

**A STUDY ON LEFT VENTRICULAR  
DIASTOLIC FUNCTION ASSESSED BY ECHO  
IN METABOLIC SYNDROME”**

*Dissertation*

*Submitted in partial fulfilment of the regulation of*

**M.D. DEGREE EXAMINATION  
BRANCH I GENERAL MEDICINE**

**DEPARTMENT OF GENERAL MEDICINE  
GOVT. STANLEY MEDICAL COLLEGE AND HOSPITAL  
CHENNAI – 600001**



**THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY  
CHENNAI**

**APRIL - 2013**

# CERTIFICATE

This is to certify that this dissertation titled  
**”A STUDY ON LEFT VENTRICULAR  
DIASTOLIC FUNCTION ASSESSED BY  
ECHO IN METABOLIC SYNDROME”**

is the bonafide work done by **Dr.RAJAKUMAR.C.R**, Post Graduate Student (2010– 2013) in the Department of General Medicine, Govt. Stanley Medical College and Hospital, Chennai under the direct guidance and supervision and in partial fulfilment of the regulations laid down by The Tamil Nadu Dr. M.G.R. Medical University, Chennai for M.D. Branch I, General Medicine Degree Examination to be held in April 2013.

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## **DECLARATION**

I, **Dr.C.R.RAJAKUMAR**, solemnly declare that the dissertation titled

**“A STUDY ON LEFT VENTRICULAR  
DIASTOLIC FUNCTION ASSESSED BY  
ECHO IN METABOLIC SYNDROME”**

is a bonafide work done by me at Govt. Stanley Medical College and Hospital from May 2012 to Oct 2012 under the guidance and supervision of my unit chief,

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PLACE: CHENNAI  
DATE:

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**Dr.C.R.Rajakumar**

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## **ABBREVIATIONS**

<b>CVD</b>	-	CARDIO VASCULAR DISEASE
<b>HT</b>	-	HYPERTENSION
<b>AACE</b>	-	AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS
<b>LDL</b>	-	LOW DENSITY LIPOPROTEINS
<b>ATPIII</b>	-	ADULT TREATMENT PANEL III
<b>NEFA</b>	-	NON ESTERIFIED FATTY ACIDS
<b>NCEP</b>	-	NATIONAL CHOLESTEROL EDUCATION PROGRAMME
<b>DM</b>	-	DIABETES MELLITUS
<b>FBG</b>	-	FASTING BLOOD GLUCOSE
<b>PPBS</b>	-	POST PRANDIAL BLOOD SUGAR
<b>TGL</b>	-	TRIGLYCERIDES
<b>BP</b>	-	BLOOD PRESSURE
<b>MS</b>	-	METABOLIC SYNDROME
<b>HDL</b>	-	HIGH DENSITY LIPOPROTEINS
<b>IR</b>	-	INSULIN RESISTANCE
<b>SHF</b>	-	SYSTOLIC HEART FAILURE
<b>DHF</b>	-	DIASTOLIC HEART FAILURE
<b>LVDD</b>	-	LEFT VENTRICULAR DIASTOLIC DYSFUNCTION
<b>HFNEF</b>	-	HEART FAILURE WITH NORMAL EJECTION FRACTION
<b>DD</b>	-	DIASTOLIC DYSFUNCTION



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## INTRODUCTION

Metabolic syndrome Characterised by four clinical elements: these are Atherogenic dyslipidemia, insulin resistance (IR), central Obesity, and high blood pressure.

The metabolic syndrome includes group of cardiac risk factors that act simultaneously.

The persons with this syndrome who are worst prognosis cardiovascular events

This is a is a group of components distressing about 20- 25% of adults population in developed countries.

In India, prevalence is about 21% to 25% in adults. elevated BP ,Hyperglycemia and central obesity harmfully affected in heart both physiologically and pathologically.

This disease and its components, such as hyper glycemia, raised BP, Lipid profile abnormalities and central obesity are progressively more common among our people due to inactive life style. These people most

commonly manifested as Heart failure but patients had normal ejection fraction (HFNEF) .

Persons with the metabolic syndrome have a high incidence of heart failure HF. patients with metabolic syndrome they are greater threat of cardiac events than not associated this disease.

This study aimed to evaluate the association between Leftventricular diastolic dysfunction and Metabolic syndrome. So far there is minimal literature in our institute regarding the study of diastolic dysfunction in subjects with metabolic syndrome.

# REVIEW OF LITERATURE

## METABOLIC SYNDROME

### HISTORY

First , **DR. JEAN VAGUE**, The Marseilles physician, in 1947, found that upper body obesity influence to other metabolic complications such as hyperglycemia, hyperlipidemia, gout and stone(1,2,3)

- **HALLER**, describe The relations of central obesity, diabetes, dyslipidemia, Elevated uric acid level, and fatty infiltration. These factors are the Synergistic property of risk factors on lipid accumulation in vessels. He first Describe the term METABOLIC SYNDROME (5)
- **SINGER** illustrate the relationships between the central obesity, hyper uricemia and hyperglycemia and elevated BP with dyslipidemia in the same year<sup>[6]</sup>
- **Gerald B. Phillips** in 1977-78 explain the theory that risk factors for MI to form joint risk factors such as hyper glycemia, elevated insulin levels , hypercholesterolemia , hyper triglyceridemia and



hypertension which are associated with elderly people and overweight patients.

He told that linking factor which lead to prevent cardio vascular disease which is sex hormones.<sup>[7][8]</sup>

- Famous professor Gerald M reaven gives lecture regarding metabolic syndrome , He described mainly associated with insulin resistance and named constellation of abnormalities syndrome X.

After that abdominal obesity included further criteria formed by WHO [1999], EGIR [1999], NACP-ATPIII [2001], AACE [2004], IDF[2006].

## **OTHER NAMES**

- Dys metabolic syndrome
  - The Deadly Quartet
  - Insulin resistance syndrome
  - Obesity syndrome
  - Syndrome X
- 
- Obesity mainly abdominal
  - Lipid profile abnormalities
  - Increased BP

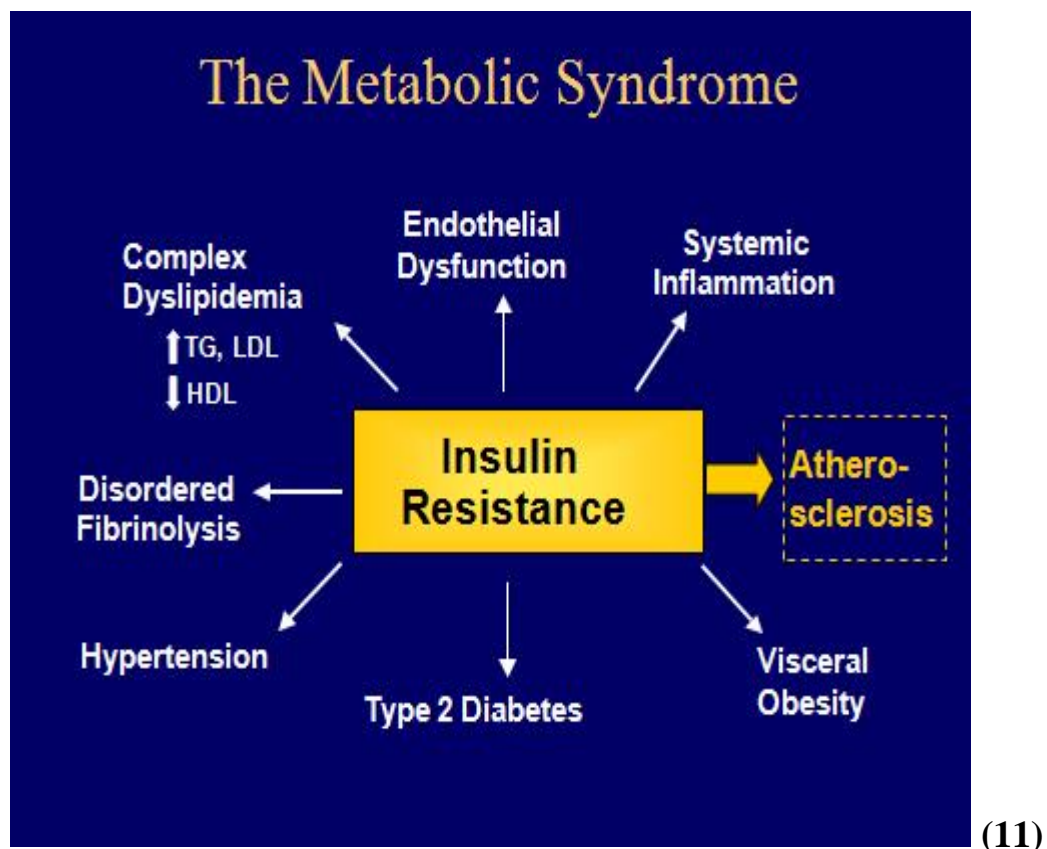
- Blood glucose abnormalities such as IR, IGT
- state of Pro inflammation
- Abnormalities of Thrombotic mechanism

These components of the metabolic syndrome, according to Adult treatment panel III may divide **underlying, major, and emerging** risk factors for CVD

- Increased weight
- sedentary life style and
- high fat food
- smokers
- Elevated BP
- High LDL level
- less HDL level
- Any h/o of premature coronary artery disease (CAD) in the family and
- Increasing age

## Emerging risk factors

- High TGL
- High LDL particles,
- Resistance to insulin,



*Figure (1) shows components of metabolic syndrome*

## Abdominal obesity

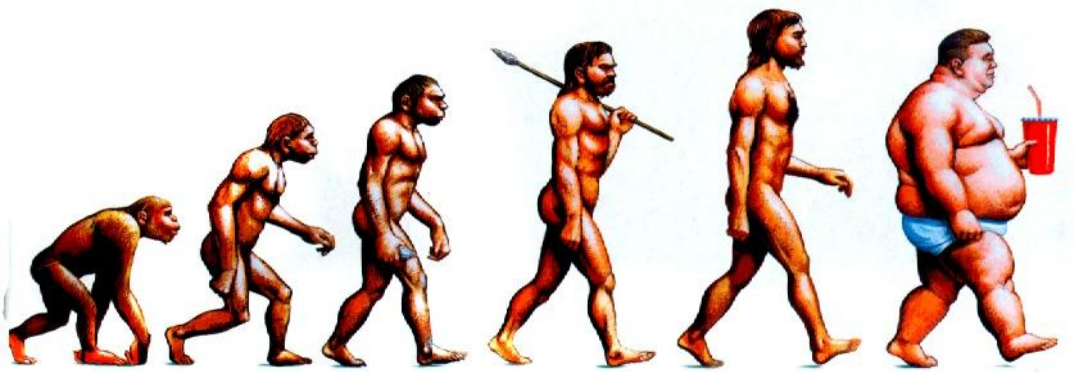
Abdominal obesity is well connected with the metabolic syndrome complications. It is clinically obtainable as increased waist circumference

## **Atherogenic dys lipidemia**

It diagnosed by lipid profile abnormalities such as elevated TGL level and less HDL level.

In comprehensive investigation of lipids ,the results commonly reveals Other abnormalities of lipoprotein, such as raised lipoproteins remnants, high apolipoprotein B level.

# **The shape of things to come**



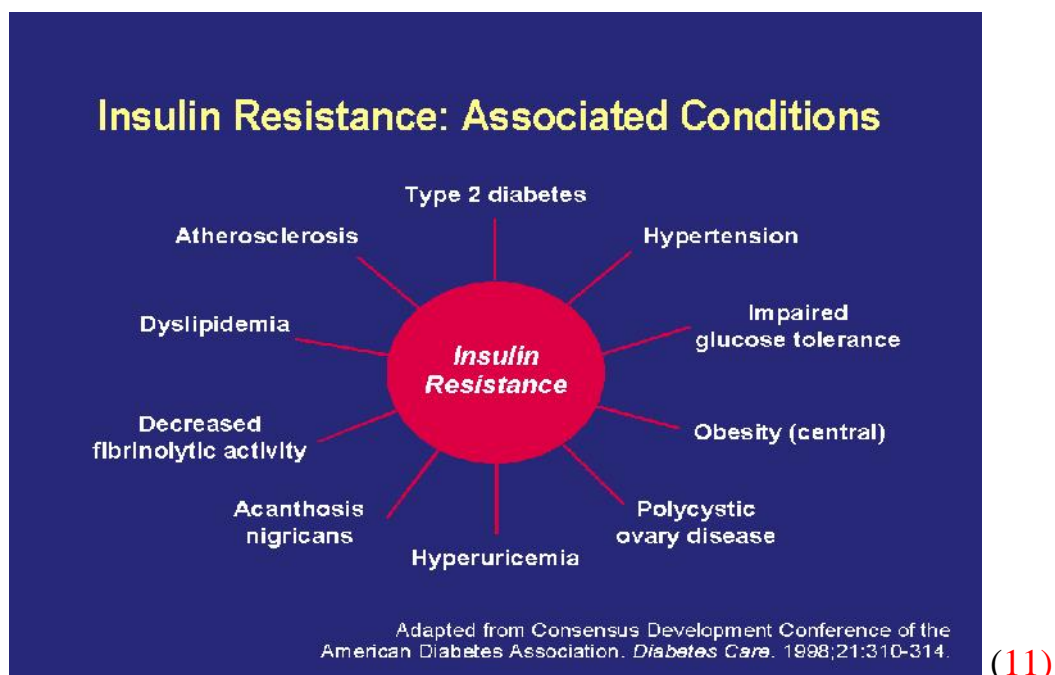
## Elevated blood pressure

Elevated BP frequently connections with central obesity and frequently occurs who are resistant to insulin.

## Insulin resistance {IR}

It is most commonly associates with the this syndrome. Insulin resistance with other risk factors are well correlates with cardio vascular events.

## INSULIN RESISTANCE - RELATED CONDITIONS



*Figure (2) shows insulin resistance associated conditions*

## **Prothrombotic state**

It is categorized by elevated fibrinogen and ( PAI- 1)plasminogen activator inhibitor which well connected with this syndrome.

