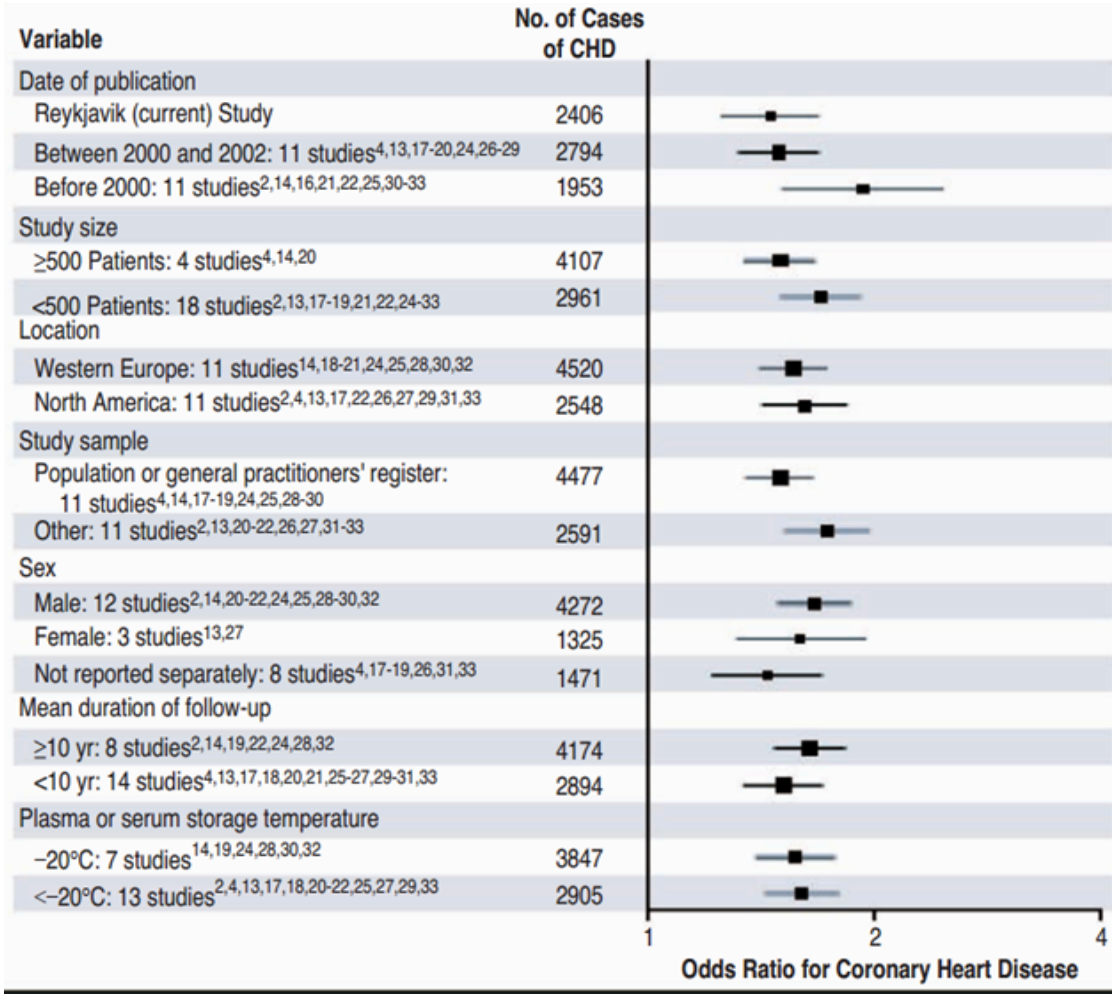
Systemic stimuli that cause chronic inflammation leading to increased CRP levels and endovascular inflammation.

CRP and Vascular Disease risk in subjects without any known vascular disease or with subclinical vascular disease.

Several prospective trails have shown that, individuals without any underlying cardiovascular disease or known preclinical vascular disease, elevated CRP levels measured by high sensitivity assays, are associated with an increased future risk of cardiovascular events.



CRP LEVEL AND THE FRAMINGHAM SCORE



22 studies on CAD risk and CRP levels

Elevated CRP levels have also been noted with obesity, type 2 diabetes, insulin resistance. Elevated CRP and IL-6 levels are shown to predict an increased risk of future development of type 2 diabetes in the Women's Health Study .

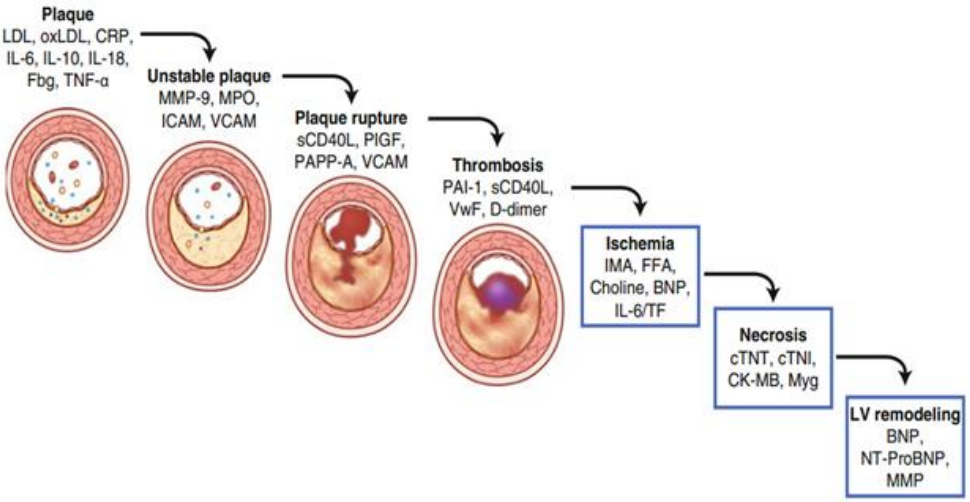


Diagram shows the steps in disease progression for acute coronary syndrome and the associated increases in serum biomarker levels

An European prospective trial on more than two thousand patients with, elevated levels of CRP and angina were at an increased risk for future myocardial infarction or sudden cardiac death .

CRP LEVELS AND RISK OF CARDIOVASCULAR DISEASES

Many studies in ACS have shown that elevated CRP levels are associated with increased risk of cardiovascular complications

including cardiac rupture and that successful reperfusion is associated with a fall in elevated CRP levels beyond that predictable on the basis of infarct size reduction .

CRP AND THERAPEUTIC INTERVENTIONS

CRP levels are elevated in presence of risk factors like obesity, insulin resistance, and smoking, importance on risk modification is needed in such cases to reduce the pro cardiovascular risk and inflammatory state .

Increased cardiovascular risk associated with elevated levels of CRP in healthy individuals was shown to be neutralised by use of aspirin in one study . The group in the lowest quartile of risk had only a 15% RRR, whereas the group in the highest quartile of risk experienced a robust 55% RRR with aspirin.

Many studies have shown that CRP levels fall with starting of statin therapy, often independent of LDL lowering, reflecting their anti inflammatory and pleiotropic effects . Some of the studies have showed that the decrease in CRP with statins occurs independent of LDL lowering.

Additional studies are needed to definitively prove whether CRP lowering is or is not related to lipid (both LDL and non LDL lipid fractions) modifying effects of statins.

Also data from the CARES secondary prevention trial showed that pravastatin was most effective in reducing cardiovascular risk in the group with elevated CRP levels . Retrospective analysis of the AFCAPS/TEXCAPS primary prevention trial also showed that increased cardiovascular risk associated with elevated CRP levels was reduced by statin therapy (lovastatin), even in subjects with average or below average cholesterol levels .

It has also been shown that CRP has an additive value across all levels of lipid screening, even after adjustment for age, smoking, blood pressure, obesity, and diabetes.hsCRP from sudden cardiac death victims showed a positive correlation with its recognition by immunostaining of plaques and as a predictor of high risk thin cap fibroatheromas.

Accumulated CRP was localized mainly to the necrotic core and surrounding macrophages where its strongest expression was found in patients with high serum CRP levels. The clinical use of CRP significantly added to the predictive value of total and HDL cholesterol.

CRP AS RISK FACTOR OF CARDIOVASCULAR EVENTS

Studies show that inflammation is linked with atherosclerosis, and low levels of CRP may be an indicator of atherosclerosis. Myocardial infarction is due to as a result of inflammation mediated atherosclerosis. This inflammation has a role in pathogenesis of cardiovascular events.

Around 50% of all myocardial infarctions happen in individuals who do not have dyslipidemia. The inclusion of measuring of CRP levels to the screening tests based on lipid levels can provide an improvised method of identifying women who are at risk of developing cardiovascular events.

Endothelial damage resultsdue to inflammation . CRP is marker for inflammation and it can be a surrogate marker for CAD risk.

The AHAssociation has classified risk groups as follows

- Low Risk with HsCRP less than 1.0 mg/L
- Average risk with HsCRP between 1.0 to 3.0 mg/L
- High risk with HsCRP more3.0 mg/L

hsCRP should not be used alone and can be combined with dyslipidemia, and blood glucose levels.

An elevated serum CRP is a predictor of the development and progression of atherosclerosis, of future coronary events including unstable angina pectoris and acute myocardial infarction.Serum CRP levels correlate well as a predictor of cardiovascular events than is LDL-cholesterol.

VARIOUS CARDIOVASCULAR RISK PREDICTION TOOLS

Risk Score	Region	Variables	End Points
Pooled cohort equations	U.S.	Age, sex, TC, HDL-C, SBP, smoking, antihypertensive medications, DM, and race	CHD death, nonfatal MI, fatal and nonfatal stroke
Framingham – ATP III, 2001	U.S.	Age, sex, TC, HDL-C, SBP, smoking, and antihypertensive medications	CHD death and nonfatal MI
Framingham – Global CVD, 2008	U.S.	Age, sex, TC, HDL-C, SBP, smoking, antihypertensive medications, DM, and known CHD, PAD, or stroke	CVD death, all CHD, stroke, heart failure, and claudication
Reynolds (men)	U.S.	Age, TC, HDL-C, SBP, smoking, FHMI, HbA1C, and CRP	CVD death, nonfatal MI, stroke, and coronary revascularization
Reynolds (women)	U.S.	Age, TC, HDL-C, SBP, smoking, FHMI, HbA1C, and hsCRP	CVD death, nonfatal MI, stroke, and coronary revascularization
SCORE	Europe	Age, sex, TC, HDL-C, SBP, and smoking	CVD death

Class IIa
In men 50 years of age or older or women 60 years of age or older with LDL cholesterol less than 130 mg/dL; not on lipid-lowering, hormone replacement, or immunosuppressant therapy; without clinical CHD, diabetes, chronic kidney disease, severe inflammatory conditions, or contraindications to statins, measurement of CRP can be useful in the selection of patients for statin therapy. (Level of Evidence: B)
Class IIb
In asymptomatic intermediate-risk men 50 years of age or younger or women 60 years of age or younger, measurement of CRP may be reasonable for cardiovascular risk assessment. (Level of Evidence: B)
Class III: No benefit
In asymptomatic high-risk adults, measurement of CRP is not recommended for cardiovascular risk assessment. (Level of Evidence: B)
In low-risk men younger than 50 years of age or women 60 years of age or younger, measurement of CRP is not recommended for cardiovascular risk assessment. (Level of Evidence: B)

RECOMMENDATIONS OF ACC/AHA FOR THE MEASUREMENT OF CRP

INTERVENTIONS THAT LOWER CRP

At present no specific therapies are available to lower CRP levels reduction

Lifestyle modification, weight loss, and stopping smoking have beneficial effects on proinflammatory markers, including CRP. Several drugs such as peroxisome proliferator activated receptors agonists , ACE inhibitors, ARBs, aspirin , niacin

,clopidogrel , and statins have also been shown to decrease serum CRP levels.

CLINICAL SIGNIFICANCE OF CRP LEVELS REDUCTION

Eventhough CRP has been studied as an independent predictor for future CV events in asymptomatic individuals,most of the epidemiologic studies report only the relative risk and fail to show the absolute risk associated with increased CRP or the receiver operating curve comparing CRP to other

risk factors, making it difficult to gauge the true incremental value of using CRP for cardiovascular risk prediction.

The factors that reduce serum CRP levels and cause a reduction in the incidence of cardiovascular events. These include the following:

Exercise; Diet high in fiber soy and nuts; Quiting Smoking; HMG-CoA reductase inhibitors; Beta adrenergic blockers and Ezetimibe a cholesterol lowering agent.

HYPERTENSION

DEFINITION.

Hypertension is defined by a sustained SBP ≥140 mmHg or a DBP ≥90 mmHg.

A single recording of elevated BP may be enough if systolic or diastolic blood pressures are significantly elevated, if symptoms are present, but very high fluctuations in blood pressure above base line BP in a healthy individual may occur transiently during acute illness or extreme physical and emotional stress .

Blood pressure ≥135/85 mmHg outside the doctor's office also could be considered elevated.The term prehypertension has been designated for BP 120–139 mmHg systolic or 80–89 diastolic. Patients with prehypertension are targets for lifestyle modifications that can prevent or delay the onset of hypertension.

Blood pressure (BP) has a continuous,normal bell shaped (Gaussian) distribution.

Hypertension is the most common cardiovascular disease.The natural course of untreated hypertension increases the risk of fatal

and nonfatal coronary artery disease, congestive heart failure, stroke,acute and chronic kidney disease and all cause mortality.

Depending on the level of hypertension, age, gender,other risk factors for target organ damage ,atherosclerosis and cardiovascular disease, the 10 year risk t varies from less than 15 % to more than 40%. Epidemiological studies indicate that > 60% of CV events happen in persons with high or moderate hypertension and who have other risk factors such as dyslipidaemia, glucose intolerance or coronary artery disease.

More than 85% of hypertension is idiopathic, while 10%–15% can be due to identifiable causes (secondary hypertension).

Essential hypertension is usually idiopathic, and inappropriate secondary retention of salt and water. Over long periods, this leads to accelerated atherosclerosis in arteries causing increased workload and hypertrophy of the heart.

APPROACH TO DIAGNOSIS AND TREATMENT OF PATIENTS WITH HTN

1) First confirm the diagnosis of hypertension.

2) Evaluate clinically for other cardiovascular risk factors, target organ damage, secondary hypertension and cardiovascular disease.

3) Initiate therapy depending on the severity of the hypertension and other comorbid risks

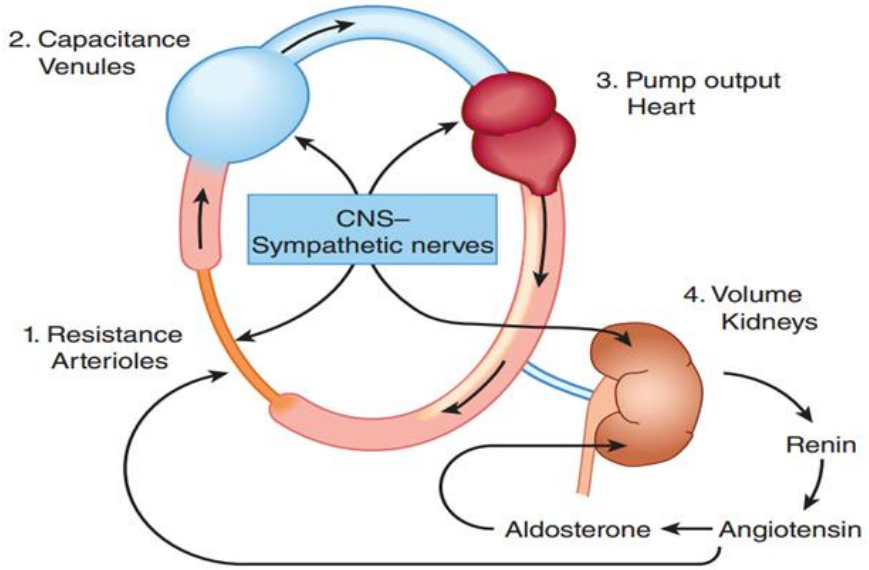
Systolic/Diastolic Pressure (mm Hg)	Category
< 120/80	Normal
120–135/80–89	Prehypertension
≥ 140/90	Hypertension
140–159/90–99	Stage 1
≥ 160/100	Stage 2

From the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. JAMA 2003;289:2560.

CLASSIFICATION OF HYPERTENSION ON THE BASIS OF BLOOD PRESSURE

Regulation of Blood Pressure

BP is the product of peripheral vascular resistance and cardiac output ,given by the equation: BP = CO × PVR.



Anatomic sites of blood pressure control

Appropriate diagnosis and management of hypertension require accurate and representative BP measurement. There is commonly a physiologic 15% to 20% variation in hour to hour BP readings. Studies using ambulatory BP monitoring

(ABPM) reveal BP is generally highest during the day, lowest during sleep, and increases during the period from 4:00 am to 12:00 pm, correlating with diurnal cortisol levels .

Risk Factors for Cardiovascular Disease	Target Organ Damage	Associated Clinical Conditions
Age >55 years	Left ventricular hypertrophy detected by	Cerebrovascular Disease
Male sex	electrocardiogram and/or echocardiography	Ischaemic stroke
Post-menopausal women	Microalbuminuria/proteinuria and/or elevation	Cerebral haemorrhage
Smoking and tobacco use	of serum creatinine (1.2 to 2.0 mg/dL)	Transient ischaemic attack
Diabetes mellitus	Ultrasound or radiological evidence of atherosclerotic	Heart Disease
Family history of premature	plaques in the carotids	Myocardial infarction
CAD (Men <55 years, Women <65 years)	Generalised or focal narrowing of retinal arteries	Angina
Increased waist-hip ratio		Coronary revascularisation
High LDL or total cholesterol, low HDL		Congestive heart failure
cholesterol and high triglycerides		Renal Disease
		Diabetic nephropathy
		Renal failure (serum creatinine 2.0 mg/dL)
		Vascular Disease
		Symptomatic arterial disease including non-specific aortoarteritis
		Dissecting aneurysm
		Advanced Hypertensive Retinopathy
		Haemorrhages or exudates
		Papilloedema

CARDIOVASCULAR RISK FACTORS AND TARGET-ORGAN DAMAGE (JNC-VII, 2003)

APPROACH TO A PATIENT WITH HTN

Investigate for damageto target organs and evidence of atherosclerotic disease, looking for evidence of cardiomegaly or heart failure, vascular insufficiency, bruits, and possible signs of secondary hypertension such as thyromegaly. Look for comorbidities such as diabetes or renal dysfunction, and calculating body mass index for cardiac risk stratification.Routine fundoscopy

USEFUL INITIAL TESTS FOR PATIENTS WITH HYPERTENSION

1) Total cholesterol,High density lipoprotein.

2) Serum potassium,sodium, creatinine (calculate glomerular filtration rate and screen for secondary causes).

3) (3)A resting electrocardiogram may show left ventricular hypertrophy, presence of coronary artery disease, and conduction blocks, important when using antihypertensive medications that have nodal blocking activity.

4) (4)Urinalysis (screen for proteinuria)

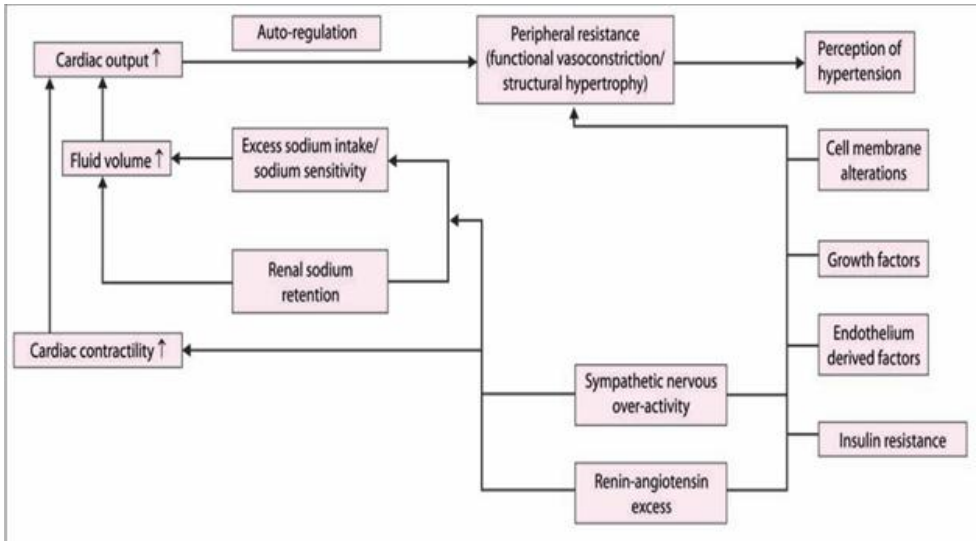
5) (5)Fasting glucose, or HBA1c (glycosylated hemoglobin).

PATHOPHYSIOLOGY OF HYPERTENSION

Hypertension is usually associated with other cardiovascular risk factors, including diabetes mellitus, hyperinsulinemia, dyslipidemia, and obesity . In combination, these risk factors are synergistic rather than merely additive.

Obesity causes a six fold increase in the probability of developing hypertension and accounts for 68% to 80% of its attributable risk .

Among patients with concomitant hypertension and dyslipidemia, coronary artery disease prevalence more than doubles compared with those with either condition alone . Smoking and alcohol use also contribute to cardiovascular morbidity.



Factors involved in the pathogenesis of hypertension

Cigarette smoking leads to endothelial damage and atherosclerosis. Consuming three or more alcoholic drinks a day increases BP, even when controlling for body mass index, cigarette smoking, and age.

SECONDARY HYPERTENSION: AN OVERVIEW

Condition	History	Physical exam	Initial tests	Screening	Definitive
Renal parenchymal disease	Renal disease, hypertension, diabetes mellitus, glomerulonephritis, chronic analgesics	Flank/abdominal mass, volume overload, diabetic neuropathy/retinopathy	Elevated creatinine and GFR, anemia, active sediment, proteinuria	Spot and 24-hour urinary protein, renal ultrasound	Renal biopsy in selected cases
Renovascular hypertension	Age < 30 y, especially female; age > 60, atherosclerosis; azotemia induced by ACE-I or ARB	Flank bruit; peripheral vascular insufficiency	Proteinuria, hyperlipidemia	Clinical prediction rules, ultrasound, CT, MRI, captopril renal scintigraphy	Renal arteriography
Coarctation of the aorta	Early onset hypertension, lower extremity claudication, mesenteric ischemia	Asymmetrical pulses and BP, systolic murmur or bruit	Bilateral ankle:brachial index, CXR	Ultrasound, MRI, CT	Transesophageal echo, aortography
Cushing syndrome	Weight gain, acne, fluid retention, bruising, adrenal mass, steroid use	Abdominal mass, moon facies, truncal obesity, striae, hirsutism	Hyperglycemia, hyperlipidemia	24-h Urinary free cortisol, low-dose dexamethasone suppression test, midnight salivary cortisol	High dose dexamethasone suppression test; if ACTH dependent, pituitary MRI +/− inferior petrosal sampling
Primary hyperaldosteronism	Onset at young age; weakness, fatigue, polyuria, polydipsia, muscle cramps		± Hypokalemia	PA/plasma renin activity, 24-h urinary aldosterone	Adrenal CT or MRI; scintigraphy +/- adrenal vein sampling
Pheochromocytoma	± Paroxysmal hypertension; palpitations, headache, sweating, autonomic instability	Tremor, orthostasis, cardiomyopathy, perspiration, incidentally discovered adrenal mass	Hyperglycemia	Plasma metanephrines; 24-h urinary metanephrines	Adrenal CT or MRI, scintigraphy, rarely PET scan
Sleep apnea	Snoring, daytime somnolence or fatigue	Obesity, increased neck circumference, micrognathia			Polysomnography

SECONDARY HYPERTENSION

PRINCIPLES OF MANAGEMENT

Goal of Antihypertensive Therapy

Antihypertensive therapy is aimed at preventing cardiovascular morbidity and mortality. Nonpharmacologic lifestyle and diet changes are essential for all patients.

Drug therapy for those with hypertension and those with prehypertension who have compelling indications, such as chronic kidney disease or diabetes . **Nonpharmacologic Treatment**

Diet and lifestyle approaches, including weight loss, exercise, and dietary adjustment, may prevent and control of hypertension (DASH) therapy.

Combining nonpharmacologic and pharmacologic therapy controls BP better than nonpharmacologic treatment alone .

Regular moderate aerobic excercises of moderate intensityf or at least 30-45 minutes per day for atleast 5 days in a week.

Restriction of salt in diet,avoiding dairy fats,stopping smoking all help in reducing hypertension.

Taking plenty of fresh fruits and vegetables,nuts like walnuts,almonds,pistachio which are rich in pottasium are good for the heart.

Table below summarizes recommendations for non-pharmacologic therapy.

RECOMMENDATIONS FOR NONPHARMACOLOGIC THERAPY

	Normotensive individuals	Prehypertensive and hypertensive patients	Health care professionals
Alcohol	Consume < 2 drinks/d for men and no more than 1 drink/d for women (1 oz ethanol, 10 oz wine, 24 oz beer)	Consume < 2 drinks/d for men and no more than 1 drink/d for women (1 oz ethanol, 10 oz wine, 24 oz beer)	Advise on effects of excess consumption, encourage reduction, refer as appropriate
Obesity	Reduce to goal body weight = BMI 18.5–24.9 kg/m^2 with diet and exercise	Reduce to goal body weight = BMI 18.5–24.9 kg/m^2 with diet and exercise	Inform patient, use proper BP cuff, refer as appropriate
Diet	Consume diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat (DASH diet)	Consume diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat (DASH diet)	Inform patient, refer as appropriate to community resources
Sodium/Salt	Minimize high-salt processed foods	Reduce intake to < 100 mmol/d (< 2.3 g sodium, < 6.0 g salt/d)	Provide information on salt content of foods, counsel on methods to reduce salt intake
Smoking	Stop smoking	Stop smoking	Advise on effects of smoking, encourage quitting, refer as appropriate
Exercise	Regularly do exercise as beneficial for weight regulation and maintaining function throughout older age	Regularly do aerobic exercise for at least 30 minutes a day most days of the week	Encourage regular, appropriate physical activity; specify mode, intensity, duration, days per week
Calcium	Consume 1200 mg/d in dietary or nondietary supplement	Consume 1200 mg/d in dietary or nondietary supplement	Advise on calcium content in foods
Stress management	Insufficient evidence to recommendation stress reduction	Insufficient evidence to recommend stress reduction	Assess social situation as appropriate
Potassium and magnesium	No evidence to recommend supplementation beyond diet rich in fruits, vegetables, and low-fat dairy	No evidence to recommend supplementation beyond diet rich in fruits, vegetables, and low-fat dairy	Encourage diet rich in fruits, vegetables, and low-fat dairy products

Abbreviation: BMI, body mass index calculated as weight in kg divided by the square of height in meters.
(*Source:* Adapted from Touyz et al. [284] and Chobanian et al. [9].)

