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A STUDY ON LEFT VENTRICULAR DIASTOLIC FUNCTION ASSESED 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 ASSESED 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 ASSESED 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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Professor of Medicine

This dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University towards the partial fulfillment of the requirement of M.D. Branch I, General Medicine degree examination.

PLACE: CHENNAI **Dr. C.R.RAJAKUMAR**
DATE:

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Last but not the least I would like to thank my patients with gratitude for their cooperation during study and for teaching us the art of medicine and inciting us to learn more.

Dr.C.R.Rajakumar

TABLE OF CONTENTS

ABBREVATIONS

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

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A STUDY ON LEFT VENTRICULAR DIASTOLIC FUNCTION ASSESED BY ECHO IN METABOLIC SYNDROME"

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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 abnomalities 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, dyslipedemia, Elevated uric acid level, and fatty infiltration. These factors are the Synergitic property of risk factors on lipid accumulation in vessels. He first Describe the term METABOLIC SYNDROME (5)

- **SINGER** illustrate the relationships between the cental obesity, hyper uricemia and hyperglycemia and elevated BP with dyslipidemia in the same year[6]

- **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 over weight patients.

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

- 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

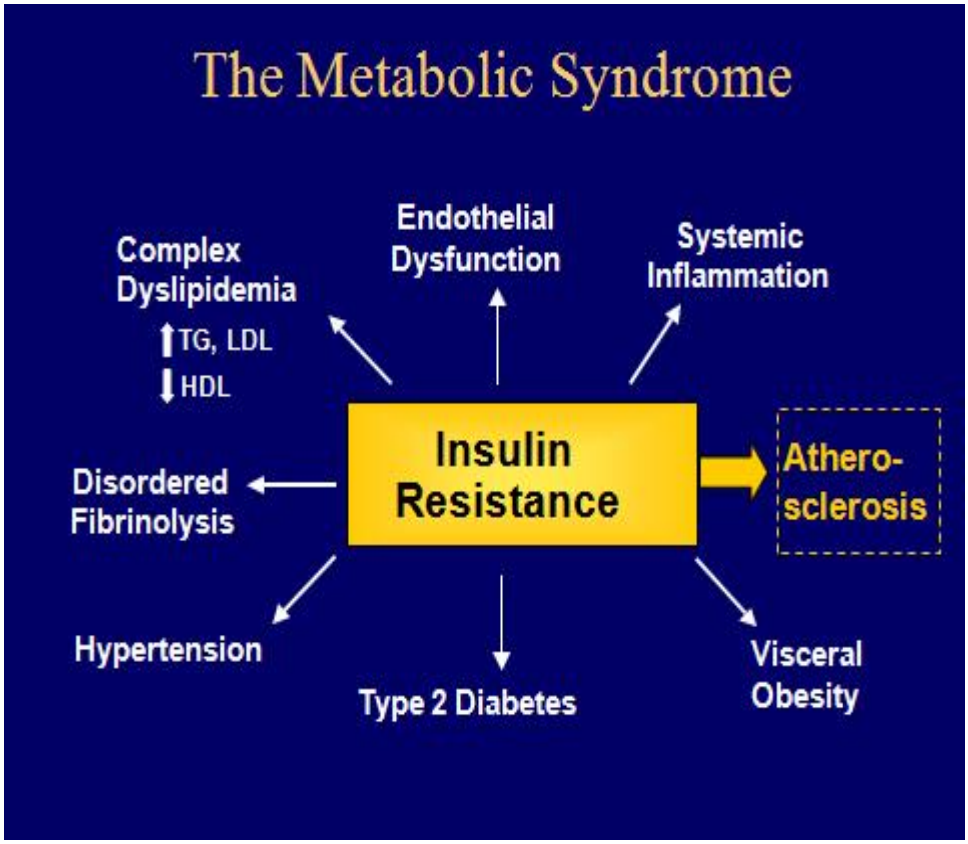
- Blood glucose abnormalities such as IR, IGT
- state of Pro inflammation
- Abnormalities of Thrombotic mechanism

These components of the metabolic syndrome, according to Adult treatment panel III may divides **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,



(11)

Figure (1) shows components of metabolic syndrome

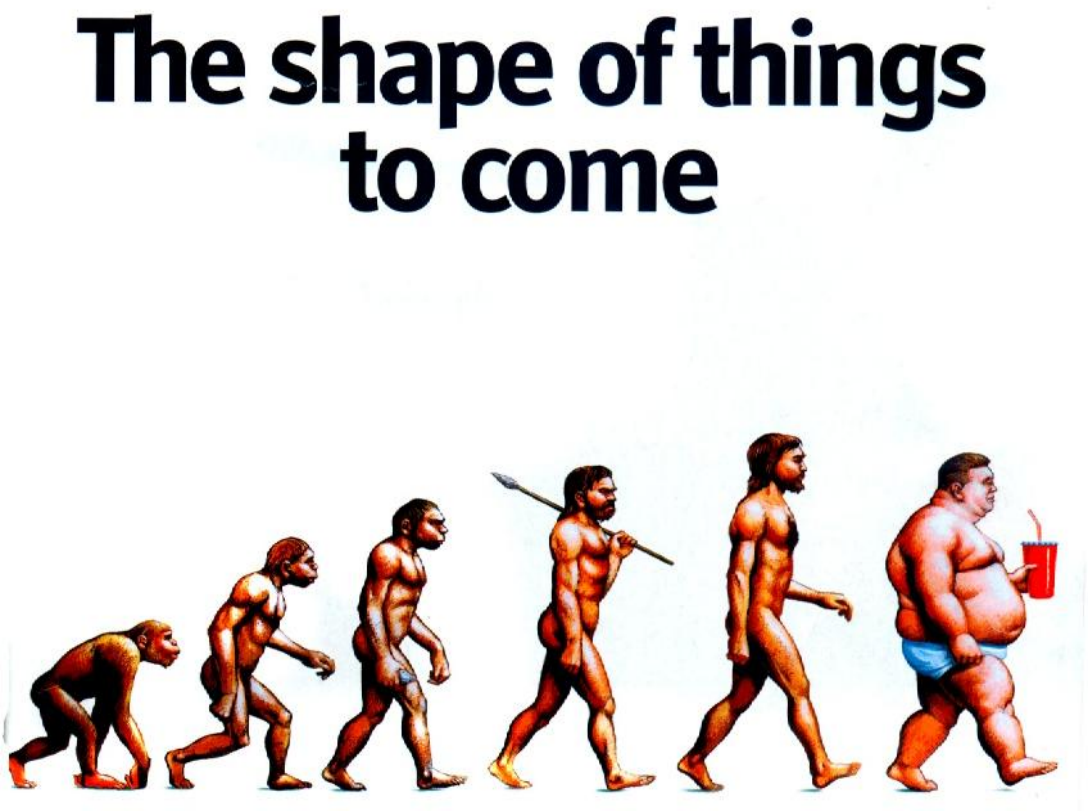
Abdominal obesity

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.



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

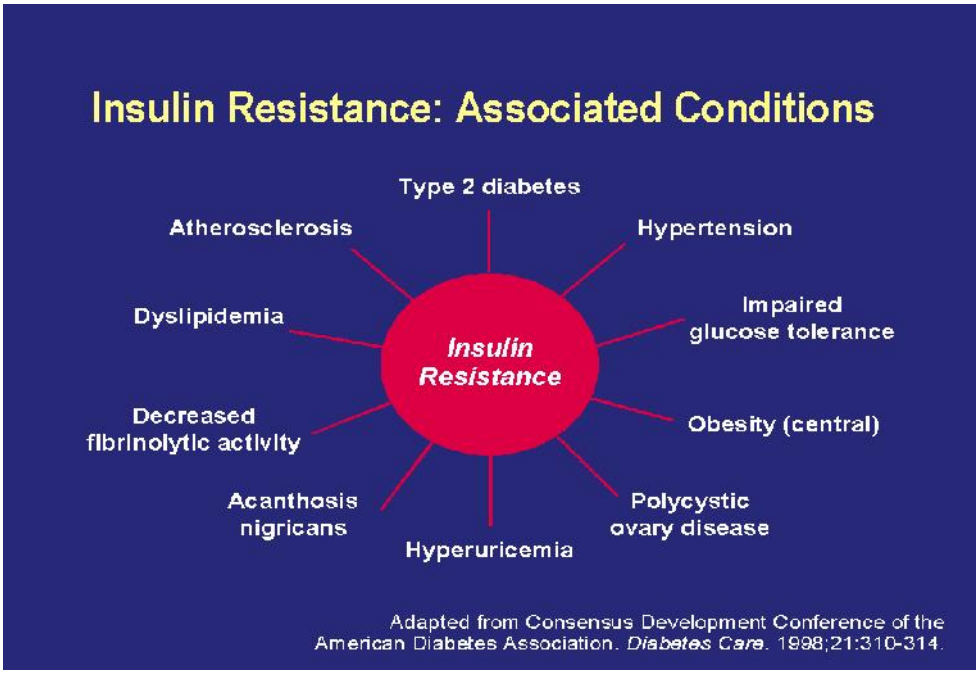


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Figure (2) shows insulin resistance associated conditions