## **METABOLIC SYNDROME - PATHOGENESIS**

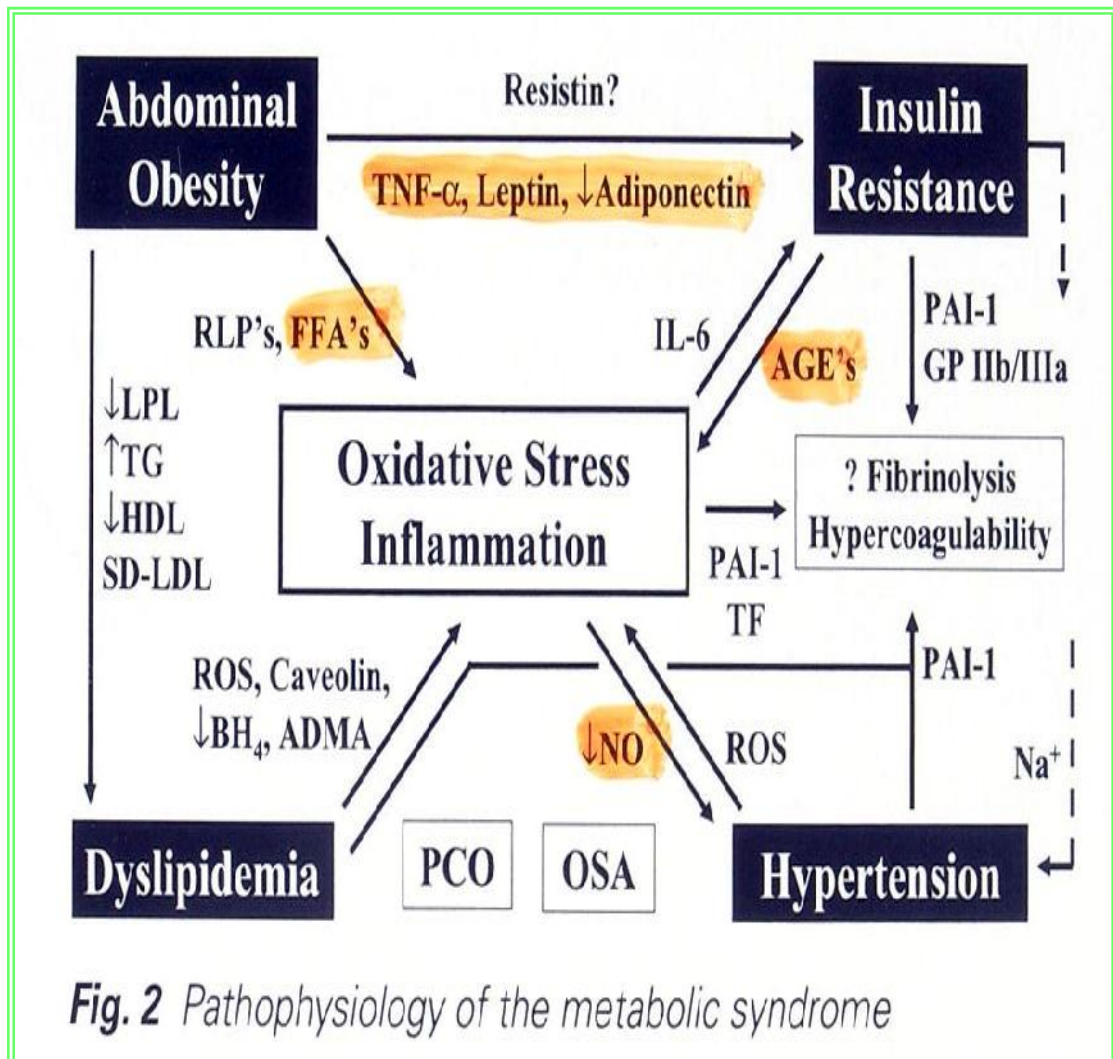
It has three etiological categories:

- a. insulin resistance**
- b. Central obesity and lipid storage abnormality;**
- c. constellation of independent factors**

**Other risk factors** are

- Increasing age
- Active inflammatory state
- &
- Endocrine abnormalities

## PATHOPHYSIOLOGY OF METABOLIC SYNDROME



*Figure( 3) shows Pathophysiology of the metabolic syndrome*

## OBESITY AND ABNORMAL BODY FAT DISTRIBUTION

Central obesity as primarily accountable for the rising occurrence of this syndrome.

Excess releases of substances from adipose tissue which exaggerate these risk factors. These are PAI-1, adiponectin, non esterified fatty acids (NEFA), and cytokines.

### **Insulin Resistance**

In pathogenesis of metabolic syndrome insulin resistance play a major role other than any factors (12,13).

Insulin resistance elevates with raising body fat mass, yet give widerange of insulin sensitivities (14).

When the Persons with obesity had body mass index more than 30 have Elevated post prandial insulin level and low sensitivity of insulin (15).

Variation of the insulin sensitivity occurs even within the obese population (14)

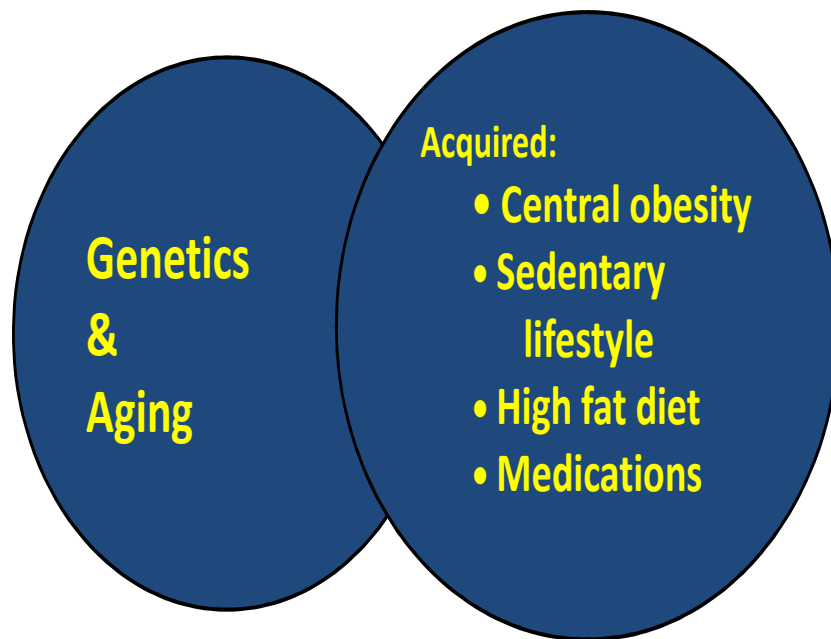
Asians population insulin resistance occurs still among BMI About 25 and provide increase to a high incidence of cardio vascular disease And hyperglycemia.



Primary insulin resistance *which is* manifested in south asians , as  
eight gain enhance the insulin resistance and metabolic syndrome Even  
in pts with primary insulin resistance(16)

## INDEPENDENT FACTORS FOR METABOLIC SYNDROME

### Factors Contributing to Insulin Resistance



(17)

*Figure (4) shows factors contributing to insulin resistance*

## **Other risk Factors**

All levels of pathogenesis affected by Advancing age so, occurrence of the metabolic syndrome rises with elderly people (18).

Many endocrine disorders had directly related to abnormality of lipid accumulations and indirectly related to this syndrome.

## DIAGNOSIS

**TABLE- 1 - ATP III CRITERIA**

<b>Factor</b>	<b>Definite Level</b>
<u><b>Central obesity ( waist circumference)</b></u>  <u>Male</u> <u>Female</u>	<u>More than 102 cm (&gt; 40 inches)</u> <u>More than 88 cm (&gt;35 inches)</u>
<u><b>TGL</b></u>	More than 150mg/dl
<u><b>HDL cholesterol</b></u> male female	Less than 40 mg/dL Less than 50 mg/dL
<u><b>Blood pressure</b></u>	more than 130 mmHg systolic BP more than 85 mmHg diastolic BP
<u><b>FBS</b></u>	More than 110 mg / dL

Diagnosis of metabolic syndrome by fulfilment of 3 out of 5 criteria.

Clinical adverse effects of metabolic syndrome was identified as Coronary heart disease and cerebrovascular disease .

Recently cut off points would be lowered FBS more than 100 mg/dL, can be considered which persons have impaired fasting glucose or taking treatment of hyper glycemia.(19).

**TABLE -2 - WHO CRITERIA**

<p>any one of the subsequent criteria:</p> <ul style="list-style-type: none"> <li>➤ Known diabetes on treatment</li> <li>➤ IFG</li> <li>➤ IGT</li> <li>➤ Normal FBS level</li> </ul>
<p><u>Plus any of the two in subsequent criteria:</u></p> <ul style="list-style-type: none"> <li>➤ Any medication for high BP and /or rised BP more than 140 mmHg in systolic or diastolic BP more than 90 mm Hg</li> </ul>
<ul style="list-style-type: none"> <li>➤ TGL LEVEL more than 150 mg/dL</li> </ul>
<ul style="list-style-type: none"> <li>➤ High density lipid level &lt; 35 mg / dL -male or &lt;39 mg / dL – female</li> </ul>
<ul style="list-style-type: none"> <li>➤ BMI more than &gt;30 and /or ratio between waist and hip more than .9 in male, more than .85 in female</li> </ul>
<ul style="list-style-type: none"> <li>➤ Albumin level in the urine more than 20 g/min or ratio between albumin and Creatinine in urine more than 30 mg/g (20, 21)</li> </ul>

In 1998, WHO define functional classification of hyperglycemia that included a implementation of criteria of this syndrome(20)

BMI or increase ratio between waist and hip was used in its place of waist Circumference alone, and micro albuminuria used a part of metabolic syndrome in this criteria.

AACE (22) propose a another criteria for Metabolic syndrome

**TABLE -3**

<b>RISK FACTOR</b>	<b>DEFINE LEVEL</b>
Body weight	BMI more than 25
Raised TGL	>150 mg / dL
less HDL Male Female	< 40mg / dl < 50mg / dl
Raised BP	More than 130 in systolic > 85 mm Hg in diastolic
Two hour glucose test	More than 140 mg/dL
FBS	110 TO 126 mg/Dl
Other risk factors	Family h/o of hyperglycemia, HT, or CVD, PCOD, Sedentary lifestyle, increasing age

**INTERNATIONAL DIABETES FEDERATION, [2005]**

**TABLE - 4**

<ul style="list-style-type: none"><li>• <b>Central obesity</b> WC more than 94 cm for male and more than 80 cm for female</li></ul>
<p><b>add any of the 2 subsequent criteria</b></p>
<ul style="list-style-type: none"><li>• <b>High Density Lipid :</b> Male - &lt; 40 mg/dL Female - &lt; 50 mg/dL taken drugs for this type of dyslipidemia</li></ul>
<ul style="list-style-type: none"><li>• <b>TGL LEVEL :</b> More than 150 mg / dl or taken any drugs for this type of Dyslipidemia</li></ul>
<ul style="list-style-type: none"><li>• <b>BP</b> BP more than 130 in systolic and or diastolic BP more than 85 mm Hg, taking any drugs HT</li></ul>
<ul style="list-style-type: none"><li>• <b>FPG:</b> More than 100 mg/dL or known case of T2DM</li></ul>

## **METABOLIC SYNDROME AS A RISK CONDITION**

MS with more risk factors carries a greater risk of adverse events in comparison to that with a single risk factor.

## **CARIO VASCULAR EVENTS**

Persons with this disorder are higher risk for Coronary heart disease(23).

Various studies shows Including the standard Framingham algorithm(24) generally most of the risk factors related with this syndrome re capture by elderly people, hypertension, lipid abnormalities, hyperglycemia, and less HDL level.

## **DIABETES AS A PREDICTOR OF CVD**

Oxford investigators study find that (25) measure of glycaemia and duration of diabetes that predict the cardio vascular events.

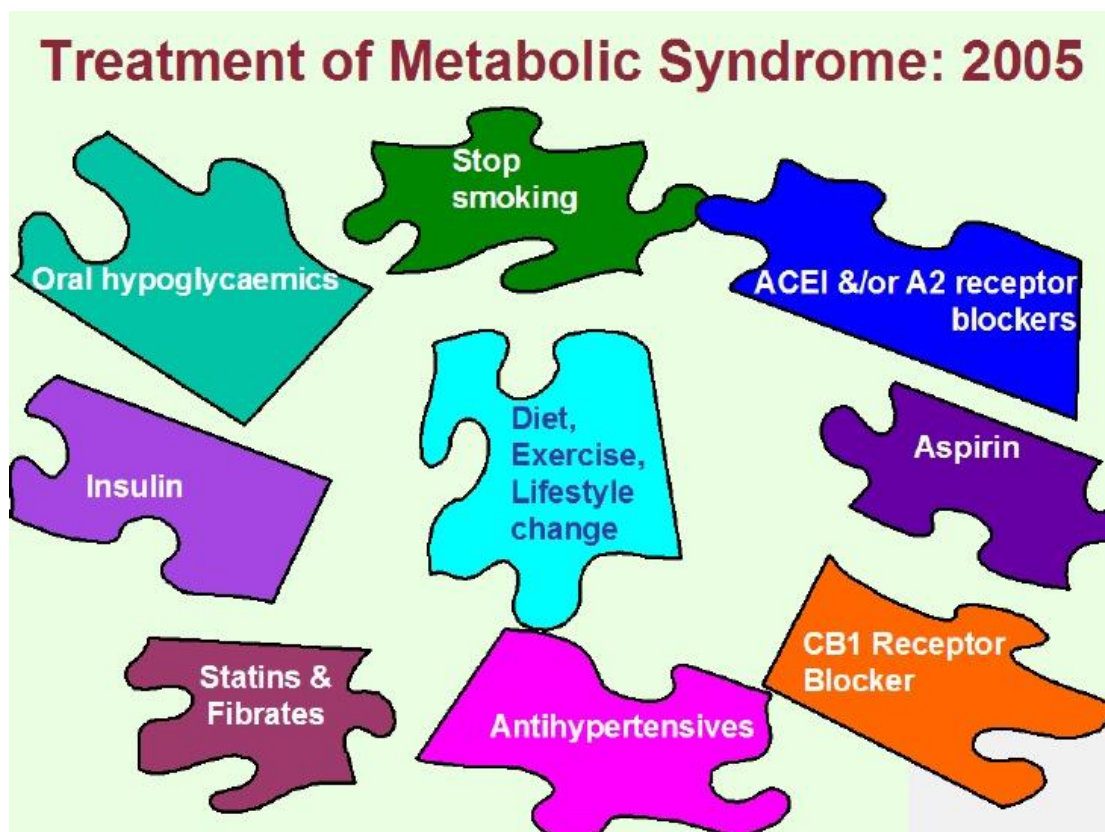


## THERAPEUTIC APPLICATIONS

### OBESITY AND LIPID DISTRIBUTION

Obesity is the the chief target of intervention for metabolic syndrome suggested by ATBIII.