RECOMMENDATIONS FOR NON PHARMACOLOGIC THERAPY

SUMMARY Drugs Used in Hypertension

Subclass, Drug	Mechanism of Action	Effects	Clinical Applications	Pharmacokinetics, Toxicities, Interactions
DIURETICS				
• Thiazides: Hydrochlorothiazide, chlorthalidone	Block Na/Cl transporter in renal distal convoluted tubule	Reduce blood volume and poorly understood vascular effects	Hypertension, mild heart failure	
• Loop diuretics: Furosemide	Block Na/K/2Cl transporter in renal loop of Henle	Like thiazides • greater efficacy	Severe hypertension, heart failure	See Chapter 15
• Spironolactone, eplerenone	Block aldosterone receptor in renal collecting tubule	Increase Na and decrease K excretion • poorly understood reduction in heart failure mortality	Aldosteronism, heart failure, hypertension	
SYMPATHOPLEGICS, CENTRALLY ACTING				
• Clonidine, methyldopa	Activate α_2 adrenoceptors	Reduce central sympathetic outflow • reduce norepinephrine release from noradrenergic nerve endings	Hypertension • clonidine also used in withdrawal from abused drugs	Oral • clonidine also as patch • *Toxicity*: sedation • methyldopa hemolytic anemia
SYMPATHETIC NERVE TERMINAL BLOCKERS				
• Reserpine	Blocks vesicular amine transporter in noradrenergic nerves and depletes transmitter stores	Reduces all sympathetic effects, especially cardiovascular, and reduce blood pressure	Hypertension but rarely used	Oral • long duration (days) • *Toxicity*: psychiatric depression, gastrointestinal disturbances
• Guanethidine	Interferes with amine release and replaces norepinephrine in vesicles	Same as reserpine	Same as reserpine	Severe orthostatic hypotension • sexual dysfunction

Drugs Used in Hypertension

Subclass, Drug	Mechanism of Action	Effects	Clinical Applications	Pharmacokinetics, Toxicities, Interactions
α BLOCKERS				
• Prazosin • Terazosin • Doxazosin	Selectively block α_1 adrenoceptors	Prevent sympathetic vasoconstriction • reduce prostatic smooth muscle tone	Hypertension • benign prostatic hyperplasia	Oral • *Toxicity:* Orthostatic hypotension
β BLOCKERS				
• Metoprolol, others • Carvedilol • Nebivolol	Block β_1 receptors; carvedilol also blocks α receptors; nebivolol also releases nitric oxide	Prevent sympathetic cardiac stimulation • reduce renin secretion	Hypertension • heart failure • coronary disease	See Chapter 10
• *Propranolol: Nonselective prototype β blocker* • Metoprolol and *atenolol: Very widely used β_1-selective blockers*				
VASODILATORS				
• Verapamil • Diltiazem	Nonselective block of L-type calcium channels	Reduce cardiac rate and output • reduce vascular resistance	Hypertension, angina, arrhythmias	See Chapter 12
• Nifedipine, amlodipine, other dihydropyridines	Block vascular calcium channels > cardiac calcium channels	Reduce vascular resistance	Hypertension, angina	See Chapter 12
• Hydralazine • Minoxidil	Causes nitric oxide release Metabolite opens K channels in vascular smooth muscle	Vasodilation • reduces vascular resistance • arterioles more sensitive than veins • reflex tachycardia	Hypertension • minoxidil also used to treat hair loss	Oral • *Toxicity:* Angina, tachycardia • Hydralazine: Lupus-like syndrome Minoxidil: Hypertrichosis
PARENTERAL AGENTS				
• Nitroprusside • Fenoldopam • Diazoxide • Labetalol	Releases nitric oxide Activates D_1 receptors Opens K channels α, β blocker	Powerful vasodilation	Hypertensive emergencies	Parenteral • short duration • *Toxicity:* Excessive hypotension, shock
ANGIOTENSIN-CONVERTING ENZYME (ACE) INHIBITORS				
• Captopril, many others	Inhibit angiotensin-converting enzyme	Reduce angiotensin II levels • reduce vasoconstriction and aldosterone secretion • increase bradykinin	Hypertension • heart failure, diabetes	Oral • *Toxicity:* Cough, angioedema • hyperkalemia • renal impairment • teratogenic
ANGIOTENSIN RECEPTOR BLOCKERS (ARBs)				
• Losartan, many others	Block AT_1 angiotensin receptors	Same as ACE inhibitors but no increase in bradykinin	Hypertension • heart failure	Oral • *Toxicity:* Same as ACE inhibitors but less cough
RENIN INHIBITOR				
• Aliskiren	Inhibits enzyme activity of renin	Reduces angiotensin I and II and aldosterone	Hypertension	Oral • *Toxicity:* Hyperkalemia, renal impairment • potential teratogen

Contd -Drugs Used in Hypertension

INDICATIONS AND CONTRAINDICATIONS FOR THE MAJOR CLASSES OF ANTIHYPERTENSIVE DRUGS

		Contraindications	
Class	**Conditions favouring the use**	**Compelling**	**Possible**
Diuretics (thiazides)	Congestive heart failure Elderly hypertensives Isolated systolic hypertension Hypertensives of African origin	Gout	Pregnancy
Diuretics (loop)	Renal insufficiency Congestive heart failure		
Diuretics (anti-aldosterone)	Congestive heart failure Post myocardial infarction	Renal failure Hyperkalaemia	
Beta-blockers	Angina pectoris Post myocardial infarction Congestive heart failure (up-titration) Pregnancy Tachyarrhythmias	Asthma Chronic obstructive pulmonary disease Atrioventricular block (grade 2 or 3)	Peripheral vascular disease Glucose intolerance Athletes and physically active patients
Calcium antagonists (dihydropyridines)	Elderly patients Isolated systolic hypertension Angina pectoris Peripheral vascular disease Carotid atherosclerosis Pregnancy		Tachyarrhythmias Congestive heart failure
Calcium antagonists (verapamil, diltiazem)	Angina pectoris Carotid atherosclerosis Supraventricular tachycardia	A-V block (grade 2 or 3) Congestive heart failure	
ACE-inhibitors	Congestive heart failure Left-ventricular dysfunction Post myocardial infarction Non-diabetic nephropathy Type 1 diabetic nephropathy Proteinuria	Pregnancy Hyperkalaemia Bilateral renal artery stenosis	
Angiotensin II-receptor antagonists (AT1-blockers)	Diabetic nephropathy Diabetic microalbuminuria Proteinuria Left-ventricular hypertrophy ACE inhibitor cough	Pregnancy Hyperkalaemia Bilateral renal artery stenosis	
Alpha-blockers	Prostatic hyperplasia (BPH) Hyperlipidaemia	Orthostatic hypotension	Congestive heart failure

DYSLIPIDEMIA

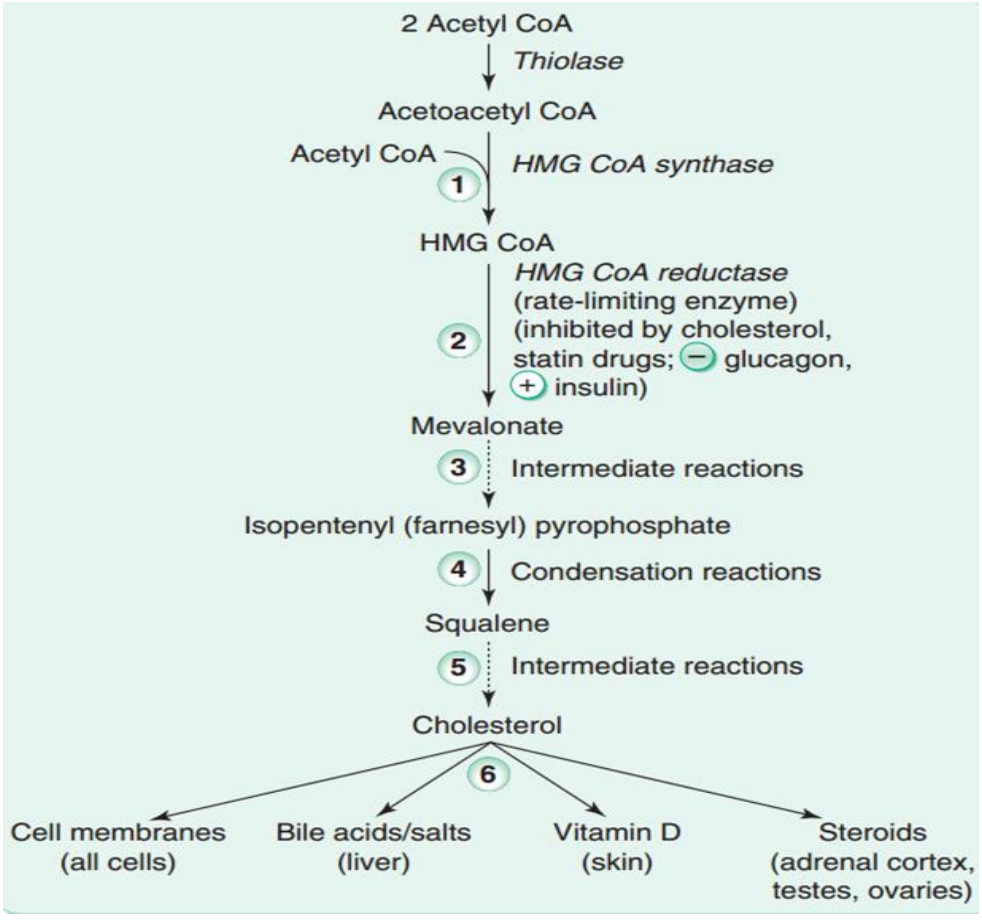
The relation of blood cholesterol with the risk of coronary artery disease (CAD) has been evaluated in many prospective observational studies and combined together in two large collaborative individual patient data meta analyses which have published relevant data.

1) The Prospective Studies Collaboration (PSC), which contains studies mainly from Europe and North America ,some from participants from studies conducted in China or Japan .

2) The Asia Pacific Cohort Studies Collaboration (APCSC), contains cohort studies on asian population.

These observational studies shows positive relation between normal levels of total cholesterol (a surrogate marker for LDL cholesterol) and the increased risk of CAD.

CHOLESTEROL SYNTHESIS AND REGULATION



STEPS IN CHOLESTEROL SYNTHESIS AND REGULATION

Step-1

1) HMG CoA is formed by 3 molecules of acetyl CoA.

2) HMG CoA is produced in the mitochondria matrix

Step-2

1) HMG CoA reductase conversion of HMG CoA to mevalonate

2) Statin drug such as atorvastatin act as competitive inhibitors with mevalonate for binding to HMG CoA reductase.

Step-3

1) farnesyl pyrophosphate (FPP) is formed from mevalonate and intermediate in cholesterol synthesis.

2) Squalene is formed by several condensation reactions involving isopentenyl pyrophosphate.

Step-4

a. Conversion of squalene to cholesterol requires NADPH.

Step-5

a. Cholesterol is excreted in bile and also used to synthesize bile acids and salts.

THE LIPOPROTEINS

Introduction

Michel Macheboeuf is known as the father of plasma lipoproteins. He was a French physician and scientist.

Physiology of lipoprotiens

Lipids are transported in the plasma on lipoproteins, they are classified by their density and electrophoretic mobility into four major groups.

1) Chylomicrons.

2) Very low density lipoproteins(VLDL).

3) Low density lipoproteins (LDL).

4) High density lipoproteins (HDL).

Chylomicrons and VLDL primarily transport triglycerides (TG) while LDL and HDL are cholesterol rich lipoproteins.

CLASS	D (nm)	d (g/mL)	MOBILITY	COMPOSITION (%)					
				Core		Surface			
				TG	CE	FC	PL	Pro	MAJOR APOS
Chylomicrons	80–500	<0.93	α_2	86	3	2	7	2	B-48, E, A-I, A-II, A-IV, C
VLDL	30–80	0.95–1.006	Pre-β	55	12	7	18	8	B-100, C-I, C-II, C-III, E
IDL	25–35	1.006–1.019	Slow pre-β	23	29	9	19	19	B-100, E
LDL	21.6	1.019–1.063	β	6	42	8	22	22	B-100
HDL_2	10	1.063–1.125	α	5	17	5	33	40	A-I, A-II
HDL_3	7.5	1.125–1.210	α	3	13	4	25	55	A-I, A-II
Lp(a)	30	1.055–1.085	Slow pre-β	3	33	9	22	33	B-100, apo(a)

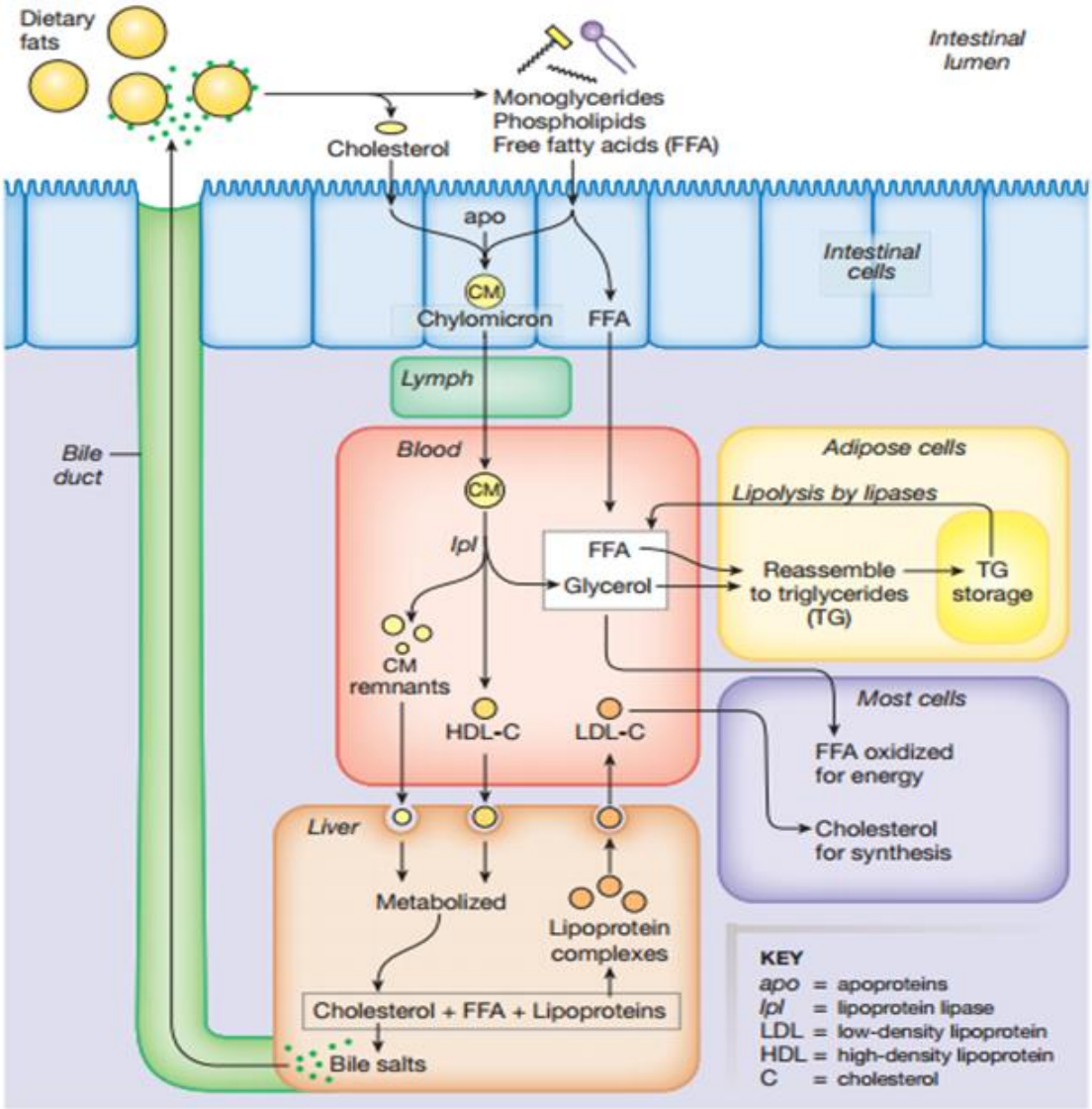
CLASSIFICATION AND PROPERTIES OF HUMAN PLASMA APOLIPOPROTEINS

Apolipoprotein	Molecular weight	Chromosomal location	Function
ApoA-I	29,016	11q23	Cofactor LCAT; facilitates both the transfer of cell cholesterol by ABCA1 to nascent HDL and the delivery of CE and FC on HDL to liver through SR-BI
ApoA-II	17,414	1q21-23	Inhibits TG hydrolysis by HL and VLDL
ApoA-IV	44,465	11q23	Activates LCAT; promotes formation of chylomicrons
ApoA-V	39,000	11q23	Stimulates proteoglycan-bound LPL
ApoB-100	512,723	2p24-p23	Secretion of VLDL from liver; binding ligand to LDLR
ApoB-48	240,800	2p24-p23	Secretion of chylomicrons from intestine
ApoC-I	6,630	19q13.2	Inhibits apoE binding to LDLR; stimulates LCAT; inhibits CETP and SR-BI
ApoC-II	8,900	19q13.2	Cofactor LPL
ApoC-III	8,800	11q23	Noncompetitive inhibitor of LPL; inhibits binding of ApoE on TG-rich lipoproteins to LDLR
ApoD	19,000	3q26.2	Promotes reverse cholesterol transport
ApoE	34,145	19q13.2	Binding ligand for LRP on chylomicron remnants and for LDLR on VLDL and IDL
ApoH	54,000	17q23	Activates LPL
ApoL	42,000	22q13.1	Made only in the pancreas; affects TG and glucose metabolism but mechanism unknown

LCAT, lecithin cholesterol acyl transferase; ABCA1, ATP-binding cassette transporter 1; HDL, high-density lipoproteins; CE, cholesteryl esters; FC, free cholesterol; SR-B1, scavenger receptor class B1; TG, triglycerides; HL, hepatic lipase; VLDL, very low-density lipoproteins; LCAT, lecithin cholesterol acyl transferase; LPL, lipoprotein lipase; LDLR, low density lipoprotein receptor; CETP, cholesteryl ester transfer protein; LRP, low density lipoprotein receptor-related protein; IDL, intermediate-density lipoproteins.

Lipoprotein Classification and Properties

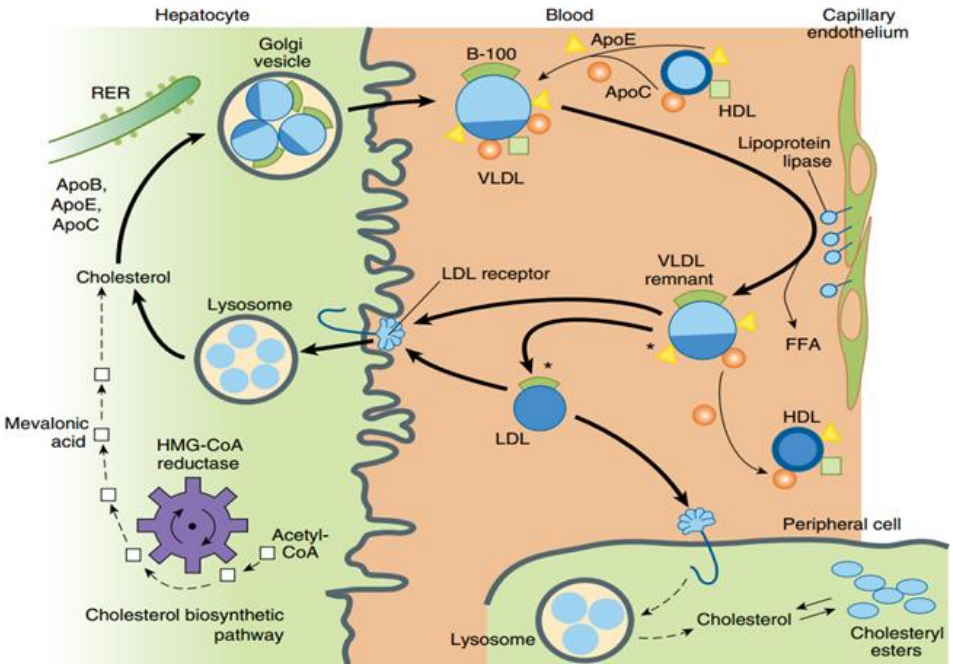
Cholesterol and triglycerides are required by peripheral tissues for multiple metabolic functions, involving the maintenance of cell membranes, synthesis of steroid hormones and bile acid, and energy utilization. These lipids are carried on a range of lipoproteins in the systemic circulation.



Transport and Fate of Dietary Fats

One of the functions of LDL particles is the transport of cholesterol into the arterial wall where it is retained by arterial proteoglycans. Macrophages are attracted to these sites and function to engulf the LDL particles. The process of engulfing LDL particles by macrophages initiates plaque formation in the arterial wall.

Increased levels of plaque formation are linked to atherosclerosis. Over time, plaques become vulnerable to rupturing, which, in turn, activates blood clotting and leads to arterial stenosis.

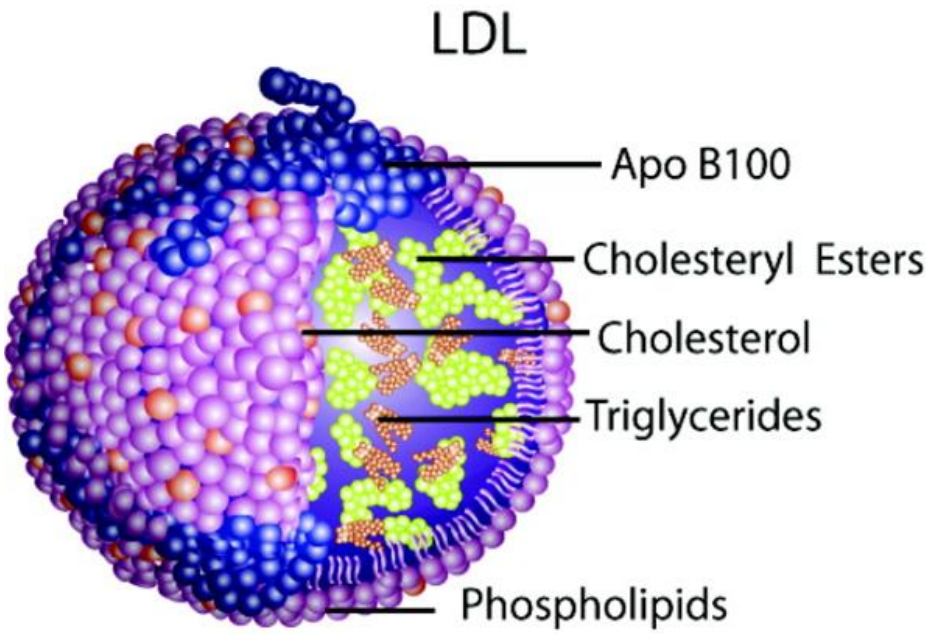


Metabolism of lipoproteins of hepatic origin

Fatty acids are transported in the blood bound to albumin. Nonabsorbable plant sterols found in soybeans reduce the absorption of cholesterol, by competing with cholesterol for esterification with fatty acids.

LIPOPROTEIN STRUCTURE

The basic lipoprotein structure typically includes a core of esterified cholesterol and triglyceride, surrounded by a surface bilayer of phospholipid, unesterified or free cholesterol, and a range of proteins (termed “apolipoproteins”).



Lipoprotein structure

Hypertriglyceridemia	Hypercholesterolemia
Diabetes mellitus	Hypothyroidism
Alcohol ingestion	Early nephrosis
Severe nephrosis	Resolving lipemia
Estrogens	Immunoglobulin-lipoprotein complex disorders
Uremia	Anorexia nervosa
HIV infection	Cholestasis
Myxedema	Hypopituitarism
Glycogen storage disease	Corticosteroid excess
Hypopituitarism	
Acromegaly	
Immunoglobulin-lipoprotein complex disorders	
Lipodystrophy	
Protease inhibitors	

SECONDARY CAUSES OF HYPERCHOLESTEROLEMIA

1) Hypothyroidism

2) Obstructive liver disease

3) Nephrotic syndrome

4) Increasing consumption of saturated fat

SECONDARY CAUSES OF HYPERTRIGLYCERIDEMIA

Diabetes mellitus, Chronic renal failure, Obesity, Nephrotic syndrome ,

Cushing syndrome, Lipodystrophy , HIV, Cigarette smoking , Excess alcohol consumption , High-carbohydrate diets

MEDICATIONS	ASSOCIATED PRIMARY LIPID DISTURBANCE		
	↑ LDL-C	↑ TG	↓ HDL-C
Cyclosporine	X		
Amiodarone	X		
High-dose chlorthalidone	X		
Hydrochlorothiazide	X		
Rosiglitazone	X		
Fibrates	X		
Oral estrogens		X	
Tamoxifen		X	
Corticosteroids		X	X
β-blockers		X	X
Retinoids		X	X
Protease inhibitors (especially ritonavir)		X	X
Bile acid binding resins		X	X
Sirolimus		X	X
L-asparaginase		X	X
Atypical antipsychotic agents		X	X

MEDICATIONS ASSOCIATED WITH DYSLIPIDEMIA RECOMMENDED LIPID GOALS

Risk category	LDL cholesterol goal (mg/dL)	LDL cholesterol for lifestyle changes (mg/dL)	LDL cholesterol for drug therapy (mg/dL)	Non-HDL cholesterol goal (mg/dL)	ApoB goal (mg/dL)
Coronary heart disease at very high risk	<70	>70	>100	<100	<80
Coronary heart disease or risk equivalent (10-year >20%)	<100	>100	>130	<130	<90
2 or more risk factors					
10-year risk 10–20%	<130	>130	>130	<160	<100
10-year risk <10%	<130	>130	>160	<160	<100
0–1 risk factors	<160	>160	>190	<190	<110

LIPOPROTEINS AND CARDIOVASCULAR BENEFIT-RISK

Plasma lipoproteins are complex biological structures which are comprised of

apolipoproteins A-1 (in high-density lipoprotein, HDL) or B-100 in the small dense particles in low density lipoproteins (LDL) and cholesterol esters. Patients with metabolic disorders, such as the metabolic syndrome and type 2 diabetes, also have lipoprotein abnormalities such as elevated triglycerides and low levels of HDL cholesterol (HDL-C).