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

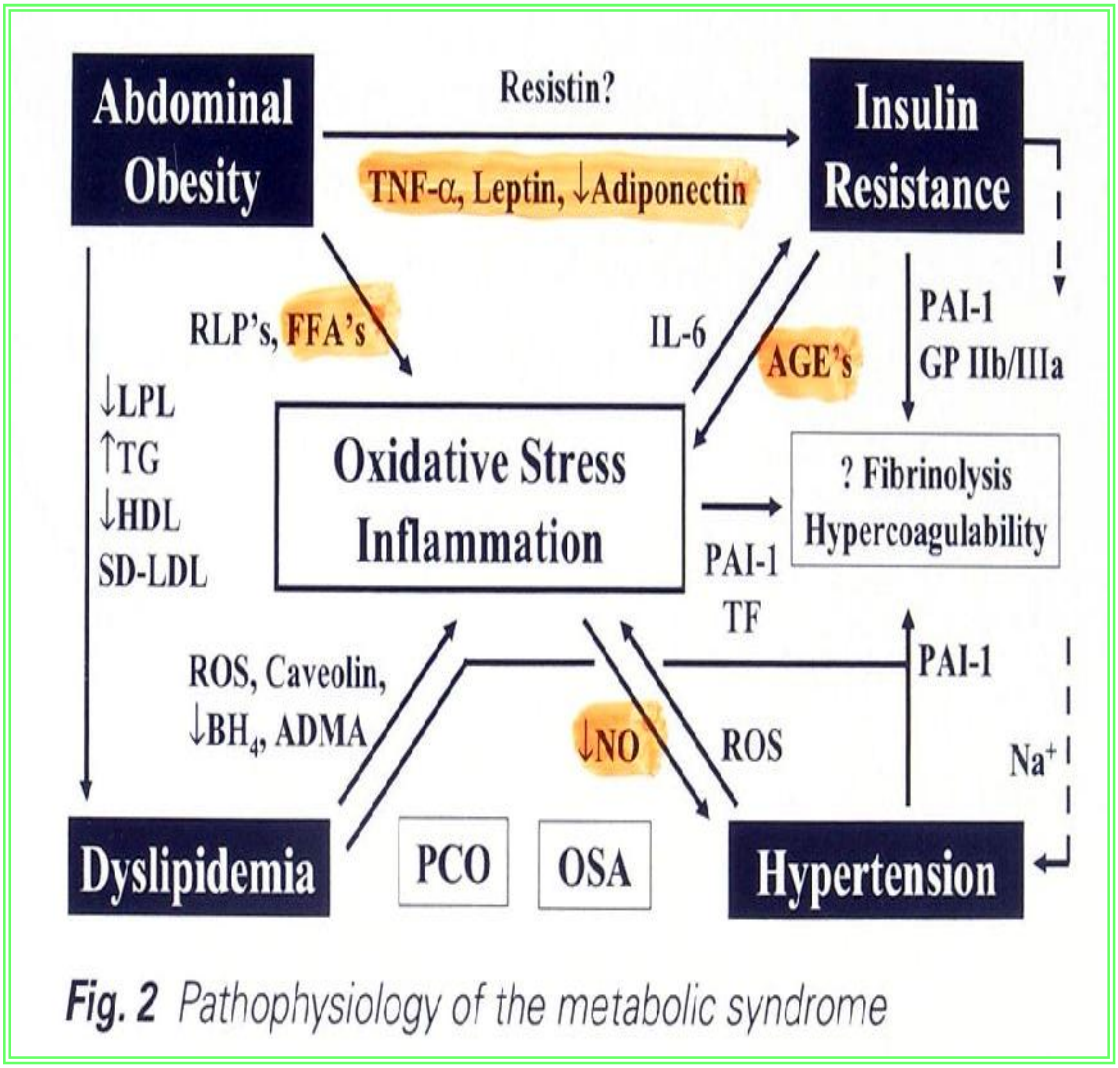


Fig. 2 Pathophysiology of the metabolic syndrome

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 mojor role other then any factors (12,13).

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

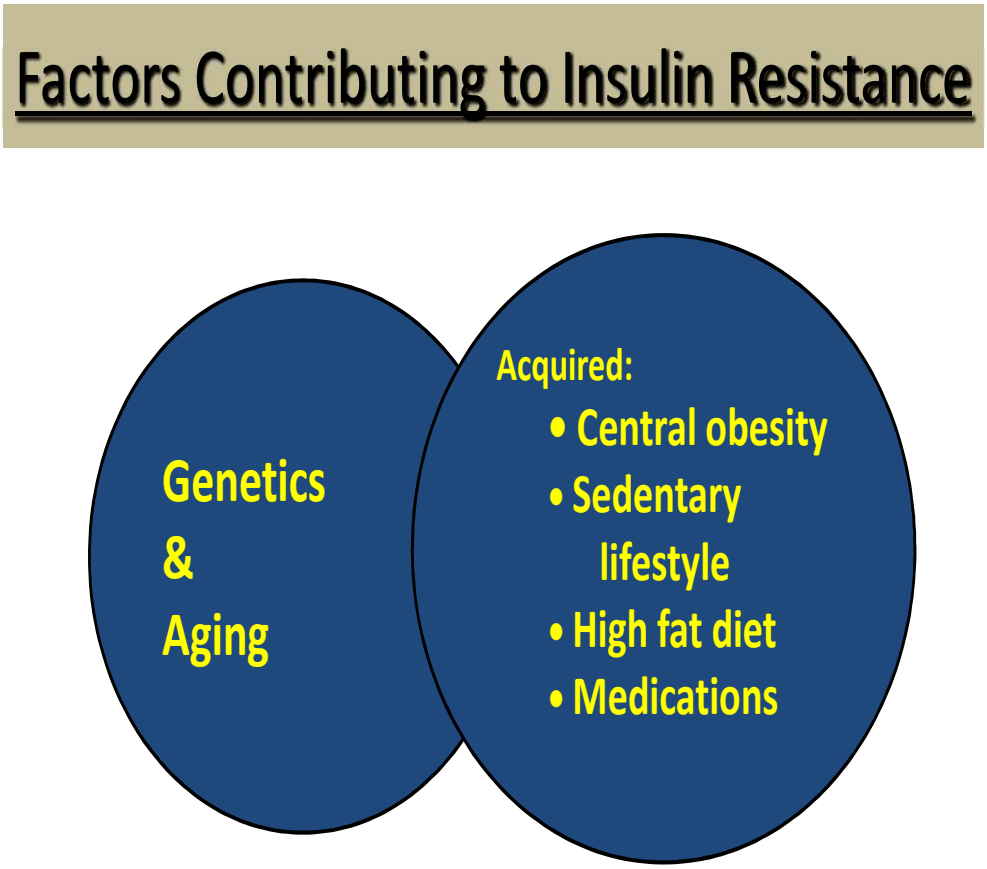
When the Persons with obesity had body mass index more than 30 have Elevated post prandial insulin level and low sensitivity of insulin (15).

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



(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**

Factor	Definite Level
Central obesity (waist circumference) Male Female	 More than 102 cm (> 40 inches) More than 88 cm (>35 inches)
TGL	More than 150mg/dl
HDL cholesterol male female	 Less than 40 mg/dL Less than50 mg/Dl
Blood pressure	more than130 mmHg systolic BP more than 85 mmHg diastolic BP
FBS	More than110 mg / dL

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

Clinical adverse effects of metabolic syndrome was identified as Cornary 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 treatmentof hyper glycemia.(19).

TABLE -2 **- WHO CRITERIA**

any one of the subsequent criteria: ➢ Known diabetes on treatment ➢ IFG ➢ IGT ➢ Normal FBS level
<u>Plus any of the two in subsequent criteria:</u> ➢ Any medication for high BP and /or rised BP more than 140 mmHg in systolic or diastolic BP more than 90 mm Hg
➢ TGL LEVEL more than150 mg/dL
➢ High density lipid level < 35 mg / dL -male or <39 mg / dL – female
➢ BMI more than >30 and /or ratio between waist and hip more than .9 in male, more than .85 in female
➢ 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)

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

RISK FACTOR	**DEFINE LEVEL**
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

• **Central obesity** WC more than 94 cm for male and more than 80 cm for female
add any of the 2 subsequent criteria
• **High Density Lipid :** Male - < 40 mg/dL Female - < 50 mg/dL taken drugs for this type of dyslipidemia
• **TGL LEVEL :** More than150 *mg* / *dl* or taken any drugs for this type of Dyslipedemia
• **BP** BP more than 130 in systolic and or diastolic BP more than85 mm Hg, taking any drugs HT
• **FPG:** More than 100 mg/dL or known case of T2DM

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.

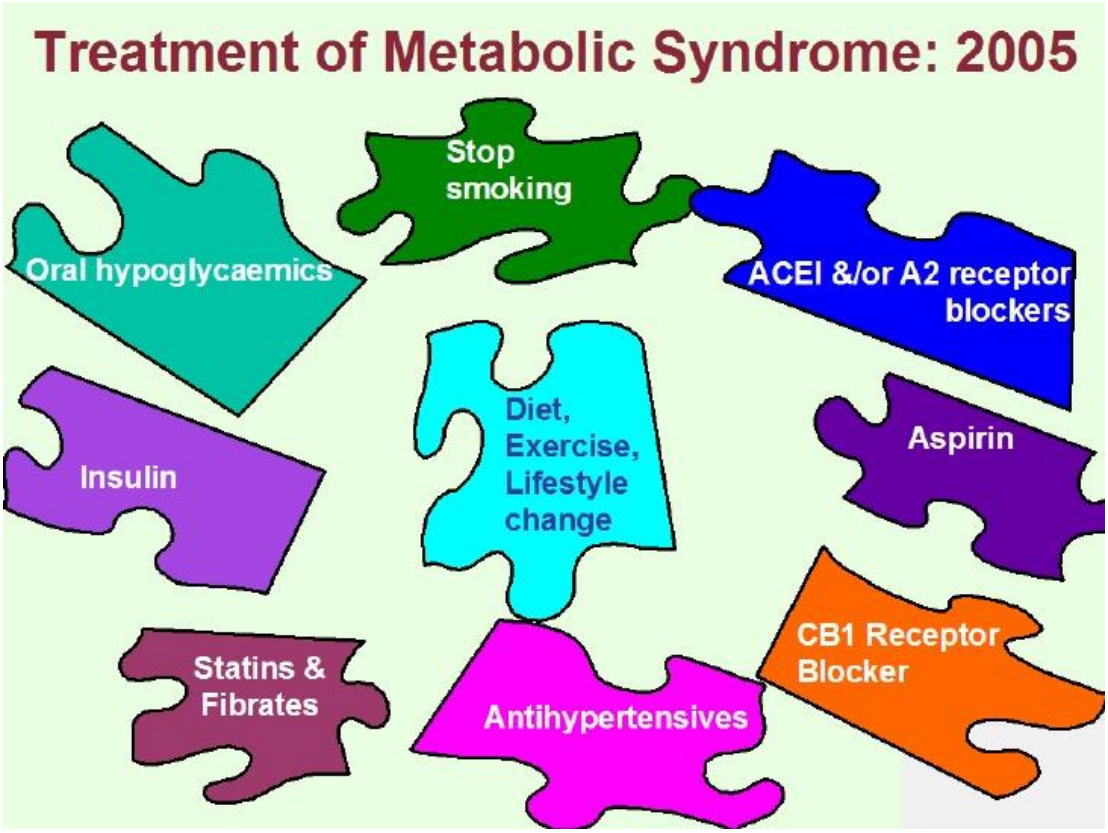


FIGURE -5 Shows treatment of metabolic syndrome

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 modificatios,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 DYSFUCTION

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 distensiablity.