Obesity approached by weight reduction by increased physical exercise and smoking cessation.



*FIGURE -5 Shows treatment of metabolic syndrome*

## **INSULIN RESISTANCE**

Metformin can be used to decrease insulin resistance of reduce the risk for Cardio vascular events in in patients with this syndrome.

## **SPECIFIC RISK FACTORS**

### **Atherogenic Dyslipidemia;**

Statins and fibrates can be useful for lowering of lipids and also reduce all apolipoprotein B-containing lipoproteins.(26)

## **HYPERTENSION**

It is treated with lifestyle modifications and weight reduction that leads to reduce blood pressure by use of antihypertensive drugs.

### **Prothrombotic State**

Anti platelet drugs can be useful for this type of risk factor associated with this syndrome. Can be used with small dose of aspirin decrease the cardiovascular events markedly.

## **Hyperglycemia**

Hyperglycemia can be treated with insulin sensitizers and **life style modifications, and physical exercise.**

## **Pro inflammatory State**

Most of the hypo lipedemic agents will decrease C –Reactive Protein levels, which leads to anti-inflammatory action.

## **LEFT VENTRICULAR DIASTOLIC DYSFUNCTION**

For a long time, all are presumed systolic dysfunction to be a primary cause of cardiac failure. But various studies and methods shows abnormality in diastolic function also in can precipitate cardiac failure and determined prognosis of the patient.

Diastolic dysfunction due to abnormal relaxation, abnormal refilling, and distensibility.

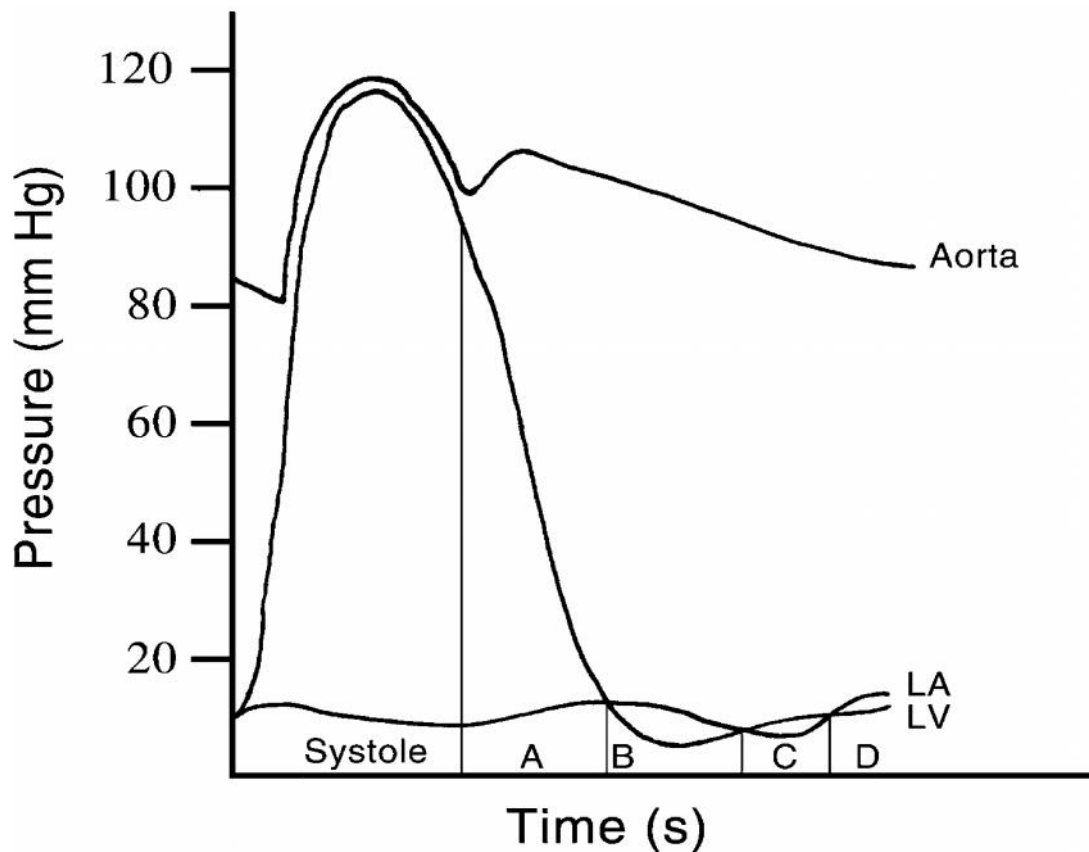
There may be considerable overlap the signs and symptoms of both diastolic and systolic heart failure.

### **PATHO PHYSIOLOGY**

Ventricular diastole has four phases

- Iso volumetric relaxation:
  - Period from closure of valve of the aorta to the opening of the valve of the mitral area

- Phase of the early rapid filling :
  - In this phase gradient of the trans mitral pressure responsible for LV filling;

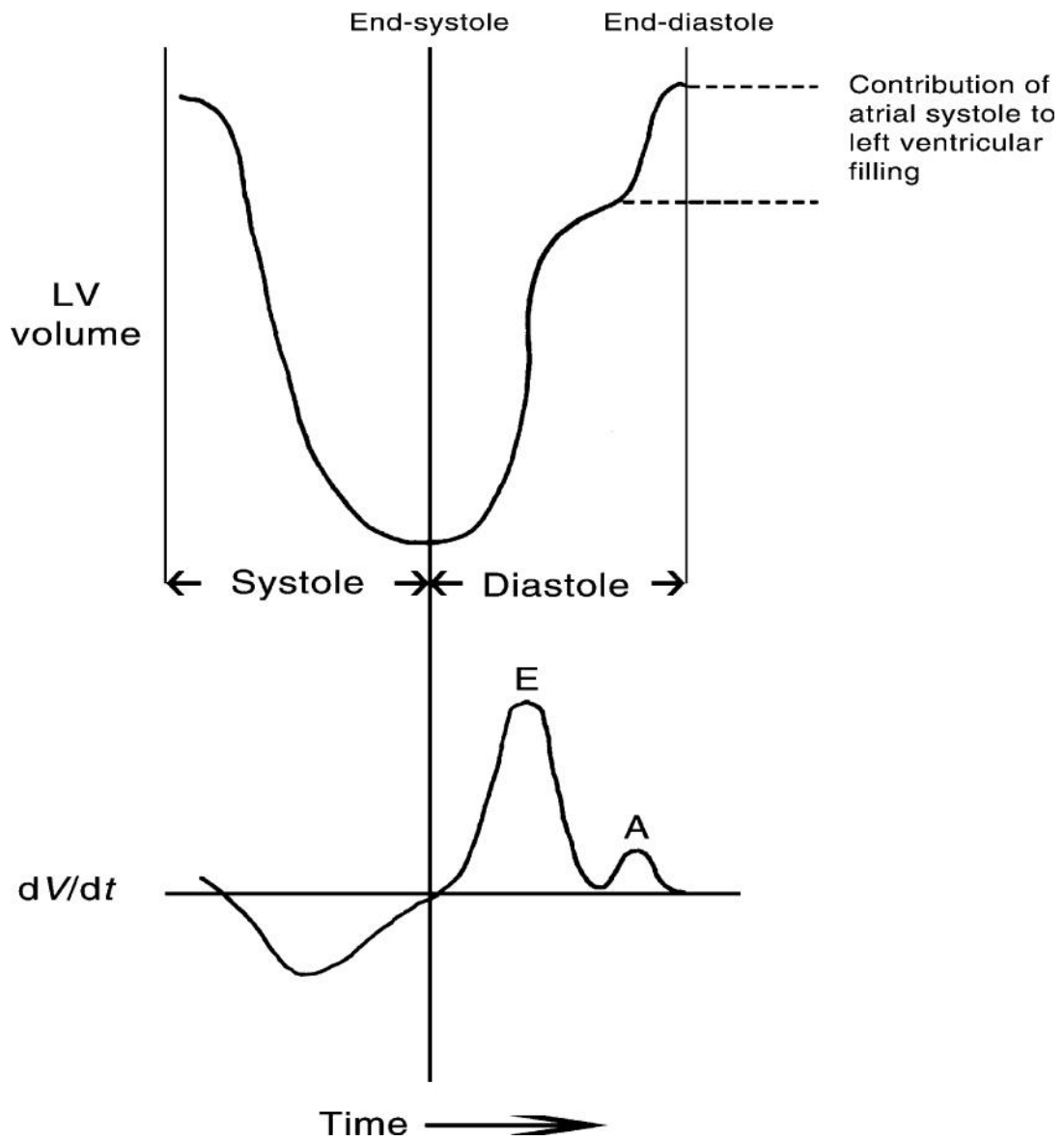


*Figure 6 - shows relationship of pressure and volume of left ventricle in the period of diastole*

- Diastasis phase:  
It is the period of less blood flow in middle phase of the diastole;

- phase of late period of rapid filling:

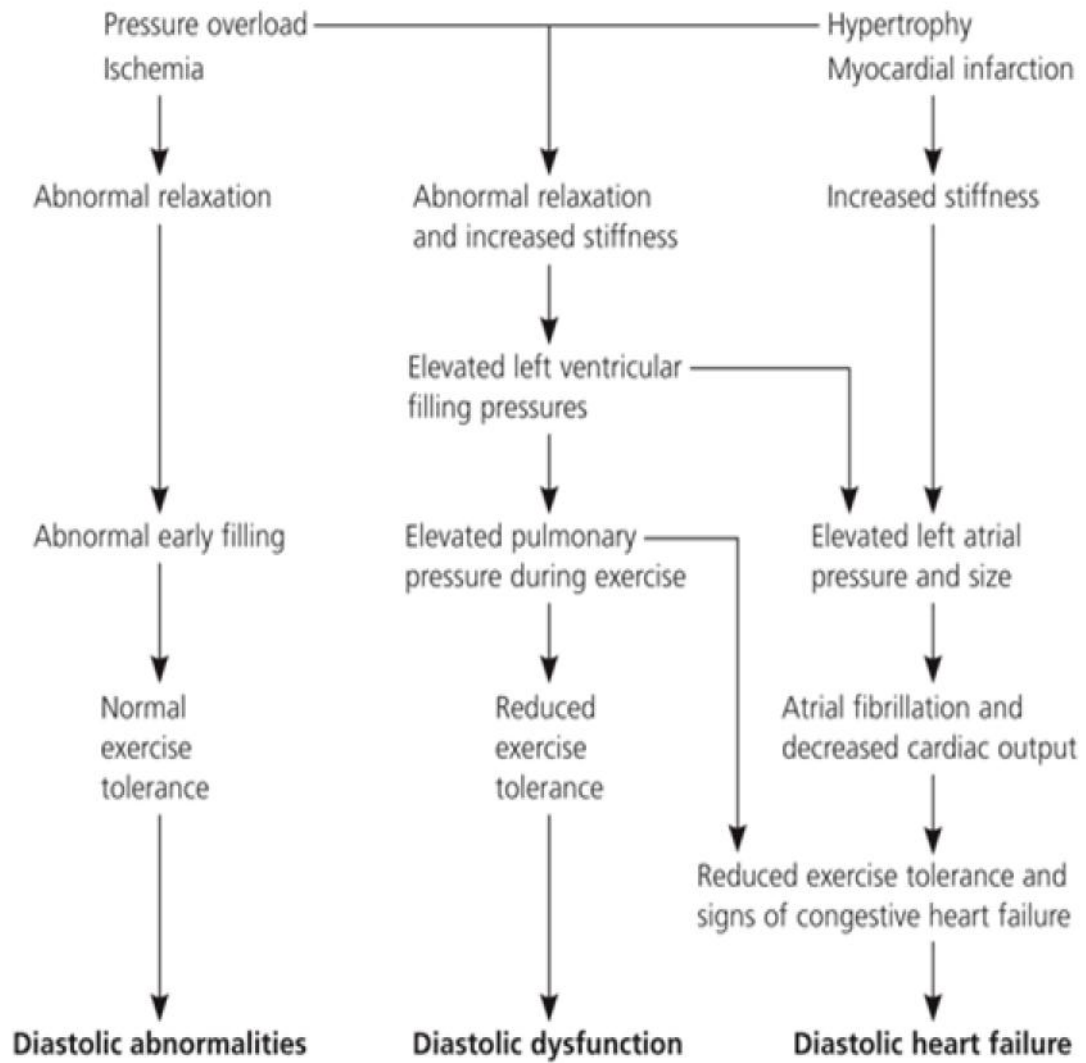
This is due to contraction of the atrium.