Elevated levels of HDL-C are linked with reduced CV events.The classical role of HDL is reverse cholesterol transport in which lipids taken from macrophage foam cells transfer their cholesterol content to HDL particles for transport to liver for degradation of cholesterol in hepatocytes, the products of which are excreted in the bile.

Epidemiological studies have shown that decreased levels of HDL-C is a risk factor for CAD. < 2% decrease in HDL-C is associated with a 3–5% increase in cardiovascular disease, while each 2 % reduction in HDL-C correlates with a 10 % increase in

deaths from coronary artery disease, which is independent of the LDL-C level.

Therapeutic class	LDL cholesterol	Triglyceride	HDL cholesterol	Comments
Statins	↓ 20–55%	↓ 15–35%	↑ 3–15%	Established clinical benefit in primary and secondary prevention. Beneficial effects on atherosclerosis progression. Nonlipid lowering properties may contribute to benefit.
Fibrates	↓ 5–20%	↓ 20–50%	↑ 5–20%	Relatively weak PPAR-α (peroxisome proliferator-activated receptor) agonists increasing transcription of HDL apolipoproteins and factors promoting reverse cholesterol transport. Anti-inflammatory properties may also be important. Variable effect of individual agents in clinical trials. Concomitant administration of gemfibrozil (Lopid) associated with higher rate of myopathy with statins.

Therapeutic class	LDL cholesterol	Triglyceride	HDL cholesterol	Comments
Bile acid sequestrants	↓ 10–25%	↑ 0–10%	↑ 3–5%	Potential increase in triglyceride levels. Often limited by GI intolerance.
Niacin	↓ 15–25%	↓ 20–50%	↑15–35%	Most effective HDL-raising drug with beneficial effects on clinical events and atherosclerosis progression. Effective lowering of Lp(a). Emerging developments aim to reduce flushing and allow more patients to achieve clinically effective high doses.
Ezetimibe	↓ 15–20%	↓ 0–10%	↑0–5%	Cholesterol absorption inhibitor. Incremental lowering of CRP when administered in combination with statin therapy.
Fish oils	↑ 3–5%	↓ 30–40%	No change	Primarily used in hypertriglyceridemic patients. Lipid benefit may contribute to efficacy in clinical trials.

THERAPIES AVAILABLE FOR DYSLIPIDEMIA ISCHAEMIC HEART DISEASE (IHD)

DEFINITION

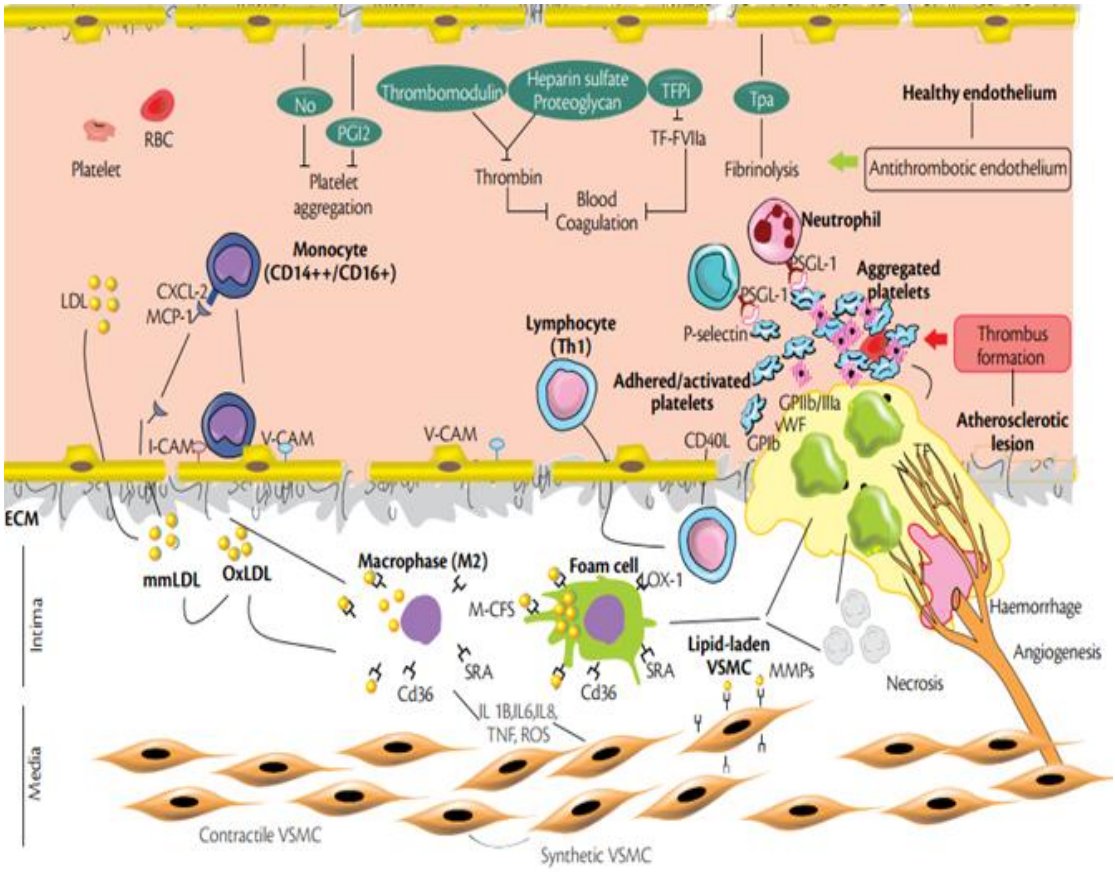
The World Health Organisation has defined ischaemic heart disease (IHD) as myocardial dysfunction due to imbalance between coronary blood flow and myocardial requirements.

The most common cause of IHD is coronary artery disease mainly due to atherosclerosis. However, imbalance between the

supply and demand can be caused by other conditions as well, like hypertrophic cardiomyopathy ,aortic valve disease, coronary artery spasm and coronary artery involvement in various collagen disorders.

Coronary artery disease(CAD) is the narrowing of the coronary arteries as a result of a plaque which is composed of the following:

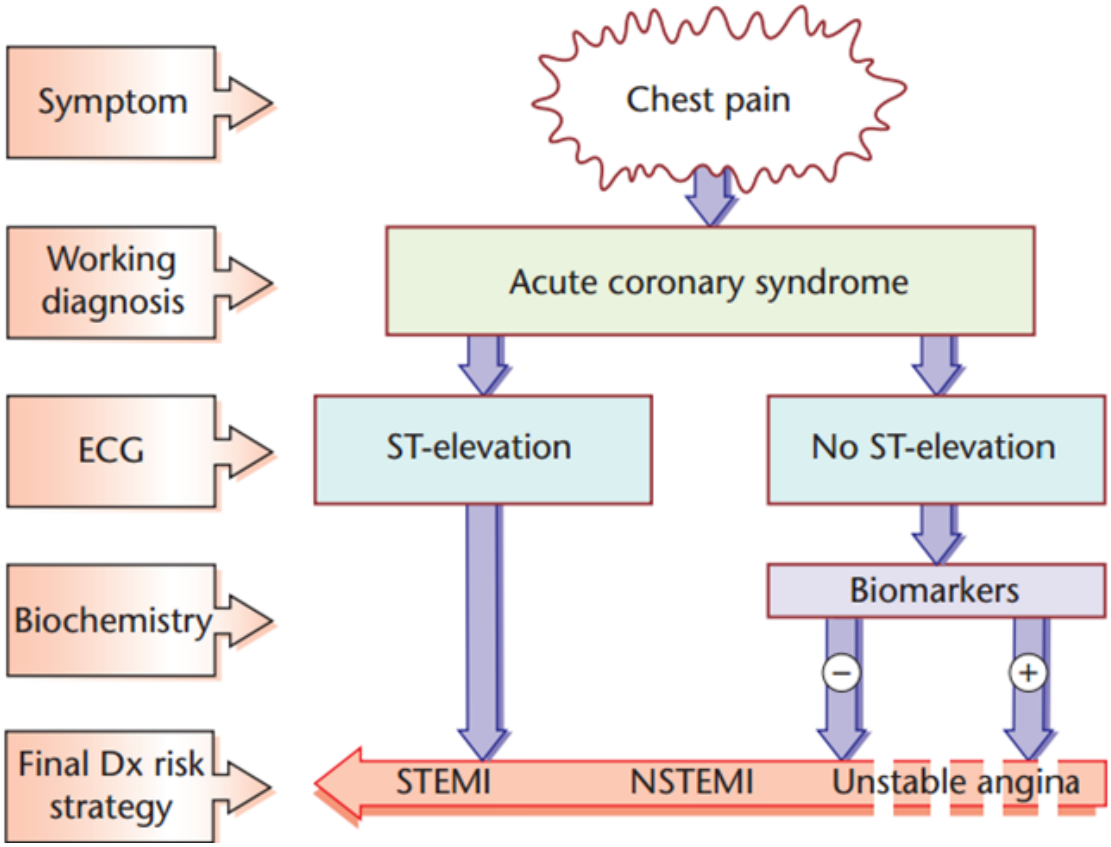
- Lipids (cholesterol esters and crystals), which are deposited at the center of the plaque also accumulate within macrophages.
- Intimal smooth muscle cells,which proliferate.
- A fibrous cap made of connective tissue.



COMPLEXITY OF EVENTS THAT DRIVE THE ATHEROSCLEROTIC PROCESS

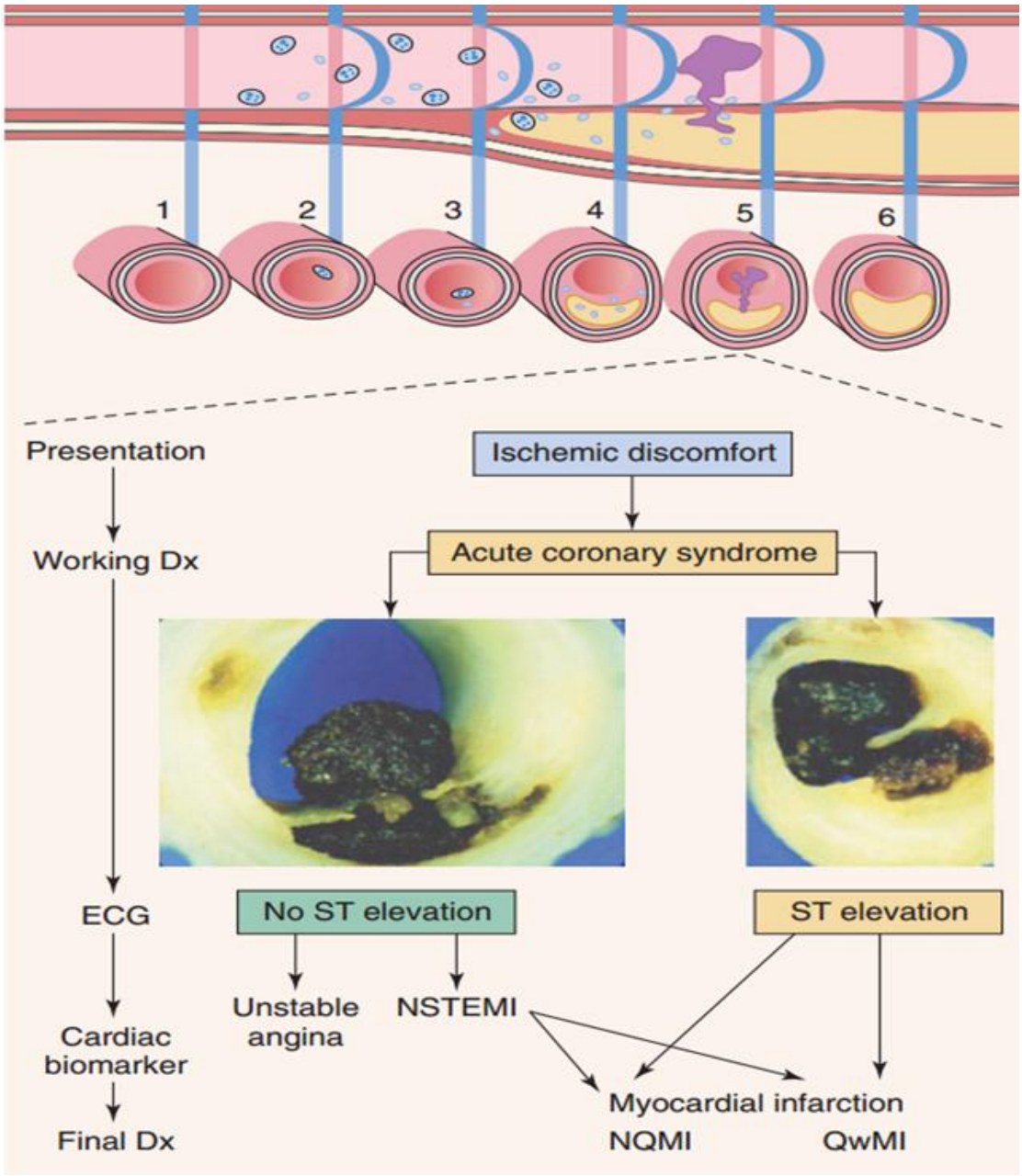
Coronary artery disease (CAD) is mainly due to coronary atherosclerosis causing various clinical syndromes of CAD .The clinical manifestations of CAD are a spectrum that includes various forms of ACS including

- ❖ Angina pectoris
- ❖ UA
- ❖ NSTEMI
- ❖ STEMI



Spectrum and definition of the acute coronary syndrome

Acute coronary syndromes result from complicated interactions between the coronary circulation and the myocardium, mainly due to coronary artery atherosclerosis as the main reason for disease.



Acute coronary syndromes

Cardiovascular diseases

- arrhythmias
- pericarditis
- myocarditis
- aortic dissection

Pulmonary diseases

- pulmonary embolism
- pleuritis
- pneumothorax

Skeletal disorders

- rip fracture/contusion
- spine diseases
- Tietze syndrome

Gastrointestinal disorders

- oesophagitis/oesophageal rupture
- pancreatitis
- gall bladder dysfunction

Others

- herpes zoster
- malignant diseases involving chest/bones

Differential diagnoses acute chest pain

Class 1: Modifiable risk factors; Interventions have been proved to lower CAD risk

1. Cigarette smoking
2. High total cholesterol
3. High LDL cholesterol
4. Low HDL cholesterol
5. High fat/cholesterol diet
6. Left ventricular hypertrophy (LVH)
7. Thrombogenic factors

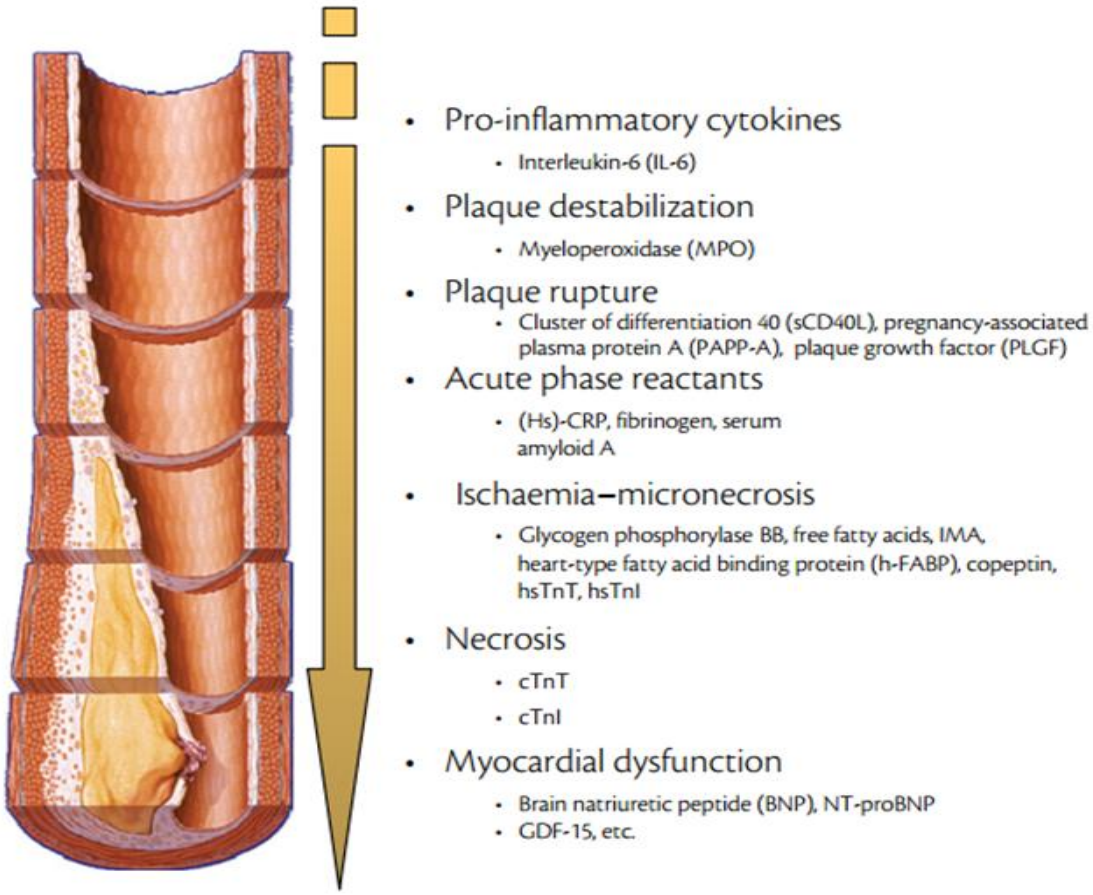
Class 2: Modifiable risk factors; Interventions are likely to lower CAD risk

8. Lipoprotein (a) or Lp(a)
9. Diabetes mellitus
10. Hypertension
11. Physical inactivity
12. Obesity
13. High triglycerides
14. High homocysteine
15. Increased high-sensitivity-CRP (hs-CRP)
16. Stress

Class 3: Non-modifiable risk factors

17. Age
18. Male gender
19. Family history of CAD

Risk factors for CAD can be classified into 3 classes



Representative biomarkers involved in the process of Atherosclerosis

NEW RISK FACTORS FOR IHD

- ❖ Prothrombin fragment 1 & 2.
- ❖ Factors V, VII, and VIII.
- ❖ D-Dimer.
- ❖ Lipoprotein(a).
- ❖ Small dense LDL.
- ❖ HDL subtypes.

- ❖ Apolipoproteins A1 and B.
- ❖ Oxidized LDL.

Risk factors for cardiovascular disease

Traditional risk factors

Modifiable	*Non-modifiable*
• Hypertension • Diabetes • Hyperlipidemia • Obesity • Tobacco use • Physical inactivity	• Age (male ≥ 45 years, female ≥ 55 years) • Gender • Family history of premature coronary artery disease*

Selected emerging risk factors

- C-reactive protein
- Small LDL particles
- Lipoprotein(a)
- Homocysteine
- Lipoprotein-associated phospholipase A2
- Coagulation and hemostatic factors
- Apolipoproteins A and B
- White blood cell count

(*Definite myocardial infarction or sudden death before 55 years of age in father or other male first-degree relative or before 65 years of age in mother or other female first-degree relative)

PATHOPHYSIOLOGY OF MECHANISM OF ISCHEMIA

Myocardial oxygen supply is reduced in conditions like

1) Coronary artery disease due to atherosclerotic lesion occluding the vessel, plaque, rupture, subintimal haemorrhage, platelet aggregates, thrombosis, and spasm on a pre existing atheromatous lesion.

2) Arterial spasm occurring de novo.

3) Coronary artery embolism, as in patients with mitral valve disease with atrial fibrillation, or myxoma of left atrium.

4) Paroxysmal supraventricular tachycardia which leads to shortening of diastole

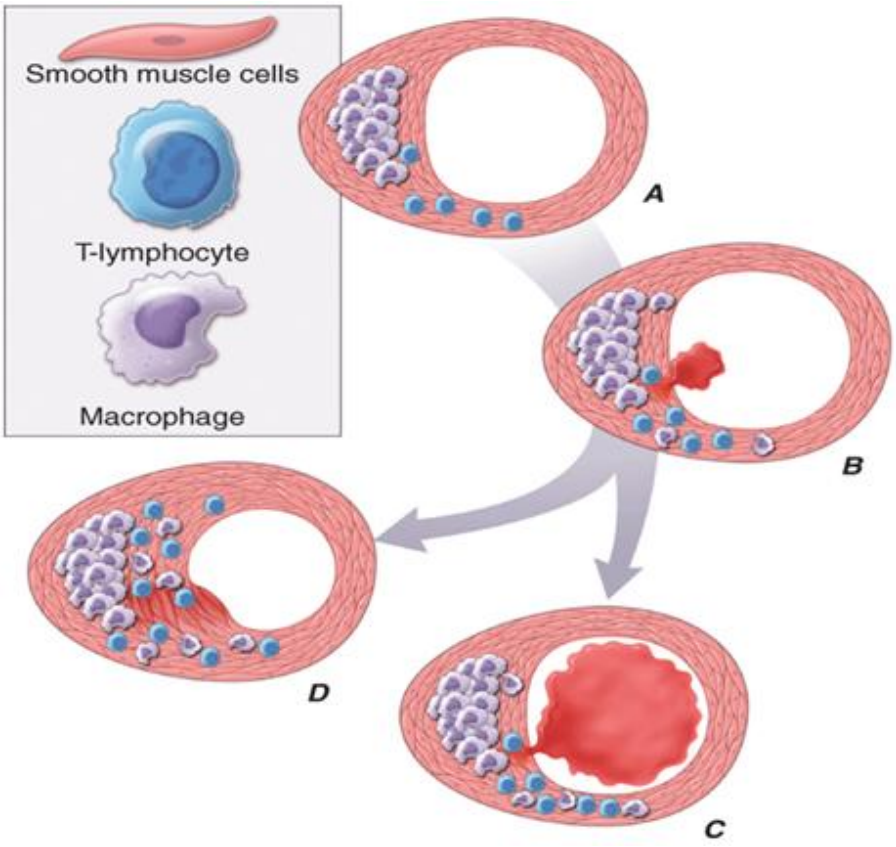
5) Coronary artery disease in collagen disorders like disseminated lupus erythematosus, polyarteritis nodosa, aortoarteritis, Kawasaki disease.

6) Anomalous origin of left coronary artery from the pulmonary artery.

7) Anemia, CO poisoning.

FOUR important pathologic processes cause an acute athero thrombotic incident :

Atherosclerotic plaque rupture that disrupts the balance of thrombosis and fibrinolysis, causing the formation of a superimposed non occlusive thrombus.



1) Arterial remodeling during atherogenesis.

2) Fibrous cap rupture of the plaque leading to thrombosis.

3) The clot disrupts endogenous fibrinolytic mechanisms

4) Thrombin causes fibrosis and a fibroproliferative response that causes artery stenosis.

ACUTE MYOCARDIAL INFARCTION /STEMI

Myocardial infarction is defined as myocardial necrosis resulting from prolonged ischemia from a pathologic process.

A recent working group from the ACC/ESC established the criteria for diagnosis of AMI as a rapid rise or fall in a cardiac necrosis biomarker, ideally troponin plus one additional factor:

1) Symptoms of ischemia.

2) ECG changes consistent with ischemia (ST deviation from J point) ≥1 mm or a new LBBB.

3) New pathological Q waves (≥0.04 mm wide and/or 1/3 the height of the QRS).

4) Imaging evidence of a new wall motion abnormality or a new loss of viability in an area of myocardium.

CLINICAL PRESENTATION

Patients with ACS typically present with angina at rest or with minimal exertion, though 50% of all MIs may be clinically silent and not recognized by the patient.