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;

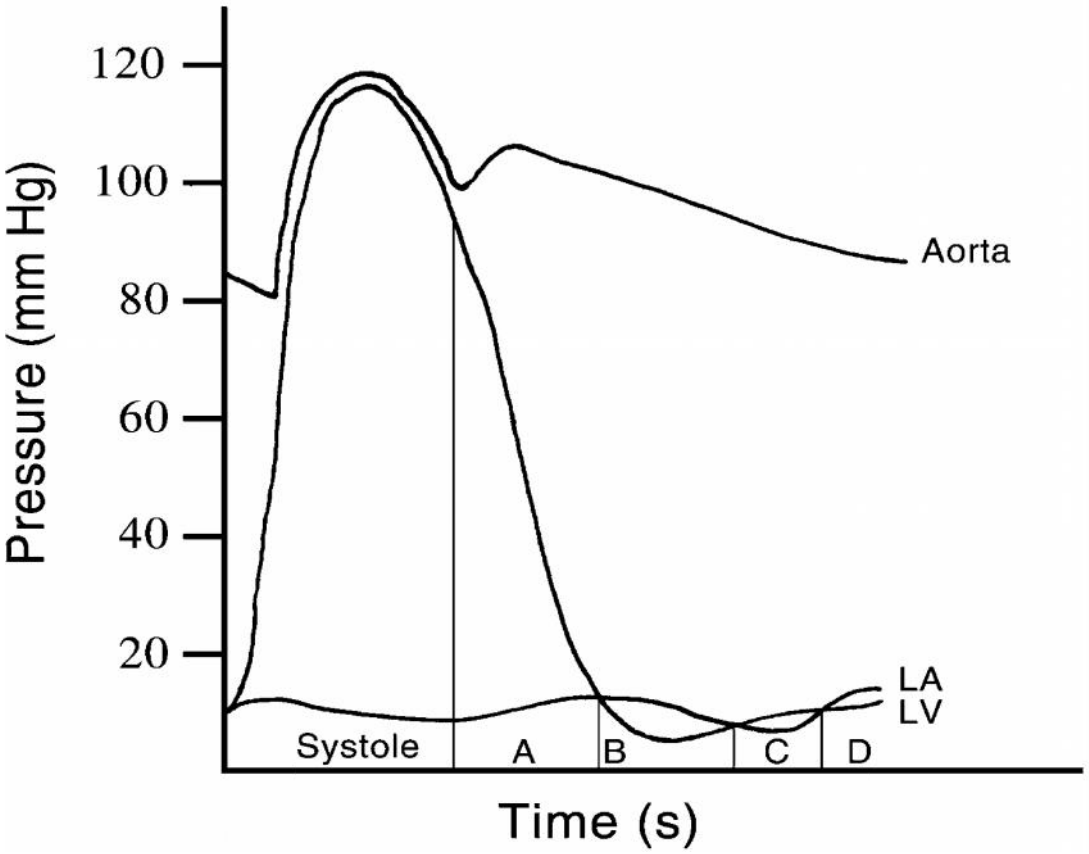


Figure 6 - shows relationship of pressure and volume of left ventricle in the period of diastole

- 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.

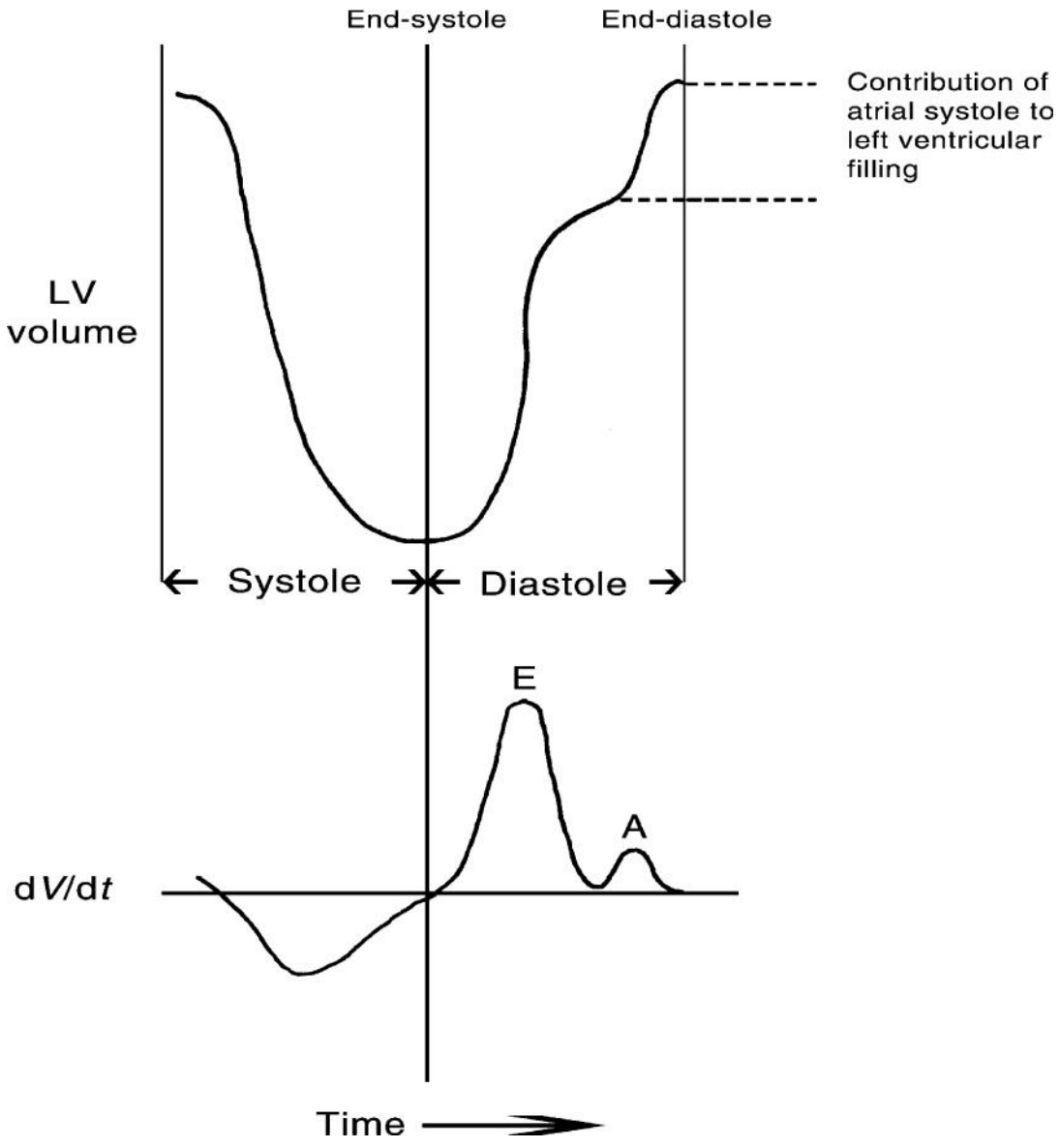
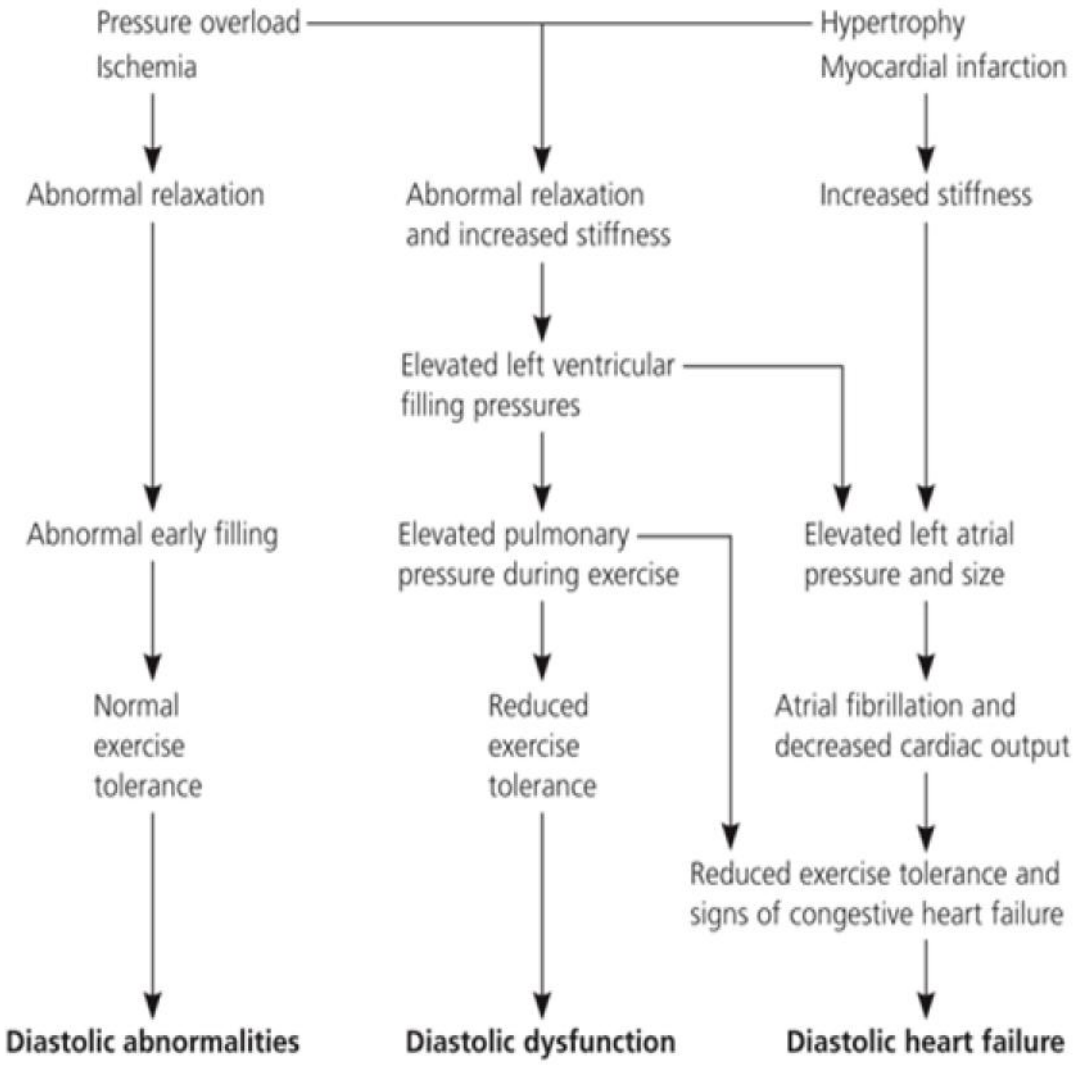