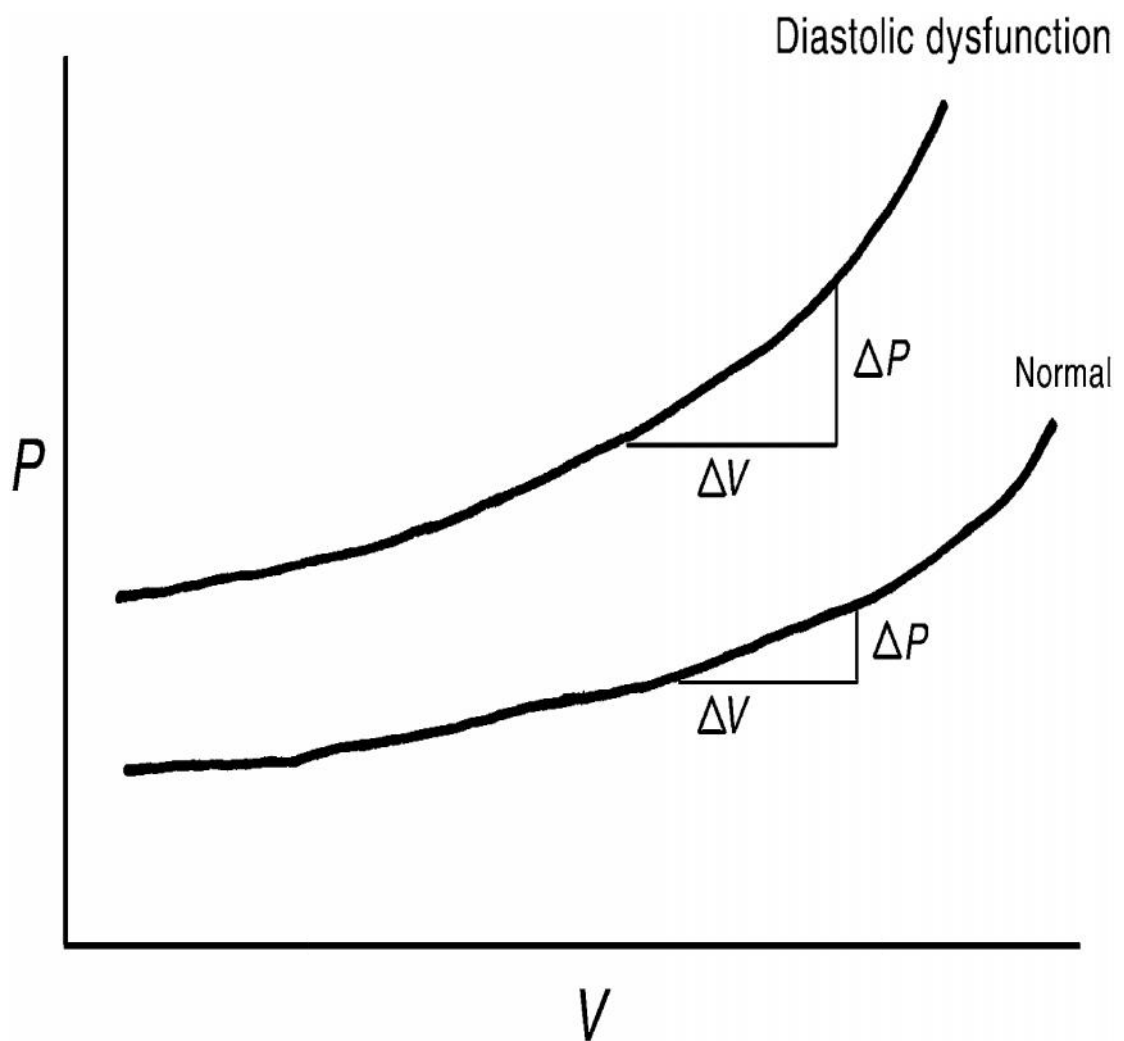
*Figure -7 shows left ventricular hemodynamics*

## PATHO PHYSIOLOGY

*Table- 5*



All these factors can lead to diastolic heart failure and diastolic dysfunction



*Figure - 8 shows graphical representation of Pressure–volume for the Left Ventricle Period of diastole. (27)*



***Table -6 Causes of Diastolic Dysfunction and Heart Failure***

**Common causes**

- Cardiac ischemia
- Elevated BP
- Increasing age
- Central Obesity
- Aortic valve stenosi

**Uncommon causes**

**Disorders of myocardium**

- Diseases of myocardium
- Infiltrative disease such as amyloidosis, sarcoidosis, fatty
- infiltration of the heart
- Non infiltrative diseases such as idiopathic and hypertrophic cardio myopathy)
- Endo myocardial diseases
- Hyper eosinophilic syndrome
- Glycogen storage disorders
- Hemochromatosis

**disorders of Pericardium**

- Constrictive pericarditis
- Pericardial effusion

## **CLINICAL FEATURES:**

Generally symptomless patient is more common than symptomatic pts who had diastolic dysfunction. When symptoms are there, DHF are very difficult to differentiate from those of Systolic heart failure .

Symptoms are

Less exercise competence;

Neuro Humoral activation with water retention;

PND, Orthopnoea.

Exercise intolerance is often an early symptoms (28)

**Table -7- SIGNS AND SYMPTOMS IN SYSTOLIC AND  
DIASTOLIC HEART FAILURE (29,30)**

	DHF (EF –more than50%)	SHF (EF -less than50%)
<b>CLINICAL SYMPTOMS</b>		
Exertional Dyspnoea	85	96
PND	55	50
Orthopnoea	60	73
<b>SIGNS</b>		
JVP elevation	35	46
crepts	72	70
apical impulse displacement	50	60
S3	45	65
S4	45	66
Liver enlargement	15	16
Oedema	30	40
<b>X-RAY - CHEST</b>		
Cardiac enlargement	90	96
Pulmonary hypertension	75	80

## **DIAGNOSIS**

Diagnosis of diastolic dysfunction may be difficult because history, clinical symptoms and signs are same as systolic dysfunction.

Various investigation may be differentiate the DHF from SHF. Among those investigations echo cardiogram play a major role in the diagnosis of the diastolic dysfunction.

Diastolic heart failure diagnosed by

- *Normal left ventricular systolic function*
- *Any abnormal myocardial relaxation*
- *Abnormal diastolic filling pressures at rest*

According to American society of cardiology all above criteria should be fulfilled.

## METHODS OF DIAGNOSIS

- M MODE ECHO CARDIOGRAM
- DOPPLER ECHO CARDIOGRAM
- TISSUE DOPPLER
- PULMONARY FLOW PATTERN

### ECHO CARDIOGRAM

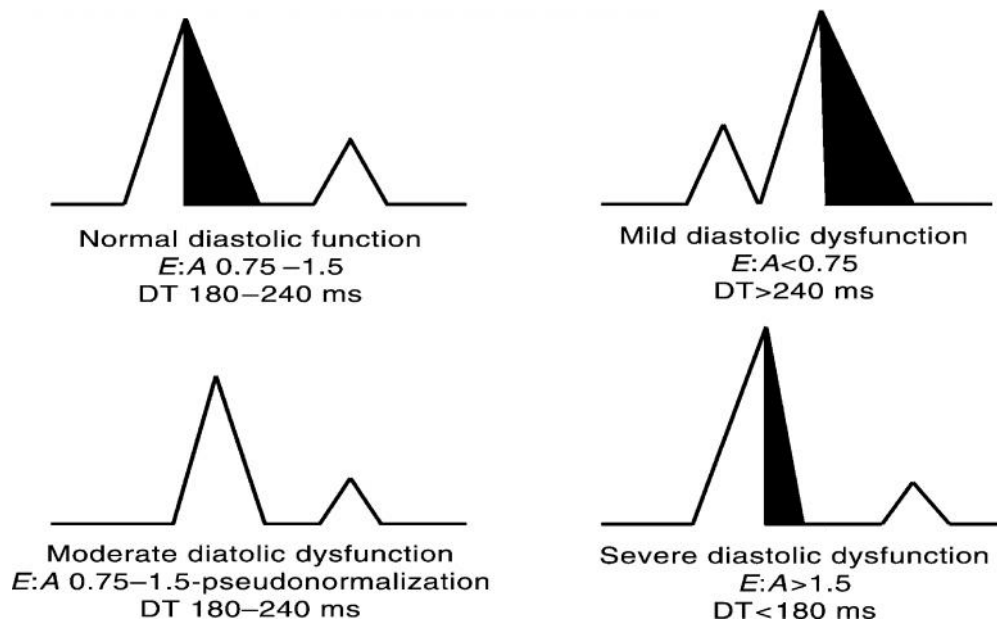
It is the Most accessible and acceptable non invasive investigation of choice

- It measures **mitral inflow velocity** it is the earliest marker of left ventricular filling abnormalities

DIASTOLIC DYSFUNCTION can be assessed In the form of

**E wave** - due to early diastolic filling

**A wave** - filling due to contraction of the atrium in late stage of Diastole



*Figure- 9 shows pictorial representation of diastolic trans mitral doppler assesment*

DT – Deceleration time

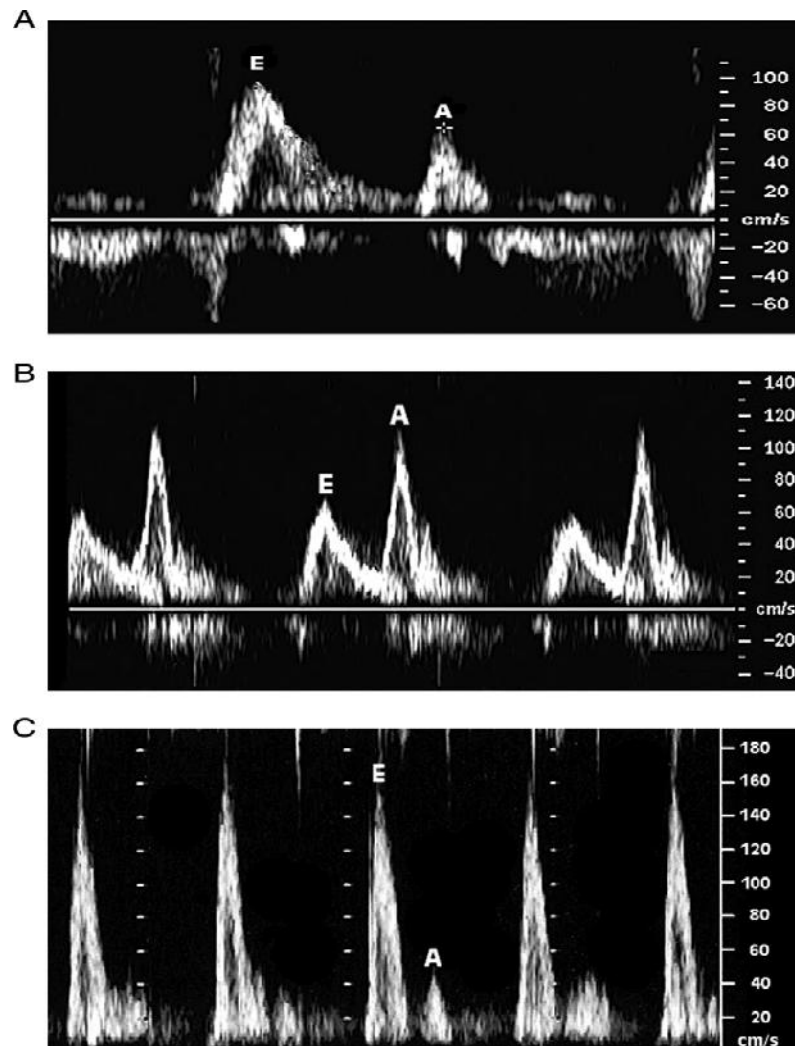
IVRT- isovolumic relaxation time

E/A RATIO

According to these value diastolic dysfunction can be graded.

## PULMONARY VENOUS FLOW:

It measure in Right upper pulmonary vein from apical 4 chamber view.



*Figure -10 shows transmitral Doppler flow pattern*

- A- Normal
- B- Pseudo normalization or stage 2 diastolic dysfunction
- C- C-advancing disease (58)

**TABLE- 8:CRITERIA FOR DIASTOLIC HEART FAILURE (59).**

Clinical features of HF	Effort dyspnoea, orthopnoea, III-IV tones, Pulmonary rales
Normal or diminished LV systolic function	EF more than 45 % LVIDDi more than 3.2 cm
abnormality Left Ventricular distension /complaine	<p>IVRT - less than 30 years - more than 92 ms,  30 to 50 years - more than 100 ms,  More than 50 yrs - more than 105 m  secs</p> <p>EA ratio less than one + DecTime – more than  220 msec + S/D less than 1.5 in below 50 yrs</p> <p>E/A - less than 0.5 + DT more than 280 ms +  S/D more than 2.5 above 50 yrs</p>



## **TREATMENT OF DIASTOLIC HEART FAILURE:**

### **INITIAL TREATMENT:**

Pt first treated with supportive therapy such as O<sub>2</sub> therapy and according to the underlying cause such as ischemia, constrictive pericarditis, atrial fibrillation Main goal To **diminish the pulmonary congestion by** Diuretics can be used with cautiously.

Because it can leads to hypo tension related complication.

If there is no respiratory compromise morphine can be given.

If blood pressure normal nitroglycerin can be given.

### **HEART RATE REDUCTION:**

It is can be achieved by the use of Beta –blockers

And Calcium channel blockers (CCB).

## **LIFE LONG TREATMENT**

Long term treatment depend upon the underlying disorder  
Such as life long anti failure treatment such as ACE inhibitor and  
spiranolactone and CABG.