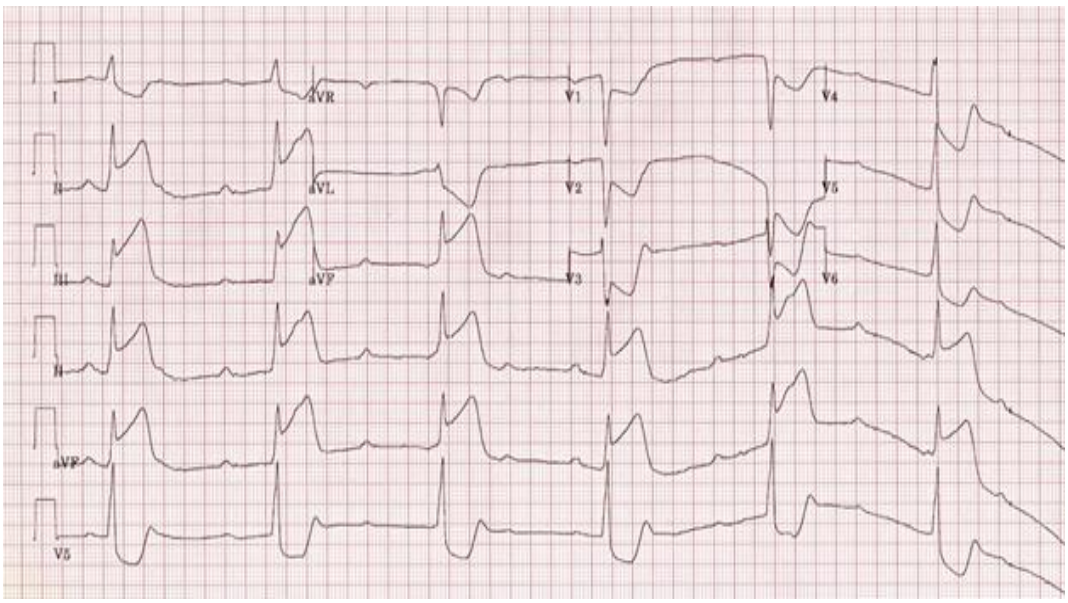
Angina is a vague not localized chest or arm discomfort, often occurring along with physical exertion or cold climate or

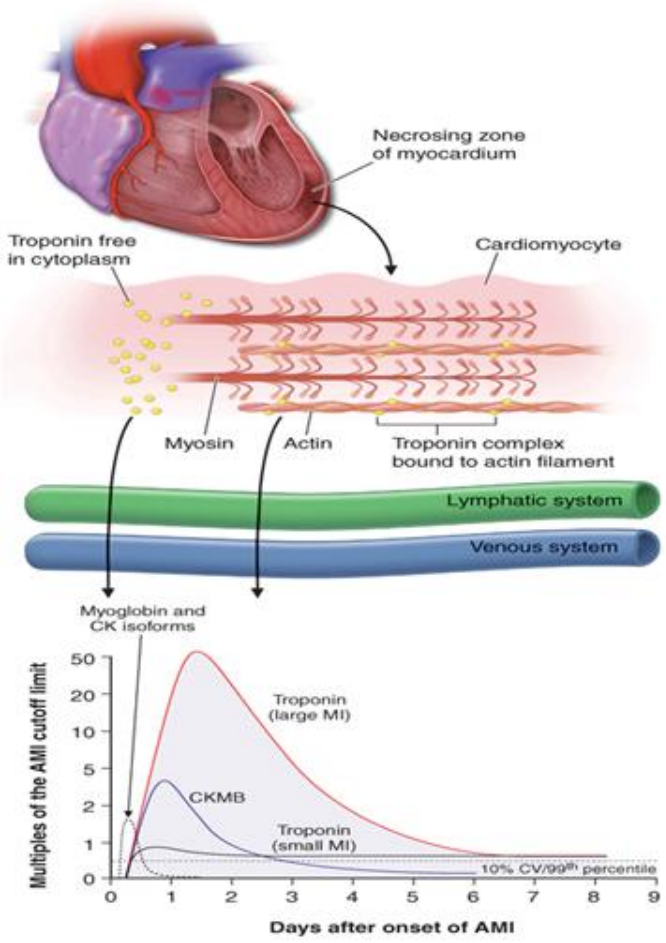
during emotional stress, it is usually relieved within 5–10 min by taking rest or nitroglycerin.

Evaluation of chest pain: A 12 lead ECG should be taken immediately.

The presence of ST segment deviation or T wave inversions in 2 contiguous leads suggestive of ischemia or infarction be further tested with cardiac troponin which is highly specific(80%) and sensitive(90%) in detecting myocardial cell necrosis.

EXTENSIVE INFERIOR WALL STEMI (ACUTE)





Cardiac Troponin elevation can be detected in the blood as early as two to four hours after onset of symptoms and detectable 7–14 days following an ACS.

Diagnosis and Treatment in STEMI: Initial diagnostic measures

1) Continuous serial ECGs; Pulse oximetry (SaO2), BP, PR.

2) Clinical history (Thrombolysis contraindications).

3) A 12-lead ECG and Chest X-ray.

Injury related to primary myocardial ischaemia

- Plaque rupture
- Intraluminal coronary artery thrombus formation.

Injury related to a supply/demand imbalance of myocardial ischaemia

- Tachy-/bradyarrhythmias
- Aortic dissection or severe aortic valve disease
- Hypertrophic cardiomyopathy
- Cardiogenic, hypovolaemic, or septic shock
- Severe respiratory failure
- Severe anaemia
- Hypertension with or without LV hypertrophy
- Coronary spasm
- Coronary embolism or vasculitis
- Coronary endothelial dysfunction without significant coronary artery disease (CAD).

Injury not related to myocardial ischaemia

- Cardiac contusion, surgery, ablation, pacing, or defibrillator shocks
- Rhabdomyolysis with cardiac involvement
- Myocarditis
- Cardiotoxic agents, e.g. anthracyclines, herceptin.

Multifactorial or indeterminate myocardial injury

- Heart failure
- Stress (Takotsubo) cardiomyopathy
- Severe pulmonary embolism (PE) or pulmonary hypertension (PH)
- Sepsis and critically ill patients
- Renal failure
- Severe acute neurological diseases, e.g. stroke, subarchnoidal haemorrhage (SAH)
- Infiltrative diseases, e.g. amyloidosis, sarcoidosis
- Strenuous exercise.

ELEVATION OF CARDIAC TROPONINS BECAUSE OF MYOCARDIAL INJURY

Novel biomarkers in ACS

- ***Copeptin:*** It is the fragment of vasopressin which is stable, and can rapidly rule out of MI if it is measured together with a hscTn, assay . There is evidence indicating that following a small infarct, copeptin is rapidly released from the pituitary gland and appears rapidly in the blood in patients with an evolving MI, while cTn is still negative . Copeptin concentrations decline fast to normal as cTn levels rise above the 99th percentile. Copeptin levels do not increase in patients with UA.

- ***MR-proatrial natriuretic peptide:*** ANP is derived from the cleavage of its precursor proatrial natriuretic peptide (proANP) . More recently, there is some evidence for a prognostic role for ANP in different settings of ACS.

- Heart fatty acid-binding protein (h-FABP)

- Ischemia-modified albumin (IMA)

- MR-proadrenomedullin.

General treatment in ACS

Drug	Dosing Regimen and Comments
Oxygen	Dosing: O_2 by nasal prongs or face mask to maintain $SaO_2 \geq 94\%$
	Comment: O_2 therapy should be used cautiously because it promotes coronary vasoconstriction and generates toxic O_2 metabolites.
Nitroglycerin	Dosing: For chest pain, 0.4 mg SL or by mouth spray, and repeat every 5 min x 2 if needed. For recurrent pain, CHF, or high BP, infuse at 5 µg/min and increase by 5–10 µg/min every 5 min to desired effect or to dose rate of 200 µg/min.
	Comment: Avoid in patients with RV infarction and for 24 hr following R_x for erectile dysfunction.
Morphine	Dosing: 2–4 mg IV with increments of 2–8 mg IV every 5–15 min as needed.
	Comment: Morphine-induced respiratory depression is uncommon in acute coronary syndromes.
Aspirin	Dosing: 162–325 mg (chewable form) initially, then 75–162 mg (enteric-coated tablets) daily.
	Comment: Initial dose should be chewed to enhance buccal absorption.
β-Blockers	Dosing: *Atenolol:* 10 mg IV, then 100 mg PO daily, or *Metoprolol:* 5 mg IV every 5 min for 3 doses, then 50 mg PO q 6 h for 48 hr, then 100 mg PO BID.
	Comment: Do NOT use in cocaine-induced chest pain or MI.

- Supplemental Oxygen 4–7 L per min.
- NTG 0.4 mg sublingual every 5 min (caution in right ventricular infarctions because of hypotension)

❖ Analgesics like Morphine (2–4 mg IV) or pethidine as needed.

SPECIFIC TREATMENT IN STEMI

Reperfusion therapy

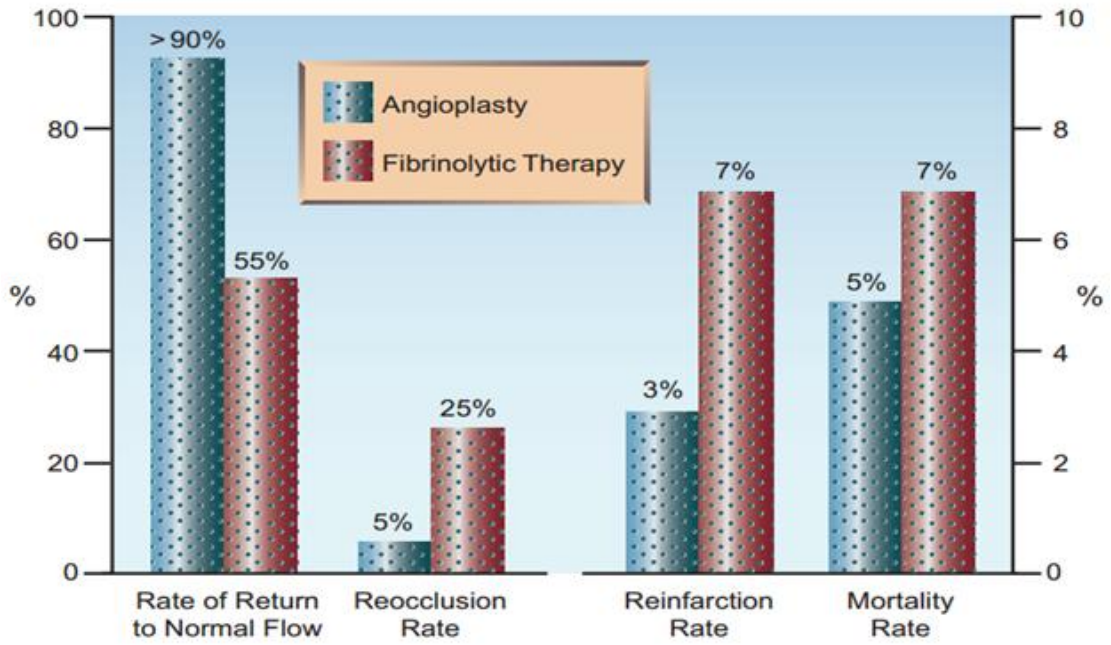
Either Primary PTCA or Thrombolysis

Situations in Which PTCA Is Clearly Preferable to Thrombolytics

- Contraindications to thrombolytic therapy
- Cardiogenic shock
- Patients in whom uncertain diagnosis prompted cardiac catheterization which revealed coronary occlusion

Situations in Which PTCA May Be Preferable to Thrombolytics

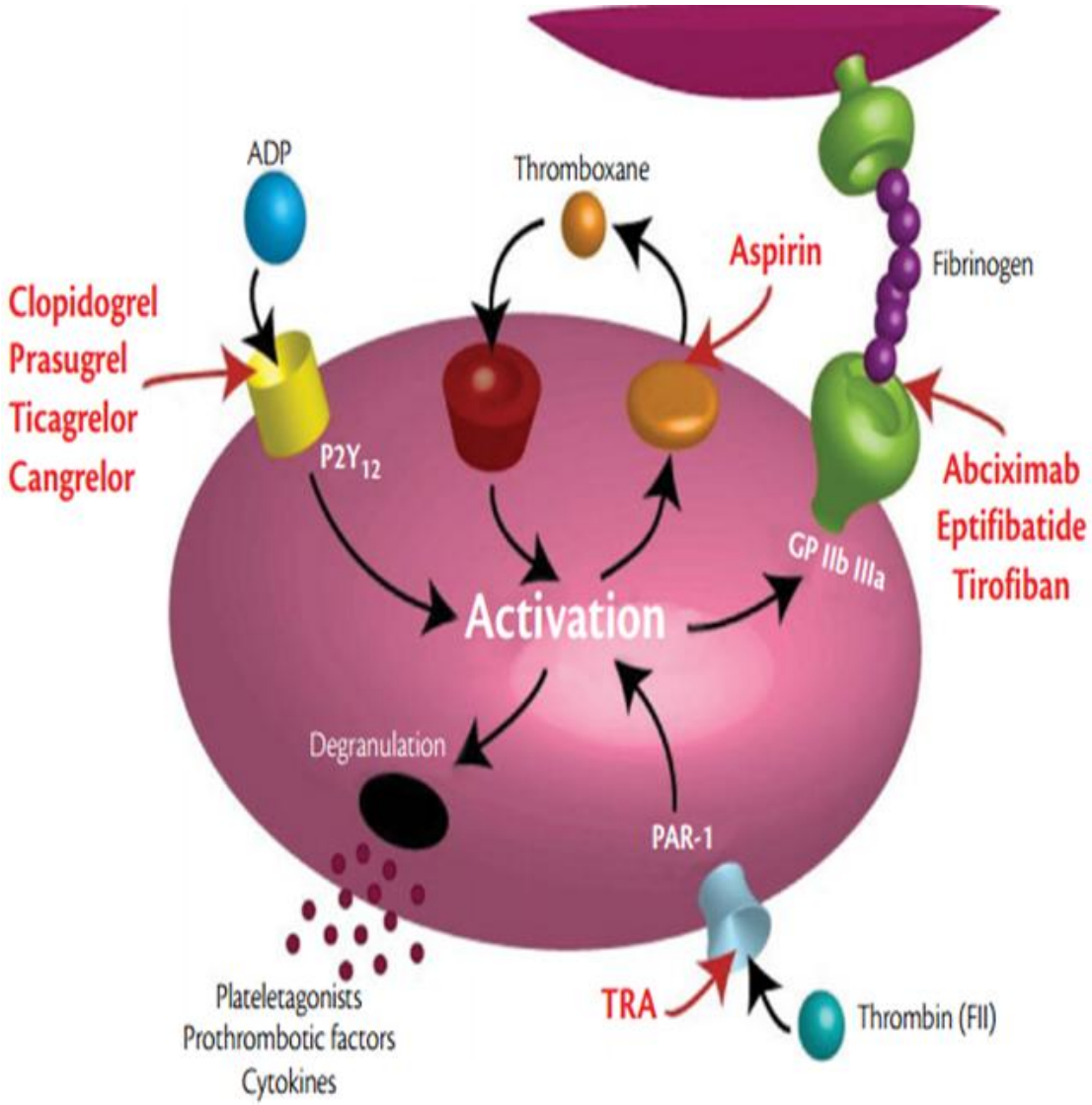
- Elderly patients (>75 years)
- Hemodynamic instability
- Patients with prior coronary artery bypass grafting
- Large anterior infarction
- Patients with prior myocardial infarction



Fibrinolytic therapy for acute myocardial infarction

	Alteplase; Tissue Plasminogen Activator (t-PA)	Reteplase	Tenecteplase (TNK-t-PA)	Streptokinase
Source	Recombinant DNA	Recombinant DNA	Recombinant DNA	Group C streptococcus
Half-life	5 minutes	15 minutes	20 minutes	20 minutes
Usual dose	100 mg	20 units	40 mg	1.5 million units
Administration	Initial bolus of 15 mg, followed by 50 mg infused over the next 30 minutes and 35 mg over the following 60 minutes	10 units as a bolus over 2 minutes, repeated after 30 minutes	Single weight-adjusted bolus, 0.5 mg/kg	750,000 units over 20 minutes followed by 750,000 units over 40 minutes
Anticoagulation after infusion	Aspirin, 325 mg daily; heparin, 5000 units as bolus, followed by 1000 units per hour infusion, subsequently adjusted to maintain PTT 1.5–2 times control	Aspirin, 325 mg; heparin as with t-PA	Aspirin, 325 mg daily	Aspirin, 325 mg daily; there is no evidence that adjunctive heparin improves outcome following streptokinase
Clot selectivity	High	High	High	Low
Fibrinogenolysis	+	+	+	+++
Bleeding	+	+	+	+
Hypotension	+	+	+	+++
Allergic reactions	0	0	+	++
Reocclusion	10–30%	–	5–20%	5–20%

2. ANTIPLATELET THERAPY



MECHANISM OF ACTION OF VARIOUS ANTIPLATELET DRUGS

Drug	Initial Medical Treatment
Antiplatelet Drugs	
1. Aspirin	162-325 mg nonenteric formulation, orally or chewed
2. Clopidogrel	LD of 300-600 mg orally, MD of 75 mg orally per day
3. Prasugrel	LD of 60 mg orally, MD of 10 mg orally per day
4. Ticlopidine	LD of 500 mg orally, MD of 250 mg orally twice daily
Anticoagulants	
1. Unfractionated heparin	LD of 60 U/kg (max 4000 U) as IV bolus
	MD of IV infusion of 12 U/kg/h (max 1000 U/h) to maintain aPTT at 1.5-2.0 times control (approximately 50-70 seconds)
2. Enoxaparin	LD of 30 mg IV bolus may be given. MD = 1 mg/kg SC every 12 hours. extend dosing interval to 1 mg/kg every 24 hours if estimated Ccr <30 mL/min
3. Fondaparinux	2.5 mg SC once daily. Avoid for Ccr <30 mL/min
4. Eptifibatide	LD of IV bolus of 180 μg/kg. MD of IV infusion of 2.0 μg/kg/min; reduce infusion by 50% in patients with estimated Ccr <50 mL/min
5. Tirofiban	LD of IV infusion of 0.4 μg/g/min for 30 minutes
	MD of IV infusion of 0.1 μg/kg/min; reduce rate of infusion by 50% in patients with estimated Ccr <30 mL/min
6. Bivalirudin	0.1 mg/kg bolus, 0.25 mg/kg/h infusion

GPIIB/IIIA INHIBITORS

Drug	Dosing Regimen
Abciximab	Dosing: Load with 0.25 mg as IV bolus, then infuse at 0.125 μg/kg/min (maximum rate is 10 μg/min) for up to 12 hr.
Eptifibatide	Dosing: Load with 180 μg/kg as IV bolus, then infuse at 2 μg/kg/min for 12–18 hr. For PCI in STEMI, repeat bolus dose in 10 min if renal function is normal. Reduce infusion rate by 50% when creatinine clearance is <50 mL/min.
Tirofiban	Dosing: Load with 25 μg/kg as IV bolus, then infuse at 0.1 μg/kg/min for 12–24 hr. Reduce infusion rate by 50% when creatinine clearance is <30 mL/min.

UNFRACTIONATED HEPARIN

Indication	Bolus	Infusion	Target aPTT/ACT
NSTE-ACS	60 U/kg (max 5000)	12–15 U/kg/hour (1000 U/hour max)	aPTT 50–70 s
STEMI (with FL)	60 U/kg (max 4000)	12 U/kg/hour for 24–48 hours (1000 U/hour max)	aPTT 50–70 s
STEMI (with primary PCI)	100 U/kg 60 U/kg if GP IIb/IIIa	–	Activated clothing time (ACT) 250–300 or 200–250 if GP IIb/IIIa

ENOXAPARIN DOSAGE GUIDELINES

Indication	Dose	Duration
NSTE-ACS	1 mg/kg subcutaneous (SC) bd (in case of PCI, no additional bolus is necessary if the last dose has been administered <8 hours before; a 0.3 mg/kg bolus is required if the last dose was given >8 hours before)	2–8 days
STEMI (FL)	30 mg IV bolus (no bolus if >75 years of age) 1 mg/kg SC bd (max 100 mg for first two doses) 0.75 mg/kg SC bd if >75 years of age (max 75 mg)	Up to 7 days
STEMI (primary PCI)	0.5 mg/kg IV bolus (additional 0.25 mg/kg in case of prolonged procedure)	

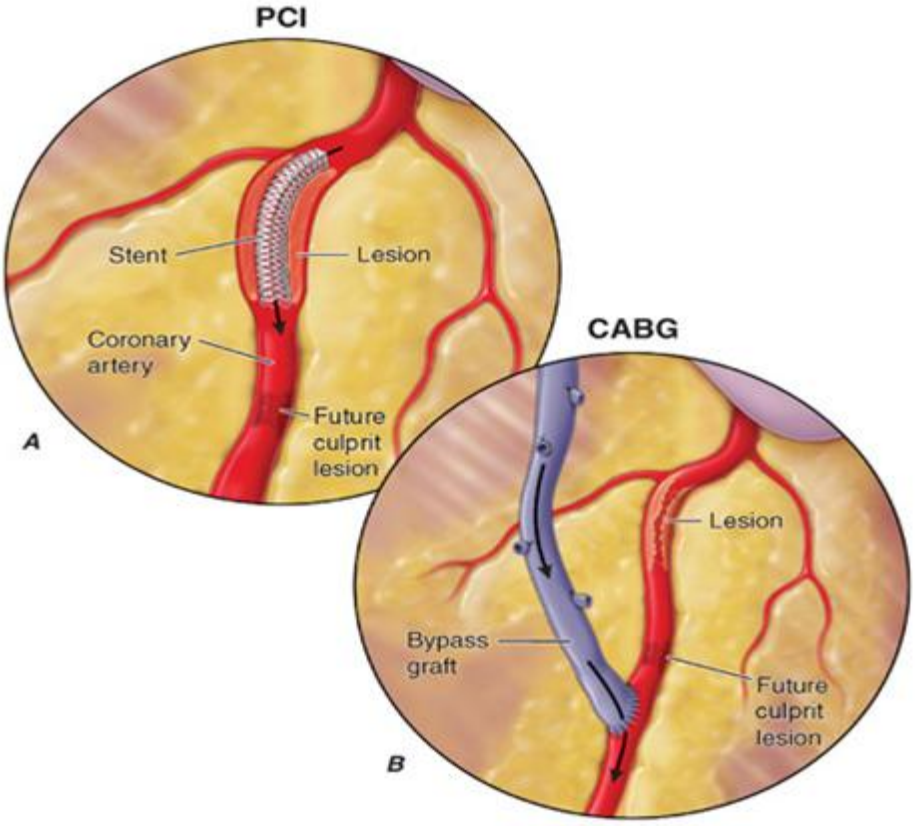
CONTRAINDICATIONS AND CAUTIONS FOR FIBRINOLYSIS IN STEMI

Absolute contraindications

- Any prior ICH
- Known structural cerebral vascular lesion (e.g. arteriovenous malformation)
- Known malignant intracranial neoplasm (primary or metastatic)
- Ischemic stroke within 3 months
- Suspected aortic dissection
- Active bleeding or bleeding diathesis (excluding menses)
- Significant closed-head or facial trauma within 3 months

Relative contraindications

- History of chronic, severe, poorly controlled hypertension
- Severe uncontrolled hypertension on presentation (SBP >180 mm Hg or DBP > 110 mm Hg)†
- History of prior ischemic stroke greater than 3 months
- History of dementia, or known intracranial pathology not covered in contraindications
- Traumatic or prolonged (> 10 minutes) CPR or major surgery (< 3 weeks)
- Recent (within 2–4 weeks) internal bleeding
- Noncompressible vascular punctures
- For streptokinase: prior exposure (> 5 days ago) or prior allergic reaction to these agents
- Pregnancy
- Active peptic ulcer
- Current use of anticoagulants: the higher the INR, the higher the risk of bleeding



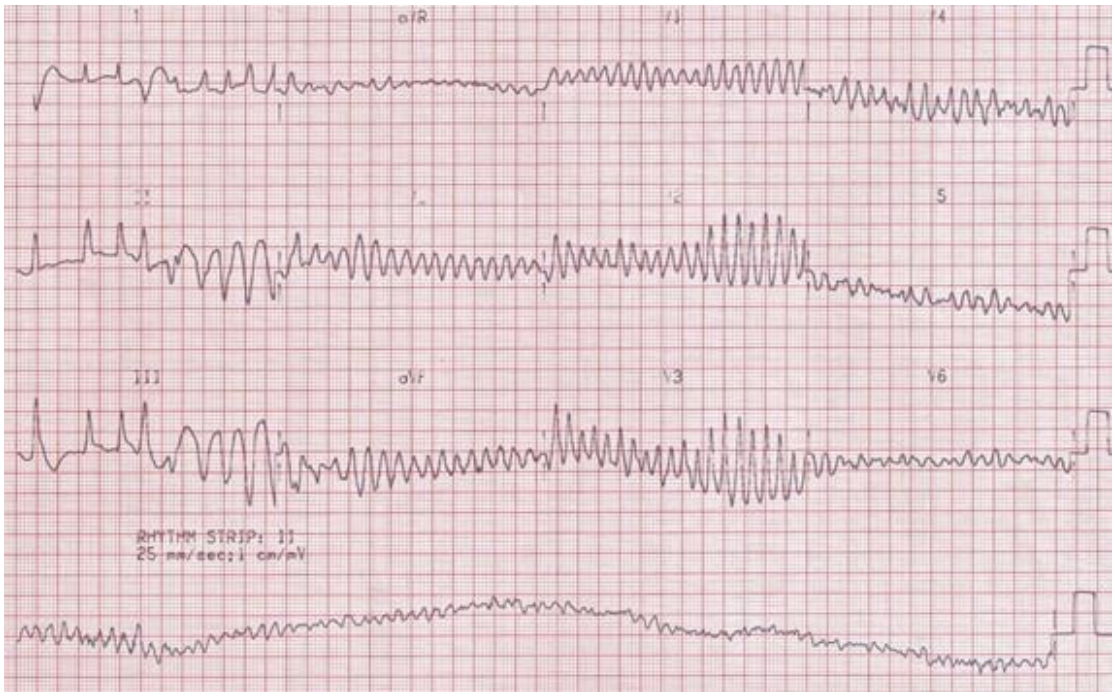
Difference between PTCA and CABG

COMPLICATIONS OF ACUTE MI

Immediate complications(within hours)

- Complete heart block.
- Hypotension.
- Right ventricular infarction.
- Cardiogenic shock Where hypotension (systolic BP <90 mmHg) Pulmonary congestion and pulmonary oedema .