Figure -7 shows left ventricular heamodynamics

PATHO PHYSIOLOGY

Table- 5



All these factors can leads to diastolic heart failure and diastolic dysfuction

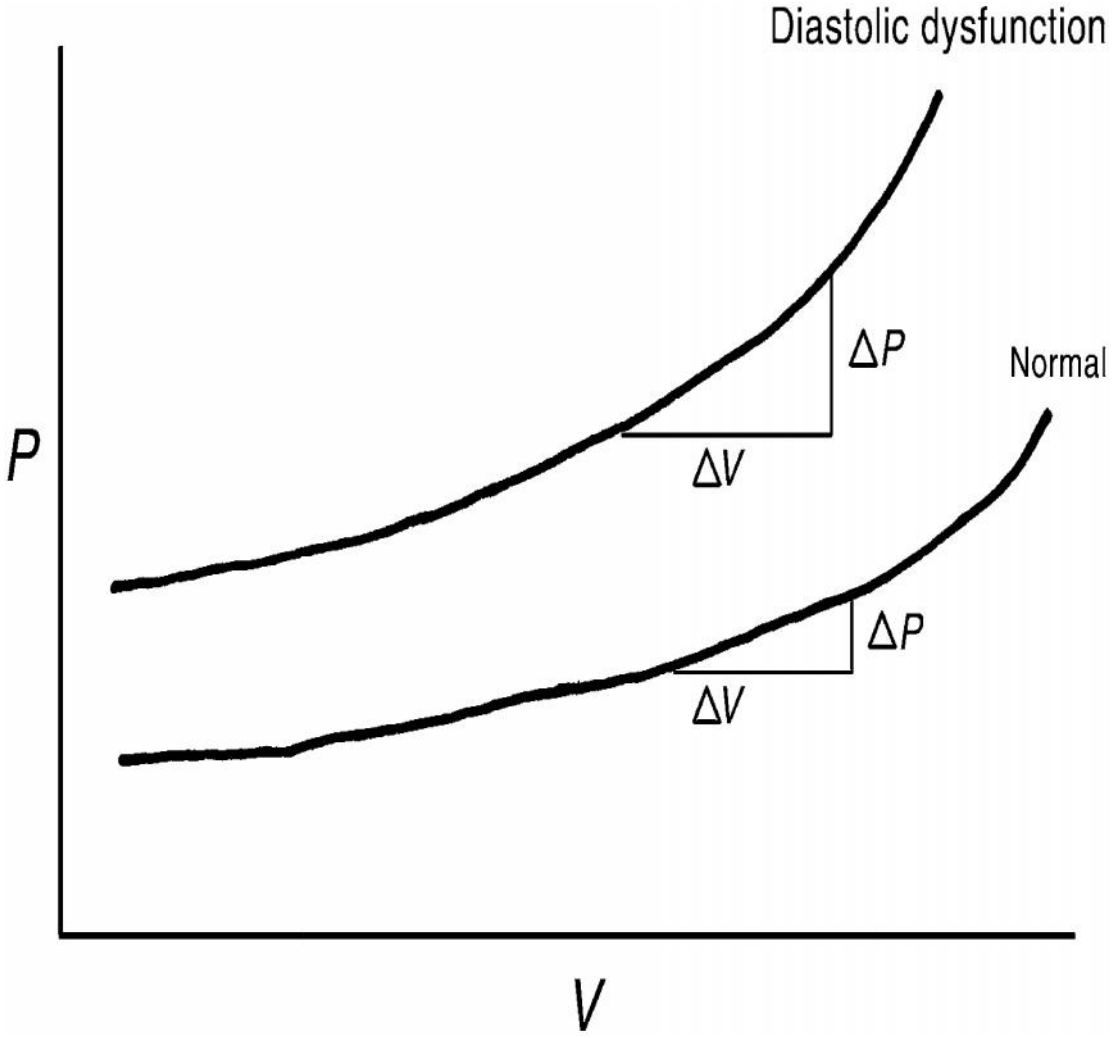


Figure - 8 shows graphical representation of Pressure–volume for the Left Ventricle Period of diastole. (27)

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%)
CLINICAL SYMPTOMS		
Exertional Dyspnoea	85	96
PND	55	50
Orthopnoea	60	73
SIGNS		
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
X-RAY - CHEST		
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

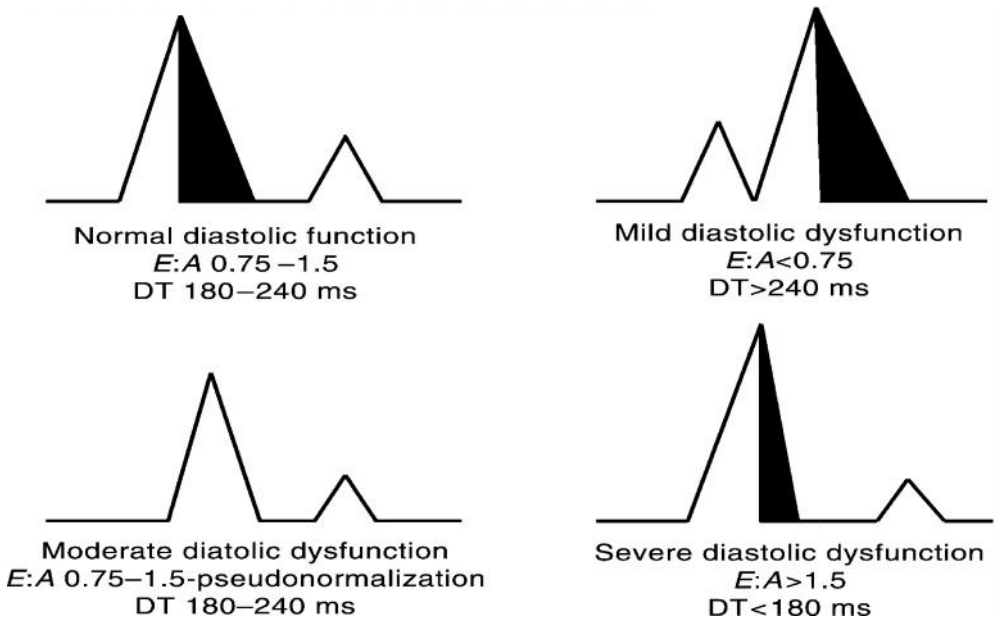


Figure- 9 shows pictorial representation of diastolic trans mitral doppler assesment

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.

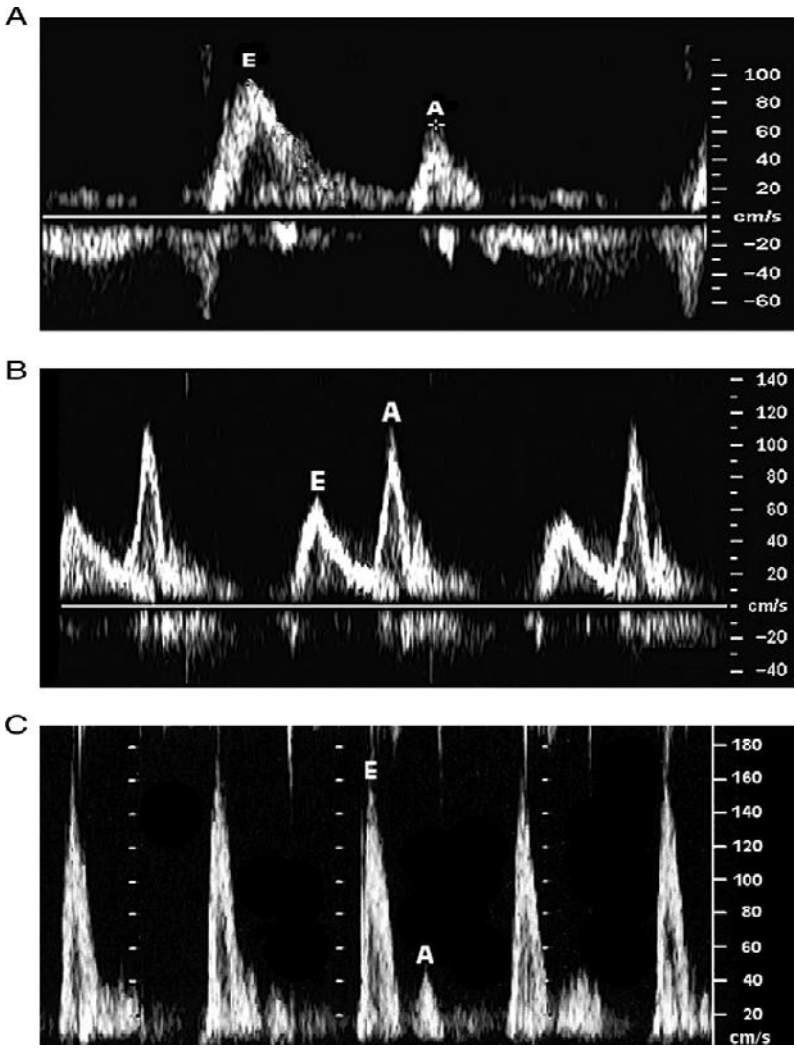


Figure -10 shows transmitral Doppler flow pattern

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 /complaince	IVRT - less than30 years - more than 92 ms, 30 to 50 years - more than 100 ms, More than 50 yrs - more than 105 m secs EA ratio less than one + DecTime – more than 220 msecs + S/D less than 1.5 in below 50 yrs E/A - less than 0.5 + DT more than 280 ms + S/D more than 2.5 above 50 yrs

TREATMENT OF DIASTOLIC HEART FAILURE:

INITIAL TREATMENT:

Pt first treated with supportive therapy such as O2 therapy and according to the underlying cause such as ischemia, constrictive pericartitis, atrial fibrillation Main goal To **diminish the pulmonary congestion by** Diuretics can be used with cautiosly.

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 fucntion

- **Hui-pinget 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 a1***(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 tha age,sex, BP, and Blood sugar level.

- **Ahn et al** *(50)* found that thecomponents 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 assesed 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

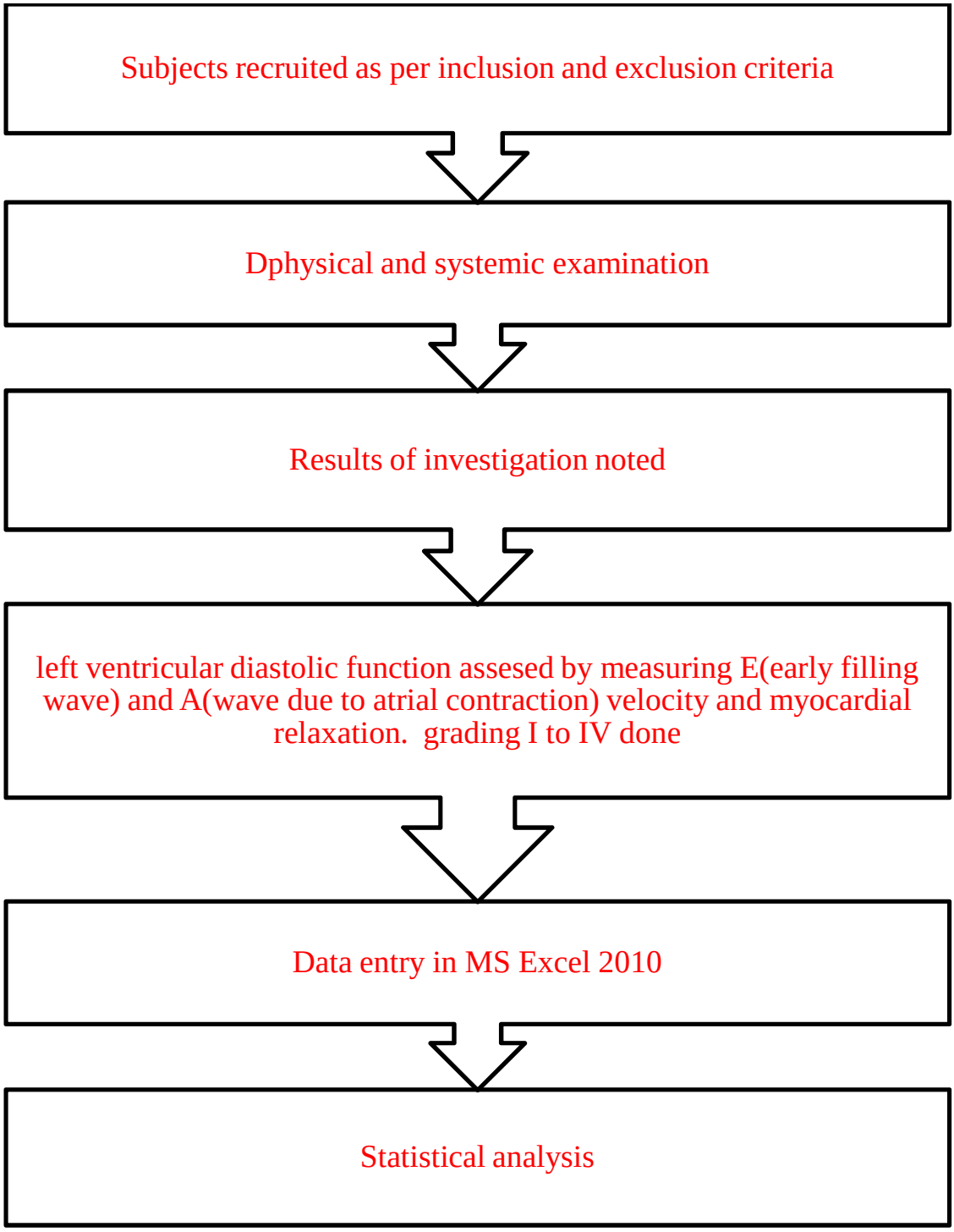


Figure (11) shows study protocol

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) sing 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 (Δd) ≥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