### **Non-pharmacological**

Dynamic and iso tonic physical activity can be useful..(33)

## **LEFT VENTRICULAR DYSFUNCTION IN METABOLIC SYNDROME**

- Obesity and hypertension are independent factors of impaired left ventricular dysfunction(34,35,36)
- Correlation of numbers of risk factors of this syndrome and presence of grading of left ventricular diastolic dysfunction is well documented(37,38,39)
- Obesity prevalence is increasing world wide and makes important risk factor for morbidity and mortality of cardio vascular disease
- Central obesity contribute the structural and functional abnormalities directed by disproportionate increase of cardiac output mediated by adrenergic stimulation and indirectly by increasing left ventricular mass(40,41,42)
- In PROCAM STUDY (Prospective cardiovascular munstar study) shows
  - Who had hypertensive only or diabetic only had 2.5 times greater risk of cardio vascular events

- If pts had both hypertension and diabetes 8 fold high risk of cardiac events
- If pts had both hypertension and diabetes and lipid profile abnormalities who had 20 fold greater risk of cardiac events.(43)
- Diabetes has independent unfavourable cardiac events which may contribute to cardiovascular morbidity in hyperglycaemia patients [44].
- There is a relation between the period of hyperglycemias' and the stages of Left Ventricular diastolic dysfunction [45].
- **Masugata H et al (46)** study shows person with this syndrome can have left ventricular diastolic dysfunction even if pt have normal cardiac function
- **Hui-ping et al(47)**in their study shows pts with these syndrome even if they have normal Ejection Fraction , Left Ventricular systolic and diastolic functions were impaired.
- **Miyazato et al (48)** FPG is a responsive indicator for Left Ventricular diastolic dysfunction in non diabetic pts and small raise

in blood glucose levels is related with abnormality in diastolic dysfunction.

- **Hwang et al(49)** in their study pts with insulin resistance commonly detected unusual left ventricular morphology and diastolic dysfunction.
- This syndrome with IR are associated with unusual Left Ventricular diastolic dysfunction and structure that is not related to the age,sex, BP, and Blood sugar level.
- **Ahn et al (50 )** found that the components of Metabolic Syndrome cluster was powerfully correlated with diastolic dysfunction.
- **Barbosa et al(51)** over weight is well correlated with ventricular dysfunction. Over weight is remain a important predictor of diastolic dysfunction
- **Chopra et al(53)** in this study if Metabolic syndrome found that, impaired relaxation grade1 DD was highly prevalent .
- **Bilal et al(54)** stated describes, females had the evidence of early ventricular dysfunction. In isolated metabolic syndrome.

- **Evrengul et al(55)** in their study found that, peak A velocity (p < 0.028) were significantly higher .
- **Stijntje et al (56)** in this study found that, irrespective of blood pressure ,pts with this syndrome shows decrease LV diastolic function .
- *Khan et al (57)* in this study found that positive correlation components of metabolic syndrome and parameters assessed by echo.

# **STUDY PROTOCOL**

## **AIMS AND OBJECTIVES:**

- 1) To assess left ventricular function in metabolic syndrome
- 2) To grade the diastolic dysfunction and clinical outcome

# **MATERIALS AND METHODS**

## **STUDY SITE**

Department of General Medicine, Government Stanley Medical college and Hospital, Chennai.

## **COLLABORATING DEPARTMENTS**

- Department of Cardiology
- Department of Medical Biochemistry

## **STUDY DESIGN**

Longitudinal study

## **STUDY PERIOD**

June 2012 to November 2012



## **SELECTION OF STUDY POPULATION**

### **INCLUSION CRITERIA**

Patients meeting criteria for metabolic syndrome without  
co morbid illness

### **EXCLUSION CRITERIA**

- Cushing syndrome
- Hypothyroidism
- Anasarca
- Known heart disease patients
- Gout
- Polycystic ovarian disease

### **EXAMINATION**

- height
- weight
- waist circumference
- pulse rate
- blood pressure

## **INVESTIGATIONS DONE**

- Complete blood count
- Blood sugar – Random, fasting and post prandial
- Blood urea
- Serum creatinine
- Serum uric acid
- Serum electrolytes
- Urine routine analysis
- Lipid profile
- Thyroid function test
- USG abdomen
- ECG
- ECHO

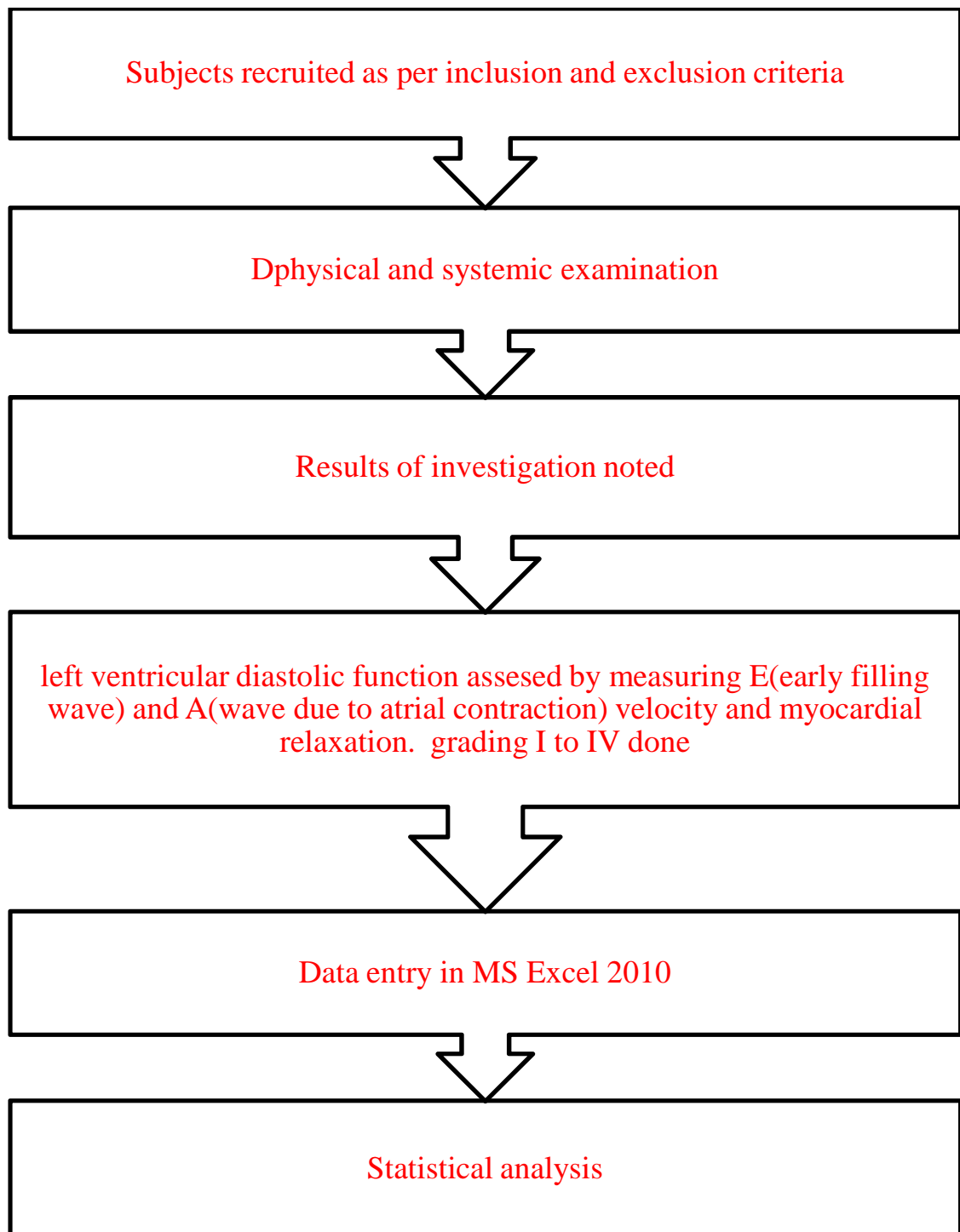
## **SAMPLE SIZE**

- Using the above mentioned criteria 50 subjects were recruited

## **SAMPLING METHOD**

- Convenience sampling method was adopted

## STUDY PROTOCOL



*Figure (11) shows study protocol*

## **ECHOCARDIOGRAPHY**

- Done by a qualified cardiologist
- Transthoracic echocardiographic examination done on all subjects in left lateral position
- Two dimensional and M-mode echocardiography was performed on using 3.5 MHz transducer
- Ejection fraction calculated measuring internal diameter of left ventricle(LV) at the end diastole (LVIDd) and at the end systole (LVIDs) using the Penn convention method
- Two dimensional and two dimensional guided M-mode echocardiogram and pulsed Doppler trans mitral and pulmonary venous flow velocity curves were obtained
- The trans mitral flow velocity curves were recorded with sample volume at the mitral tips, and the pulmonary venous flow velocity curves were recorded with the sample volume 1 to 2 cm into the right superior pulmonary vein using the guidance of color flow Doppler imaging with the transducer placed at the cardiac apex
- The averaged values of all echo cardio graphic parameters of at least 3 consecutive beats were used for the analysis
- Doppler velocity curves were recorded at a horizontal sweep speed of 100mm/s

- Left ventricular diastolic dysfunction was assessed by evaluating the mitral in flow velocity curves(MIVC)

Normal E/A ratio is defined as E/A ratio an age and sex adjusted mean value – 2SD and pulmonary venous A duration – mitral A duration ( d) 0

- E deceleration time [E(dt)] and pulmonary venous A wave amplitude(P va) were other values calculated

**Table – (9) Grades of diastolic dysfunction – ECHO**

<b>Diastolic Dysfunction Stages</b>	<b>E/A Ratio (Cm/s)</b>	<b>DT (ms)</b>	<b>IVRT ( ms)</b>	<b>M-Mode (Vp cm/s)</b>	<b>Tissue Em (cm/s)</b>
<b>Normal Pattern</b>	>1	160-210	70- 90	>45	>8
<b>I -Stage Of Delayed Relaxation</b>	<1	>220	>95	<45	<8
<b>II) Pseudonormal Pattern</b>	1-2	150-200	60 – 95	<45	<8
<b>Iii. Restrictive Filling Stage</b>	>2	<150	<60	<45	<8

## STATISTICAL ANALYSIS

Statistical analysis was done using

- Percentages
- Mean values
- Standard deviation
- Standard error
- Chi square test
- T-test unpaired

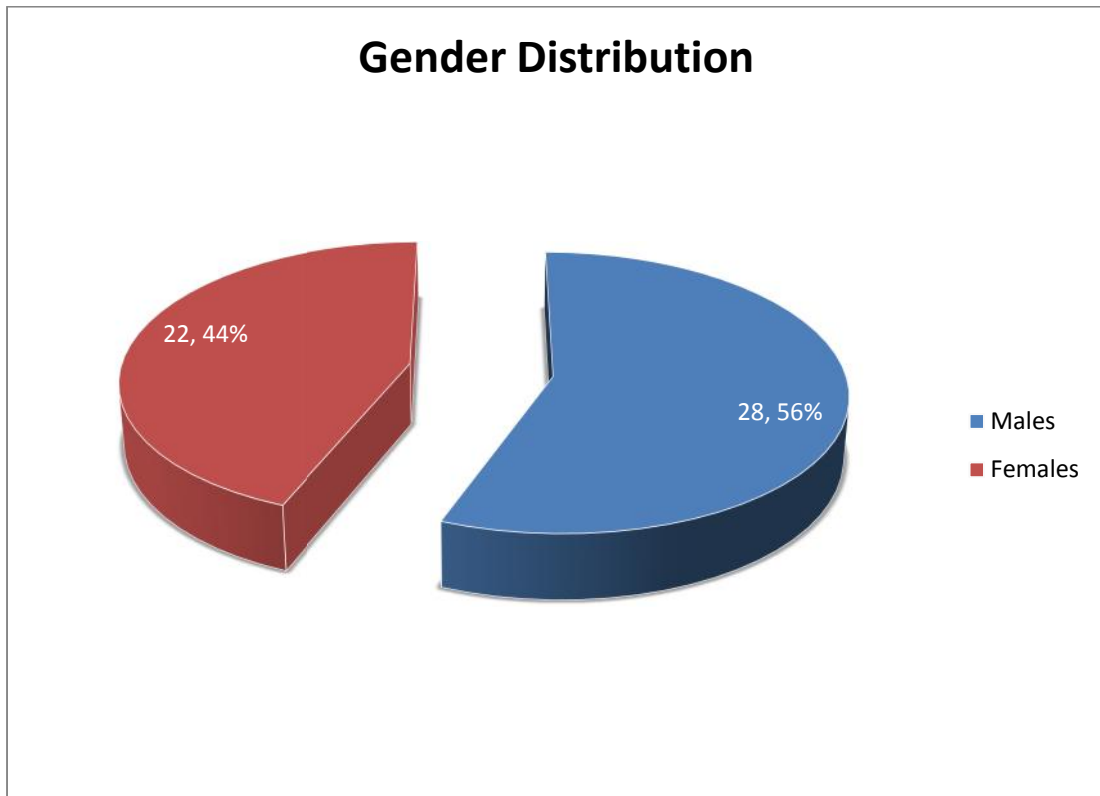
Level of significance used is 0.05 for the corresponding degree of freedom to draw the inference. A p value  $<0.05$  was considered statistically significant.

## RESULTS

A longitudinal study consisting of 50 metabolic syndrome outpatients and inpatients attending the Department of Medicine, Government Stanley medical college hospital, Chennai was undertaken to assess the left ventricular diastolic function.