Ventricular premature beats
Ventricular tachycardia
Ventricular fibrillation
Accelerated idioventricular rhythm
Atrial premature beats
Atrial tachycardia
Atrial fibrillation



Ventricular fibrillation

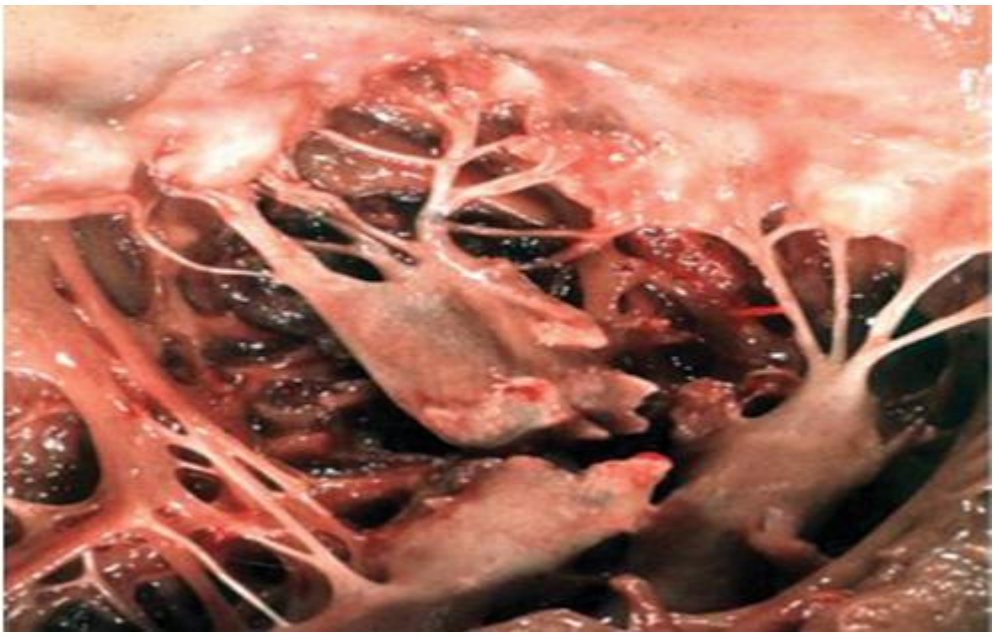
Class	Clinical Features	Mortality
Killip I	MI with no HF	6%
Killip II	MI with mild HF (basal rales)	17%
Killip III	MI with severe HF (rales ≥50% of lung fields)	38%
Killip IV	Cardiogenic shock	81%

KILLIP CLASSIFICATION OF CARDIOGENIC SHOCK

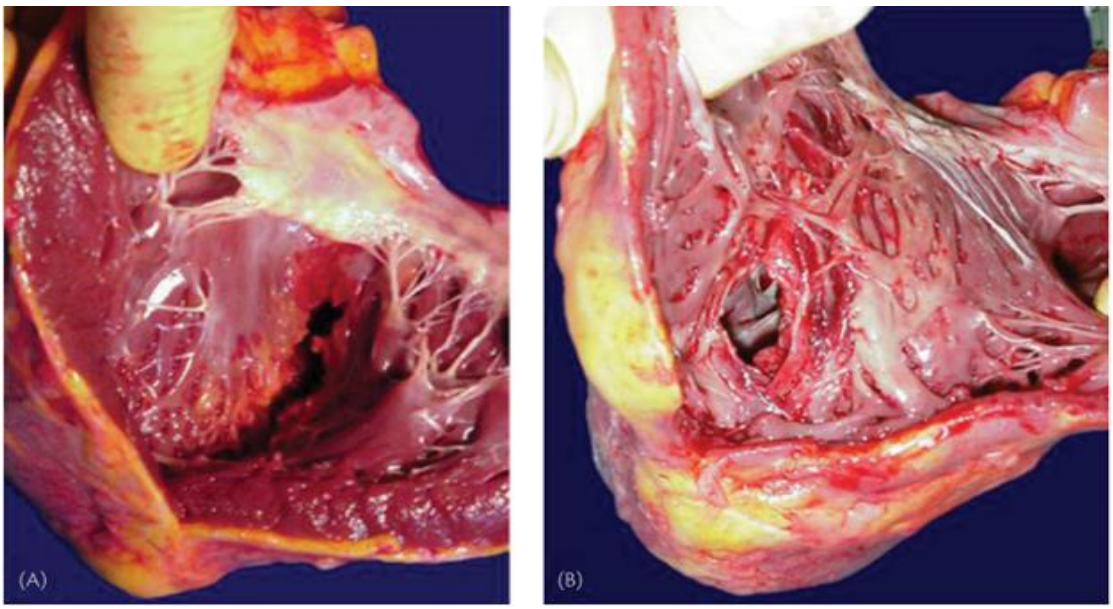
Early complications(within days)

- New murmur.

- Mitral regurgitation due to papillary muscle rupture.



Complete rupture of the posterior papillary muscle Ventricular septal rupture



Rupture of myocardial free wall

- Pericarditis can happen 35% of patients with STEMI within the 7 days.

- **Late complications (several weeks)**

- **Dressler syndrome:** A form of post infarction pericarditis, occurs 7 days to 7 weeks after the acute event characterised by pleuritic chest pain,fever, elevated ESR.

- **Left ventricular aneurysm:** Develops most commonly after a large transmural anterior myocardial infarction.

Oral pharmacotherapy	Given in acute setting	Given in chronic setting
Aspirin	Yes	Lifelong
Clopidogrel	Yes	12 months
β-blocker	With caution	For angina, rate control, and heart failure
CCB	No	For angina, rate control, and hypertension
angiotensin-converting enzyme inhibitors (ACE-I)/ angiotensin receptor blocker (ARB)	No	Yes
Aldosterone antagonist	No	Yes
Statins	Yes	Yes
Anti-factor Xa (rivaroxaban)	No	Consider at low dose (2.5 mg)
Magnesium, lidocaine, n-3 polyunsaturated fatty acids, glucose–insulin–potassium	No	No

Long-term secondary prevention therapy

Unstable angina (UA) and non-ST elevation myocardial infarction (NSTEMI) Both UA and NSTEMI are continuity of the acute coronary syndrome (ACS) spectrum which includes STEMI.

Unstable angina is characterized by following features

- ❖ Angina occurring at rest
- ❖ Recent onset

Table 1: Braunwald Clinical Classification of Unstable Angina

	Secondary UA (A)	Primary UA (B)	Post-MI Angina (C)
New onset angina (I)	I A	I B	I C
Angina at rest not within preceding 48 hours (II)	II A	II B	II C
Angina at rest within 48 hours (III)	III A	III B-T Positive III B-T Negative	III C

Arrow indicates that with increasing severity prognosis worsens.

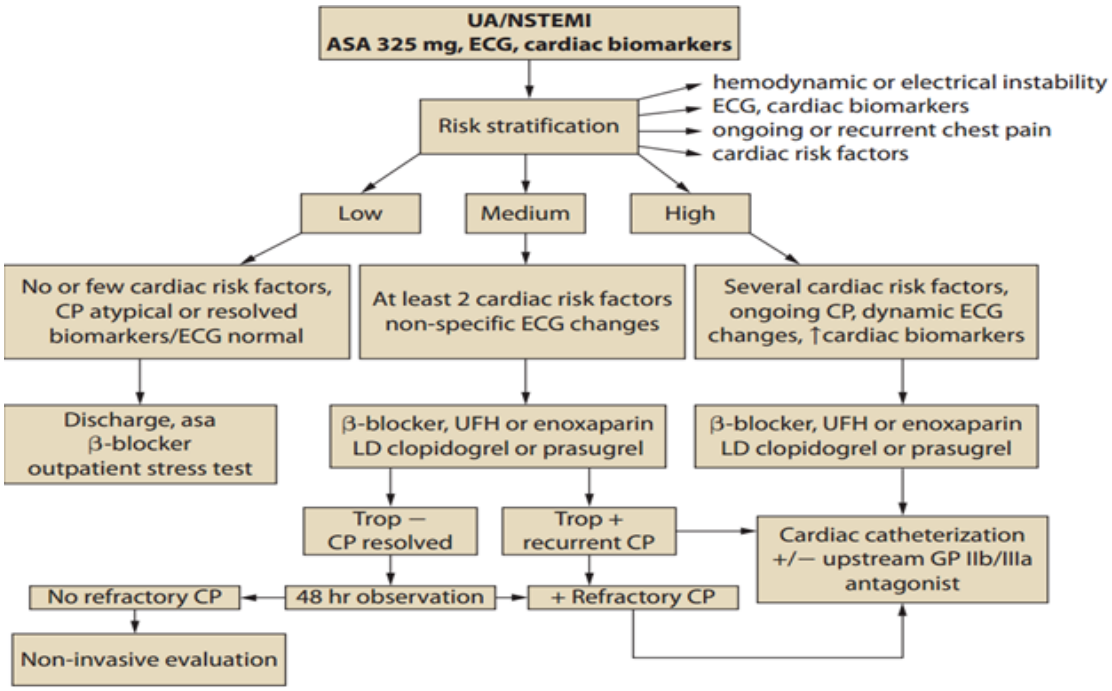
Patients with ACS are risk stratified on the basis of certain criteria, to assess which of them would benefit from early invasive therapy PCI (percutaneous coronary intervention) and who will be managed conservatively. Many risk profile models like TIMI , GRACE have been proposed for triage assessment.

The TIMI risk score is determined by seven variables, each of which is assigned one point. Patients with scores of five or more have been shown to have a higher risk of adverse events and a higher mortality and these patients should be advised early coronary angiography and revascularisation.

TIMI Risk Score (No. of Risk Factors)*	Risk of Death, MI, or Urgent Revascularisation (%)
0 or 1	~ 5%
2	~ 10%
3	~ 15%
4	~ 20%
5	~ 25%
6	~ 40%

** Risk factors include: Age ≥ 65 years; ≥ 3 CAD risk factors; Known CAD (>50% stenosis); Prior aspirin therapy; ≥ 2 anginal episodes in last 24 hours; ST deviation ≥ 0.5 mm; Elevated Troponins.*

TIMI Risk Score



General overview of the treatment of UA/NSTEMI-ACS 1

MATERIALS AND METHODS

SETTING

This study was conducted at the Hypertension clinic, Rajiv Gandhi Government General Hospital and Madras Medical College.

ETHICAL COMMITTEE APPROVAL

Obtained.

STUDY DURATION

This study was conducted over a period of six months.

STUDY POPULATION

Patients coming to hypertension clinic for hypertension management.

SAMPLE SIZE

50 patients

TYPE OF STUDY

Cross sectional,Observational study

INCLUSION CRITERIA

- Adult hypertensives with B.P controlled or uncontrolled with anti hypertensive treatment.
- Duration of hypertension since diagnosis ≥6 months

EXCLUSION CRITERIA

- Patients with fever.
- Patients with acute or chronic inflammatory diseases.
- CAD,CVA,PVD,CKD.
- Acute or chronic infectious diseases.
- Diabetes,IBD,TB,COPD,Connective tissue diseases.
- h/o hypothyroidism.
- On treatment with NSAIDS, steroids,aspirin and statins.

DATA COLLECTION AND METHODS

Informed consent was obtained from all the patients participating in the study.

Patients were subjected to detailed history taken according to a questionnaire and clinical examination.

- CBC .
- RFT
- LFT.
- FBS,PPBS

- Fasting lipid profile.
- Urine analysis.
- Standard 12 lead ECG .
- Body mass index.
- Echocardiography.
- HsCRP done in every case.

Patients were classified according to JNC 7 staging,classification of HTN.

B.P was measured in right upper limb in sitting posture with a digital sphygmomanometer.

PROCEDURE / INVESTIGATION DETAILS

Blood samples are collected from the antecubital vein using 2cc syringe transferred to a test tube and analyzed by standard proceedures.

- HsCRP-levels measured by fully automated nephelometry
- Fasting Lipid profile measured by Photometry.
- Total cholesterol measured by CHOD POD assay.

- HDL-C measured by Enzyme selective protection assay.
- LDL –C measured by Homogenous enzymatic colorimetrics assay.
- Triglycerides measured by Enzymatic colorimetric method.

All the data collected was entered in the Proforma [enclosed].

STATISTICS AND ANALYSIS

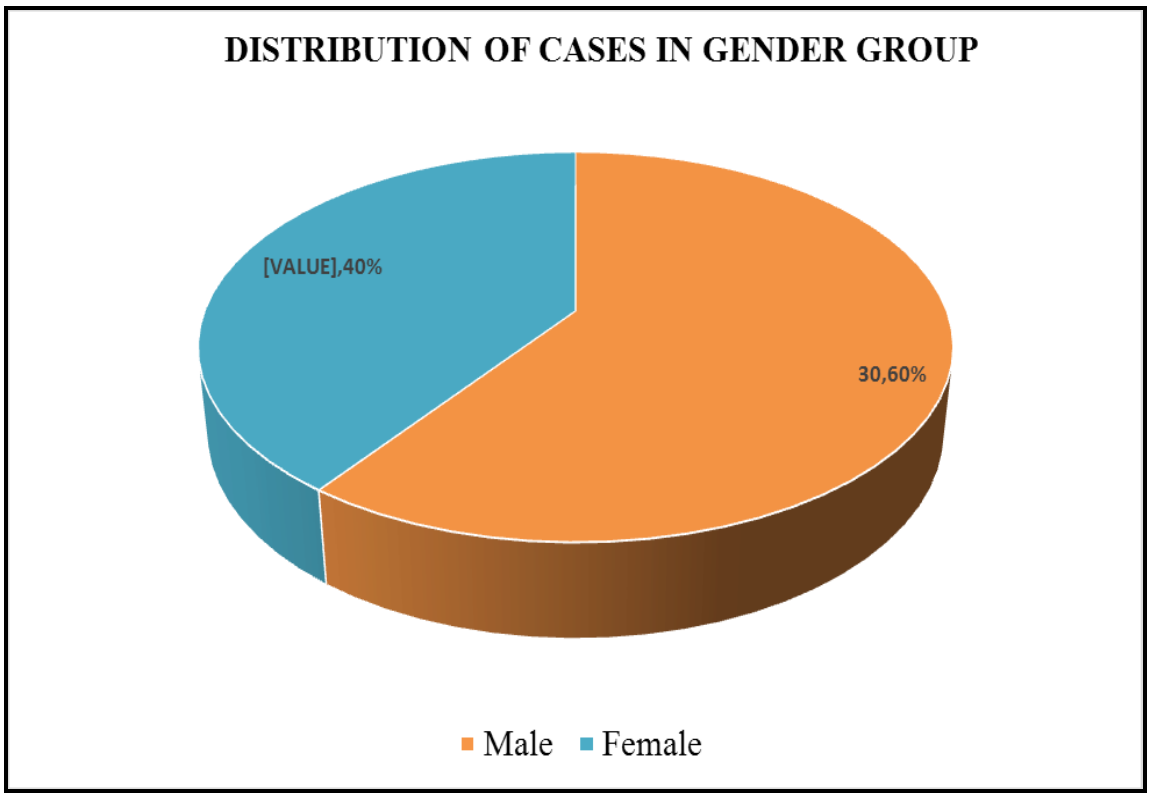
Data was analyzed using Software: SPSS, Version 20.0

- If the p value is 0.000 to 0.010 then it implies significant at 1 level (highly significant)
- If the p value is 0.011to 0.050 then it implies significant at 5 level.
- If the p value is 0.051 to 1.000 then it implies not significant at 5 level (not significant)
- Association between 2 variable categories was made using the chi square test.

OBSERVATION AND RESULTS

SEX DISTRIBUTION IN STUDY GROUP

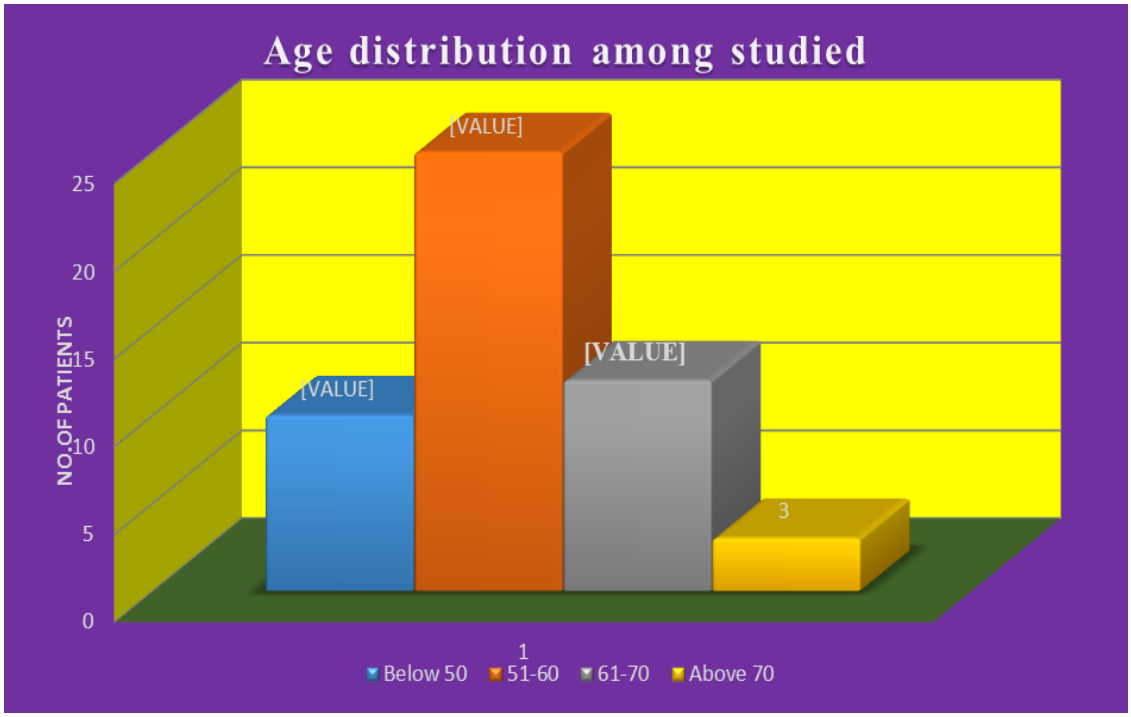
Gender		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Male	30	60.0	60.0	60.0
	Female	20	40.0	40.0	100.0
	Total	50	100.0	100.0	



No of patients study group were total 50 out of which 60% male and 40% females.

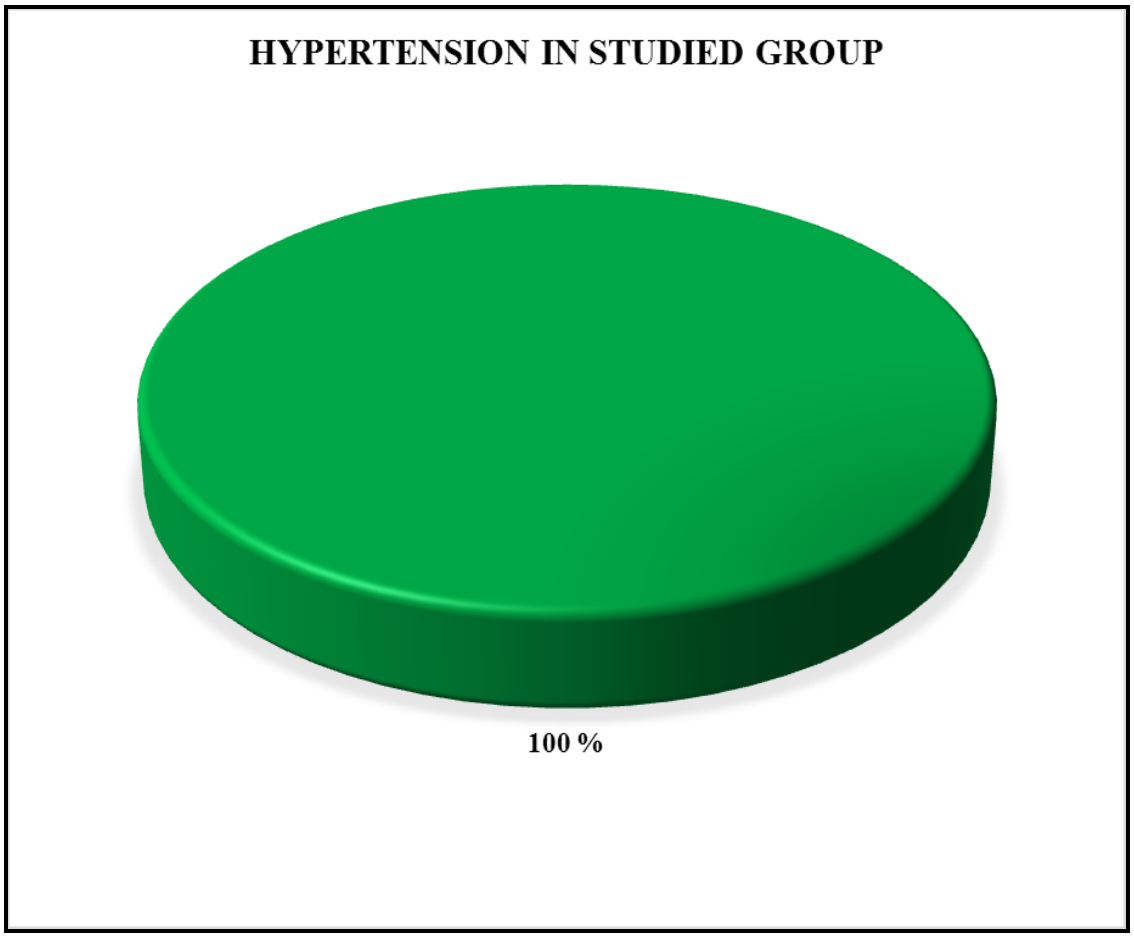
AGE DISTRIBUTION AMONG STUDIED

Age in years		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Below 50	10	20.0	20.0	20.0
	51-60	25	50.0	50.0	70.0
	61-70	12	24.0	24.0	94.0
	Above 70	3	6.0	6.0	100.0
	Total	50	100.0	100.0	



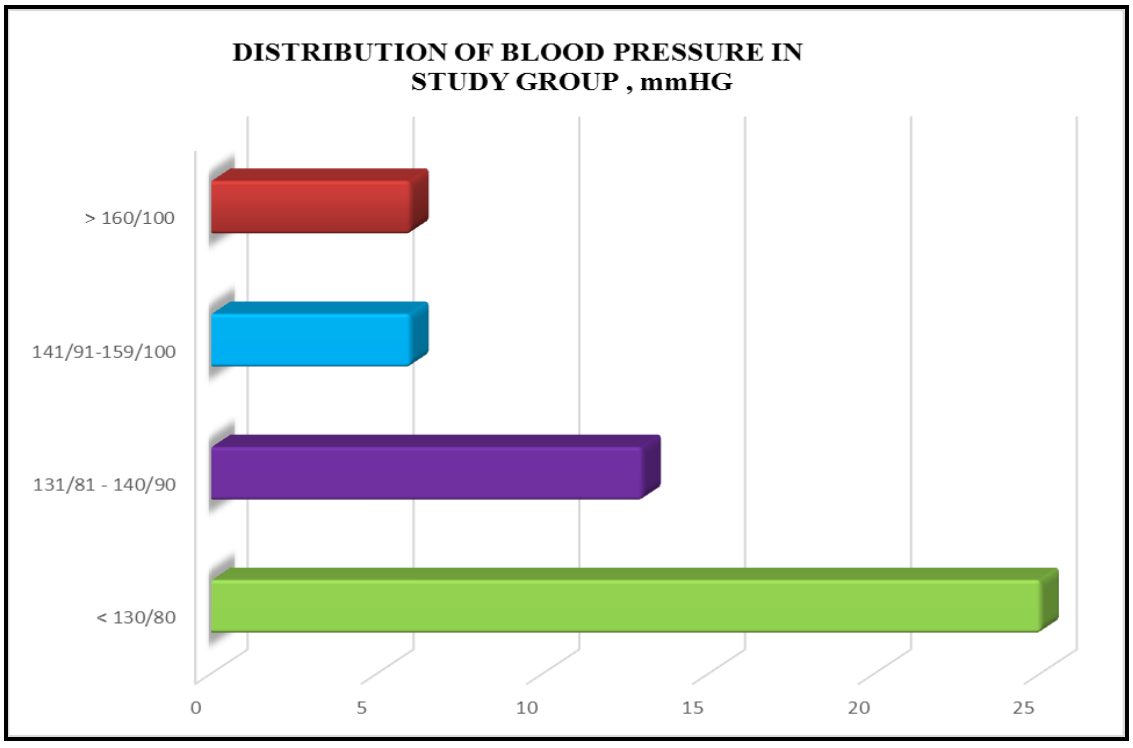
HYPERTENSION IN STUDIED GROUP

HTN		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	50	100.0	100.0	100.0



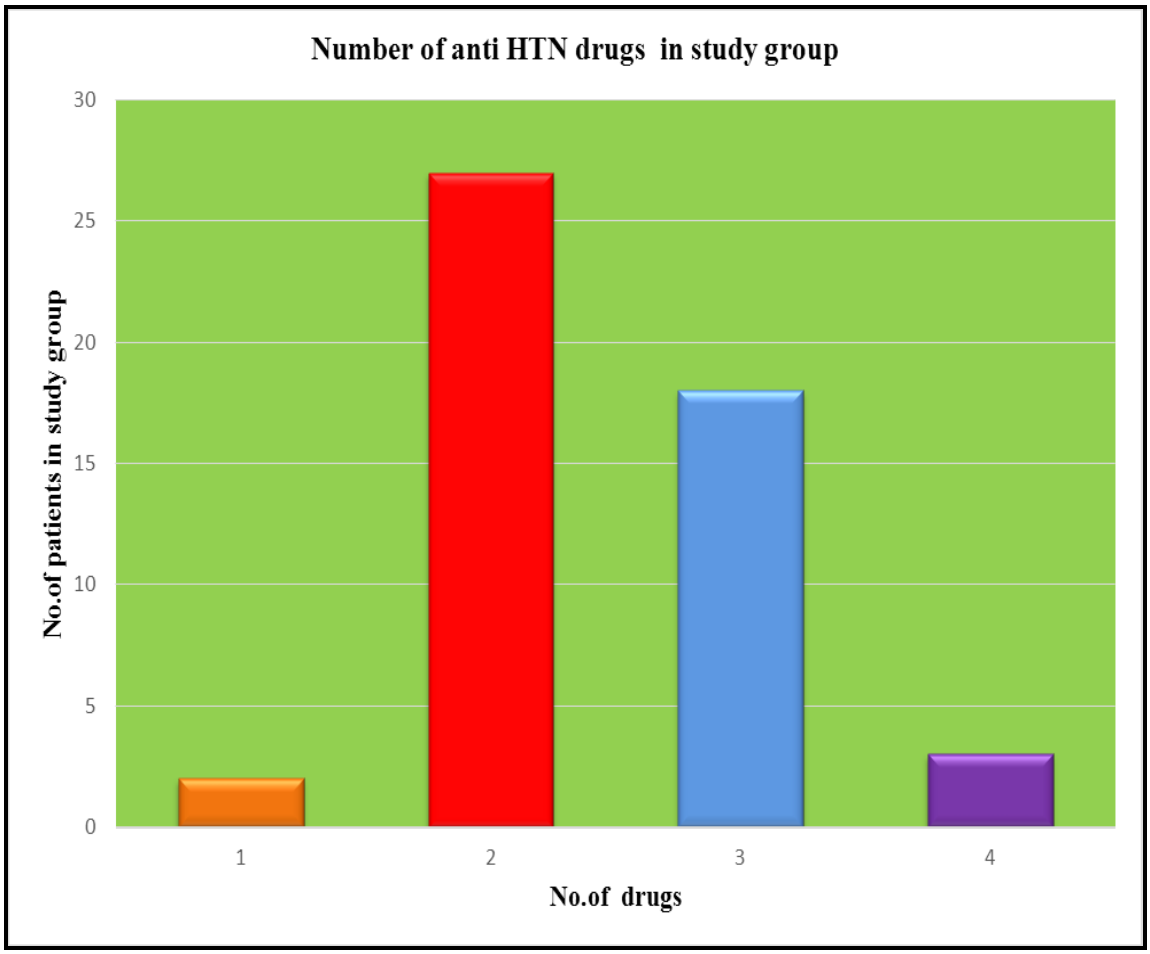
DISTRIBUTION OF BLOOD PRESSURE IN STUDY GROUP , MMHG

BP mmHG		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	< 130/80	25	50.0	50.0	50.0
	131/81 – 140/90	13	26.0	26.0	76.0
	141/91-159/100	6	12.0	12.0	88.0
	> 160/100	6	12.0	12.0	100.0
	Total	50	100.0	100.0	



