# STUDY OF DIASTOLIC DYSFUNCTION IN DIABETES MELLITUS

***submitted to***
***The Tamil Nadu Dr.M.G.R.Medical University***

**M.D. DEGREE EXAMINATION**
**BRANCH – I (GENERAL MEDICINE)**

**KILPAUK MEDICAL COLLEGE**

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

**APRIL 2011**

# BONAFIDE CERTIFICATE

This is to certify that this dissertation titled **"DIASTOLIC DYSFUNCTION IN DIABETES MELLITUS"** is a bonafide work of the candidate **Dr. P.SARAVANAKUMAR,** post graduate student under my supervision in the Department of General Medicine, Government Kilpauk Medical college, Chennai during the academic period 2008-2011 and being submitted to the Tamilnadu Dr. M.G.R. Medical University, Chennai in partial fulfilment of the University regulation for the award of the degree of Doctor of Medicine (MD General Medicine) March 2011.

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# ACKNOWLEDGEMENT

I thank **Prof.Dr.V.Kanagasabai, M.D**.,Dean, Govt. Kilpauk Medical College, for permitting to use the resources and clinical material of this hospital.

I owe special thanks to the superintendent Prof. **Dr.K.Thiyagarajan, M.S., MCH, DNB (URO), Prof.Dr.N.Gunasekaran, M.D., D.T.C.D** deputy superintendent, Govt Royapettah Hospital, for permitting me to use the resources.

I thank **Prof.Dr.G.Rajendran, M.D.,** Professor and Head of the Department of Medicine for granting me permission to conduct this study.

I thank, **Prof.Dr.T.Jeyakumar, M.D.,** professor of medicine, **Prof. Dr.Swaminathan M.D., D.M., Prof.Dr.N.K.Senguttuvan, M.D., D.M.,** for their valuable guidance.

I thank **Prof.Dr.K.Rajendran, M.D., Prof.Dr.N.Raghu**, **M.D**., for their encouragement and support during the course of study.

I am grateful to **Dr.P.Paranthaman, M.D., Dr.G.Ranjani, M.D., Dr.S.Kalaichelvi, M.D., and Dr.N.Jayaprakash, M.D.,** for their support during the course of study. I am grateful to all Assistant Professors of GRH and KMC for all their help during the study.

I also thank my fellow Post Graduates and House Surgeons for all their timely help they rendered. Most importantly I am indebted to all the patients, without whom this study was not possible. I am grateful to my parents, wife and my friend without whom nothing is possible. Above all I thank Almighty Lord with whom all thing is possible.

# CONTENTS

# INTRODUCTION

## DIASTOLIC DYSFUNCTION:

Diastolic dysfunction is an abnormality of diastolic distensibility, filling, or relaxation of the left ventricle and the heart fills more slowly, asynchronously or only with an increase in filling pressure.

HEART FAILURE :

Heart failure (HF) is generally defined as inability of the heart to supply sufficient blood flow to meet the body's needs.

Heart failure is a common, costly, disabling, and potentially deadly condition.

Around 2% of adults suffer from heart failure, but in those over the age of 65, this increases to 6–10% [1,2] , the condition usually worsens with time.

Heart failure is the leading cause of hospitalization in people older than 65. [3] Although some people survive many years, progressive disease is associated with an overall annual mortality rate of 10%. [4]

Heart failure [HF] is classified in to

- HF with decreased ejection fraction
- HF with normal ejection fraction [DHF]

DHF has a prevalence of almost 50 % of total heart failure, and is increasing in incidence every year thus causing a high burden to the community and health care. [5]

Eventhough earlier studies showed better prognosis for DHF, recently concluded various studies have indicated morbidity and mortality similar to HF with decreased EF [6,7] .

In addition to the traditional causes of DHF such as hypertension, aortic stenosis and others, Diabetes as a cause of Diastolic dysfunction and hence to DHF has an increased recognition in recent years.

Various studies has shown a prevalence of diastolic dysfunction to be 55 to 65 % among Diabetic individuals [120,189].

With Diabetes increasing in incidence, with increase in longevity, sedentary lifestyle and obesity, Diabetes will form a major cause of DHF, particularly, these individual risk factors most often co-exist.

With this background presence of Diastolic dysfunction in diabetic patients was studied in our hospital.

# AIM OF STUDY

1) To find out the Diastolic dysfunction among the Diabetes mellitus patient attending Diabetic OPD in GRH.
2) To find out whether the following parameters affect the occurrence of Diastolic dysfunction in Diabetic individuals.
    a. Age
    b. Sex
    c. Duration of Diabetes
    d. Smoking
    e. Alcohol
    f. Body Mass Index
    g. Diabetic Retinopathy
    h. Proteinuria
    i. Dyslipidemia

# REVIEW OF LITERATURE

## Physiology of diastole

Diastole includes the part of the cardiac cycle starting at the aortic valve closure – when LV pressure falls below aortic pressure and finishing at the mitral valve closure.

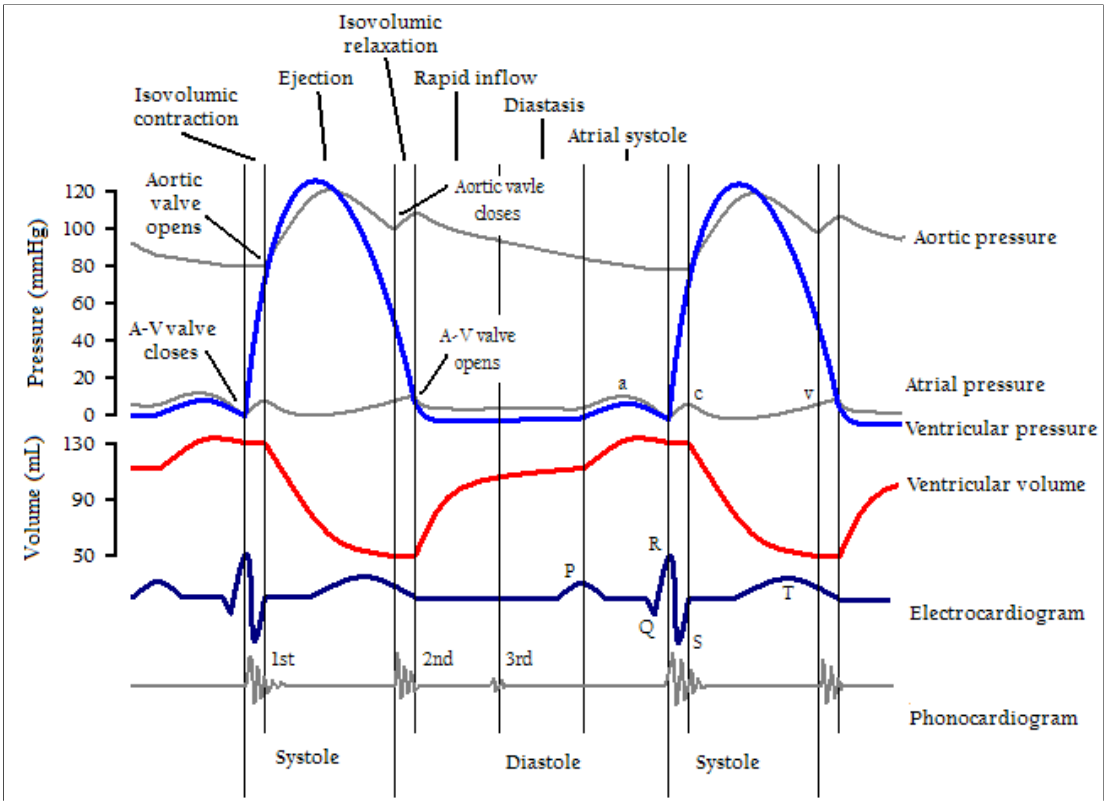
A normal LV diastolic function may be clinically defined as the capacity of the left ventricle to receive a LV filling volume able, in its turn to guarantee an adequate stroke volume, operating at a low pressure regimen.