### Gender

Chart 1

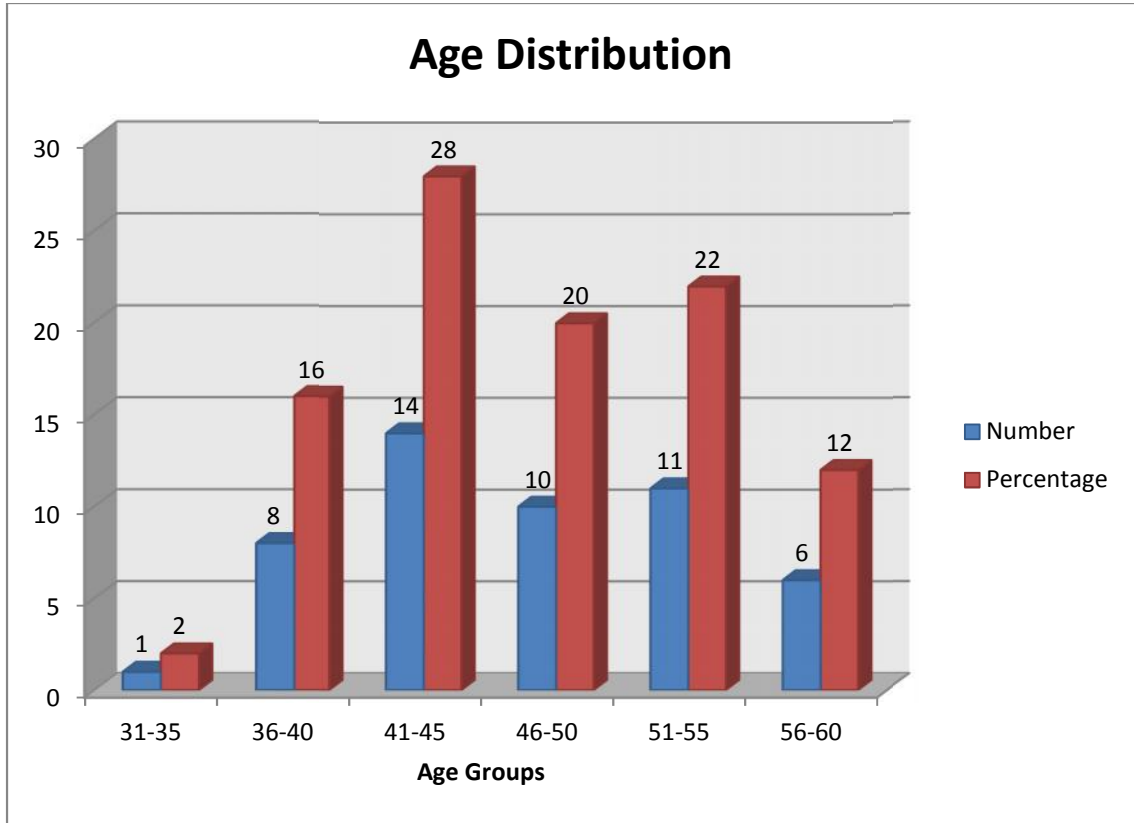


A total of 50 patients diagnosed with metabolic disorder were included in the study. Males constituted 28 % (n=28) of the sample population and females constituted 44% (n=22) (Chart 1)



## Age distribution

Chart 2



Most of the patients were clustered in the 41-45 years age group (n=14, 28%) followed by the 51-55 years age group (n=11, 22%) (Chart 2). Minimum age was 38 years and the maximum age is 57 years. The mean age was 46.96 years with standard deviation 6.61.

## Blood pressure

Table 10

<b>Blood pressure</b>	<b>Number(n)</b>	<b>Mean</b>	<b>Standard Deviation(SD)</b>
<b>SBP in mm Hg</b>	50	133.08	10.69
<b>DBP in mm Hg</b>	50	85.44	4.68

The mean systolic blood pressure and diastolic blood pressure are  $133.08 \pm 10.96$  and  $85.44 \pm 4.68$  respectively.

## Waist measurement

Table 11

<b>Waist measurement</b>	<b>Number(n)</b>	<b>Mean</b>	<b>Standard Deviation(SD)</b>
<b>Men</b>	28	96.14	5.42
<b>Women</b>	22	95	6.36

The mean waist measurement is  $96.14 \pm 5.42$  in males and  $95 \pm 6.36$  in females respectively.

## Blood sugar

Table 12

<b>Blood sugar</b>	<b>Number(n)</b>	<b>Mean</b>	<b>Standard Deviation(SD)</b>
FBS mg/ml	50	113.14	10.94

The mean fasting blood sugar levels among the study subjects is  $113.14 \pm 10.94$ .

## Serum Triglycerides

Table 13

<b>Serum Triglycerides</b>	<b>Number(n)</b>	<b>Mean</b>	<b>Standard Deviation(SD)</b>
TGL mg/ml	50	161.78	14.04

The mean triglyceride levels among the study subjects are  $161.78 \pm 14.04$ .

## High density lipoproteins

Table 14

<b>High density lipoproteins</b>	<b>Number(n)</b>	<b>Mean</b>	<b>Standard Deviation(SD)</b>
Males	28	43.78	5.29
Females	22	48.27	6.19

The mean high density lipoprotein levels among the study subjects are  $48.27 \pm 6.19$ .

## ECHO parameters

### E/A ratio

Table 15 (A)

<b>E/A</b>	<b>Number</b>	<b>Mean</b>	<b>Standard deviation</b>	<b>Maximum</b>	<b>Minimum</b>
	50	0.74	0.13	0.46	1.01

The E/A ratio ranged from 0.46 to 1.01 in cases with a mean of  $0.74 \pm 0.13$ .

Table15 (B)

<b>E/A ratio</b>	<b>Number</b>	<b>Percentage</b>
< 1.0	47	94%
>1.0	3	6%
Total	50	100%

94% had abnormal diastolic function as defined by E/A ratio. 3% had normal diastolic function.

### Deceleration time of E (DT of E)

Table 16 (A)

<b>DT (msec)</b>	<b>Number</b>	<b>Mean</b>	<b>Standard Deviation(SD)</b>	<b>Minimum</b>	<b>Maximum</b>
	50	242.86	12.87	212	265

The Deceleration time of E ranged from 212 to 265 in subjects with a mean of 242.86  $\pm$  12.87.

Table 16(B)

<b>DT (msec)</b>	<b>Number</b>	<b>Percentage</b>
<b>150 -200 msec</b>	3	6%
<b>160-210 msec</b>	31	62%
<b>&gt;220 msec</b>	16	32%
<b>Total</b>	50	100%

Three patients had DT values between 150-200 msec and 31 patients were present between 160-210 msec and 16 had values greater than 220 msec.



## Isovolumetric relaxation time

Table 17(A)

IVRT (msec)	Number	Mean	Standard Deviation(SD)	Minimum	Maximum
	50	92.2	17.62	57	123

In the present study, the mean ad SD of IVRT group was  $92.2 \pm 17.62$  msec, with a minimum value of 57 msec and maximum value of 123 msec.

Table 17 (B)

IVRT (msec)	Number	Percentage
<60 msec	3	6%
70-90 msec	31	62%
>95 msec	16	32%
<b>Total</b>	50	100%

Three patients had < 60 msec and 31 had between 70-90 msec and 16 had > 95 msec.

## Left ventricular diastolic dysfunction in study subjects

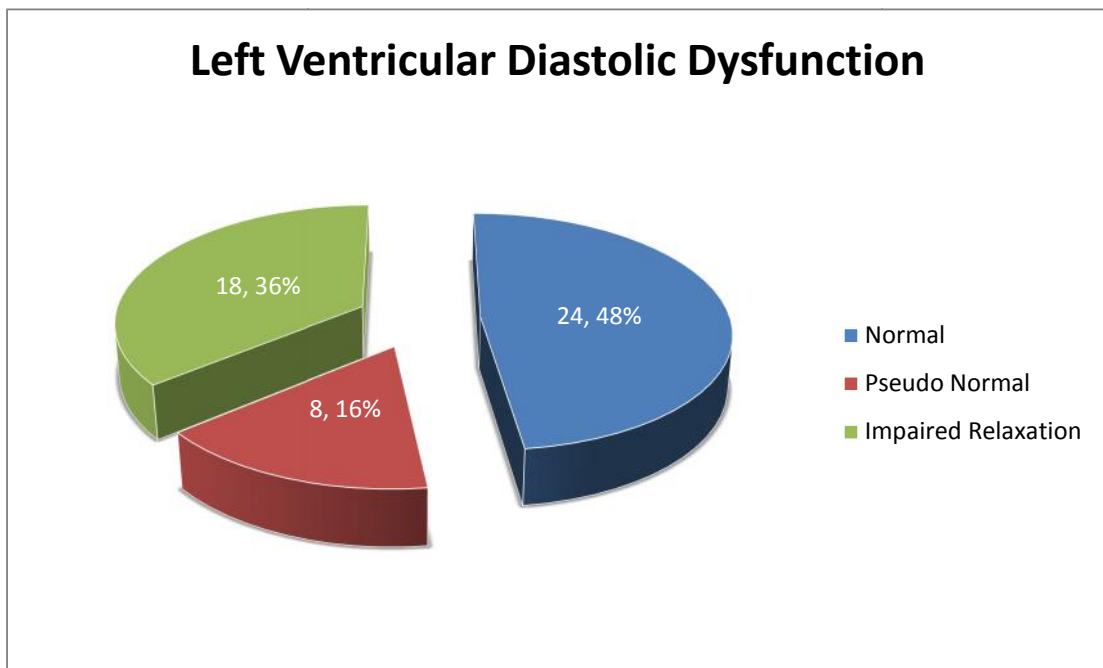
Table 18

Cardiac Dysfunction	Number	Percentage
Normal	24	48
Impaired Relaxation	18	36
Pseudonormal	8	16
Total	50	100

As shown in table and chart , out of 50 subjects,

- 24(48%) had normal diastolic function
- 18(36%) had impaired relaxation
- 8(16%) had pseudonormal pattern
- Thus 26(52%) subjects had diastolic dysfunction

Chart 3



## Mean values of Diastolic dysfunction parameters

Table 19

<b>ECHO Parameters</b>	<b>Left Ventricular Diastolic Dysfunction</b>		
	<b>Normal</b>	<b>Impaired Relaxation</b>	<b>Pseudonormal</b>
<b>E/A ratio</b>	1.08	0.82	1.12
<b>DT</b>	166.33	157.83	186.75
<b>IVRT</b>	90.08	86.56	96.25

The table above shows the following

E/A ratio

- E/A ratio is 1.08 in the normal group
- 0.82 is the reading in the impaired relaxation group
- Pseudonormal group has a value of 1.12

DT

- Deceleration time in the normal group is 166.33 ms
- In the impaired relaxation group it is 157.83 ms
- 186.75 ms is the value in the Pseud normal group

IVRT

- Isovolumetric relaxation time is 90.08 ms in the normal group
- The value in the impaired relaxation group is 86.56 ms
- In the Pseudonormal group the value is 96.25 ms

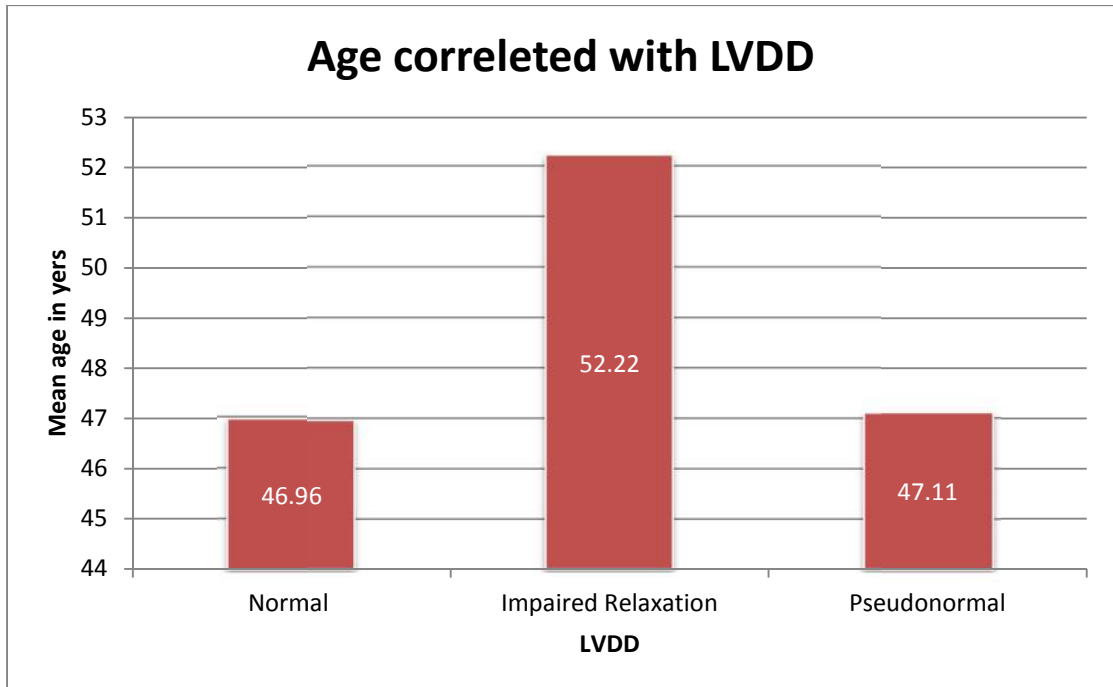
**Mean values of study parameters in relation to left ventricular diastolic dysfunction**

Table 20

Study parameters	Left Ventricular Diastolic Dysfunction			P value
	Normal	Impaired Relaxation	Peudonormal	
Age in years	46.96	52.22	47.11	0.086
Systolic BP mm Hg	133.08	139.56	146.11	0.969
Diastolic BP mm Hg	85.44	88.57	90.32	0.809
Waist (male) cms	96.14	95.32	95.98	0.442
Waist (female) cms	95	94.63	94.11	0.454
FBS mg/dl	113.14	128.36	131.75	0.300
TGL mg/dl	161.78	131.11	122.38	0.220
HDL mg/dl	43.78	42.96	41.00	0.611