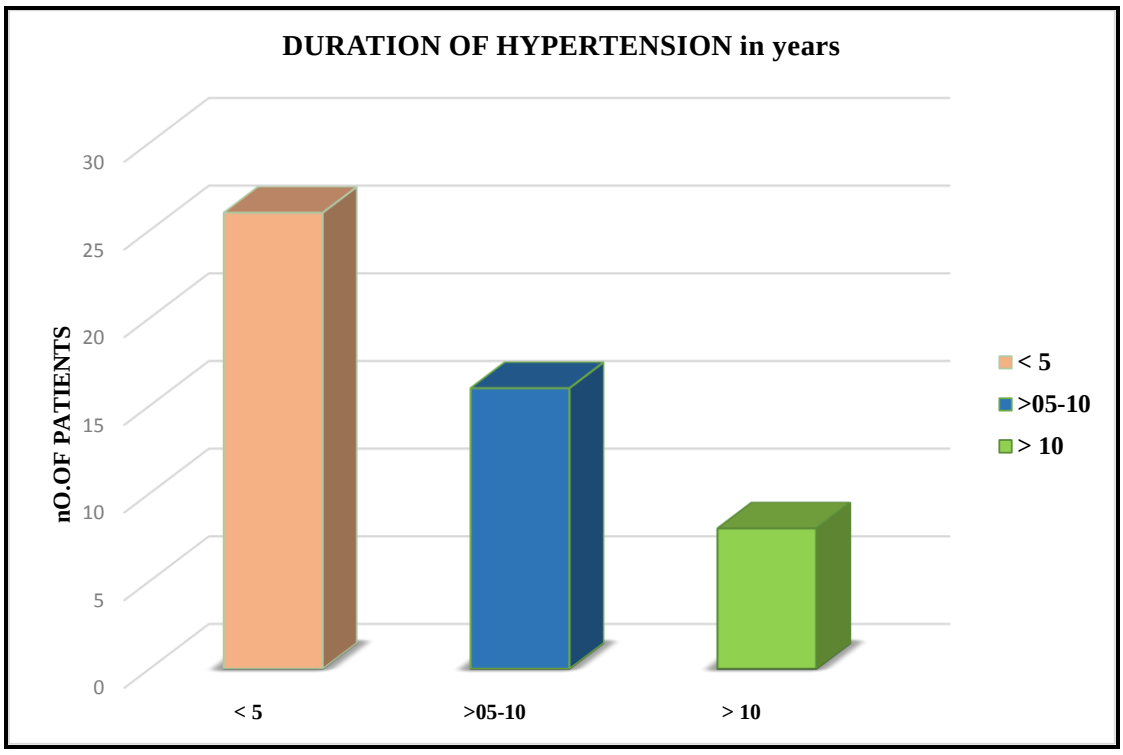
NUMBER OF ANTI HTN DRUGS IN STUDY GROUP

Number of Drugs		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	2	4.0	4.0	4.0
	2	27	54.0	54.0	58.0
	3	18	36.0	36.0	94.0
	4	3	6.0	6.0	100.0
	Total	50	100.0	100.0	



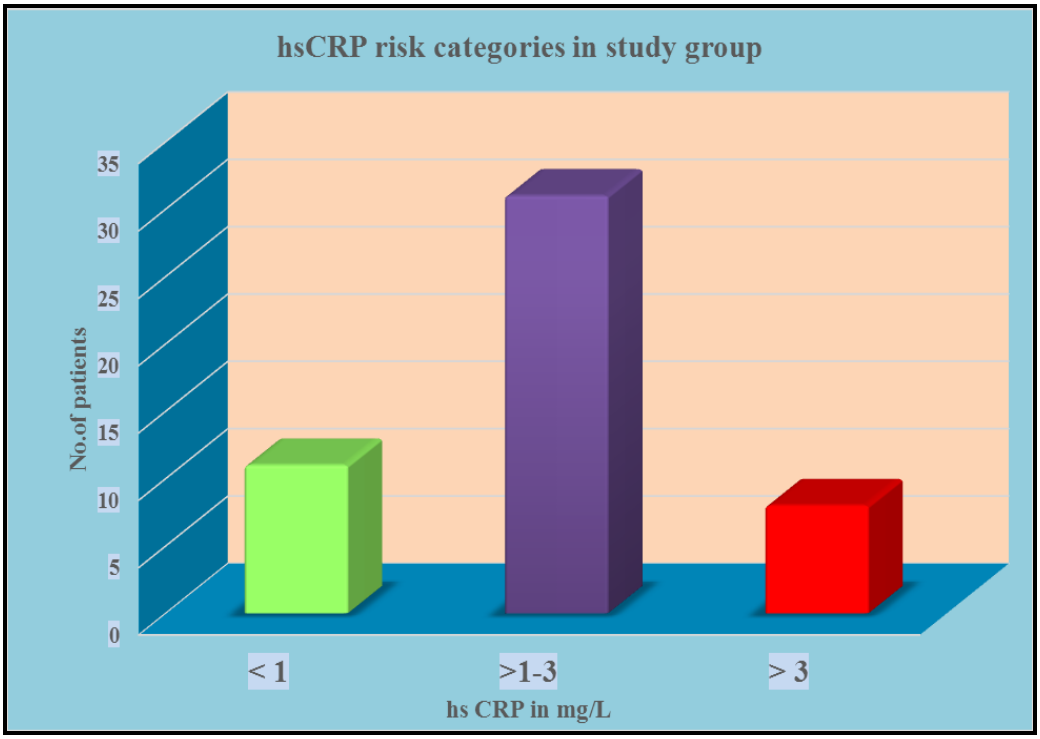
DURATION OF BP IN STUDIED GROUP

Duration of BP in years		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	< 5	26	52.0	52.0	52.0
	6-10	16	32.0	32.0	84.0
	> 10	8	16.0	16.0	100.0
	Total	50	100.0	100.0	



HS-CRP LEVELS WITH RISK CATAGORIES MG/L

Hs-CRP mg/L		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	< 1	11	22.0	22.0	22.0
	1-3	31	62.0	62.0	84.0
	> 3	8	16.0	16.0	100.0
	Total	50	100.0	100.0	

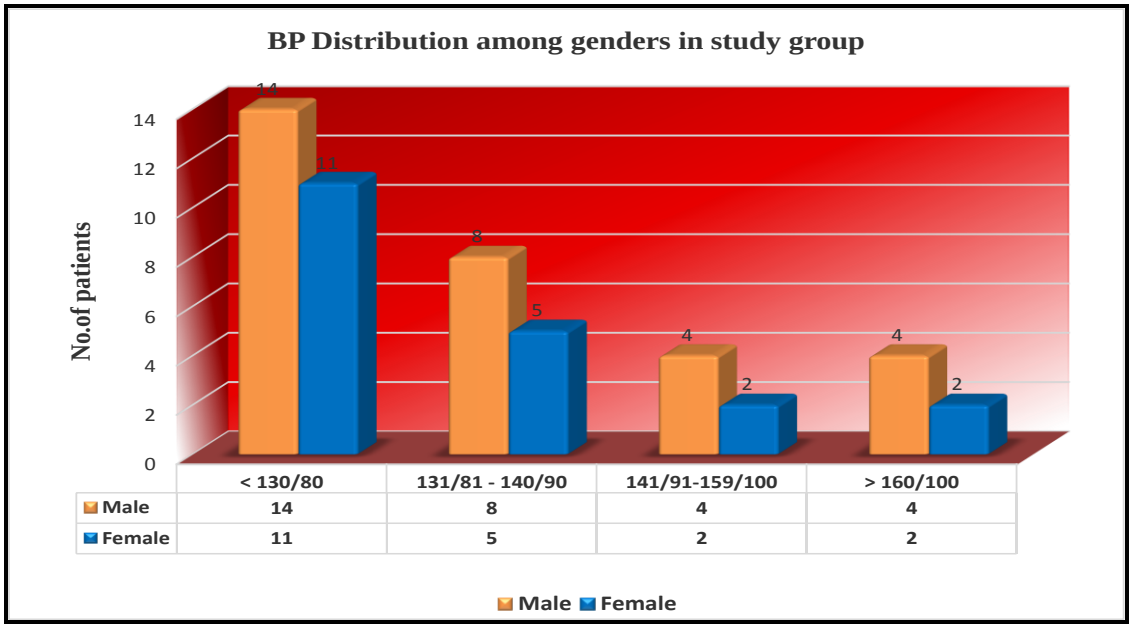


	Hs-CRP mg/L
Chi-Square(a)	18.760
df	2
Asymp. Sig.	.000

p value is < 0.001 is highly significant

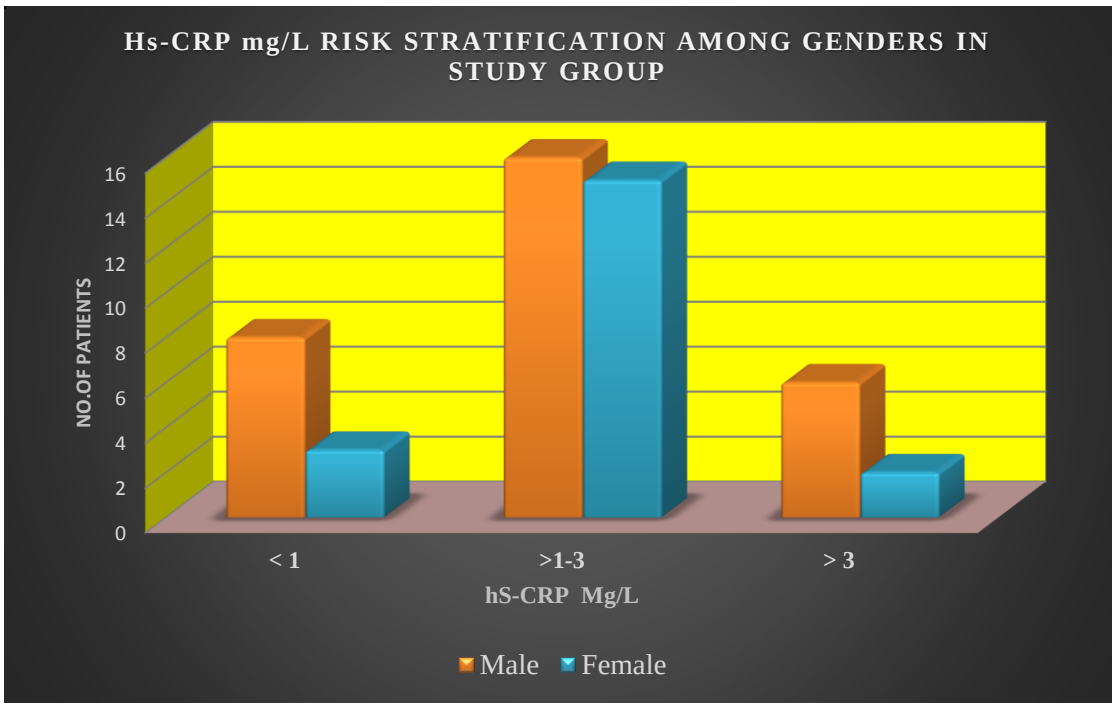
BP DISTRIBUTION AMONG GENDERS IN STUDY GROUP

BP mmHg * Sex			Sex		Total
			Male	Female	
Number	< 130/80	Count	14	11	25
		% within BP mmHg	56.0%	44.0%	100.0%
		% within Sex	46.7%	55.0%	50.0%
	131/81 - 140/90	Count	8	5	13
		% within BP mmHg	61.5%	38.5%	100.0%
		% within Sex	26.7%	25.0%	26.0%
	141/91-159/100	Count	4	2	6
		% within BP mmHg	66.7%	33.3%	100.0%
		% within Sex	13.3%	10.0%	12.0%
	> 160/100	Count	4	2	6
		% within BP mmHg	66.7%	33.3%	100.0%
% within Sex		13.3%	10.0%	12.0%	
Total		Count	30	20	50
		% within BP mmHg	60.0%	40.0%	100.0%
		% within Sex	100.0%	100.0%	100.0%



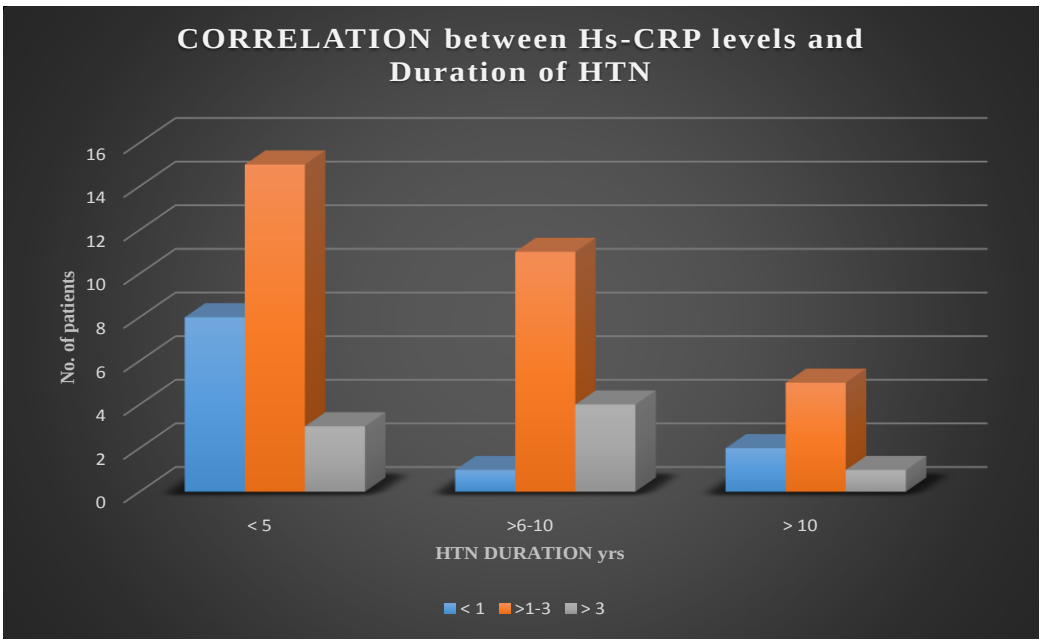
HS-CRP MG/L RISK STRATIFICATION AMONG GENDERS IN STUDY GROUP

Hs-CRP mg/L * Sex			Sex		Total
			Male	Female	
Hs-CRP mg/L	< 1	Count	8	3	11
		% within Hs-CRP mg/L	72.7%	27.3%	100.0%
		% within Sex	26.7%	15.0%	22.0%
	1-3	Count	16	15	31
		% within Hs-CRP mg/L	51.6%	48.4%	100.0%
		% within Sex	53.3%	75.0%	62.0%
	> 3	Count	6	2	8
		% within Hs-CRP mg/L	75.0%	25.0%	100.0%
		% within Sex	20.0%	10.0%	16.0%
Total		Count	30	20	50
		% within Hs-CRP mg/L	60.0%	40.0%	100.0%
		% within Sex	100.0%	100.0%	100.0%



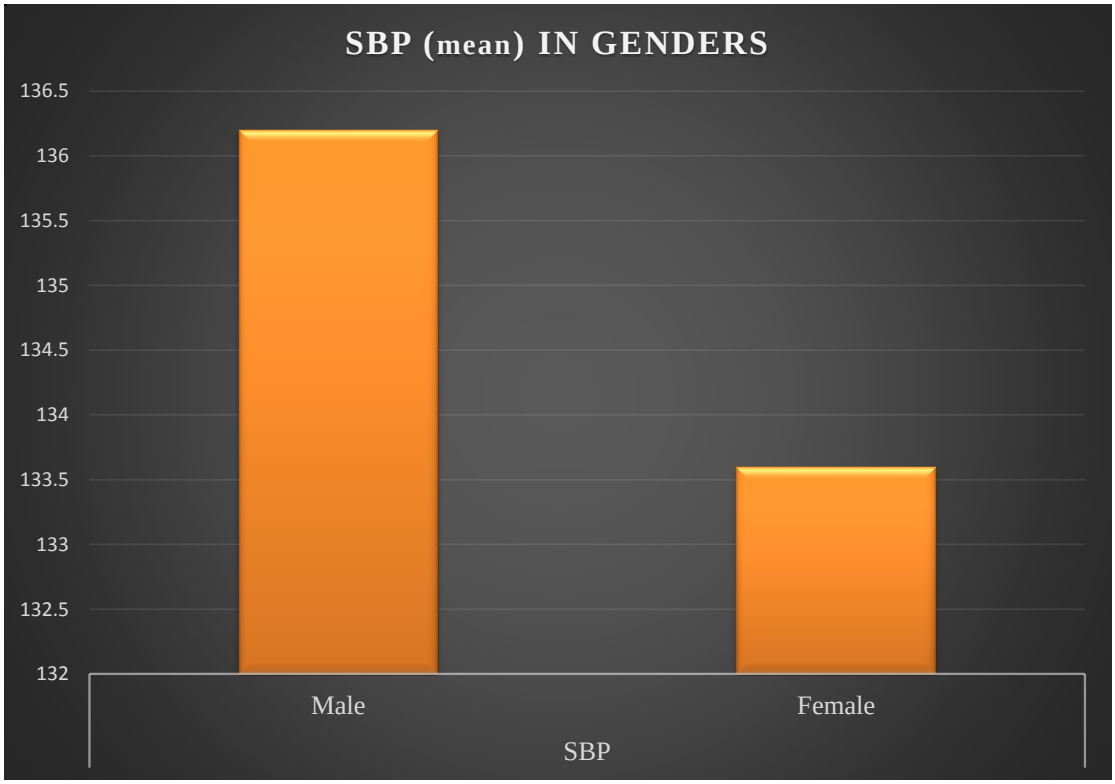
CORRELATION BETWEEN HS-CRP LEVELS AND DURATION OF HTN

			Hs-CRP mg/L			Total
			< 1	1-3	> 3	
Duration of BP years	< 5	Count	8	15	3	26
		% within Duration of BP	30.8%	57.7%	11.5%	100.0%
		% within Hs-CRP mg/L	72.7%	48.4%	37.5%	52.0%
	6-10	Count	1	11	4	16
		% within Duration of BP	6.3%	68.8%	25.0%	100.0%
		% within Hs-CRP mg/L	9.1%	35.5%	50.0%	32.0%
	> 10	Count	2	5	1	8
		% within Duration of BP	25.0%	62.5%	12.5%	100.0%
		% within Hs-CRP mg/L	18.2%	16.1%	12.5%	16.0%
Total		Count	11	31	8	50
		% within Duration of BP	22.0%	62.0%	16.0%	100.0%
		% within Hs-CRP mg/L	100.0%	100.0%	100.0%	100.0%



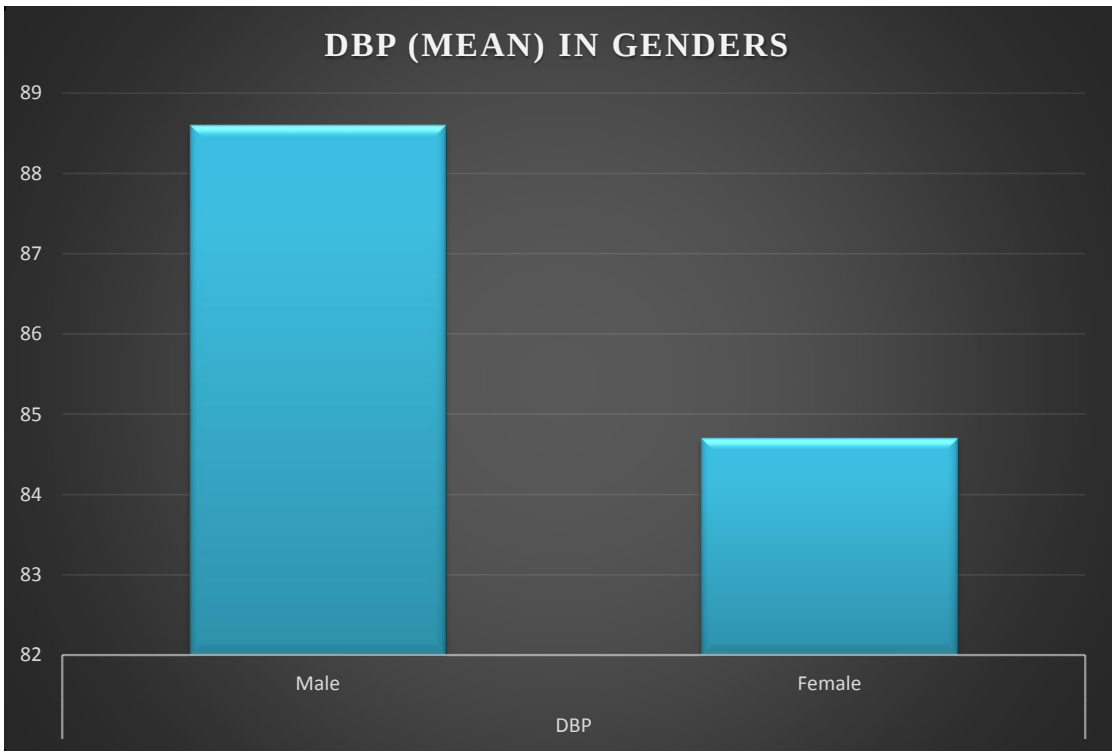
BP (MEAN) IN GENDERS

	Sex	N	Mean	Std. Deviation	Std. Error Mean
SBP	Male	30	136.20	16.529	3.018
	Female	20	133.60	15.446	3.454
DBP	Male	30	88.60	8.122	1.483
	Female	20	84.70	9.021	2.017



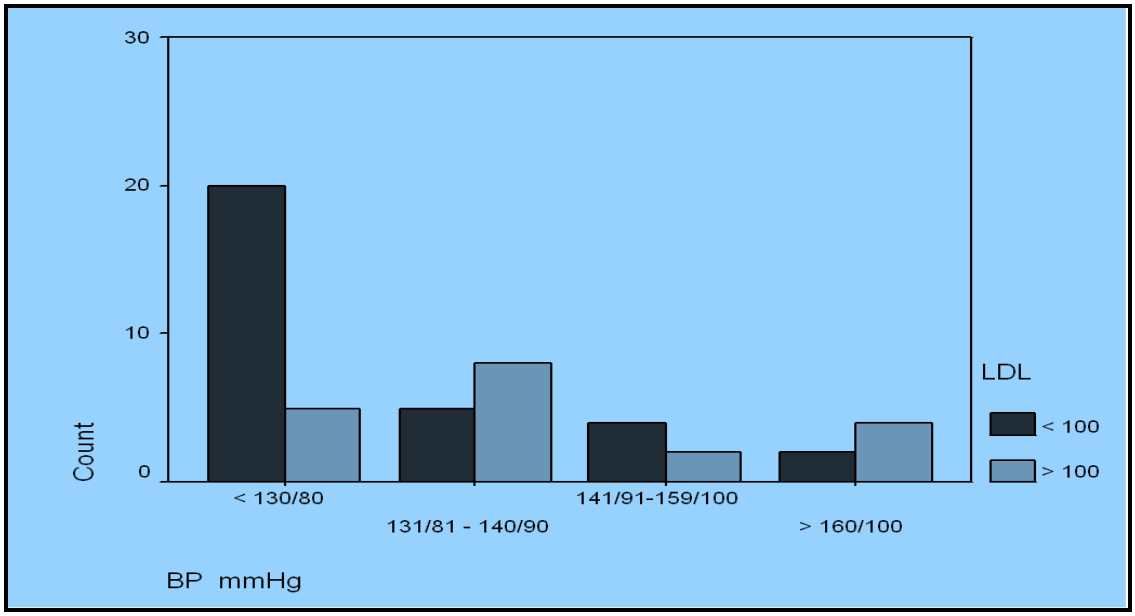
DBP (MEAN) IN GENDERS

	Sex	N	Mean	Std. Deviation	Std. Error Mean
SBP	Male	30	136.20	16.529	3.018
	Female	20	133.60	15.446	3.454
DBP	Male	30	88.60	8.122	1.483
	Female	20	84.70	9.021	2.017