In merely descriptive terms, diastole can be divided in 4 phases [10]:

1. Isovolumetric relaxation, period occurring between the end of LV systolic ejection (= aortic valve closure) and the opening of the mitral valve, when LV pressure keeps going its rapid fall while LV volume remains constant. This period is mainly attributed to the active LV relaxation, with a lower, variable contribution of elastic recoil of the contracted fibers;

2. LV rapid filling, which begins when LV pressure falls below left atrial pressure and the mitral valve opens. During this period the blood has an acceleration which achieves a maximal velocity, directly related to the magnitude of atrio-ventricular pressure, and stops when this gradient ends. This

period represents a complex interaction between LV suction (= active relaxation) and visco-elastic properties of the myocardium (= compliance);




The above figure shows **cardiac cycle events** occuring in the left ventricle.

3. Diastasis, when left atrial and LV pressures are almost equal and LV filling is essentially maintained by the flow coming from pulmonary veins – with left atrium representing a passive conduit – with an amount depending of LV pressure, function of LV "compliance";

4. Atrial systole, which corresponds to left atrial contraction and ends at the mitral valve closure. This period is mainly influenced by LV compliance,

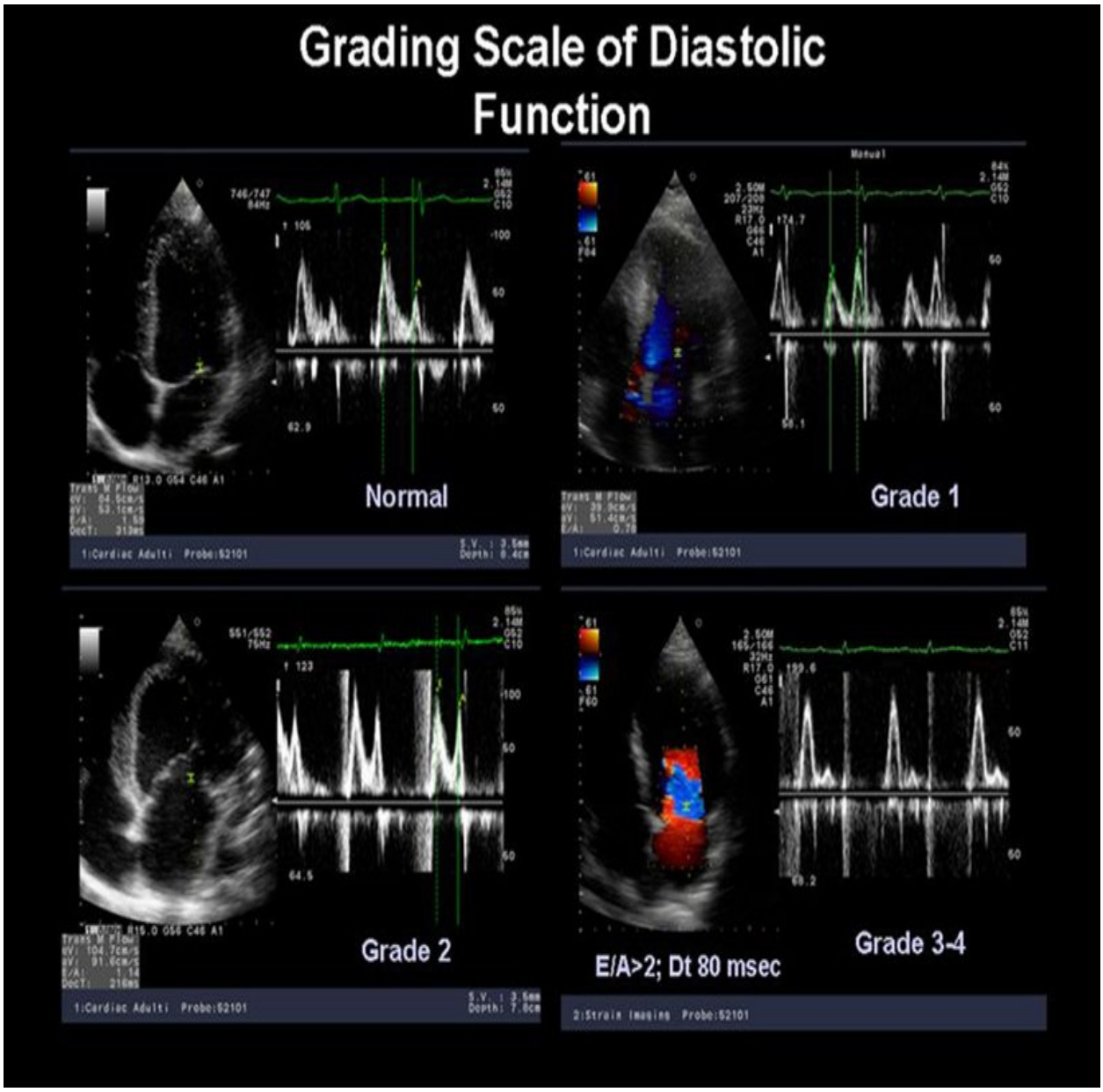



**FIGURE 1:** Grading of diastolic dysfunction from normal to severe dysfunction (grade 3-4), evaluated by Pulse Wave (PW) Doppler of mitral inflow. Normal: DT 140-240 msec; E/A 0.75-1.5. Grade 1: DT> 240 msec, E/A <0.75. Grade 2: DT 140-240 msec, E/A 0.75-1.5. Grade 3-4: DT < 140 msec, E/A > 1.5; in grade 3, the E/A ratio is reversible, when compared to grade 4, with the pre-load changes.