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

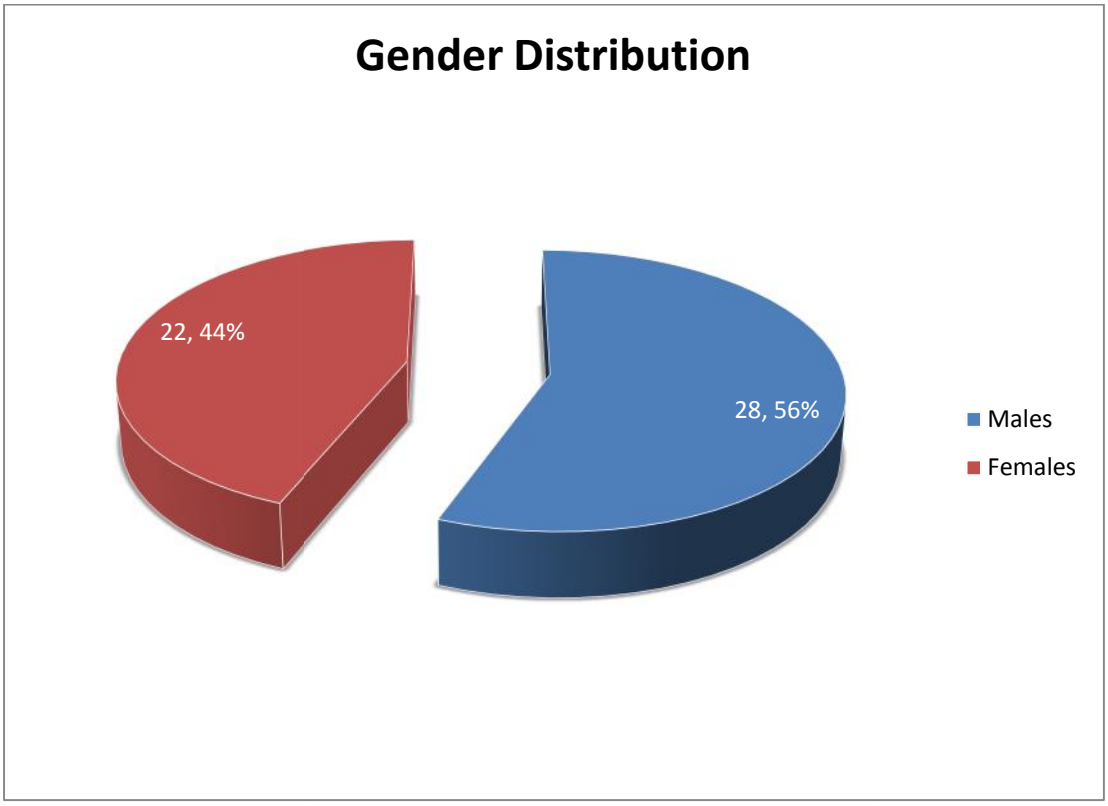
Level of significance used is 0.05 for the corresponding degree of freedom to draw the inference. A p value <0.05 was considered statistically significant.

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

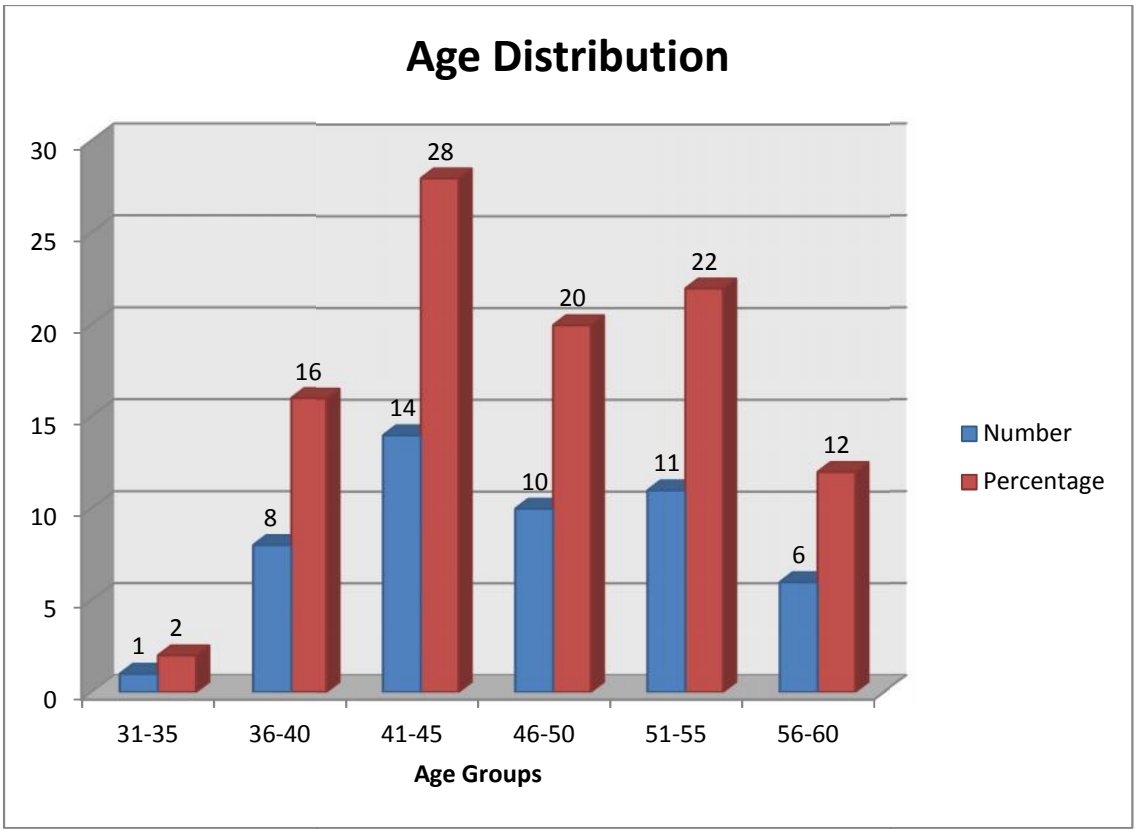
Chart 1



A total of 50 patients diagnosed with metabolic disorder were included in the study. Males constituted 28 %(n=56) 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

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

The mean systolic blood pressure and diastolic blood pressure are 133.08±10.96 and 85.44±4.68 respectively.

Waist measurement

Table 11

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

The mean waist measurement is 96.14 ±5.42 in males and 95 ±6.36 in females respectively.

Blood sugar

Table 12

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

The mean fasting blood sugar levels among the study subjects is 113.14 ±10.94.

Serum Triglycerides

Table 13

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

The mean triglyceride levels among the study subjects are 161.78 ±14.04.

High density lipoproteins

Table 14

High density lipoproteins	Number(n)	Mean	Standard Deviation(SD)
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 ± 6.19.

ECHO parameters

E/A ratio

Table 15 (A)

E/A	Number	Mean	Standard deviation	Maximum	Minimum
	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 ± 0.13.

Table15 (B)

E/A ratio	Number	Percentage
< 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)

DT (msec)	Number	Mean	Standard Deviation(SD)	Minimum	Maximum
	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 ± 12.87.

Table 16(B)

DT (msec)	Number	Percentage
150 -200 msec	3	6%
160-210 msec	31	62%
>220 msec	16	32%
Total	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)

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

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

Table 17 (B)

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

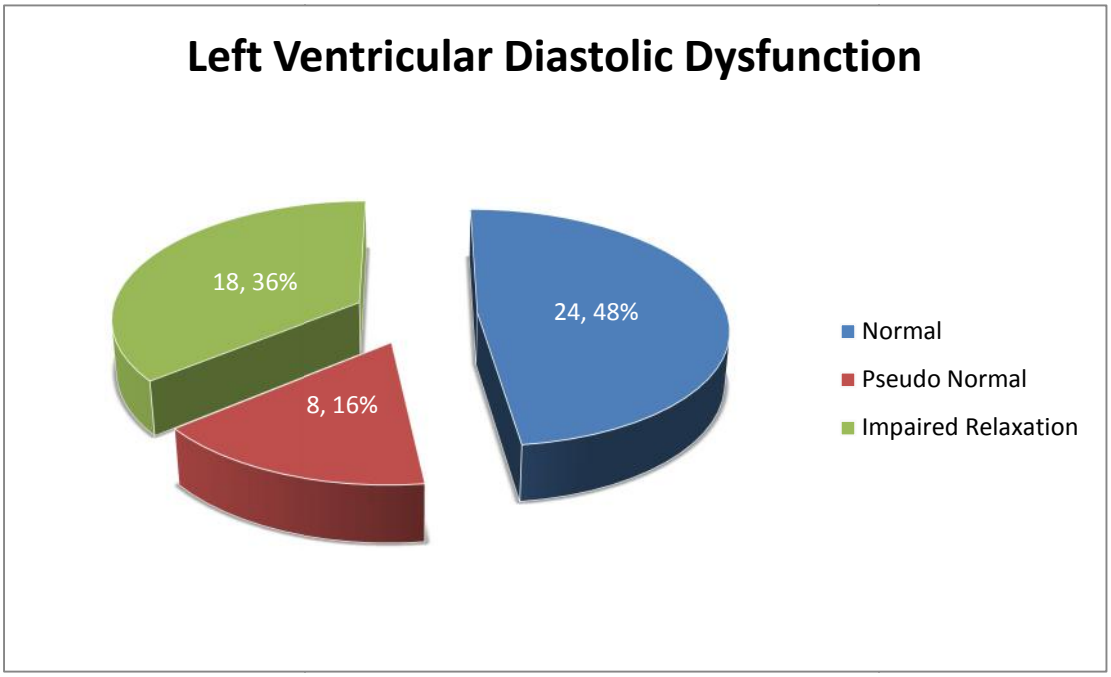
Table 18

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 nrmal 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