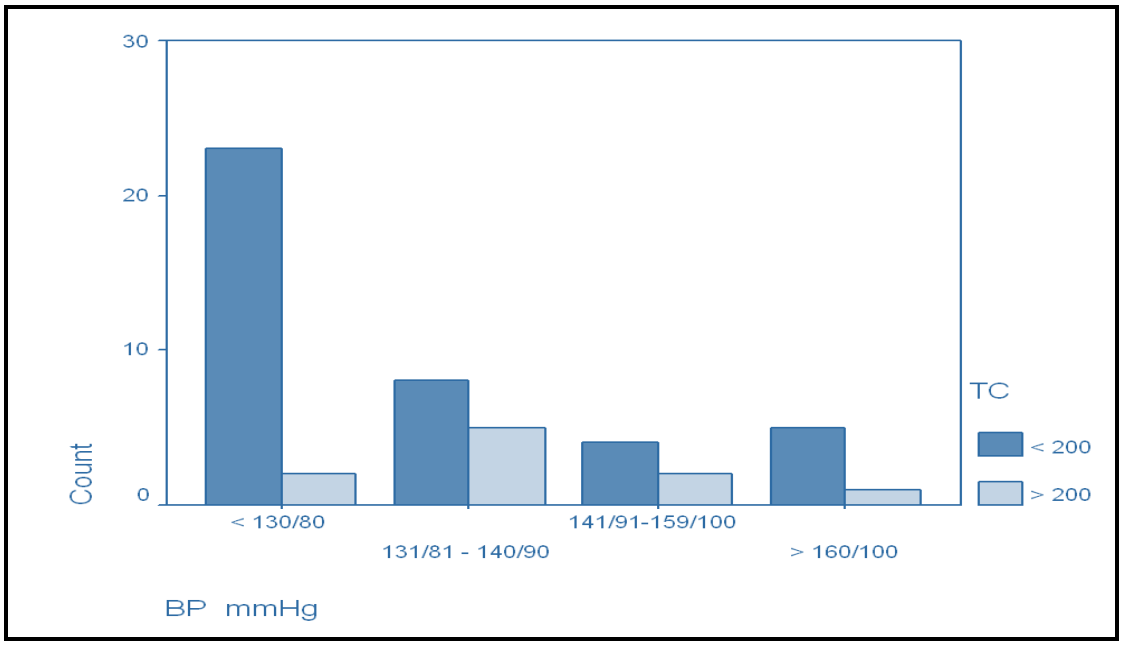
HTN CLASSES AND LDL-C LEVELS

			LDL		Total
			< 100	**> 100**	
BP mmHg	< 130/80	Count	20	5	25
		% within BP mmHg	80.0%	20.0%	100.0%
		% within LDL	64.5%	26.3%	50.0%
	131/81 - 140/90	Count	5	8	13
		% within BP mmHg	38.5%	61.5%	100.0%
		% within LDL	16.1%	42.1%	26.0%
	141/91-159/100	Count	4	2	6
		% within BP mmHg	66.7%	33.3%	100.0%
		% within LDL	12.9%	10.5%	12.0%
	> 160/100	Count	2	4	6
		% within BP mmHg	33.3%	66.7%	100.0%
% within LDL		6.5%	21.1%	12.0%	
Total		Count	31	19	50
		% within BP mmHg	62.0%	38.0%	100.0%
		% within LDL	100.0%	100.0%	100.0%



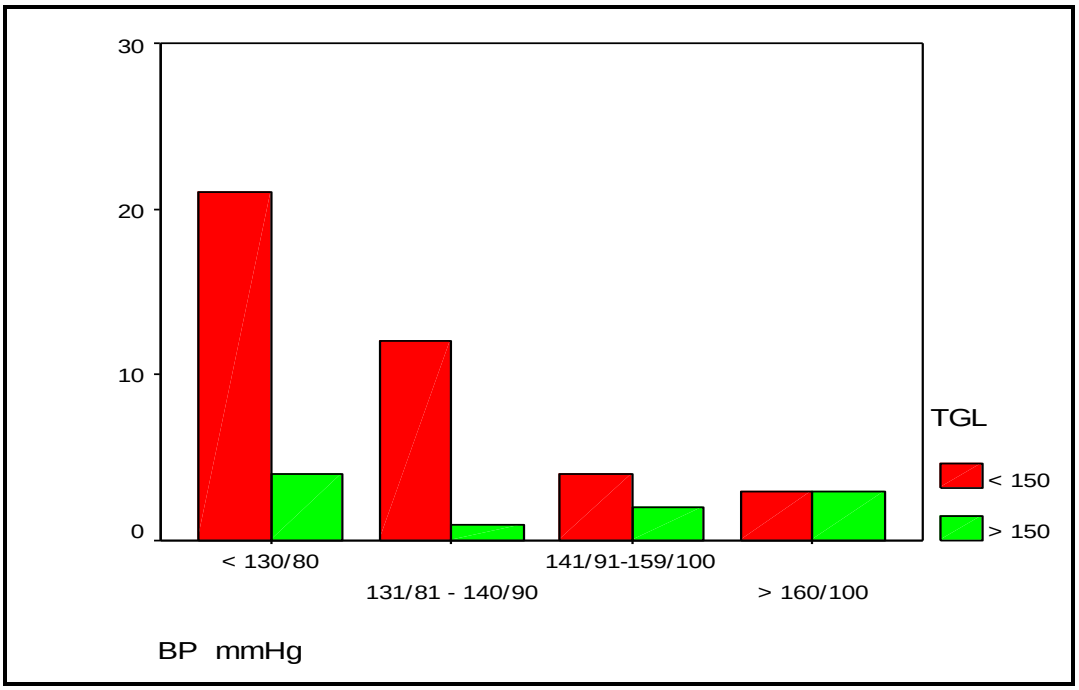
HTN CLASSES AND TOTAL CHOLESTEROL LEVELS

			TC		Total
			< 200	> 200	
BP mmHg	< 130/80	Count	23	2	25
		% within BP mmHg	92.0%	8.0%	100.0%
		% within TC	57.5%	20.0%	50.0%
	131/81 - 140/90	Count	8	5	13
		% within BP mmHg	61.5%	38.5%	100.0%
		% within TC	20.0%	50.0%	26.0%
	141/91-159/100	Count	4	2	6
		% within BP mmHg	66.7%	33.3%	100.0%
		% within TC	10.0%	20.0%	12.0%
	> 160/100	Count	5	1	6
		% within BP mmHg	83.3%	16.7%	100.0%
% within TC		12.5%	10.0%	12.0%	
Total		Count	40	10	50
		% within BP mmHg	80.0%	20.0%	100.0%
		% within TC	100.0%	100.0%	100.0%



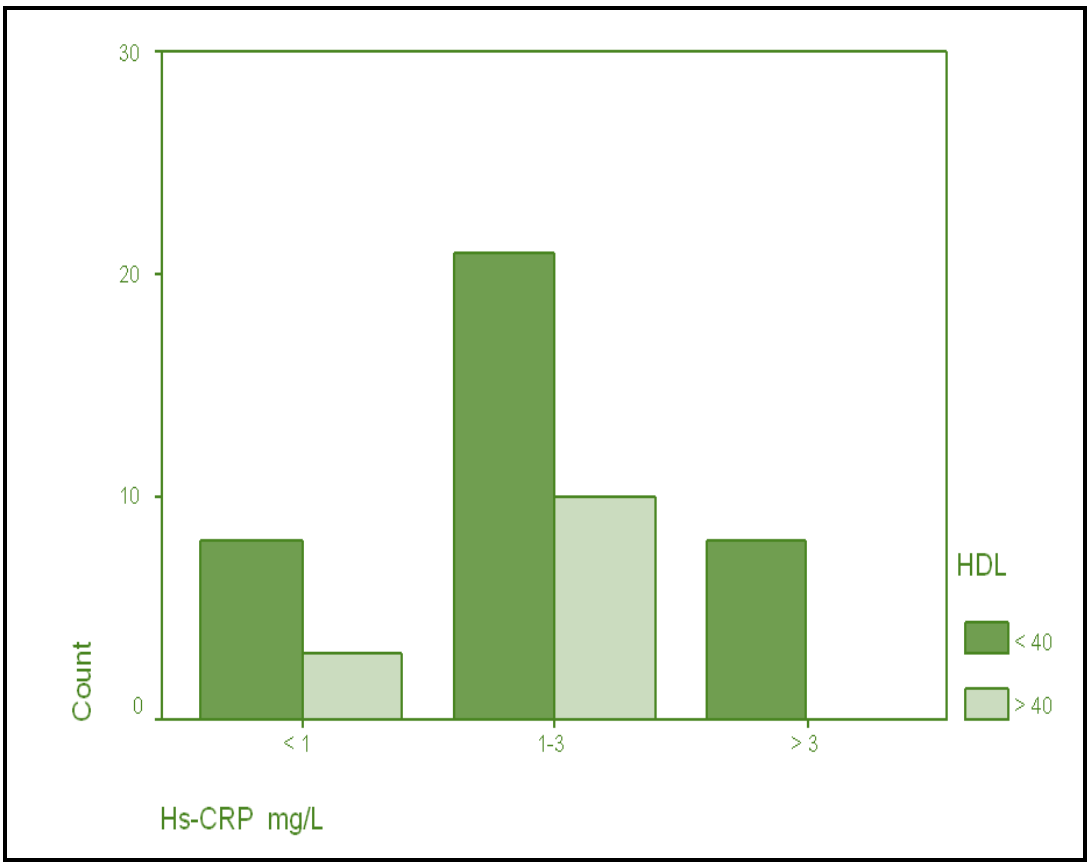
HTN CLASSES AND TRIGLYCERIDE LEVELS

			TGL		Total
			< 150	> 150	
BP mmHg	< 130/80	Count	21	4	25
		% within BP mmHg	84.0%	16.0%	100.0%
		% within TGL	52.5%	40.0%	50.0%
	131/81 - 140/90	Count	12	1	13
		% within BP mmHg	92.3%	7.7%	100.0%
		% within TGL	30.0%	10.0%	26.0%
	141/91-159/100	Count	4	2	6
		% within BP mmHg	66.7%	33.3%	100.0%
		% within TGL	10.0%	20.0%	12.0%
	> 160/100	Count	3	3	6
		% within BP mmHg	50.0%	50.0%	100.0%
% within TGL		7.5%	30.0%	12.0%	
Total		Count	40	10	50
		% within BP mmHg	80.0%	20.0%	100.0%
		% within TGL	100.0%	100.0%	100.0%



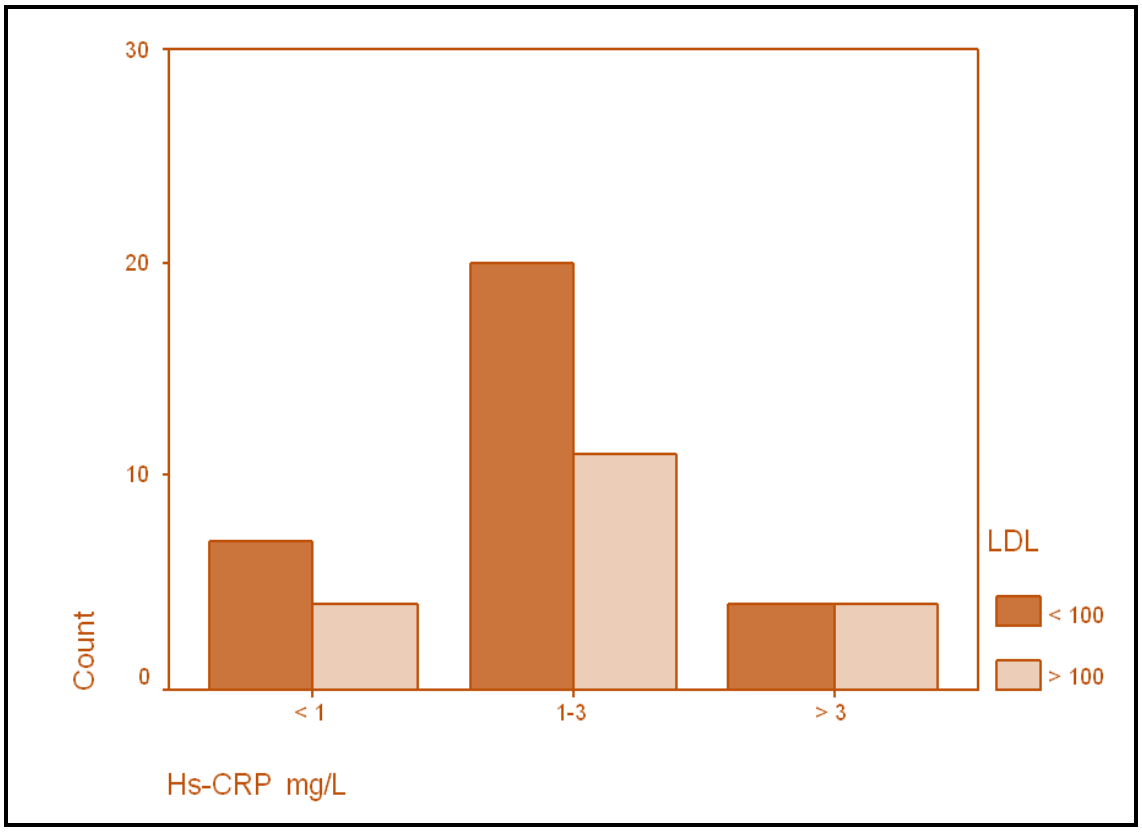
HSCRP CLASSES AND HDL-C LEVELS

			HDL		Total
			< 40	> 40	
Hs-CRP mg/L	< 1	Count	8	3	11
		% within Hs-CRP mg/L	72.7%	27.3%	100.0%
		% within HDL	21.6%	23.1%	22.0%
	1-3	Count	21	10	31
		% within Hs-CRP mg/L	67.7%	32.3%	100.0%
		% within HDL	56.8%	76.9%	62.0%
	> 3	Count	8	0	8
		% within Hs-CRP mg/L	100.0%	.0%	100.0%
% within HDL		21.6%	.0%	16.0%	
Total		Count	37	13	50
		% within Hs-CRP mg/L	74.0%	26.0%	100.0%
		% within HDL	100.0%	100.0%	100.0%



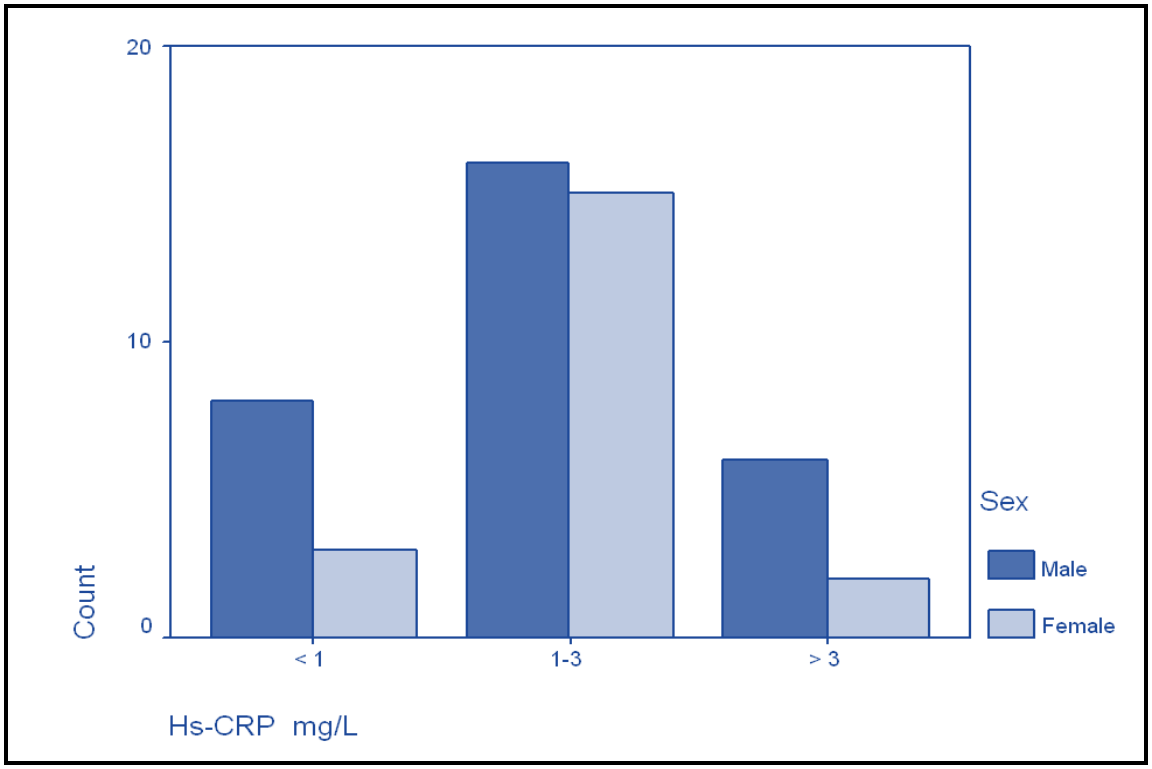
HSCRP CLASSES AND LDL-C LEVELS

			LDL		Total
			< 100	> 100	
Hs-CRP mg/L	< 1	Count	7	4	11
		% within Hs-CRP mg/L	63.6%	36.4%	100.0%
		% within LDL	22.6%	21.1%	22.0%
	1-3	Count	20	11	31
		% within Hs-CRP mg/L	64.5%	35.5%	100.0%
		% within LDL	64.5%	57.9%	62.0%
	> 3	Count	4	4	8
		% within Hs-CRP mg/L	50.0%	50.0%	100.0%
% within LDL		12.9%	21.1%	16.0%	
Total		Count	31	19	50
		% within Hs-CRP mg/L	62.0%	38.0%	100.0%
		% within LDL	100.0%	100.0%	100.0%



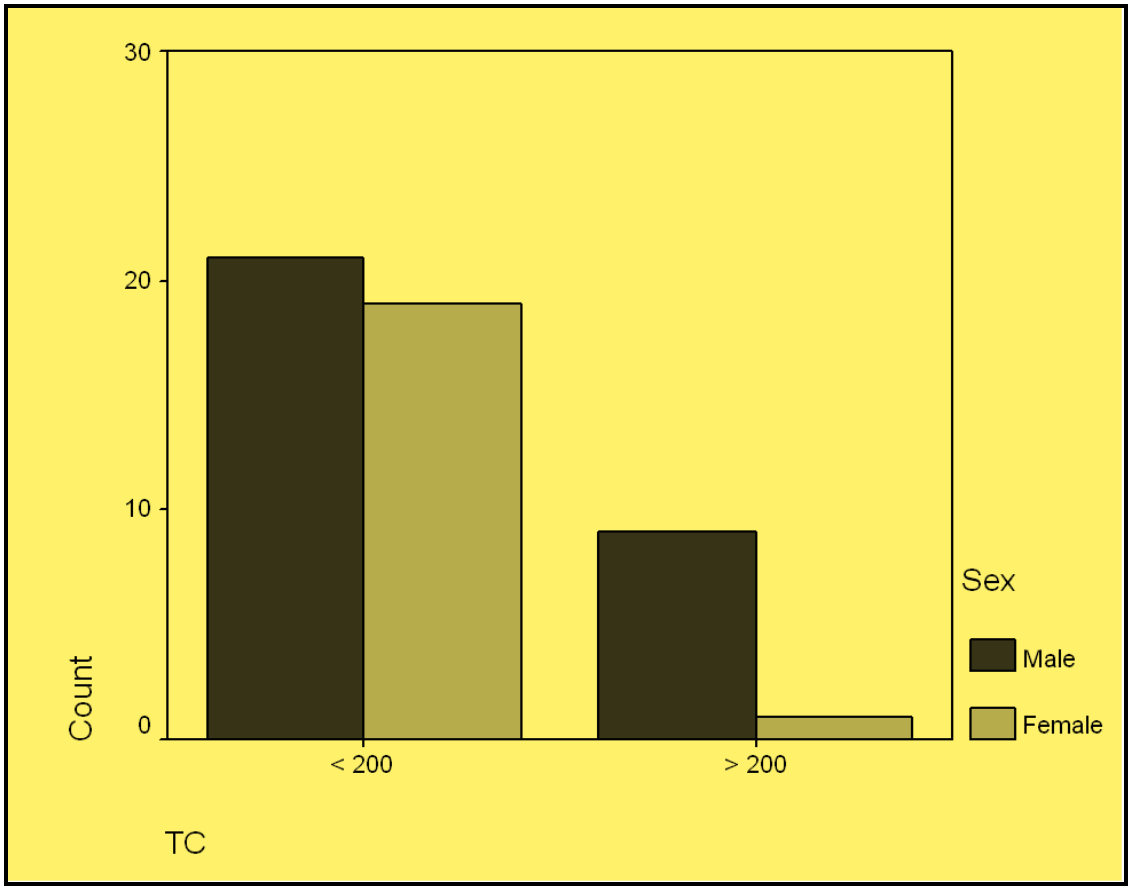
HSCRP CLASSES IN GENDERS

			Sex		Total
			Male	Female	
Hs-CRP mg/L	< 1	Count	8	3	11
		% within Hs-CRP mg/L	72.7%	27.3%	100.0%
		% within Sex	26.7%	15.0%	22.0%
	1-3	Count	16	15	31
		% within Hs-CRP mg/L	51.6%	48.4%	100.0%
		% within Sex	53.3%	75.0%	62.0%
	> 3	Count	6	2	8
		% within Hs-CRP mg/L	75.0%	25.0%	100.0%
% within Sex		20.0%	10.0%	16.0%	
Total		Count	30	20	50
		% within Hs-CRP mg/L	60.0%	40.0%	100.0%
		% within Sex	100.0%	100.0%	100.0%



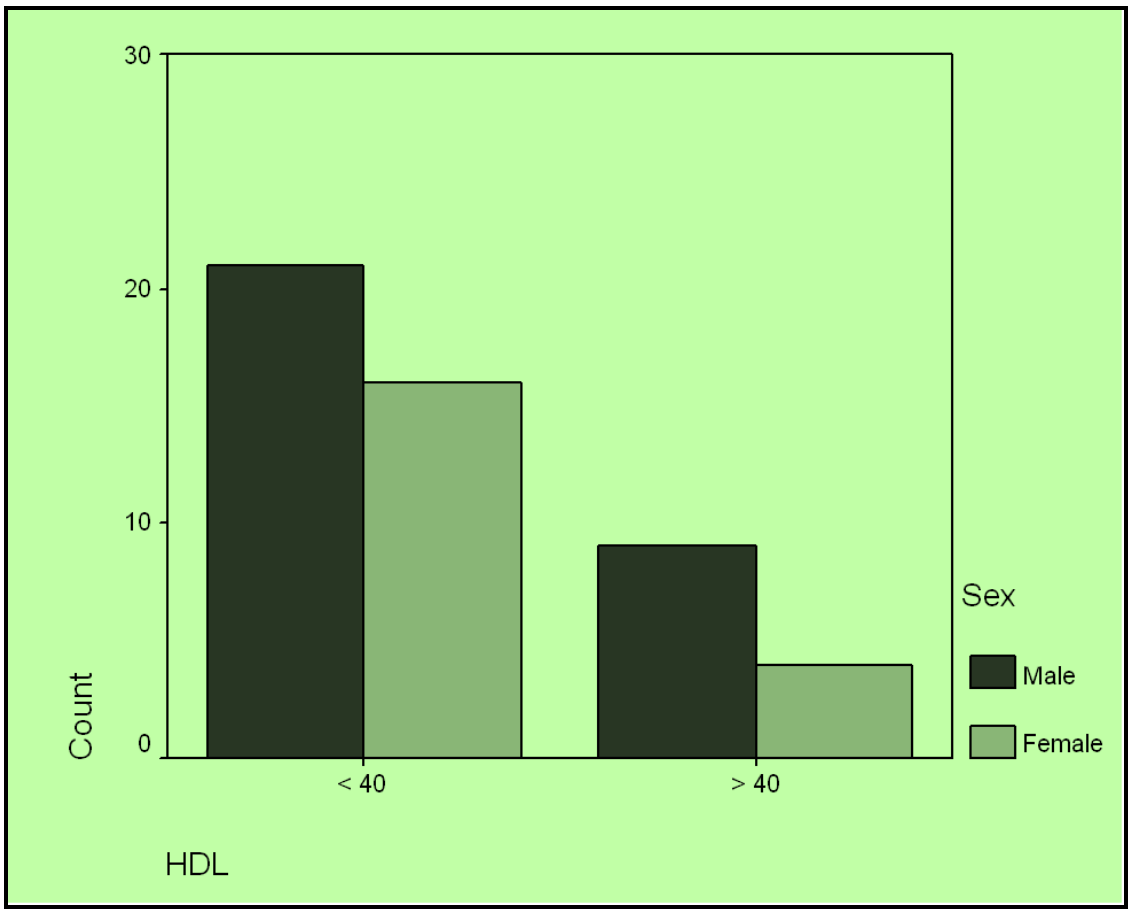
TOTAL CHOLESTEROL GENDER WISE

			Sex		Total
			Male	Female	
TC	< 200	Count	21	19	40
		% within TC	52.5%	47.5%	100.0%
		% within Sex	70.0%	95.0%	80.0%
	> 200	Count	9	1	10
		% within TC	90.0%	10.0%	100.0%
% within Sex		30.0%	5.0%	20.0%	
Total		Count	30	20	50
		% within TC	60.0%	40.0%	100.0%
		% within Sex	100.0%	100.0%	100.0%



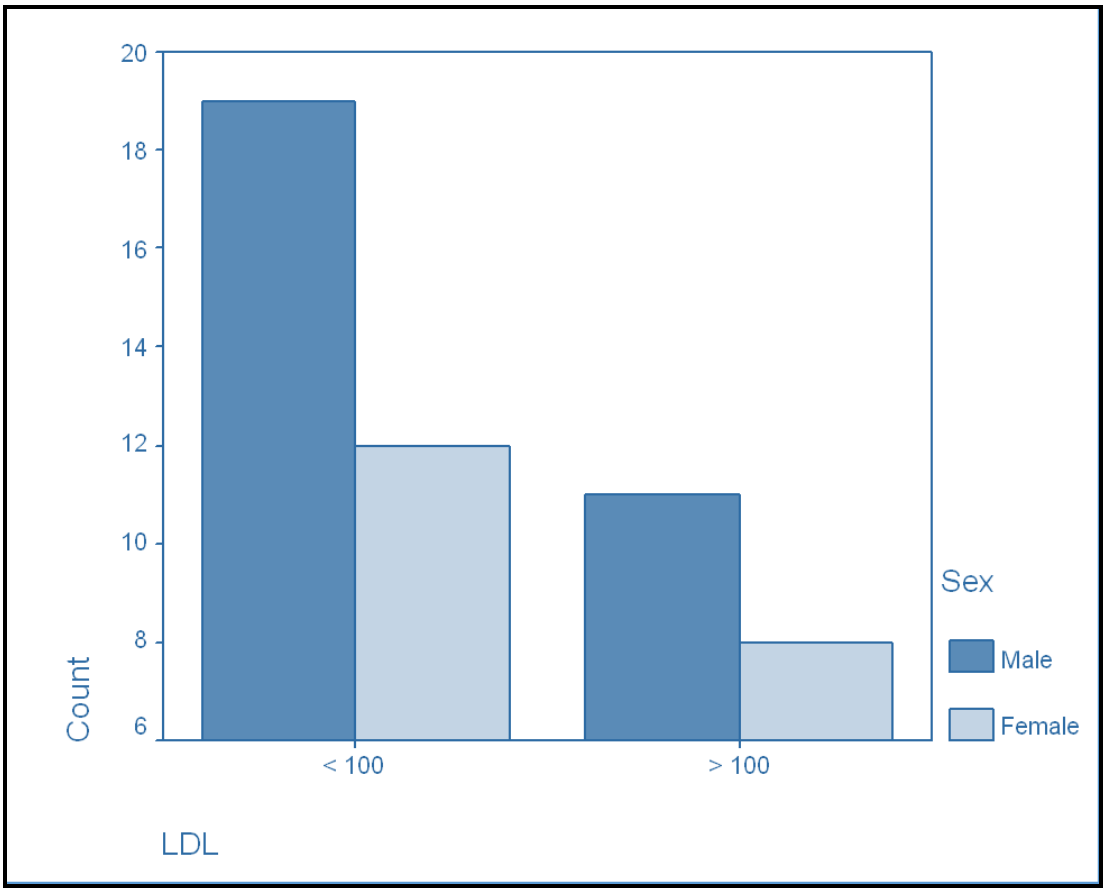
HDL- CHOLESTEROL GENDER WISE

			Sex		Total
			Male	Female	
HDL	< 40	Count	21	16	37
		% within HDL	56.8%	43.2%	100.0%
		% within Sex	70.0%	80.0%	74.0%
	> 40	Count	9	4	13
		% within HDL	69.2%	30.8%	100.0%
% within Sex		30.0%	20.0%	26.0%	
Total		Count	30	20	50
		% within HDL	60.0%	40.0%	100.0%
		% within Sex	100.0%	100.0%	100.0%



LDL- CHOLESTEROL GENDER WISE

			Sex		Total
			Male	Female	
LDL	< 100	Count	19	12	31
		% within LDL	61.3%	38.7%	100.0%
		% within Sex	63.3%	60.0%	62.0%
	> 100	Count	11	8	19
		% within LDL	57.9%	42.1%	100.0%
% within Sex		36.7%	40.0%	38.0%	
Total		Count	30	20	50
		% within LDL	60.0%	40.0%	100.0%
		% within Sex	100.0%	100.0%	100.0%



RESULTS

SEX DISTRIBUTION

No of patients study group were total 50 out of which 60% male and 40% females.