## Correlation of age with left ventricular diastolic dysfunction

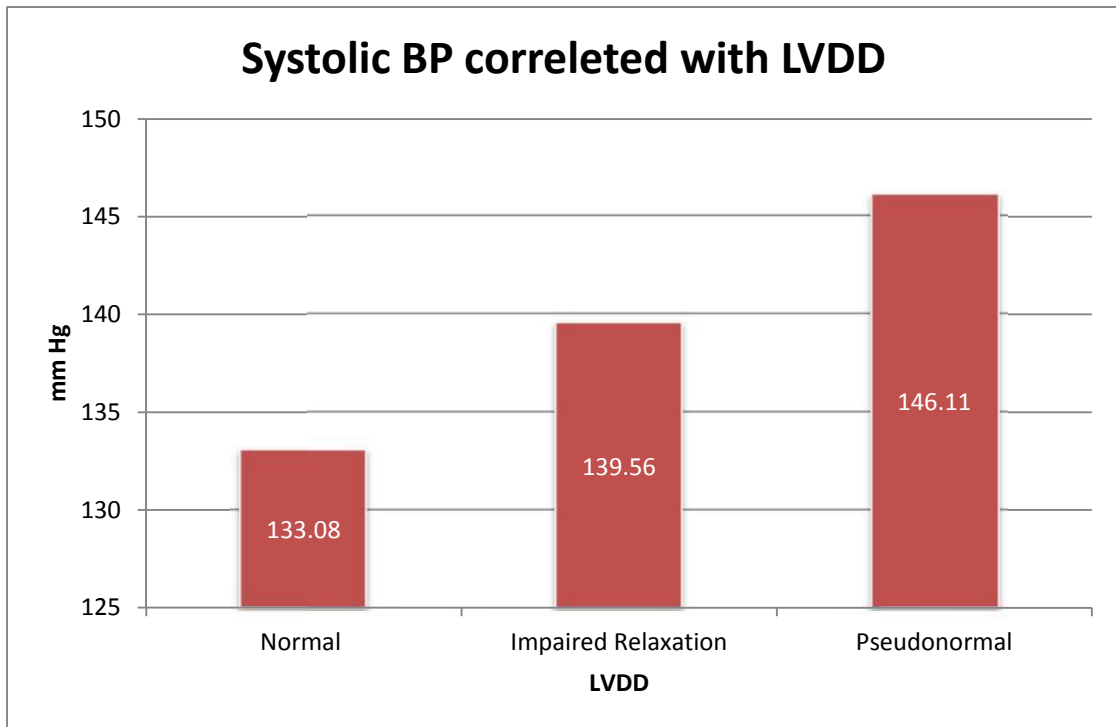
Chart 4



As depicted in table 13 and chart 4 mean age in the normal group is 46.96 years, in impaired relaxation group it is 52.22 years and in the pseudonormal group is 47.11 years. Though the age range was higher in impaired relaxation group, it was not statistically significant ( $p=0.086$ ).

## Correlation of systolic BP with left ventricular diastolic dysfunction

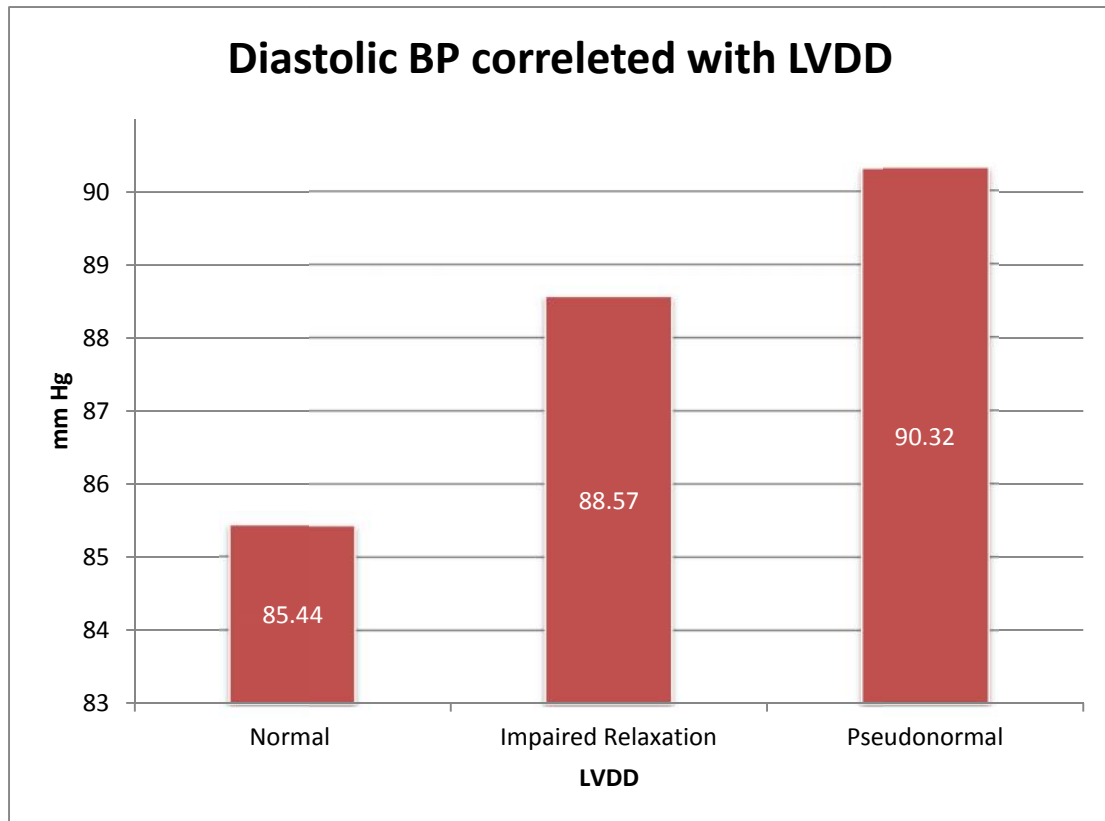
Chart 5



As depicted in table 13 and chart 5 mean systolic BP in the normal group is 133.08 mm Hg, in impaired relaxation group it is 139.56 mm Hg and in the pseudonormal group is 146.11 mm Hg. Though the systolic BP values are higher in pseudonormal group, it was not statistically significant ( $p=0.969$ ).

## Correlation of diastolic BP with left ventricular diastolic dysfunction

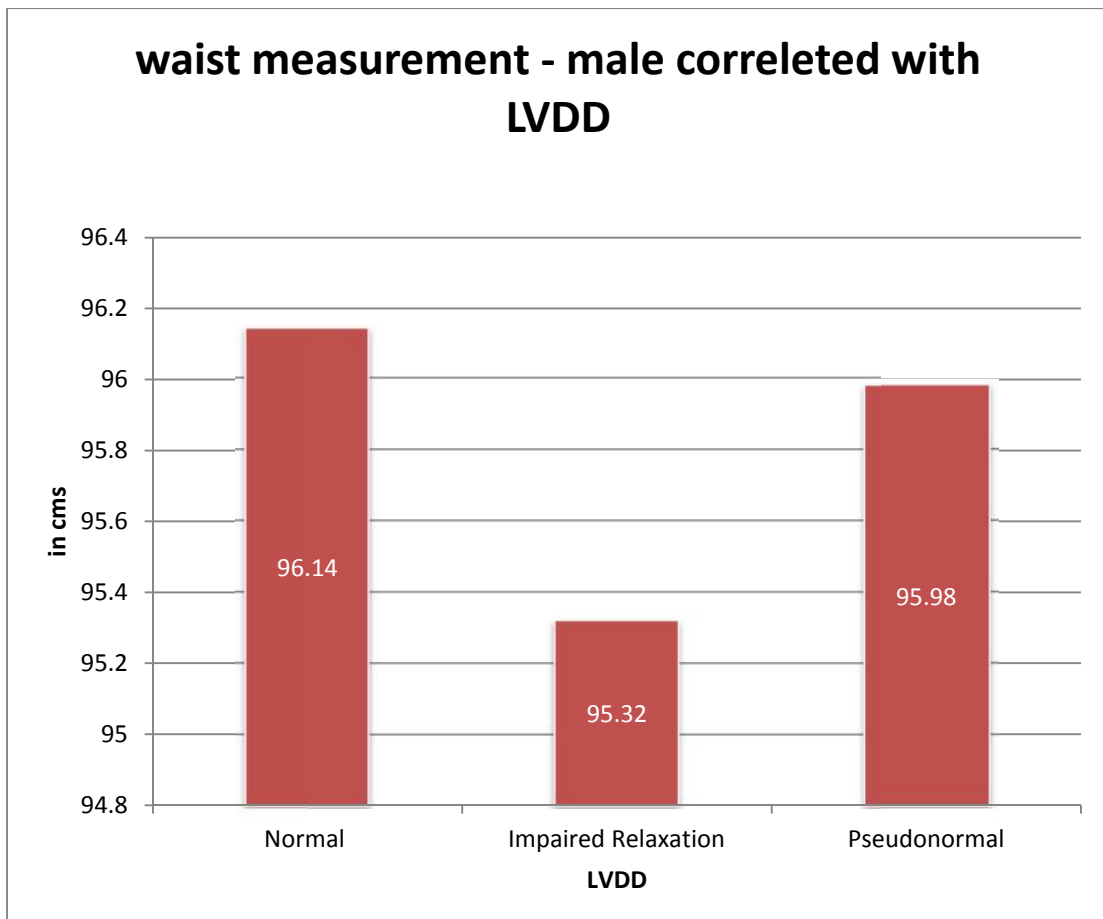
Chart 6



As depicted in table 13 and chart 6 mean diastolic BP in the normal group is 85.44 mm Hg, in impaired relaxation group it is 88.57 mm Hg and in the pseudonormal group is 90.32 mm Hg. Though the diastolic BP values are higher in pseudonormal group, it was not statistically significant ( $p=0.809$ ).

## Correlation of waist measurement - male with left ventricular diastolic dysfunction

Chart 7

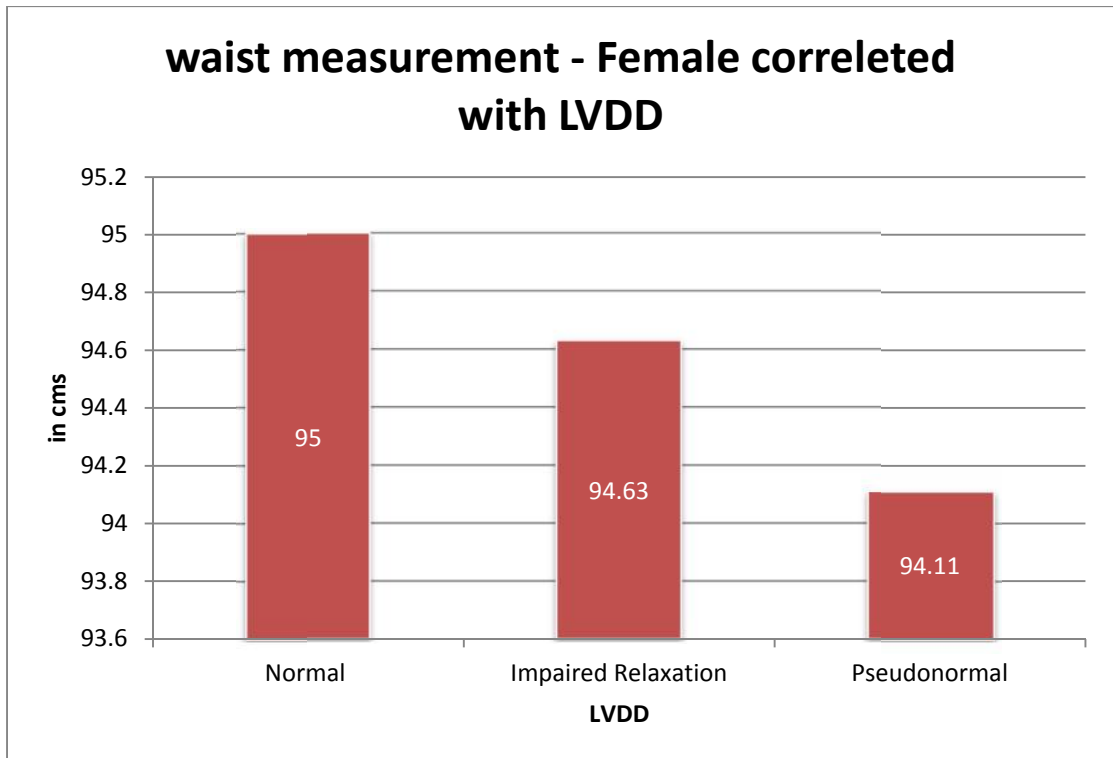


As depicted in table 13 and chart 7 mean waist measurement - male in the normal group is 96.14 cms, in impaired relaxation group it is 95.32 cms and in the pseudonormal group is 95.98 cms. Though the mean waist measurement - male values are higher in normal group, it was not statistically significant ( $p=0.442$ ).