ECHO Parameters	Left Ventricular Diastolic Dysfunction		
	Normal	Impaired Relaxation	Pseudonormal
E/A ratio	1.08	0.82	1.12
DT	166.33	157.83	186.75
IVRT	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

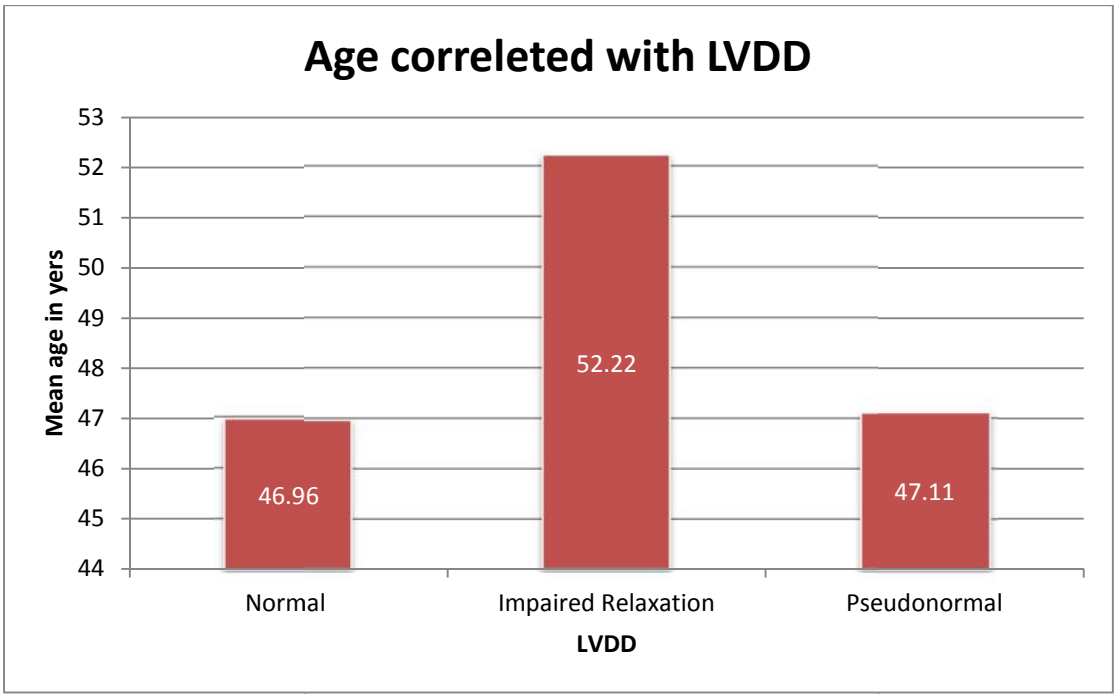
Mean values of study parameters in relation to left ventricular diastolic dysfunction