AGE DISTRIBUTION

The percent of patients with HTN in study group belonging to age below 50yrs was 20%, those belong to age 51-60yrs was 50%, those belongs to age 61-70 was 24% and above 70yrs of age 6%

Significant **number** of patients belonged to 61-70yrs of age group in the study.

HYPERTENSION IN STUDY GROUP

100% of patients in study group had HTN which was either controlled or uncontrolled on Anti Hypertension treatment.

DISTRIBUTION OF BP IN MMHG IN STUDY GROUP

BP < 130/180 mmHg : 55%.

BP 131/81 – 140/90 mmHg : 26%

BP 141/91-159/99 mmHg : 12%

BP 160/100 mmHg : 12%

Significant number of patients had BP <130/80 mmHg

PATIENTS WITH NO. OF ANTI HYPERTENSION DRUGS IN STUDY GROUP

a.Patients with 1 drug were 4%

b.Patients with 2 drugs were 54%

c.Patients with 3 drugs were 36%

d.Patient with 4 drugs were 6%

Significant no of patients on antihypertension treatment was on 2 drugs at the time of study.

DURATION OF HTN AND WITH DURATION OF HTN >6 MONTHS

Patients with duration of BP

<5yrs were -52%

6-10yrs were -32%

>10yrs were -16%

Significant no. of patients had HTN of duration more than <5 yrs.

HS-CRP LEVELS WITH RISK CATEGORIES IN MG/L

Patients with HSCRP <1mg LOW risk category was 22%

HRCP >1-3 MODERATE risk category was 62%

HRCP >3mg HIGH risk category was 8%

Highly Significant (**p value is 0.001)** no of patient had HsCRP levels of >1-3mg/L belonging to moderate risk category.

BP DISTRIBUTION AMONG GENDERS IN STUDY GROUP

1) Bp <130/80 mmhg no.of males was 14(56%) and no.of females was 11(44%).

2) Bp 131/81-140/90 mmhg no.of males was 8 (61.5%) and no.of females was 5(38.5%).

3) Bp 141/91-159/100 mmhg no.of males was 4 (66.7%) and no.of females was 2 (33.3%).

4) Bp > 160/100 mmhg no.of males was 4 (66.7%) and no.of females was 2 (33.3%).

HS-CRP MG/L RISK STRATIFICATION AMONG GENDERS IN STUDY GROUP

1) Male patients with

HsCRP <1mg LOW risk category was 8 (72.7%)

HsCRP >1-3 mg MODERATE risk category was 16 (51.6%)

HsCRP >3 mg HIGH risk category was 6 (75.0%)

2) Female Patients with

HsCRP <1mg LOW risk category was 3 (27.3%)

HsCRP >1-3 MODERATE risk category was15 (48.4%)

HsCRP >3mg HIGH risk category was 2 (25.0%)

CORRELATION BETWEEN HS-CRP LEVELS AND DURATION OF HTN

1) With Duration of BP < 5 years with HsCRP <1mg no.of patients was 8(30.8%), with HsCRP >1-3 no.of patients was 15(57.7%), with HsCRP >3 no.of patients was 3(11.5%)

2) With Duration of BP 6-10 years with HsCRP <1mg no.of patients was 1 (6.3%), with HsCRP >1-3 no.of patients was 1(68.8%), with HsCRP >3 no.of patients was 4(25%)

3) With Duration of BP > 10 years with HsCRP <1mg no.of patients was 2(25%), with HsCRP >1-3 no.of patients was 5(62.5%), with HsCRP >3 no.of patients was 1(12.5%).

Mean SYSTOLIC and DIASTOLIC BP in males and female subjects

Mean SBP in male subjects was 136 mmhg.

Mean SBP in female subjects was 133mmhg.

Mean DBP in female subjects was 84 mmhg.

DISCUSSION

HsCRP levels can be used as a marker of latent atherosclerosis and cardiovascular risk. 50% of all ACS occur in persons who do not have dyslipidemia. Studies have shown that that the combined evaluation of CRP levels and lipid profile may improve risk stratification and also identify asymptomatic individuals at higher risk of cardiovascular events

AHA and CDC recommended the utility of testing of CRP levels as an adjunct to CV risk assessment. CRP was recommended over the other inflammatory biomarkers whichare available because it is advanced and validated clinical assay and has a larger supporting data for its accuracy and validity.

Risk categorization by HsCRP levels interpretation guidelines: Less than 1mg/L, lower risk; between 1–3 mg/L, intermediate risk and more than 3 mg/L, higher risk. Testing of CRP as a optional use was recommended for those at intermediate risk (8–15% absolute 10 year risk of CAD events) by the Framingham Risk Score.

HsCRP adds prognostic value at all levels of LDL-C,Framingham coronary risk score, and BP levels, also in those individuals with and without subclinical atherosclerosis.In clinical settings, HsCRP should be used in combination with lipid profile evaluation.

Advanced knowledge of cardiovascular risks can lead to better lifestyle and pharmacological interventions targeted to prevent future CV events.

In this observational study subjects with hypertension were categorized according to JNC7 classification of hypertension.

Subjects grouped into duration of hypertension were compared with HsCRP levels and subjects categorized into 3 risk categories of <1mg/L,1-3mg/L and >3mg/L.

There was significant no.of patients in the moderate risk category with HsCRP levels between 1-3mg/L **(p value is < 0.001)** but no statistical significance observed when HsCRP levels were correlated with the duration of hypertension or with levels of Total cholesterol, LDL-C and HDL-C.

CONCLUSION

In summary ,this study observed that HsCRP levels of >1-3mg/L were elevated significantly in subjects with hypertension **(p value is < 0.001)** irrespective of their BP levels and duration of hypertension.

There was no statistical significance and correlation between levels of HsCRP and hypertension with levels of LDL-C or HDL-C in the study group.

CLINICAL IMPORTANCE

HsCRP levels can be evaluated in hypertensive individuals who do not have symptomatic CAD irrespective of abnormal Lipid profile and can be provided with primary prevention to prevent future cardiovascular events.

LIMITATIONS OF STUDY

The main limitation in this study was the small size of study group.

Further follow up study of patients in moderate to high risk category with elevated levels of HsCRP is needed.

A larger study group with evaluation of the complete clinical profile of persons with hypertension and also comparing the type of

antihypertensive with the lipid profile and HsCRP levels could have provided with better risk stratification,leading to providing better primary prevention of CAD.

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STUDY ON HIGH SENSITIVITY C REACTIVE PROTIEN (hsCRP) LEVELS & CORRELATION WITH LIPID PROFILE IN HYPERTENSION

PROFORMA

Name :

Age/Sex : Weight :

IP/OP No : Diagnosis :

Patient ID No : Duration :

Patient characteristics	**Medications**
□ Systemic hypertension	□ Calcium channel blockers
□ Diabetes	□ Statins
□ Smoking	□ Beta blockers
□ Diet	□ ACE inhibitors
□ Alcoholism	□ Others
Vascular complications	
□ Coronary events	□ Cerebrovascular events
□ Peripheral vascular diseases	

Symptoms:

Chest pain: Dyspnoea:

Cough: Palpitations:

Sweating: Presyncope/Syncope:

Swelling Of Legs: Easy Fatigability:

Facial Puffiness: Decreased Urine Output:

Others:

Past history:

Diabetes mellitus: Coronary artery disease:

Recent infection: Recent hospitalization:

Connective tissue disorders: Other comorbid illnesses:

Hypertension: Kidney disease:

Stroke: Hematological illness:

Heart failure: Liver disease:

Tuberculosis: Recent surgery/trauma:

COPD: Br.Asthma:

Drug history:

Family history:

Personal history:

- Diet
- Sleep
- Bowel/bladder
- Substance abuse

Menstrual history:

VITALS:

Pulse: JVP:

Respiratory Rate: **Blood Pressure**:

General examination:

Weight: Height:

Body mass index: Icterus:

Pallor: Lymphadenopathy:

Cyanosis Pedal edema:

Clubbing:

Systemic examination:

CVS:

Apical impulse

Heart sounds(S1,S2,S3,S4)

Murmurs

Basal crepitations

RS:

ABDOMEN:

CNS:

Investigations:

COMPLETE BLOOD COUNT	
Total leucocyte count	cells/cu.mm
Neutrophils	%
Lymphocytes	%
Eosinophils	%
Basophils	%
Monocytes	%
Hemoglobin	g/dl
Hematocrit	%

ESR			mm/1 hour		
RBC count			Million/cu.mm		
Platelet count			Cells/cu.mm		
RFT			**LFT**		
Glucose(F)		mg/dl	Total bilirubin		mg/dl
Urea		mg/dl	Direct bilirubin		mg/dl
Creatinine		mg/dl	SGOT		U/l
Na+		mEq/l	SGPT		U/l
K+		mEq/l	ALP		U/l
			Total protein		g/dl
			Albumin		g/dl

hsCRP	

Urine analysis:

FASTING LIPID PROFILE	
Total cholesterol	mg/dl
Triglycerides	mg/dl
LDL	mg/dl
HDL	mg/dl
VLDL	mg/dl

ECG:

Echocardiography: Regional wall motion abnormality:

Ejection fraction:

INFORMATION SHEET

We are conducting a study on **"HIGH SENSITIVITY C REACTIVE PROTIEN (HSCRP) LEVELS & CORRELATION WITH LIPID PROFILE IN HYPERTENSION"** among patients attending Rajiv Gandhi Government General Hospital, Chennai and for that your specimen may be valuable to us.

The purpose of this study is to evaluate **HIGH SENSITIVITY C REACTIVE PROTIEN (hsCRP) LEVELS & CORRELATION WITH LIPID PROFILE IN HYPERTENSION"** to identify and risk stratify patients at risk for cardio vascular events & primary prevention of coronary artery disease..

We are selecting certain cases and if you are found eligible, we may be using your blood samples to do special studies which in any way do not affect your final report or management.

The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of Investigator	Signature of Participant
Date :	
Place :	

PATIENT CONSENT FORM

Study Detail : **"HIGH SENSITIVITY C REACTIVE PROTIEN (hsCRP) LEVELS & CORRELATION WITH LIPID PROFILE IN HYPERTENSION"**

Study Centre : Rajiv Gandhi Government General Hospital, Chennai.

Patient's Name :

Patient's Age :

Identification Number :

Patient may check (√) these boxes

a) I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction. ☐

b) I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected. ☐

c) I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ☐

d) I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms. ☐

e) I hereby consent to participate in this study. ☐

f) I hereby give permission to undergo complete clinical examination and hematological tests and ECHO Cardiography. ☐

Signature/thumb impression

Signature of Investigator

Patient's Name and Address

Study Investigator's Name:

Dr. DEVANAND KUMAR.G

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

EC Reg No.ECR/270/Inst./TN/2013
Telephone No. 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr.Devanand Kumar G
Postgraduate M.D.(General Medicine)
Madras Medical College
Chennai 600 003

Dear Dr.Devanand Kumar G

The Institutional Ethics Committee has considered your request and approved your study titled **"High Sensitivity C Reactive Protein (hsCRP) levels and correlation with Lipid Profile in Hypertension" No.15072015.**

The following members of Ethics Committee were present in the meeting held on 07.07.2015 conducted at Madras Medical College, Chennai-3.

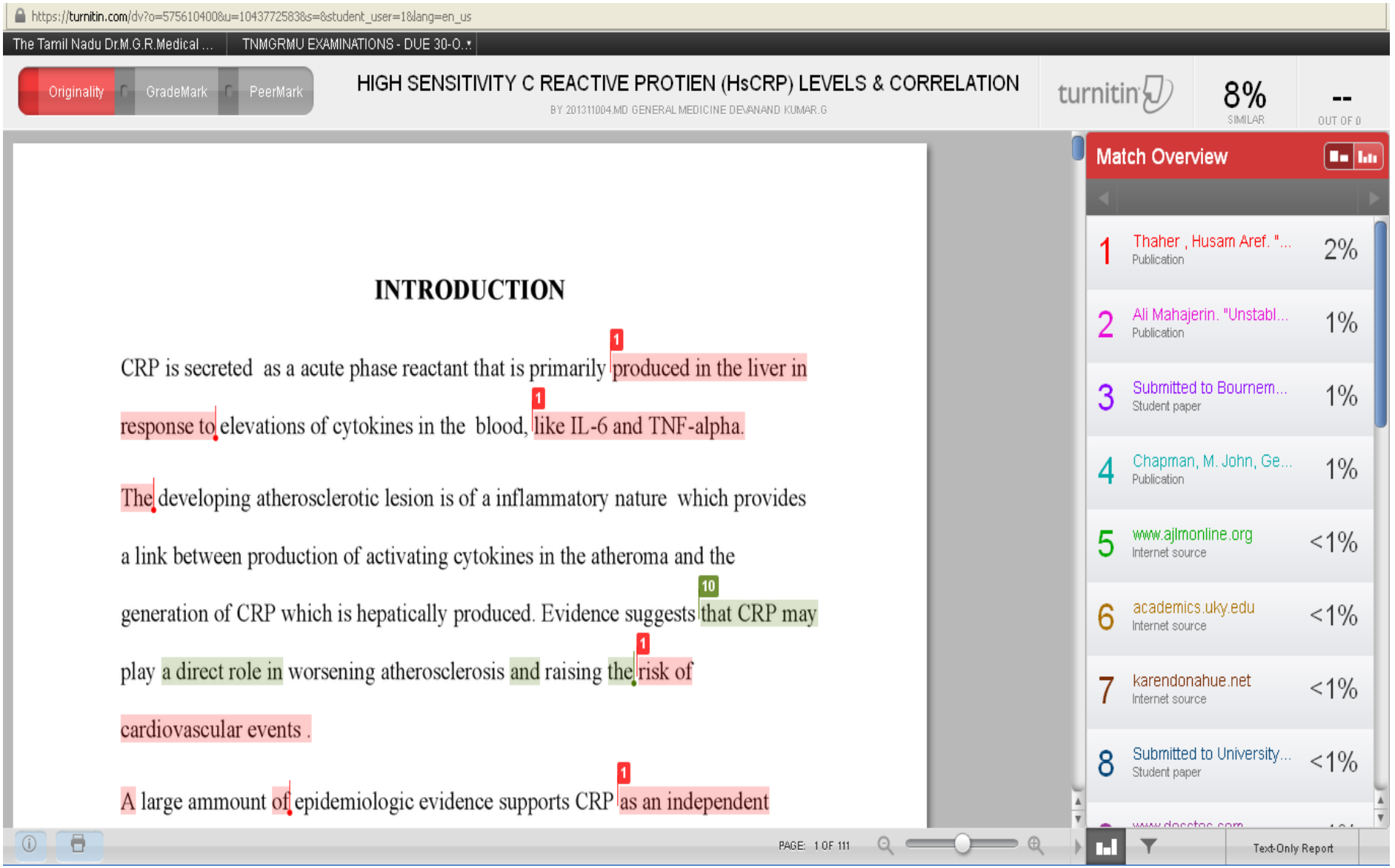
1. Prof.C.Rajendran, M.D.,	: Chairperson
2. Prof.R Vimala, M.D , Dean, MMC, Ch-3	: Deputy Chairperson
3. Prof.Sudha Seshayyan, M.D., Vice-Principal, MMC, Ch-3	: Member Secretary
4. Prof.B.Vasanthi, M.D., Professor Pharmacology, MMC	: Member
5. Prof.P.Ragumani, M.S , Professor, Inst of Surgery, MMC	: Member
6. Prof.Md.Ali, M.D., D.M., Prof. & HOD of Medl.G.E., MMC	: Member
7. Prof.Baby Vasumathi, Director, Inst.of O&G, Ch-8	: Member
8. Prof.K.Ramadevi, Director, Inst.of Biochemistry, MMC	: Member
9. Prof.Saraswathy, M.D., Director, Inst. Of Pathology, MMC	: Member
10. Prof.Srinivasagalu, Director, Inst.of Inter Med. MMC	: Member
11. Thiru S.Rameshkumar, B.Com , MBA	: Lay Person
12. Thiru S.Govindasamy, B.A., B.L.,	: Lawyer
13. Tmt.Arnold Saulina, M.A., MSW.,	: Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003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INTRODUCTION
CRP is secreted as a acute phase reactant that is primarily produced in the liver in response to elevations of cytokines in the blood, like IL-6 and TNF-alpha.
The developing atherosclerotic lesion is of a inflammatory nature which provides a link between production of activating cytokines in the atheroma and the generation of CRP which is hepatically produced. Evidence suggests that CRP may play a direct role in worsening atherosclerosis and raising the risk of cardiovascular events .
A large ammount of epidemiologic evidence supports CRP as an independent
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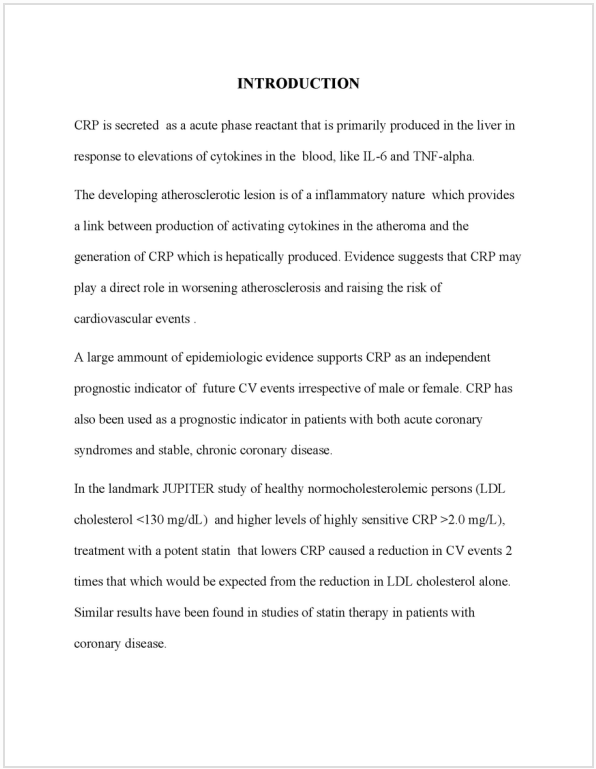

INTRODUCTION

CRP is secreted as a acute phase reactant that is primarily produced in the liver in response to elevations of cytokines in the blood, like IL-6 and TNF-alpha.

The developing atherosclerotic lesion is of a inflammatory nature which provides a link between production of activating cytokines in the atheroma and the generation of CRP which is hepatically produced. Evidence suggests that CRP may play a direct role in worsening atherosclerosis and raising the risk of cardiovascular events .

A large ammount of epidemiologic evidence supports CRP as an independent prognostic indicator of future CV events irrespective of male or female. CRP has also been used as a prognostic indicator in patients with both acute coronary syndromes and stable, chronic coronary disease.

In the landmark JUPITER study of healthy normocholesterolemic persons (LDL cholesterol <130 mg/dL) and higher levels of highly sensitive CRP >2.0 mg/L), treatment with a potent statin that lowers CRP caused a reduction in CV events 2 times that which would be expected from the reduction in LDL cholesterol alone. Similar results have been found in studies of statin therapy in patients with coronary disease.

MASTER CHART

S.No	Age	Sex	HTN	SBP	DBP	Drugs	Duration of BP	Hs_CRP	TC	HDL	LDL	TGL
1	48	1	1	150	90	AC	2	0.39	141	34	74	137
2	53	1	1	140	90	BC	3	1.51	205	53	116	99
3	45	2	1	160	90	ABC	5	1.60	196	36	110	168
4	52	1	1	140	96	AC	1	2.13	140	32	96	90
5	58	2	1	120	76	BC	7	1.73	174	36	90	164
6	56	1	1	150	100	BCD	7	2.45	219	36	102	190
7	49	2	1	110	70	AC	3	1.72	186	48	124	148
8	62	1	1	140	90	ABC	6	3.01	114	38	70	54
9	56	2	1	150	90	ABC	10	2.40	194	32	56	130
10	68	1	1	160	100	BCD	18	3.10	136	30	72	80
11	50	2	1	170	100	A	1	6.00	198	35	110	181
12	54	1	1	160	90	BC	5	0.76	156	33	106	112
13	52	1	1	150	100	ACD	5	1.80	210	46	106	96
14	69	2	1	140	90	ACD	10	1.35	156	34	97	100
15	68	1	1	120	86	BC	8	3.05	185	33	96	109
16	46	1	1	110	80	BC	3	1.18	181	36	96	259
17	55	2	1	120	80	A	3	1.62	178	32	110	93
18	62	1	1	140	100	CD	9	7.09	220	30	130	150
19	76	2	1	136	90	ABCD	21	2.08	251	33	104	134
20	52	1	1	170	100	ARCD	1	1.90	183	45	94	174
21	54	1	1	100	80	BC	3	1.42	148	32	95	132
22	57	2	1	130	90	BC	6	0.89	156	38	100	160
23	60	2	1	130	80	ABC	7	1.90	170	35	82	88
24	70	1	1	130	80	AC	21	0.16	223	57	129	159
25	56	2	1	140	90	ACD	3	0.42	125	44	72	76
26	75	1	1	140	90	BC	19	1.20	205	44	118	161
27	48	1	1	120	84	BC	1	4.20	130	31	75	71
28	66	1	1	110	76	ABCD	13	2.00	174	62	82	74
29	58	2	1	130	80	ABC	7	2.35	146	32	92	102

S.No	Age	Sex	HTN	SBP	DBP	Drugs	Duration of BP	Hs_CRP	TC	HDL	LDL	TGL
30	67	1	1	140	80	ABC	19	0.65	194	46	106	92
31	54	1	1	130	80	AD	4	0.99	186	32	96	98
32	52	2	1	130	80	BC	1	1.40	102	36	68	75
33	63	1	1	120	80	BC	9	2.12	140	52	74	82
34	48	1	1	160	100	ABC	2	3.05	208	31	108	64
35	59	2	1	140	100	AB	6	4.02	176	36	116	68
36	53	1	1	156	100	ACD	6	1.99	138	32	82	164
37	50	2	1	110	80	AD	4	2.00	154	32	84	71
38	72	2	1	146	96	ACD	16	2.80	168	30	48	98
39	58	1	1	120	84	AB	1	1.64	162	46	84	76
40	65	2	1	130	72	ABC	3	0.56	132	30	86	76
41	70	2	1	120	84	AD	20	1.78	148	34	88	108
42	55	1	1	130	96	ACD	6	1.80	138	36	76	78
43	60	1	1	130	90	AC	5	2.40	224	36	78	140
44	62	2	1	140	86	ABC	9	2.30	180	52	106	92
45	58	1	1	130	80	AC	1	1.26	150	32	106	72
46	56	2	1	120	70	AD	3	1.14	194	42	106	92
47	60	1	1	130	86	AB	2	0.68	154	36	66	106
48	48	1	1	140	90	AD	1	0.98	206	32	110	128
49	48	1	1	130	80	ABC	8	1.21	132	32	82	68
50	55	1	1	140	80	AC	5	0.52	146	38	98	120