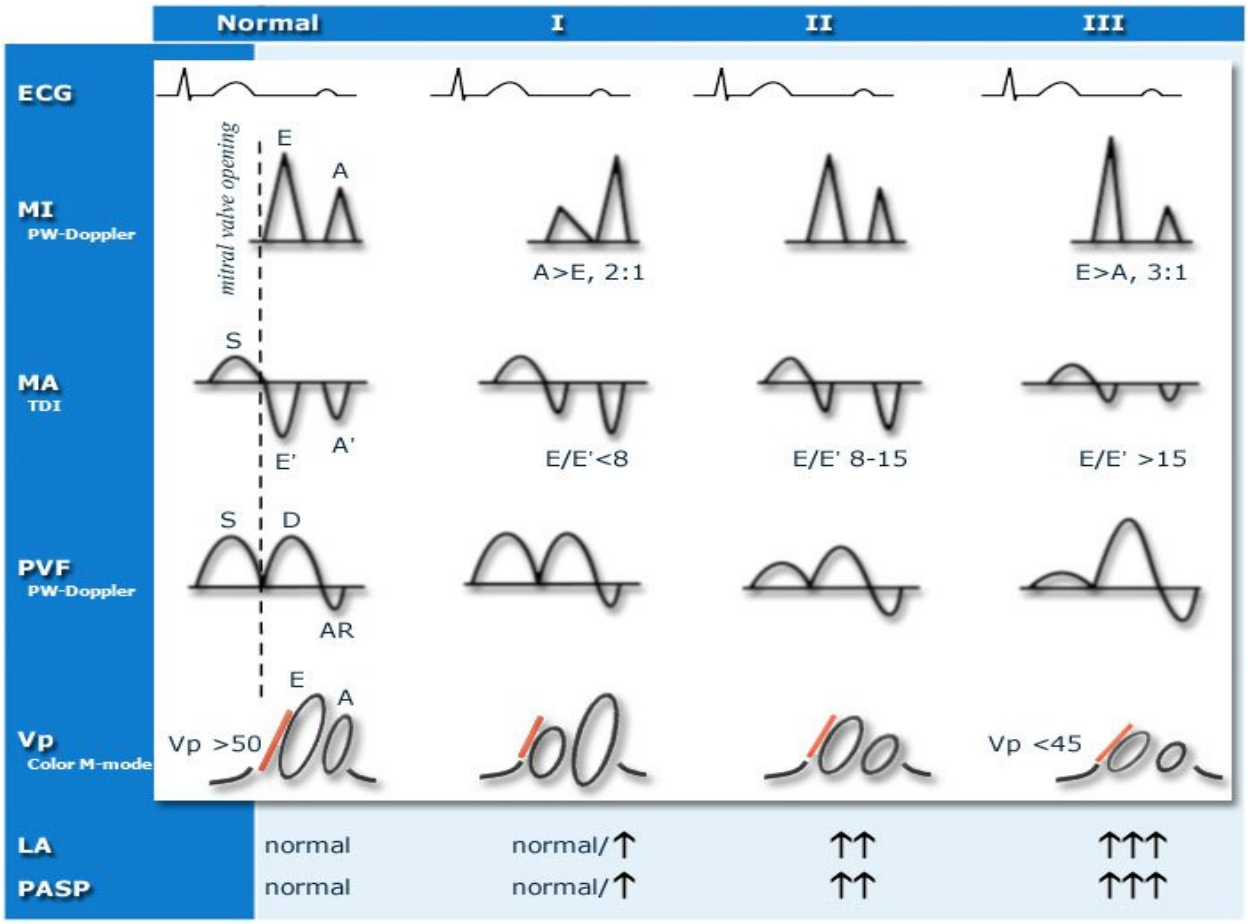



**FIGURE 2 :** Diagramatic representation - Grading of diastolic dysfunction (N, G1, G2, G3)

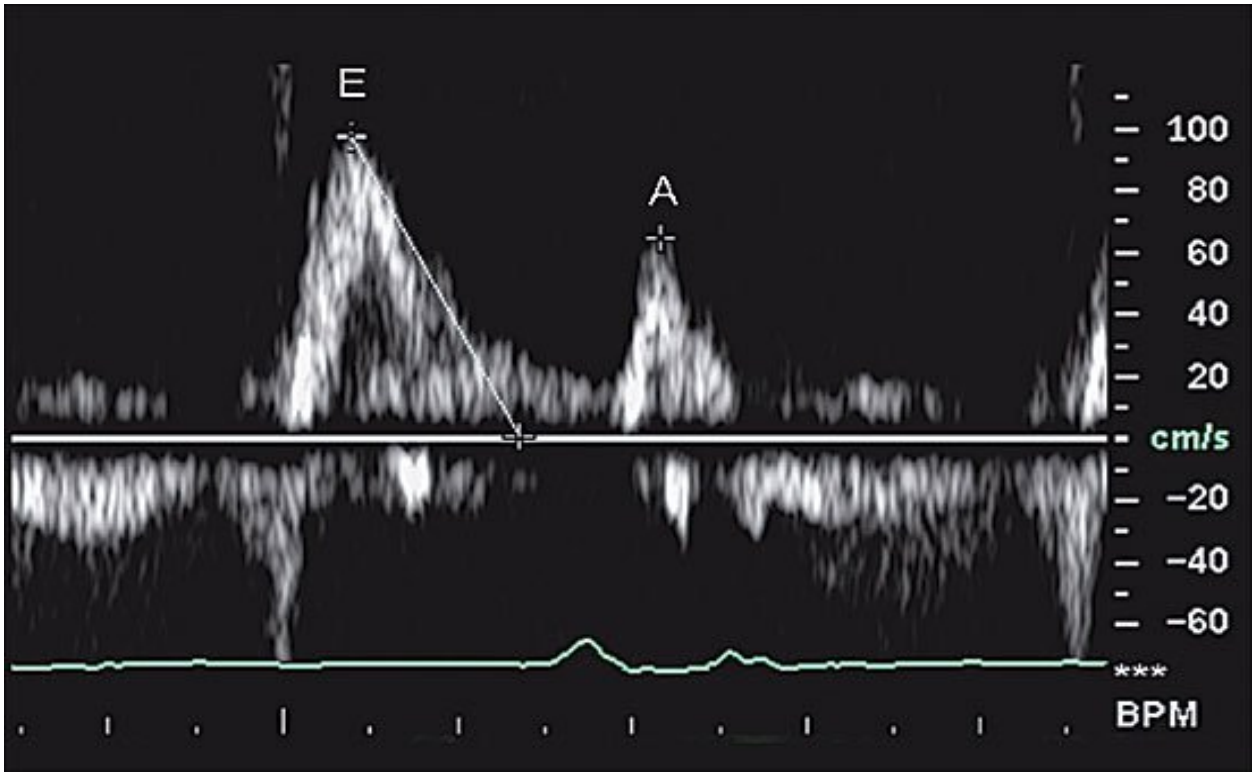



**FIGURE 3:** Normal trans–mitral-valve spectral Doppler flow pattern. The E-to-A-wave ratio is approximately 1.4 to 1.0.