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

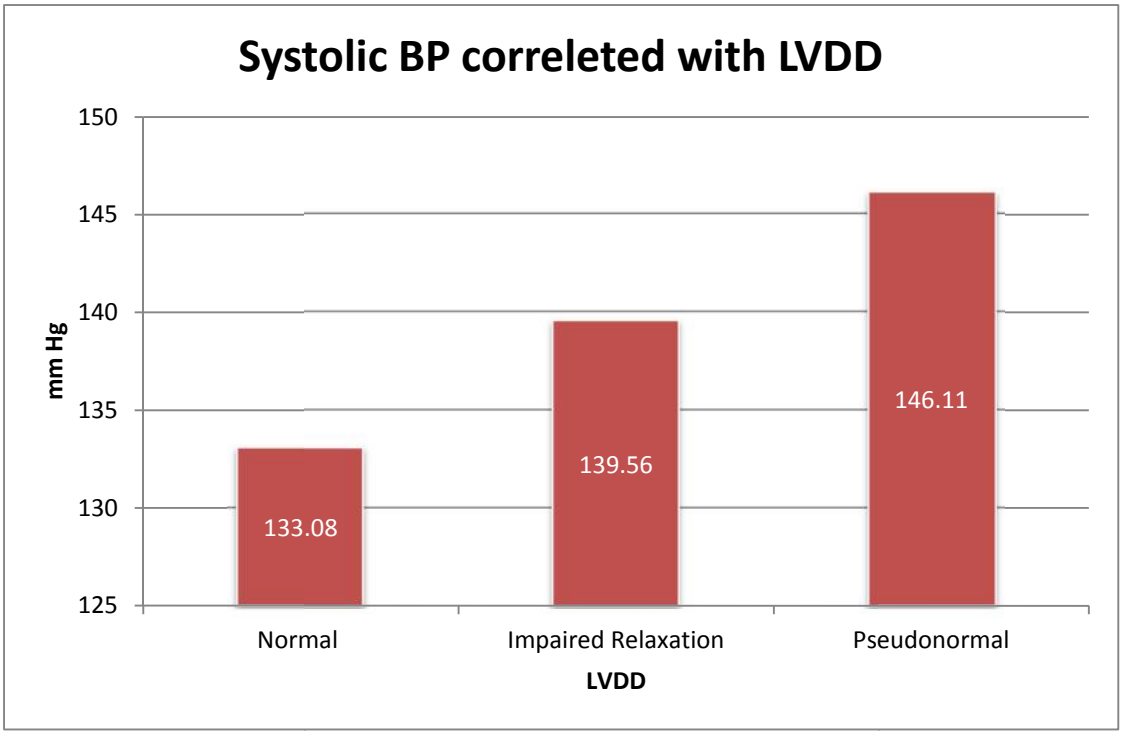
Chart 4



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

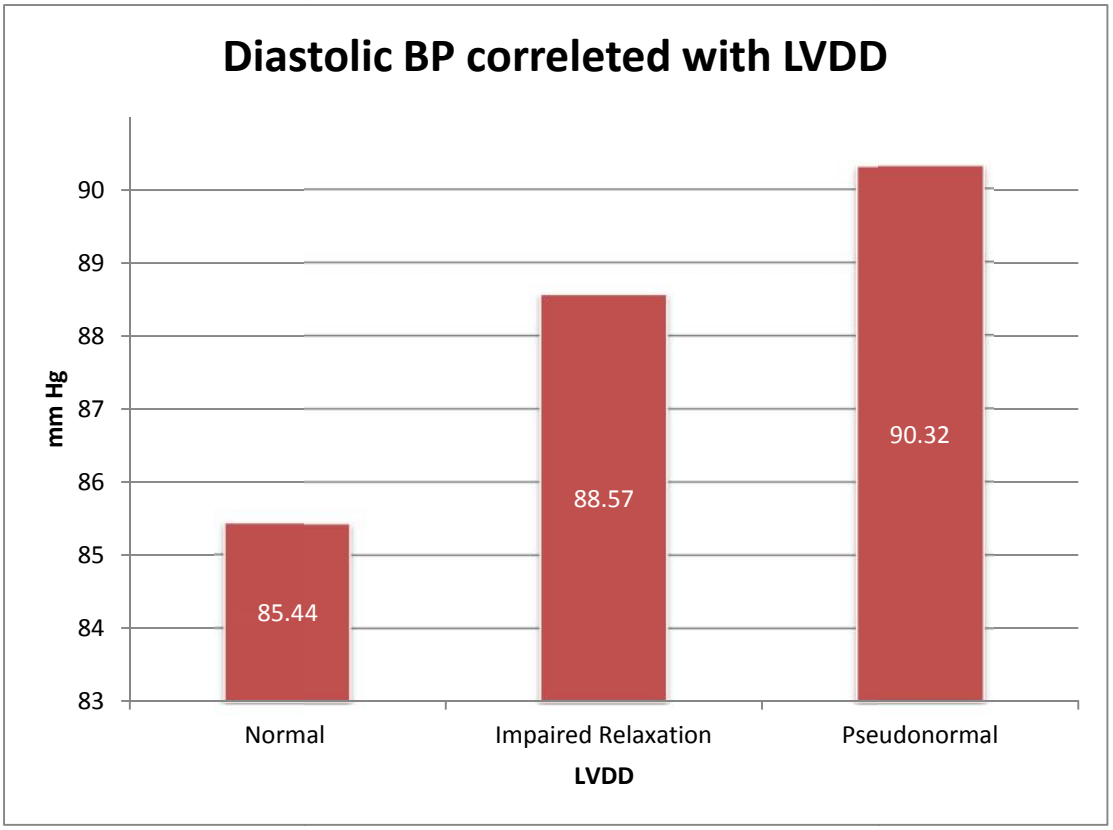
Chart 5



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

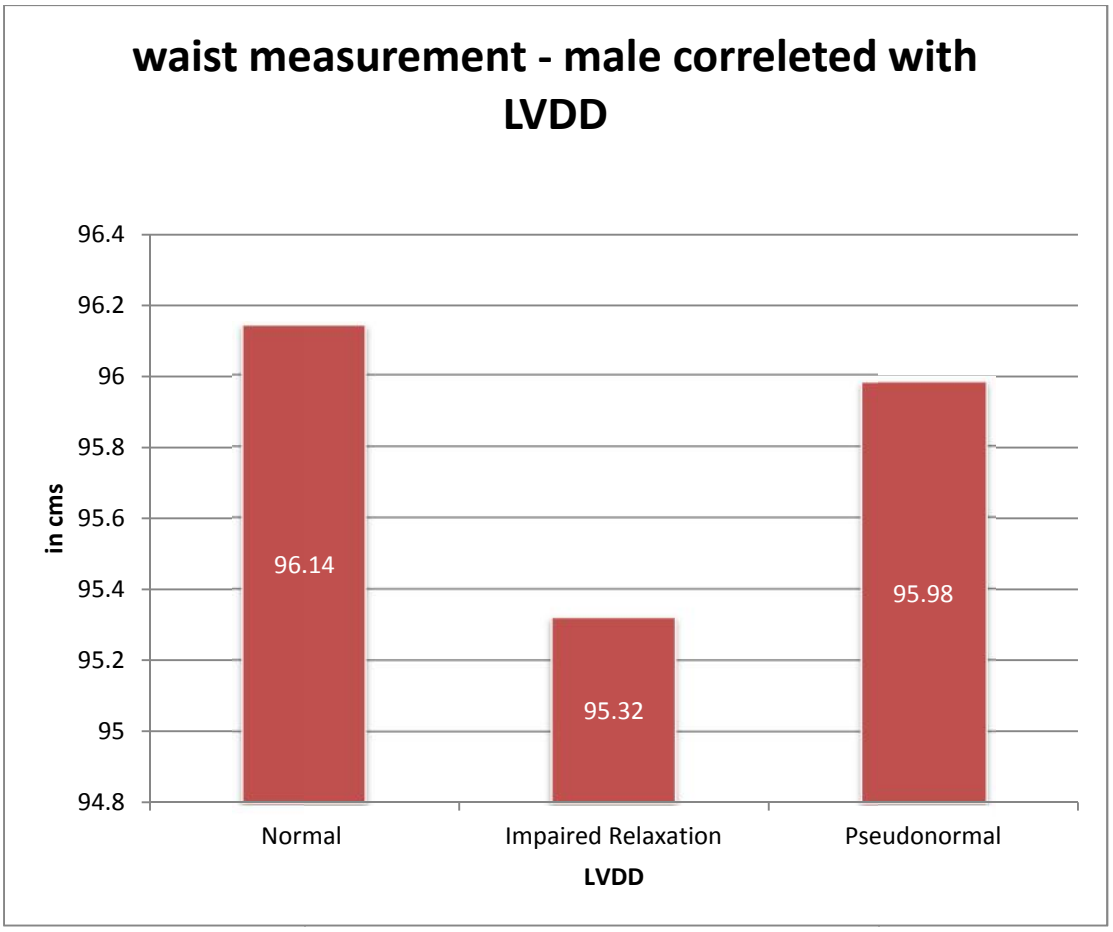
Chart 6



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

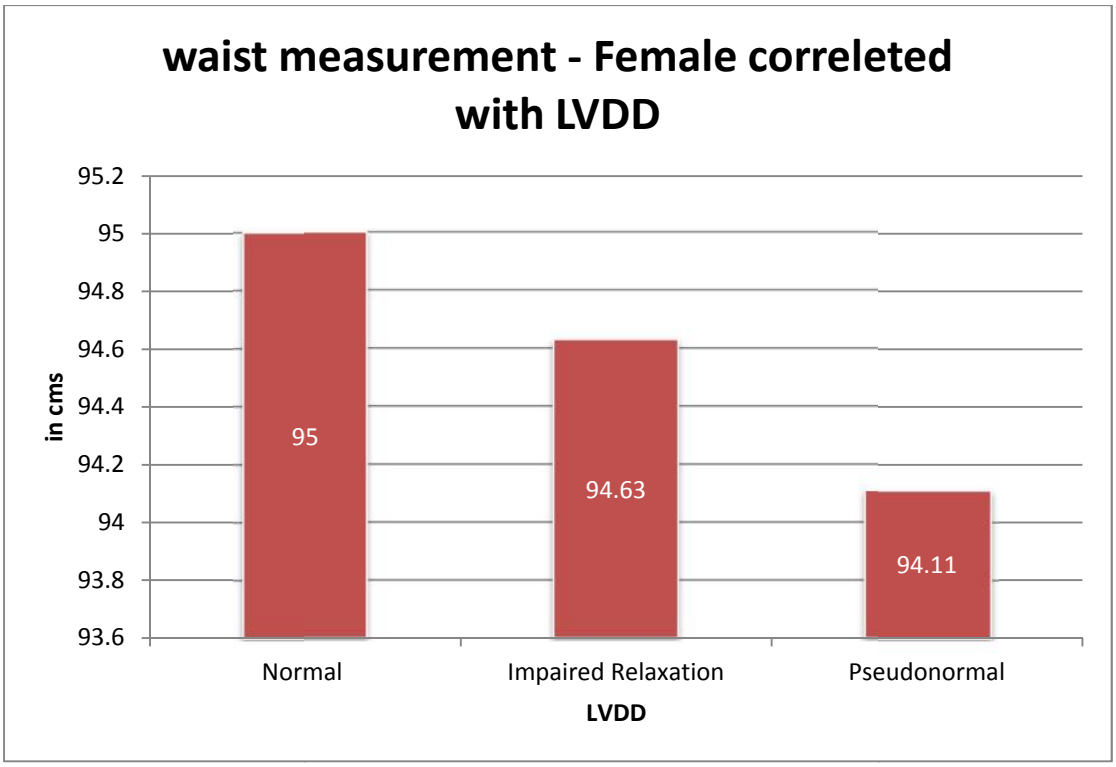
Chart 7



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

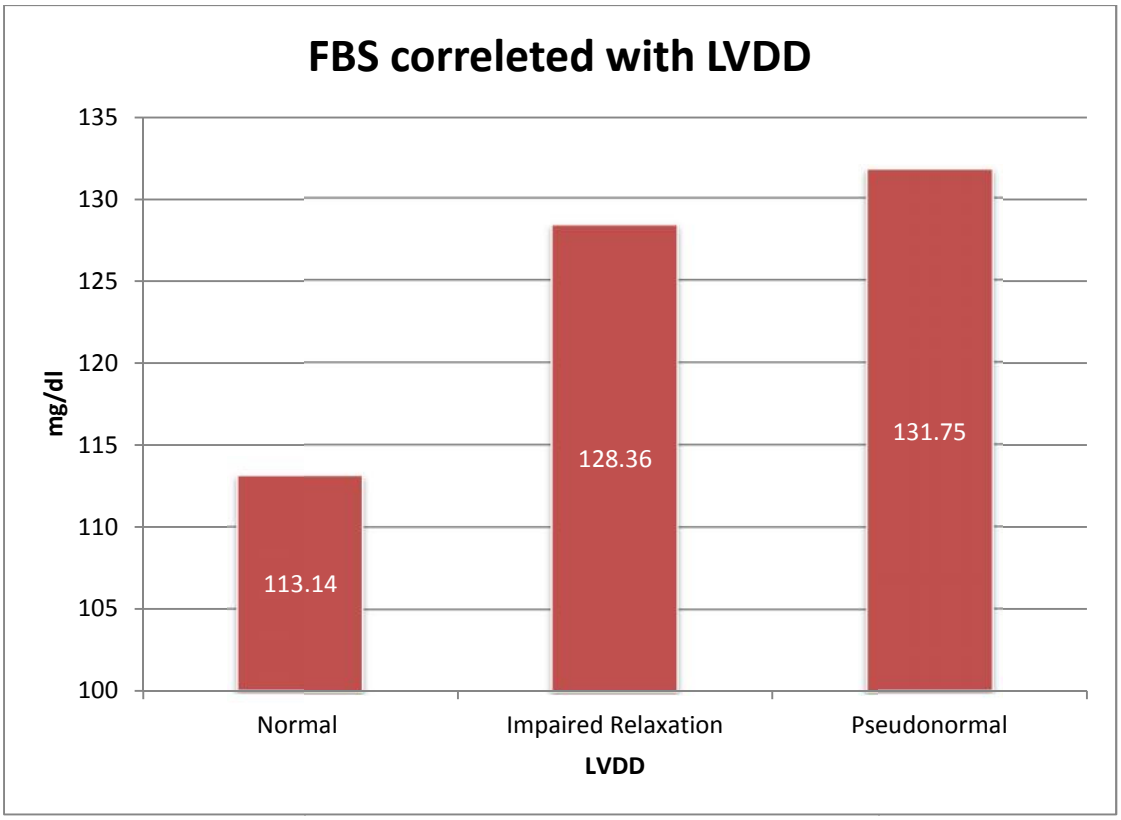
Chart 8



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

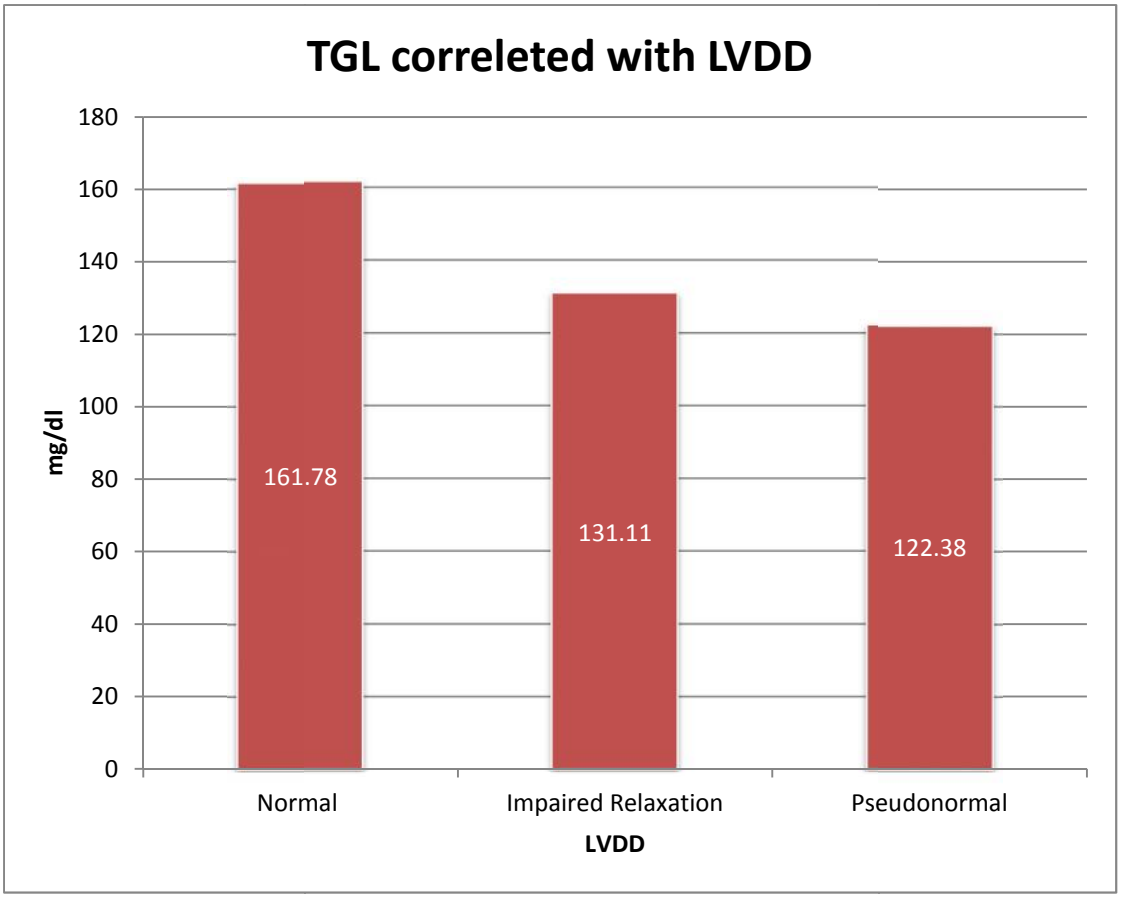
Chart 9



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

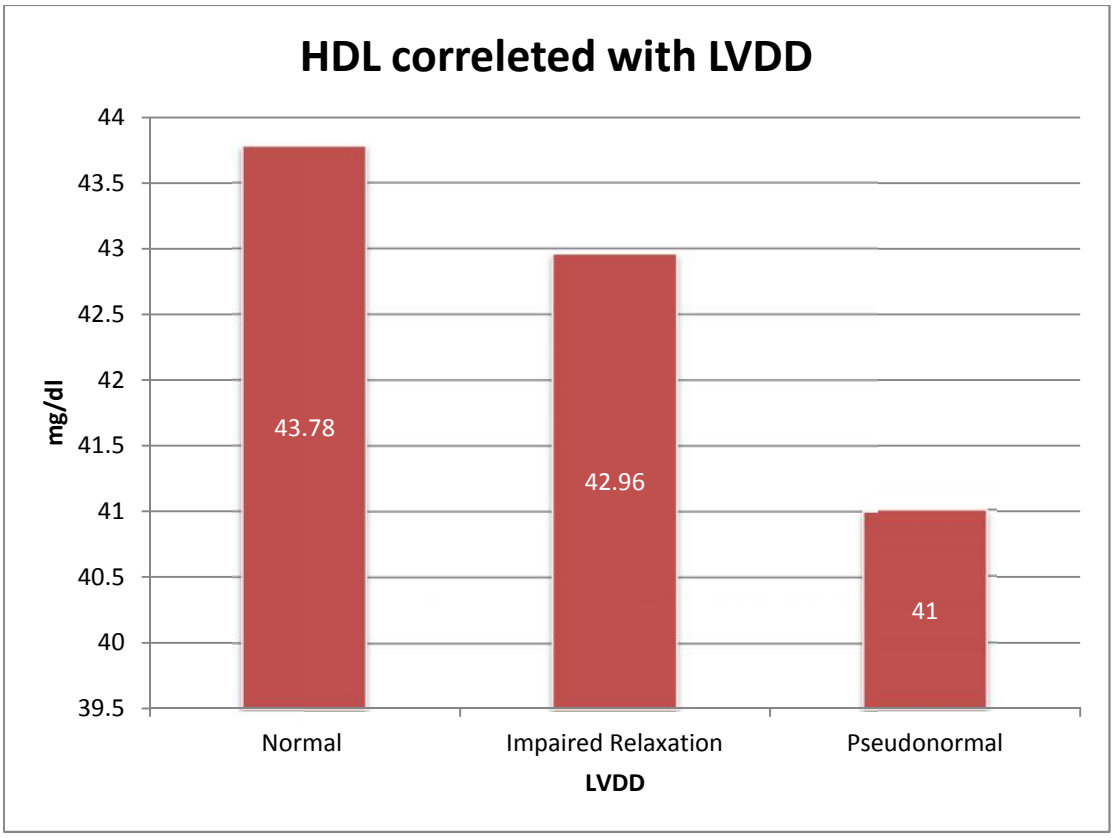
Chart 10



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 ([62]who reported LVDD 36% and Antonio Nicolino A et al [63] 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 ([64,65,66])

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 th 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/0P 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

HT - Hypertension

DM - Diabetes mellitus

WC - Waist circumferance

ECHO - Echo cardiogram

DT - Decelaration time

IVRT - Isovolumetric relaxation time

SBP - Systolic blood pressure

DBP - Diastolic blood pressure

FBS - Fasting blood sugar

TGL - Triglycerides

TC - Total cholesterol

EF - Ejection fraction

LVH - left ventricular hypertrophy

																	ECHO				
S.NO	NAME	AGE	SEX Male=1 Female=2	SMOKING No=0 Yes=1	PAST H/O HT No=0 Yes=1	PAST H/O DM No=0 Yes=1	WEIGHT(KG)	WAIST CIR(CM)	SBP	DBP	FBS	TOAL CHO	TGL	HDL	LDL	ECG Normal=1 Tachy=2 LVH=3	EF%	E (m/s)	A(m/s)	E/A	DcT(ms)	IVRT
1	CHINRAJ	55	1	1	1	0	76	98	130	90	122	198	220	47	11O	1	62	0.55	0.83	0.6626506	245	87
2	RANI	52	2	0	0	0	82	102	134	88	117	156	187	48	108	2	63	0.56	0.73	0.76712329	236	65
3	SAMPATH	44	1	1	1	0	72	92	130	90	114	185	157	44	98	1	66	0.67	0.98	0.68367347	247	90
4	MANIVEL	42	1	0	0	0	66	97	126	80	120	176	176	45	96	1	65	0.78	0.96	0.8125	228	121
5	KALYANI	36	2	0	0	0	70	96	130	80	118	156	167	44	88	1	62	0.68	0.87	0.7816092	241	87
6	SUBBARAO	39	1	1	0	1	73	92	142	88	128	178	167	46	93	3	65	0.56	0.98	0.57142857	256	105
7	PARVARHY	53	2	0	0	0	68	88	156	80	98	156	145	52	94	1	60	0.67	0.76	0.88157895	234	98
8	MALAKONDAIA	57	1	0	0	0	66	92	160	90	124	145	167	55	97	1	62	0.77	0.88	0.875	238	58
9	NIZAR	44	1	1	0	0	76	104	126	80	118	167	176	40	98	1	64	0.9	0.89	1.01123596	221	97
10	KANMANI	40	2	0	0	0	77	94	128	80	123	186	156	45	88	1	62	0.67	0.92	0.72826087	238	99
11	AZHAGAMMAL	49	2	0	0	1	78	93	146	94	98	198	156	55	110	3	66	0.55	0.78	0.70512821	249	88
12	VELU	42	1	1	0	0	72	88	138	80	123	187	152	38	98	1	62	0.67	0.88	0.76136364	248	98
13	KAMATCHI	54	2	0	0	0	75	90	136	90	129	178	145	50	102	1	64	0.76	0.78	0.97435897	230	98
14	CHELLASAMY	46	1	1	0	0	78	89	120	80	108	165	156	38	98	1	65	0.57	0.73	0.78082192	248	123
15	JEYALAKSHMI	37	2	0	0	0	81	93	120	82	98	174	152	40	89	1	65	0.67	0.78	0.85897436	237	112
16	MOH RIYAZ	42	1	0	0	0	88	87	134	88	90	176	143	43	92	1	65	0.68	0.89	0.76404494	256	105