## Correlation of waist measurement - female with left ventricular diastolic dysfunction

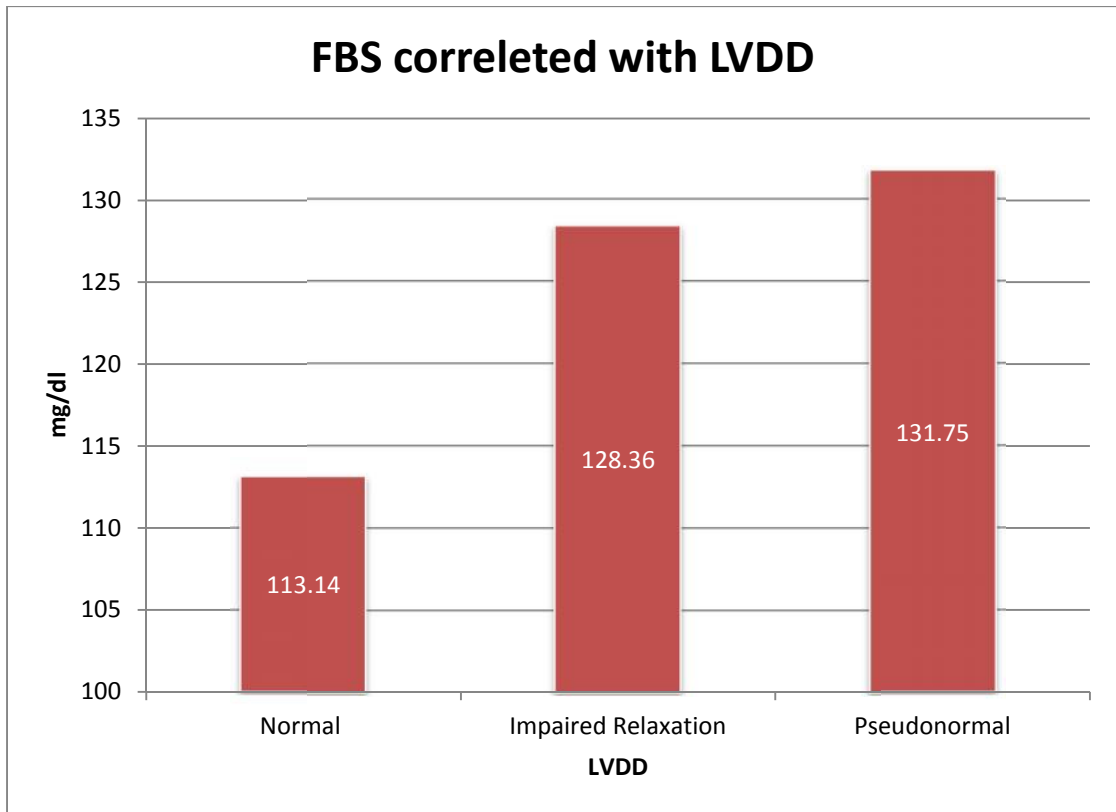
Chart 8



As depicted in table 13 and chart 8 mean waist measurement - female in the normal group is 95.00 cms, in impaired relaxation group it is 94.63 cms and in the pseudonormal group is 94.11 cms. Though the mean waist measurement - female values are higher in normal group, it was not statistically significant ( $p=0.454$ ).

## Correlation of fasting blood sugar with left ventricular diastolic dysfunction

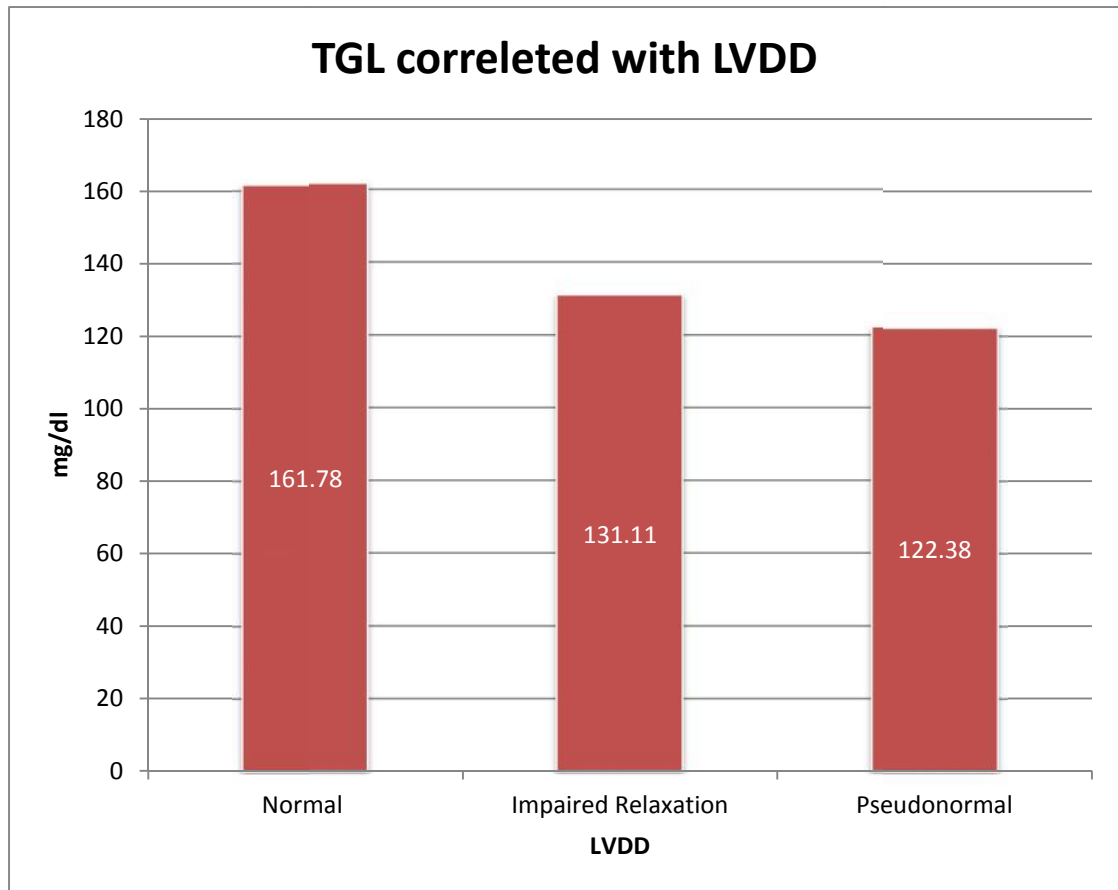
Chart 9



As depicted in table 13 and chart 9 mean fasting blood sugar in the normal group is 113.14 mg/dl, in impaired relaxation group it is 128.36 mg/dl and in the pseudonormal group is 131.75 mg/dl. Though the mean fasting blood sugar values are higher in pseudonormal group, it was not statistically significant ( $p=0.300$ ).

## Correlation of triglycerides with left ventricular diastolic dysfunction

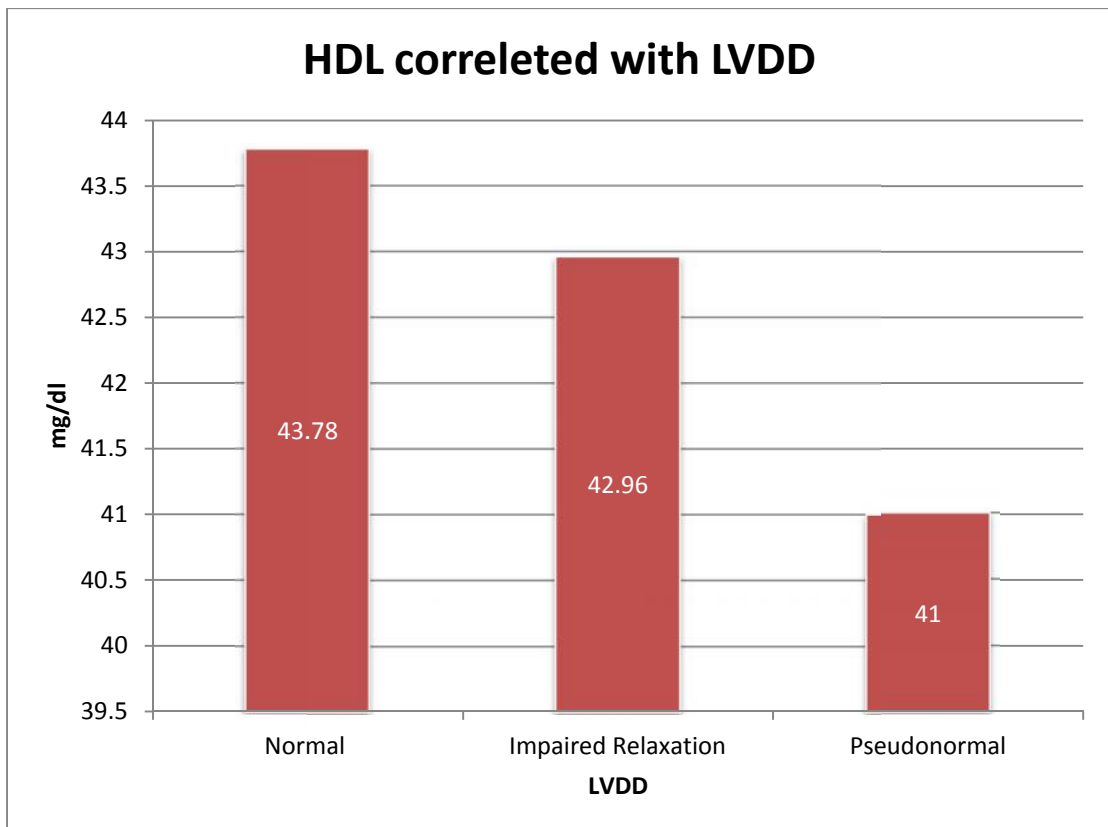
Chart 10



As depicted in table 13 and chart 10 mean triglyceride in the normal group is 161.78 mg/dl, in impaired relaxation group it is 131.11 mg/dl and in the pseudonormal group is 122.38 mg/dl. Though the mean triglyceride values are higher in normal group, it was not statistically significant ( $p=0.220$ ).

## Correlation of high density lipoproteins with left ventricular diastolic dysfunction

Chart 11



As depicted in table 13 and chart 11 mean high density lipoprotein in the normal group is 43.78 mg/dl, in impaired relaxation group it is 42.96 mg/dl and in the pseudonormal group is 41.00 mg/dl. Though the mean high density lipoprotein values are higher in normal group, it was not statistically significant ( $p=0.611$ ).

## DISCUSSION

Left ventricular diastolic dysfunction may be the earliest marker of metabolic syndrome induced heart disease, which leads to progressive development of cardiac failure. Thus it is important to detect left ventricular diastolic dysfunction at an early stage. This will prevent progression of disease to failure.

Left ventricular diastolic dysfunction may also be caused by other medical conditions. In our study the subjects with the above conditions, which affect LVDD were excluded.

Previous studies like Tarumi et al <sup>(62)</sup> who reported LVDD 36% and Antonio Nicolino A et al <sup>(63)</sup> reported LVDD from 32-40%. But in our study we reported a prevalence of 52%. When compared to the above mentioned studies, we had studied the pseudo normal pattern.

Hence the reason for high prevalence levels of LVDD in our study. The recognition of pseudo normal pattern is important because it is an intermediate stage impaired relaxation and restrictive filling which is a more advanced stage of LVDD.

In our study mean age in the normal group is 46.96 years, in impaired relaxation group it is 52.22 years and in the pseudonormal group is 47.11 years. The p value obtained was not statistically significant (p=0.086).

Systolic and diastolic BP, waist measurement, FBS, TGL and HDL levels did not correlate with LVDD and were not statistically significant. Similar results were seen in Paul Poirier et al, N H Anderson et al and Rajesh Rajput et al studies (<sup>64,65,66</sup>)

## SUMMARY AND CONCLUSION

- Left ventricular diastolic dysfunction was observed in 52% of total subjects and 48% of total subjects have normal left ventricular function. 36% impaired relaxation cases and 16% pseudo normal cases contributed to the 52% prevalence of LVDD.
- Recognition of pseudonormal pattern of utmost importance. It is an intermediary stage between mild impaired relaxation state and advanced restrictive filling stage.
- LVDD had no correlation with blood pressure, fasting blood sugar, waist measurement, triglycerides and high density lipoproteins level.
- LVDD is the earliest manifestation of metabolic disease related cardiomyopathy. Hence detecting it early will prevent disease progression to symptomatic cardiac failure and bring down the disease burden.
- The clinical significance of the findings in terms of prognosis and treatment needs to be determined.

- This study is a hypothesis generating study.
- Hence results from our study needs to be reinvestigated using robust research designs like cohort studies.
- Conventional echocardiography is a simple economical test for detecting LVDD in metabolic syndrome patients who are asymptomatic.
- ECHO diagnostic factors like E/A ratio, DT and IVRT should be should be studied further and developed into accurate cost effective screening tools for screening asymptomatic LVDD.



## **LIMITATIONS OF THE STUDY**

1. Low sample size
2. Selection bias while selecting subjects
3. Low financial support
4. Inability to use research design like cohort study due to a lack  
resources

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## PROFORMA

Serial No :

Date :

Unit :

Name :

IP/OP No :

Age :

Sex :

Address :

Phone :

Education :

Occupation :

Income :

Social Class :

Past history :

HT

T2DM

Hypothyroidism

Heart disease

## **EXAMINATION**

Weight :

Height :

Waist circumference :

Pulse rate :

Blood pressure :

## **INVESTIGATIONS**

CBC:

HB

TC

DC

ESR

PLATELET COUNT

PCV

URINE ROUTINE

BLOOD SUGAR(R)

FBS

PPBS

BLOOD UREA

SERUM CREATININE

ELECTROLYTES

Sodium

Potassium

Chloride

bicarbonate

SERUM URIC ACID

LIPID PROFILE

TOTAL CHOLESTEROL

HDL

TGL

LDL

VLDL



THYROID FUNCTION TEST:

FREE T3

FREE T4

TSH

SERUM CORTISOL

USG ABDOMEN

ECG

ECHO

## **FOLLOW UP**

BP:

FBS:

LIPID PROFILE:

TOTAL CHOLESTEROL

HDL

LDL

VLDL

TRIGLYCERIDES

ECHO:

## CONSENT FORM

- 1) i agree to participate in study titled a study on left ventricular diastolic function assessed by echo in metabolic syndrome.
- 2) i confirm that i have been told about this study in my mother tongue & have had the oppurtunity to ask questions.
- 3) i understand that my partipation is voluntery & i may refuse to participate at any time without giving any reason and without affecting my benefits.
- 4) i agree not to restrict the use of any date or results that arise from the study
- 5) i agree to subject myself for echocardiogram which is part of management tool for my disease.

Name of the participant:

Sign/Thumb print

Investigator

## KEY WORDS

<b>HT</b>	- Hypertension
<b>DM</b>	- Diabetes mellitus
<b>WC</b>	- Waist circumference
<b>ECHO</b>	- Echo cardiogram
<b>DT</b>	- Deceleration time
<b>IVRT</b>	- Isovolumetric relaxation time
<b>SBP</b>	- Systolic blood pressure
<b>DBP</b>	- Diastolic blood pressure
<b>FBS</b>	- Fasting blood sugar
<b>TGL</b>	- Triglycerides
<b>TC</b>	- Total cholesterol
<b>EF</b>	- Ejection fraction
<b>LVH</b>	- left ventricular hypertrophy