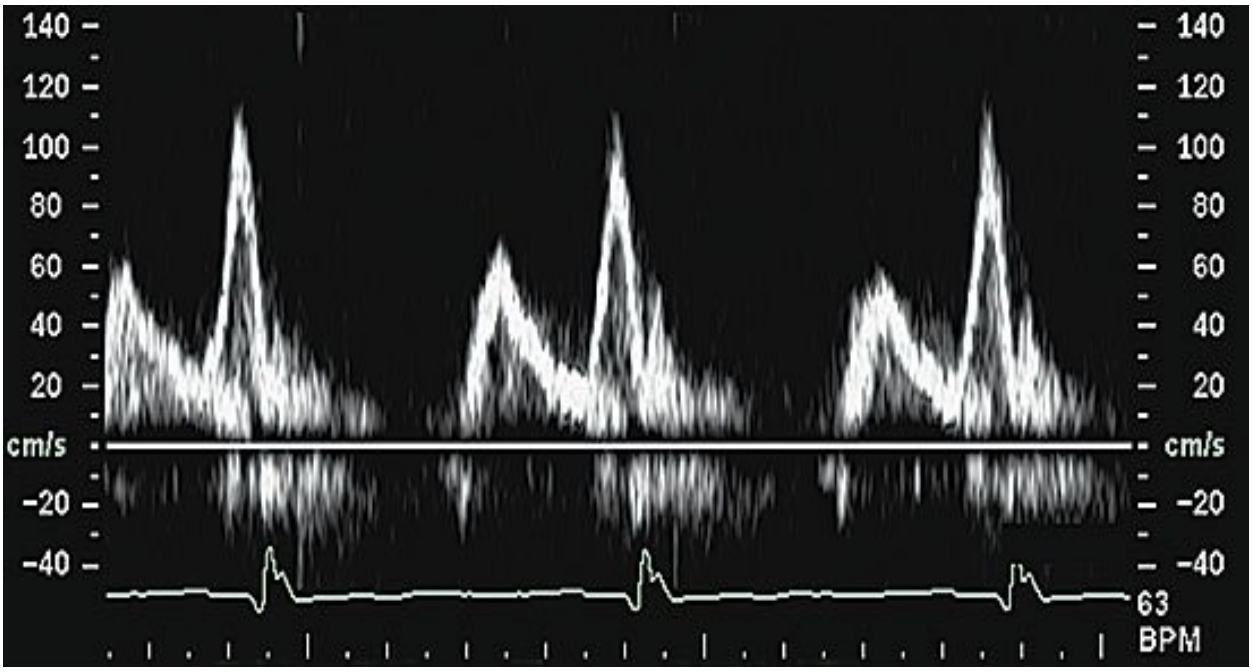



**FIGURE 4 :** Trans–mitral-valve Doppler flow tracing in a patient with mild diastolic dysfunction (abnormal relaxation). The E-to-A-wave ratio is less than 1.0.

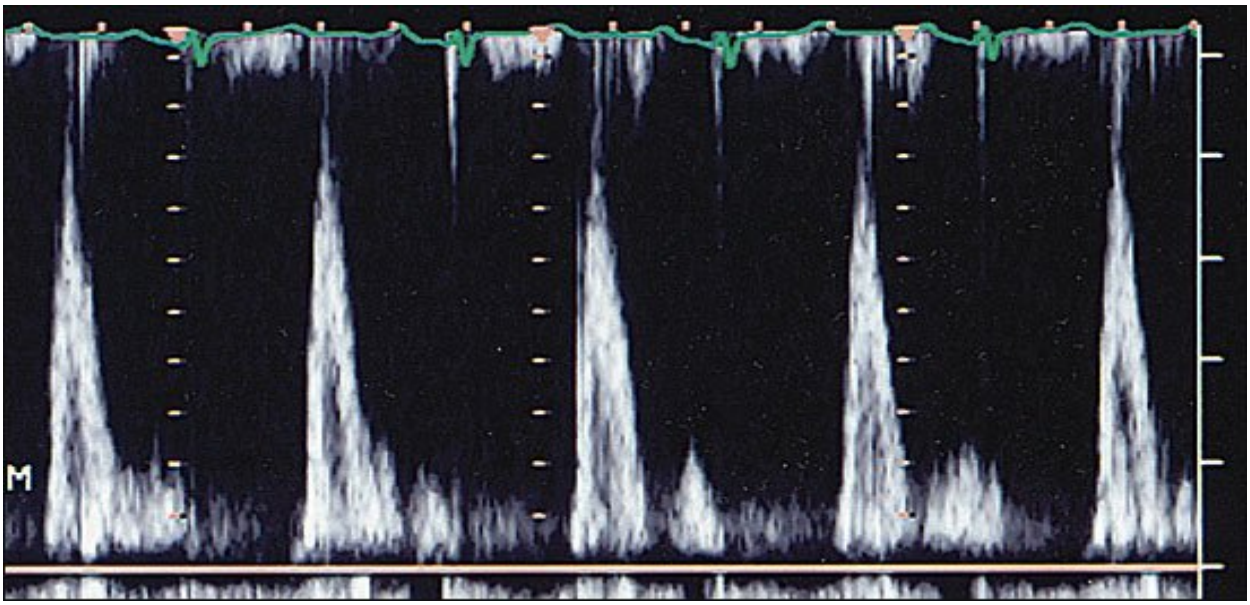



**FIGURE 5:** Trans–mitral-valve Doppler flow pattern in a patient with severe (restrictive) diastolic dysfunction. The E-to-A-wave ratio is abnormally high, and the A-wave velocity is extremely low.

but depends also by the pericardial resistance, by the atrial force and by the atrioventricular synchronicity (= ECG PR interval).

Cardiac catheterization allows to assess the pressure-volume relation along the overall cardiac cycle. Among the various hemodynamic measurements, $\tau$ (= time constant of the isovolumic pressure decline) and DP/DV ratio, expression of LV end-diastolic myocardial stiffness, are the main invasive measurements of LV diastolic function [10]. On the other hand, Doppler recording of transmitral and pulmonary venous flow measure - flow velocities and time intervals, whose variations occur in relation to analogous variations of left atrial and LV pressures [11,12]. Thus, Doppler parameters provide important information about dynamics of LV filling and LV diastolic properties during disease evolution or improvement [13].

**Ultrastructural features of diastolic dysfunction**

The extracellular matrix (ECM), corresponding to fibrillar collagen, is an important structure for processes of both myocardial contraction and relaxation. It facilities the arrangement of the cardiomyocytes into the most suitable allocation for the development of force and shortening, giving a substantial support to the maintenance of an effective myocardial performance [14].

The myocardial remodelling is accompanied by changes of myocardial cell factors but also of the ECM where fibroblast proliferation, alteration of the collagen network and increase in interstitial and perivascular collagen are strongly promoted by renin-angiotensin-aldosterone system [15]. ECM has, therefore, to be considered a dynamic entity playing a fundamental role into the myocardial adaptation to physiologic and pathologic stress [14]. ECM undergoes an intense turnover, due to balanced action of metalloproteases, proteolytic enzymes activated by several factors including also BNP, and tissue inhibitors counterbalancing the activity of metalloproteases [16]. Thus, if the collagen destruction alters both geometry and function of contractile myocardium throughout an upregulation of metalloproteases, on the other hand myocardial fibrosis occurs because of an imbalance where collagen deposition prevails over its degradation.

According to the ultrastructural view, we can hypothesize two opposite pathologic conditions: the first one, when the collagen loss, e.g, after acute myocardial infarction, deprives myocardium of its indispensable support structure, thus inducing a reduction of myocardial systolic function; the second one, when the accumulation of the same collagen, main component of myocardial fibrosis, determines both systolic and diastolic myocardial dysfunction. In this context not only the total amount of collagen is main

determinant of LV diastolic stiffness but also distribution, configuration, disorganization of collagen fibers (crosshatching), and ratio of collagen type I to collagen type III play an important role [14].

**Clinical, hemodynamic and diagnostic aspects of diastolic dysfunction:**

Clinical Aspects :

In the clinical setting the coexistence of systolic and diastolic dysfunction in patients with symptomatic HF occurs very often. In fact, LV stiffness (or compliance) is related to the length of myocardial fibers, reflecting in its turn on LV end-diastolic dimensions. LV diastolic function, through the influence on left atrial and capillary wedge pressures, determines the onset of symptom in patients with prevalent LV systolic dysfunction too. In parallel to the ultra-structural level, the clinical progression of HF may follow two different routes. In the first one, as it happens after acute myocardial infarction, postinfarction LV dilation (= remodelling) leads to systolic dysfunction and/or systolic heart failure. In the second one, LV structural abnormalities (= LV concentric geometry) induce functional alterations of DD. When diastolic dysfunction becomes symptomatic – that is, when dyspnoea occurs – diastolic heart failure rises. The majority of patients affected by isolated diastolic HF show symptoms not at rest but in relation to stress conditions (II NYHA class). Symptoms can be induced or worsened by, firstly, physical exercise but also by

events as anaemia, fever, tachycardia and some systemic pathologies. In particular, tachycardia reduces the time needed for global LV filling, thus inducing an increase of left atrial pressure and consequent appearance of dyspnoea, because of accumulation of pulmonary extravascular fluid.