17	SAGUNTHALA	43	2	0	0	0	72	84	140	82	108	149	176	52	87	1	64	0.68	0.98	0.69387755	254	108
18	RAJU	52	1	1	0	0	73	96	156	90	118	187	153	53	98	1	64	0.55	0.89	0.61797753	249	79
19	NATARAJAN	49	1	1	1	0	94	104	152	88	124	176	143	43	88	1	65	0.69	0.87	0.79310345	245	106
20	JOTHY	34	2	0	0	0	76	86	120	80	119	187	152	55	92	1	64	0.891	0.89	1.0011236	229	88
21	GANESAN	39	1	1	1	0	81	94	134	90	123	174	157	40	98	1	62	0.59	0.87	0.67816092	234	88
22	SELVARAJ	46	1	0	0	1	92	98	120	80	128	156	176	43	89	1	63	0.65	0.97	0.67010309	249	89
23	DHEEPA	38	2	0	0	0	84	94	128	84	98	156	162	43	92	1	65	0.56	0.87	0.64367816	256	105
24	TAMILARASI	42	2	0	0	0	79	93	132	84	116	176	158	40	97	1	64	0.57	0.78	0.73076923	245	99
25	BALAKRISHNAN	56	1	0	1	0	67	88	138	92	106	187	145	39	97	1	62	0.55	0.87	0.63218391	259	60
26	ELUMALAI	52	1	1	0	0	73	92	148	90	102	164	157	38	101	1	60	0.67	0.78	0.85897436	238	73
27	KALA	41	2	0	0	1	82	86	128	84	123	176	154	55	102	1	65	0.58	0.78	0.74358974	243	108
28	RAJENDRAN	47	1	1	0	0	91	96	120	80	119	203	162	39	108	1	59	0.58	0.93	0.62365591	251	123
29	SUBBULAKSHMI	45	2	0	0	1	79	98	142	88	135	198	178	38	105	1	64	0.52	0.93	0.55913978	264	78
30	KALIMUTHU	38	1	1	0	0	72	95	120	84	120	176	178	40	98	1	65	0.45	0.98	0.45918367	265	88
31	PITCHAIMUTHU	53	1	0	0	0	80	96	148	90	98	168	167	44	97	1	67	0.55	0.78	0.70512821	238	76
32	MADHU	43	1	1	0	0	84	93	144	80	90	178	142	39	101	1	66	0.66	0.78	0.84615385	223	98
33	VALLI	49	2	0	0	0	76	98	126	90	99	186	154	55	101	1	67	0.55	0.78	0.70512821	229	87
34	FATHIMABEEBI	43	2	0	0	0	88	102	124	82	116	176	152	55	98	1	67	0.45	0.79	0.56962025	256	76
35	JOHN	50	1	1	0	0	78	98	128	90	118	165	154	40	96	1	66	0.47	0.96	0.48958333	260	69
36	GOWRI	48	2	0	0	0	68	92	138	92	119	198	178	40	98	1	65	0.51	0.89	0.57303371	248	79
37	CHELLAMMAL	56	2	0	0	0	76	98	134	90	102	169	156	52	108	1	64	0.67	0.79	0.84810127	226	67
38	MARIYAPPAN	45	1	1	0	0	78	99	120	82	118	187	167	45	109	1	67	0.67	0.87	0.77011494	238	99
39	RAGHU	41	1	1	0	0	82	104	130	80	102	224	157	54	119	1	66	0.8	0.87	0.91954023	221	77
40	ANSAR BASHA	58	1	1	0	0	86	105	120	80	112	204	157	45	98	1	66	0.67	0.87	0.77011494	246	109
41	GEETHA	57	2	0	0	1	92	106	138	90	111	198	149	42	98	1	65	0.67	0.94	0.71276596	248	123
42	SEETHALAKSHMI	53	2	0	0	0	75	93	128	84	119	178	178	55	89	1	65	0.56	0.89	0.62921348	256	107
43	SUBRAMANI	48	1	0	0	0	78	98	134	86	112	220	173	49	98	1	63	0.57	0.8	0.7125	247	106
44	CHINNATHAMBI	55	1	1	0	0	82	93	142	80	117	185	165	45	88	1	65	0.79	0.98	0.80612245	234	97
45	CHINNAMMMAL	52	2	0	1	0	76	94	138	88	116	178	154	45	92	1	65	0.58	0.98	0.59183673	256	87
46	RAJA	48	1	1	0	0	78	95	120	80	93	189	176	39	98	1	65	0.78	0.97	0.80412371	220	98
47	KANNIYAPPAN	55	1	1	0	0	82	103	130	80	115	209	157	55	109	1	65	0.79	0.78	1.01282051	212	58
48	JAMUNA	38	2	0	0	0	90	108	120	92	98	240	171	56	107	1	64	0.89	0.98	0.90816327	231	108
49	VELAMMAL	44	2	0	0	0	94	102	120	88	116	187	152	45	98	1	62	0.57	0.87	0.65517241	265	109
50	JEYACHANDRAN	58	1	0	1	0	91	106	138	92	119	167	157	40	109	1	63	0.45	0.87	0.51724138	256	57