The diagnosis of HF can be performed obviously by the simple clinical examination but the identification of the diastolic origin needs an instrumental assessment. In fact, the objective examination of patients with diastolic HF allows to notice the same signs occurring for systolic HF and even the thoracic X-ray can not be useful to distinguish the two entities. ECG can show signs of LVH, due to hypertensive cardiomyopathy or other causes. DD may be asymptomatic and, therefore, identified occasionally during a Doppler echocardiographic examination.

ECHO-Doppler :

The diagnostic importance of this tool rises from the high feasibility of transmitral Doppler indexes of diastolic function, shown even in studies on population [17], such to be suitable and accurate also for serial evaluations over time. To date, standard Doppler indexes may be efficaciously supported by the evaluation of pulmonary venous flow[18] and by new ultrasound technologies as Tissue Doppler [19] and color M-mode derived flow propagation rate [20]. The application of maneuvers (Valsalva, leg lifting) [21,22] to Doppler transmitral

pattern and/or different combination of standard transmitral Doppler with the new tools (ratio between atrial reverse velocity duration and transmitral A velocity duration, ratio between transmitral E peak velocity and Tissue Doppler derived Em of the mitral annulus or flow propagation velocity [Vp]) are sufficiently reliable to predict capillary wedge pressure and to distinguish accurately variations of LV end-diastolic pressure [23,24]. Some of these tools are effective even in particular situations as sinus tachycardia [25] and atrial fibrillation[26] while the pulmonary venous flow or the Valsalva maneuver applied to transmitral inflow has to be preferred in the case of mitral valve prosthesis and aortic valve regurgitation, respectively [27]. In addition, Tissue Doppler is also able to "read" the percentage of myocardial fibrosis [28], *primum movens* of DD. Alone or, better, combined together, these tools permits to recognize normal diastole as well as to diagnose and follow the progression of DD from the pattern of abnormal relaxation (grade I of DD) until pseudonormal (grade II) and restrictive (grade III-IV) patterns.

Hemodynamics :

By the hemodynamic point of view, the differences between diastolic and systolic HF are expressed by the pressure-volume loop [29]. When systolic HF occurs, increased LV filling pressures correspond to increased LV volumes, with a displacement of the loop upon and at right. In the case of diastolic HF,

the increase of LV filling pressures occur in the presence of normal or even reduced LV volumes, thus moving the loop up and to the left. It is obvious that in the more advanced stages of HF, diastolic and systolic dysfunction coexist.

**Determinants of diastolic dysfunction:**

LV DD develops in several cardiac diseases [30] as well as in extra - cardiac pathologies involving the heart (accumulation diseases as amyloidosis, thyroid disorders, acromegaly and others) [31,32] and in myocardial ischemia due to coronary artery stenosis or even to isolated dysfunction of coronary microcirculation [33]. Till now, the main cause of DD is arterial hypertension [8,9,70]. Overweight and obesity, often coexisting with the same hypertension, deeply affects LV diastolic function, forcing the left ventricle to a working overload [34]. In this view, DD represents one of the cardiac consequences of pluri-metabolic syndrome, where arterial hypertension, obesity, glucose intolerance and hypertriglyceridemia cohabit in the same subject, having their common matrix in the insulin resistance. High levels of insulin resistance, often evident in arterial hypertension [35], are positively associated with the prolongation of isovolumic relaxation time, independent of LV geometric changes and of increased afterload[36].

The alteration of diastolic isovolumic relaxation is probably due to an increment of intracellular calcium, which has been observed in insulin resistant hypertensives and is induced in its turn by an abnormal re-uptake of calcium by sarcoplasmic reticulum [37]. Also the hormones produced by adipose tissue, as leptin – involved into the control of body weight throughout food absorption and energy-giving cost – negatively affects LV diastolic function [38]. The association of arterial hypertension and diabetes mellitus worsens further Doppler indexes of LV diastolic function as shown into the population of the Strong Heart Study [39].

It is controversial whether LV DD is necessarily accompanied on the development of LVH or rises up independent of it [8,9,40-43,70]. It is true that DD is a direct sequence of pressure overload, associated to elevated 24-hour blood pressure [40] and even more to the increment of nighttime diastolic blood pressure [43]. Recent studies point out that the diastolic abnormalities of hypertensive patients are related to inappropriately high levels of LV mass, disproportionate to the hemodynamic load predicted by the individual body size and cardiac load, more than to the values of LV mass which traditionally define LVH [44]. Inappropriately high LV mass is a potent predictor of cardiovascular risk in hypertensive patients, in presence as in absence of clear cut LVH [45]. The concept of DD onset preceding the appearance of LVH is

consistent with the observation that BNP, whose levels grow gradually with the progression of DD grading (from abnormal relaxation until restrictive Doppler patterns) [46], are increased in patients with diastolic HF independent of the magnitude of LV mass [47]. Even a new ultrasound technology as Tissue Doppler supports the hypothesis of an early evidence of DD: myocardial DD (= Em/Am ratio < 1 at the level of multiple LV walls in the apical views) is detectable before the appearance of the abnormalities involving LV transmitral inflow and is uniform in non hypertrophic patients while it becomes prominent at the septum in presence of overt LVH [48]. It is now clear that diastolic HF is associated to both increase of collagen amount and LV concentric geometry [49]. This concept is further supported by the HyperGEN study where delayed LV relaxation is independently associated with concentric LV geometry in hypertensive patients including obese and diabetic patients [50].

**Definition and classification criteria for diastolic HF:**

The evidence of acute HF in absence of overt LV systolic dysfunction raised by the experience of Gandhi and coworkers [51]: where hypertensive patients affected by pulmonary oedema, undergoing echocardiographic examination during the acute episode and after clinical stabilization respectively (1–3 day after), did not show significant variations of LV EF (50 ± 15% and 50 ± 13% respectively, NS) and of wall motion score index between

the two examinations. This clinical condition, defined as heart failure with preserved systolic function or, better, with normal EF, has been made equal to isolated diastolic heart failure. A truly correct definition of this clinical entity should, however, be done on the grounds of direct estimation of LV diastolic function and establishment of reference normal values. Strong controversy has been developed in the previous years about this issue, with opposite scientific positions.

The American point of view, corresponding to the Framingham Heart Study investigators, has sustained the concept that diastolic HF is "definite" only when an invasive hemodynamic assessment shows diastolic alterations in the temporal proximity of the acute episode [52]. On the other hand, the European point of view (European Group on Diastolic Heart Failure)has defined diastolic HF according to criteria including clinical examination, echocardiographic assessment (normal EF) and Doppler indexes (derived by both transmitral inflow and pulmonary veins flow)[53].

Despite the obvious superiority of the invasive technique [54], it has to be taken into account that the need of cardiac catheterization for establishing a definite diagnosis of diastolic HF raises practical and even ethical issues. Practical issues are related to the low priority such examination would have in a cath-lab overloaded by coronary procedures and to the poor interest of

hemodynamists in the assessment of indexes of LV diastolic function. Ethical concern lies upon the fact that the present reliance on echo-Doppler examination of LV diastolic function makes cardiac catheterization an useless invasive procedure to this end, except very particular cases. Moreover, if it is true that the prevalence of abnormal Doppler indexes (from 38% of isovolumic relaxation time to 64% for deceleration time) is much lower to that showed by the more reliable invasive measurements (92 % for LV end-diastolic pressure and 79 % for $\tau$) [55], is also true that this can be, at least partially, due to the confounding influence of physiologic variables as age [56] and heart rate[57]. In this view, reference normal values of Doppler indexes of LV diastolic function should be done considering ranges of both age and heart rate.

It is now current opinion that the diagnosis of diastolic HF can be made even without measurement of diastolic function if three criteria are present: 1)symptoms and signs of HF (Framingham criteria), 2) LV EF> 50%, and 3) ability to rule out mitral stenosis, pericardial disease, and non cardiac causes of dyspnoea, oedema and fatigue [58]. Recent evidences further sustain the definite role of Doppler echocardiography to diagnose diastolic HF [59,60].

To date, however, no certain definition of diastolic HF exists and the recognition of its existence is not unanimously accepted [49]. Studies performed by both standard Doppler echocardiography [61] and Tissue Doppler [62,63]

demonstrated how sub-clinic alterations of myocardial systolic function are already overt in diastolic HF. Because of the use of LV EF is a rather insensitive indicator of true LV myocardial contractility, the assessment of LV long-axis function by the simple M-mode of the mitral lateral annulus could help to identify initial LV systolic dysfunction [64]. Finally, it has also to be taken into account how concomitant variables, including obesity, chronic obstructive lung disease and even myocardial ischemia,can be confounding factors leading to "false" diagnosis of diastolic HF, particularly in the elderly population [65].

**Prevalence of diastolic HF:**

The studies performed until now have assessed above all the prevalence of HF with normal EF, using standard echocardiography without Doppler. In a first meta-analysis of 1995, the investigators of the Framingham Heart Study [66] showed wide variability in the prevalence of this kind of HF (range = 13–74%) while a subsequent study involving the Framingham offspring cohort pointed out a 51% prevalence of overall HF [67]. Very recently, Hogg et al collected ten "cross-sectional" studies on population, in the United States as in several European countries, and found very high variability of HF with normal EF. The explanation of this variability is related mostly to different age and

gender of participants. It has to be considered that this kind of HF is particularly frequent in the elderly population, occurs more often in the female gender and is associated much more with arterial hypertension and atrial fibrillation than to coronary heart disease [68]. The data collected between 1995 and 1999 from Italian Network on Congestive Heart Failure (IN-CHF) are strongly consistent with these results [69]. The choice of different cut-off points for normal LV EF can be an additional reason of variability for the prevalence of diastolic HF in the above mentioned studies. As per recent studies HF with preserved EF constitutes almost half of the total [5].

**Clinical course and Prognosis of DHF :**

Morbidity in Diastolic Heart Failure and Diastolic Dysfunction

It is well known that morbidity associated with diastolic heart failure is generally quite high [74,78-84]. The 1-year hospital readmission rate can approach 50% in some series [71-73]. Patients with diastolic heart failure also tend to have frequent outpatient visits. For these reasons, the expenditures associated with diastolic heart failure rival that of systolic heart failure [85]. In CHARM-Preserved study [76], At a mean follow-up interval of 3.5 years, roughly 18% of the patients were admitted to the hospital for worsening heart failure, with 4.2% having more than 3 admissions. In study conducted by Gottdiener et al

[86] patients with diastolic heart failure are at risk for nonfatal myocardial infarction and stroke. Increased morbidity has also been documented in patients with isolated diastolic dysfunction, as opposed to overt diastolic heart failure. Even studies that examine asymptomatic, relatively young patients with documented normal coronary anatomy suggest increased morbidity in the setting of diastolic dysfunction.

Mortality in Diastolic Heart Failure and Diastolic Dysfunction**:**

The mortality rate in patients with diastolic heart failure ranges from 5% to 8% annually, as compared with 10% to 15% in patients with systolic heart failure [72,73,87]. As shown in the study done by, Redfield et al [71], Isolated diastolic dysfunction carries an elevated mortality risk as does diastolic heart failure.

Recent studies have also shown that the prognosis in diastolic dysfunction is the same as that in systolic dysfunction [6,7].

**Prognostic Indicators :**

- Clinical Predictors

  1. New York Heart Association class : Higher the class more the mortality [75]
  2. Renal function : worsening renal function as determined by glomerular filtration rate [88] affects prognosis

3. Age : age is a strong predictor of mortality in diastolic heart failure.[72,75,88]

- Brain Natriuretic Peptide

The level of brain natriuretic peptide (BNP), which correlates with diastolic abnormalities as seen on echocardiogram,[89] has received some attention as a possible predictor of outcome.

- Echo-Doppler

Diastolic heart failure is a highly prevalent disease whose incidence will likely grow in the near future, considering the high prevalence of hypertension, diabetes, and obesity [77] as well as the increasing mean age Data concerning prognosis are accumulating from prospective cross-sectional and population-based studies, especially those involving echocardiography. These data will likely improve the clinical approach to these patients by highlighting those at high risk for complications and mortality.

**DIABETES AS A CAUSE OF DIASTOLIC DYSFUNCTION :**

Diabetes is associated with increased cardiovascular complications, the most common of which are ischemic cardiomyopathy and left ventricular (LV) dysfunction. Diabetes is also associated with heart failure, mainly through its association with hypertension and coronary artery disease [90]. However, the

existence of a primary myocardial disease, “diabetic cardiomyopathy”, has been proposed as evidence has accumulated for the presence of myocardial dysfunction in diabetic patients in the absence of ischemic, valvular or hypertensive heart disease [91-97]. The existence of a diabetic cardiomyopathy was first proposed by Rubler et al in 1972 on the basis of postmortem findings [91]. Subsequently, abnormalities in both systolic and diastolic performance in diabetic subjects have been demonstrated in animal [98] and human studies [99-103]. Diastolic dysfunction has been described as an early sign of this diabetic heart muscle disease preceding the systolic damage. The pathogenesis of this ventricular dysfunction remains unknown and has been somewhat controversial [104].

Numerous studies have shown that impairment of the LV diastolic function may be detected in patients with diabetes. Diastolic LV abnormalities have been initially disclosed by cardiac catheterisation [99,105] and later by non – invasive methods. Regan et al [99] and Paillole et al [117], demonstrated in normotensive, diabetic patients without coronary artery disease, free of microangiopathy, and without clinical evidence of heart failure, increased left-ventricular end-diastolic pressure, a decreased left-ventricular end-diastolic volume with a normal ejection fraction. Non-invasive studies subsequently demonstrated abnormalities of diastolic function in the diabetic population by

using several methods: abnormal time intervals by phonocardiograms [106,107], abnormal LV filling by standard and digitized echocardiography [108-111], radionuclide studies [112] and subsequently Doppler echocardiography [113,114]. Of note, impairment of the LV diastolic function was observed in patients free of diabetic complications, hypertension and symptomatic coronary artery disease.

Diastolic abnormalities present in diabetic patients without diabetic complications or cardiovascular disease has been suggested as an earliest functional effect of a specific diabetic cardiomyopathy [115,116]. Various abnormalities in diastolic function, e.g. prolonged isovolumic relaxation period, delayed mitral valve opening and impairment in rapid diastolic filling, increased atrial contribution of LV filling, reduced E/A mitral ratio have been characteristics findings. In the large majority of studies, abnormalities of LV diastolic function have been demonstrated in diabetic patients with intact systolic function. Raev et al[116], demonstrated a high prevalence of diastolic dysfunction with preserved systolic function in asymptomatic, young, type 1 diabetic patients. Diastolic dysfunction began 8 years after the onset of diabetes while systolic dysfunction was found much later, occurring after 18 years of diabetes duration. These studies have demonstrated a shift in the filling pattern from the early passive filling phase to the late atrially augmented filling phase.

Surprisingly, until recently, the existence of the pseudonormal LV filling pattern, a more advanced stage of LV diastolic dysfunction, was not evaluated in all the previous Doppler studies. Indeed, identification of a pseudonormal filling can be easily overlooked if preload reducing maneuvers (Valsalva maneuver, Glyceryl Trinitrate) or if new echo Doppler indices are not used. In very recent studies, a pseudonormal diastolic function was reported in 17 to 28% of asymptomatic, normotensive type 2 diabetics using Valsalva maneuver[119,120] and with Glyceryl Trinitrate [121]. These studies led to the conclusion that LV diastolic dysfunction could be much more common than previously reported in this population.

The influence of diabetic complications on LV diastolic dysfunction has been investigated in several studies. Varying results have been obtained between the severity of diabetic microvascular complications and LV diastolic dysfunction [103,106-109, 113,116, 122-126].

**Diabetic Retinopathy :**

Studies performed in diabetic patients free of coronary artery disease, have demonstrated that patients with mild to severe retinopathy exhibited LV diastolic dysfunction (lower E/A values) compared to age-matched controls [114,127] or patients without retinopathy [123,128]. In the most recent report, [129] a

higher prevalence of retinopathy (49%) was encountered in patients with abnormal mitral filling pattern (E/A ratio < 1) compared to patients with a normal diastolic function (20%). This relation with retinopathy was however not constantly found. [118,130]

**Nephropathy :**

In large number of studies, [123,131-133 ], there was a gradual decrease in E/A ratio in type 1 diabetic patients according to the presence of microalbuminuria and proteinuria. It was not constant, as shown in other studies.[129 ,134]

**Autonomic neuropathy :**

Cardiac autonomic neuropathy, affecting the sympathetic or parasympathetic sections or both, has been suggested to be a potential contributor to impaired diastolic function in several studies. As shown by Echocardiography,[118] correlation between DD and,

1. Severity of cardiac autonomic neuropathy evidenced by radionuclide study.[112]
2. Myocardial sympathetic innervation function score derived from scintigraphy. [135]
3. Sympathetic dysfunction, evaluated clinically, by abnormal systolic blood pressure response to standing. [129]

4. Parasympathetic neuropathy. [130, 136,137]

**Relation with glycemic control**

Initial studies performed in diabetic animals have revealed impaired myocardial contraction and relaxation and biochemical changes reversed after adequate insulin therapy [138,139], the degree of reversibility depending on the dose of insulin [140].

The relationship between diastolic dysfunction and glycemic control in diabetic patients is still a matter of debate. In a study individuals with type 1 diabetes [141], severity of diastolic dysfunction, evaluated by computer assisted analysis of M-mode echocardiograms (time interval between minimal cavity dimension and mitral valve opening), was related to the long-term quality of metabolic control (mean value of HbA1c over the last two years).

Fiorina et al [142] demonstrated a reduction in the rate of diastolic dysfunction, evaluated using radionuclide ventriculography, in every uremic patient after a kidney - pancreas transplantation. This amelioration of LV diastolic dysfunction appeared to be positively associated with glycemic control.

Other studies have however shown a lack of correlation between impaired diastolic function and HbA1c levels, performed in type 1 diabetics [115, 103, 124, 143].

In type 2 diabetics, prospective studies reached varying conclusions, a few studies shows a positive correlation between the good glycemic control and improvement in diastolic dysfunction. [127, 144, 145]

On the other hand, some studies showed that improvement in glycemic control was not associated with changes in diastolic function even with 12 months of follow-up [146-148].

**Relation with severity of glycemic disturbance**

Few, small studies have shown relation of glucose homeostasis with Diastolic dysfunction.

In a study, subjects with normal glucose tolerance, with impaired glucose tolerance and with type 2 diabetes mellitus diagnosed by an oral glucose tolerance test according to the recommendations of the World Health Organization, they found early signs of diastolic dysfunction (assessed by E/A mitral flow ratio), not only in patients with diabetes but also in those with impaired glucose tolerance, independent of the confounding role of ischemia, body weight, and blood pressure[151,152]. They suggested that cardiac function is related to the concentration of glucose and HbA1c already below the threshold of diabetes. The limitation of the study is that done in a small population.

**Diastolic dysfunction and diabetes duration**

Older studies showed that, Evidence of an alteration in LV diastolic function at an early stage of type 1 diabetes without correlation with specific complication, in which all patients were free of cardiovascular diseases and had diabetes mellitus for less than 5 years. However, the evaluation of diastolic function used an imperfect parameter assessed by M-mode echocardiography and phonomechanography. [144,149,150]

Similar findings have been reported with Doppler echocardiography (E/A ratio), in newly diagnosed type 2 diabetic patients free of microvascular complications, without evidence of hypertension and coronary artery disease[103,143,146,147]. These observations of an impaired diastolic function in patients with newly diagnosed diabetes or with a short duration of the disease and with no microangiopathic complications suggest that this alteration may occur early in the history of type 2 diabetes and would not be related to microvascular complications. The lack of correlation between the occurrence of LV diastolic dysfunction and the duration of diabetes in these studies suggests that diabetic microangiopathy is not the only factor contributing to this dysfunction.

**Pathogenesis :**

Besides the experimental findings in animal studies, numerous studies in humans have explored the association of diabetes with histopathological abnormalities. Alterations in intramyocardial coronary arteries, similar to those seen in other organs of diabetic patients have been reported. Endothelial proliferation and subendothelial hyaline thickening with PAS-positive material in the vessel wall have been described in some but not all patients with or without overt congestive heart failure [153]. Capillary basement membrane thickening and capillary microaneurysms have also been observed in hearts of diabetics [154,155]. In the study of Zoneraich et al [156] conducted in young normotensive type 1 diabetics, a small vessel disease was reported in 72% of diabetic patients while it was present in only 12% of non diabetic subjects. Interstitial accumulation of advanced-glycated end products (AGEs), which include collagen, elastin and other connective tissue proteins, as well as fibrosis in the myocardium have been reported in biopsy or post-mortem studies of human diabetic hearts [99, 157-160]. The mechanism of collagen accumulation in the diabetic myocardium seems to be due to impaired degradation rather than enhanced synthesis [161]. The interstitial abnormalities could explain an increase in end-diastolic stiffness as well as LV mass and contribute to the diastolic dysfunction [99]. In the less advanced forms of tissue

abnormality, the interstitial changes seem to predominate for some time and are associated with preserved cell morphology that is consistent with normal systolic function. As a potential diagnostic tool, it has been suggested that collagen accumulation in the extracellular matrix of the heart is responsible for abnormal acoustic properties of the myocardium in diabetic patients [123]. The coexistence of diabetes and hypertension, has been considered as a major factor in the expression of the abnormalities in human diabetic myocardium. This concept initially suggested in diabetic rats studies [162] was illustrated in the human study of Van Hoeven et al [160]. They demonstrated, in hearts obtained at autopsy, that interstitial and replacement fibrosis and myocytolitic necrosis were substantially more prominent in heart of hypertensive diabetics than in patients with isolated diabetes or hypertension. From these data emerged the concept that this association, which is very frequent in this population, is very likely to have synergistic relationship as a cause of LV dysfunction. The pathogenesis is however not completely elucidated, which explains why the relationship of type, duration and severity of the diabetes to the myocardial abnormalities still remain uncertain.

**Concept of Coronary Flow Reserve (CFR) :**

Diabetes and coronary microvascular dysfunction :

The alterations of myocardial composition and, thus, of diastolic properties and LV filling pressure might be mediated by changes in the coronary microcirculation. Microvascular damage experienced by the diabetic heart [205] may lead to myocardial cell injury and reactive fibrosis/ hypertrophy. Although focal microvascular alterations have not seemed sufficient to account for diffuse interstitial fibrosis [206], these observations looked at structure but not dynamics of coronary microvessels. Today, the function of coronary circulation may be evaluated by transthoracic echocardiography, by visualizing the distal left anterior descending artery [207-209], and by measuring coronary flow reserve (CFR) as hyperemic to the resting velocities ratio [207-209]. The CFR has excellent concordance with intracoronary Doppler flow wire-derived CFR [207], high feasibility [208], and reproducibility [208]. In the absence of epicardial coronary stenosis, impaired CFR indicates coronary microvascular dysfunction [209]. A reduction of CFR has been documented in both type 1 and type 2 DM and seems to be a direct consequence of elevated glycemia [210,211]. An alternative explanation is insulin resistance, which alters CFR during a cold pressure test, a completely endothelium-dependent stimulus [212]. Endothelial function, another possible determinant of CFR, is impaired in early DM [213].

Also, increased cardiac sympathetic activity may account for abnormal CFR in diabetic patients [214].

The link between coronary microvascular and diastolic dysfunction in diabetes:

Diastolic dysfunction is evident in type 1 diabetic patients free of CAD when CFR impairment is also detectable [214]. A similar relationship between the magnitude of CFR reduction and the degree of myocardial DD was found in uncomplicated hypertension [215], another condition characterized by impaired coronary microcirculation. This association is not surprising because coronary flow occurs predominantly during diastole. A change in the time constant of LV isovolumic pressure fall **τ**, measured by catheterization, is associated with decreased coronary flow even in patients without CAD [216]. Both reduced CFR and DD are associated with insulin resistance [213,217], with LV concentric remodeling/ hypertrophy [204,218], with disorders of the sympathetic nervous system [214], with abnormalities of the angiotensinrenin system [219], and with endothelial dysfunction [220]. We can, therefore, suppose that coronary microvascular damage plays a mechanistic role for DD [221] or even vice versa, considering DD as the main expression of myocardial fibrosis. Determinants of microvascular dysfunction in DM, such as hyperglycemia and insulin resistance, and factors including sympathetic overdrive, endothelial dysfunction, and LV concentric remodeling, also contribute to the development

of DD. Comprehensive transthoracic Doppler evaluation of diabetic patients should include assessment of diastolic function with estimation of LVFP by tissue Doppler, and of coronary microvascular function by CFR test.

**Clinical significance of LV diastolic dysfunction in diabetes :**

Congestive heart failure is a major public health problem. Several epidemiological investigations have confirmed that up to half of patients in the community have heart failure due to diastolic dysfunction despite normal LV ejection fraction [163]. Some epidemiological and clinical arguments suggest that diastolic abnormalities may contribute to the high morbidity and mortality among diabetic patients. Indeed, in the community setting, data from the Framingham Heart Study have shown an increased incidence of congestive heart failure in diabetic subjects irrespective of coronary heart disease and hypertension [92]. It was also observed in patients enrolled in clinical trials of myocardial infarction. Despite similar LV systolic function, patients with diabetes have more pronounced heart failure symptoms, use more diuretics, and have an adverse prognosis compared with those without diabetes. One putative explanation for this discrepancy is diastolic dysfunction of the left ventricle [164]. The prognostic implications of diastolic dysfunction have been recently underlined. Diastolic dysfunction as rigorously defined by

comprehensive Doppler techniques is common, often not accompanied by recognized cardiac heart failure, and associated with marked increases in all-cause mortality [165]. It has also been demonstrated that a reduced mitral E/A ratio is independently associated with increased all-cause mortality as well as cardiovascular mortality in a population based sample of middle-aged and elderly adults [166]. It is important to point out that these prognostic data included diabetic patients for whom no specific analysis was performed. By the way, to date, the prognostic impact of isolated diastolic dysfunction in diabetics is not clearly known. The impact of isolated diastolic dysfunction in diabetes only concerned exercise ability but did not address mortality evaluation. Indeed, some studies have demonstrated that in absence of LV systolic dysfunction, the impairment of LV relaxation can influence exercise tolerance [167, 168]. LV diastolic dysfunction was supposed to influence maximal treadmill performance and explain lower maximal performance observed in patients with type 2 diabetes.

**Treatment of DHF :**

Acute Diastolic Heart Failure :

When the patient presents in acute pulmonary oedema, the management is very similar to that of systolic heart failure. The use of oxygen, morphine, nitrates and diuretics to reduce venous congestion and relieve the hypoxia is

life saving. [169,170] However, even in this acute stage, awareness that this may be diastolic heart failure as opposed to systolic heart failure would influence our management. In patients who fit the diastolic heart-failure profile of being elderly, diabetic, hypertensive, African or Asian, we need to be cautious against too aggressive a diuresis. Aggressive diuresis may cause severe hypotension, as the left ventricle has a steep pressure-volume curve. Also, tachycardia is very poorly tolerated in diastolic heart failure, and in the presence of atrial fibrillation, early use of betablockers or calcium channel blockers is warranted. [171,172]

Intermediate-Term Treatment of Diastolic Heart Failure :

After appropriate diuresis and stabilisation of the patient, one has to consider the aetiology behind the diastolic heart failure in order to define the therapeutic strategy.

Long-Term Management :

While the acute - and intermediate - term management strategies have obvious clinical benefits or good evidence base, the long-term management of diastolic heart failure lies much more in the evidence-based vacuum. However, two large-scale randomised controlled trials have recently provided some evidence base for the treatment of diastolic heart failure.

The Candesartan in Heart Failure - Assessment of Reduction in Mortality (CHARM) - Preserved study[173] use of candesartan added patients, had significantly fewer hospitalisations, and there was a trend towards reduction in the primary composite end point of heart-failure hospitalisation and death from cardiac cause.

The Seniors trial[174] use of nebivolol in diastolic heart failure with NYHA of II-IV, there was a significant reduction of the primary outcome of all-cause mortality and cardiovascular hospitalization. This implies that betablockade has identical benefit in diastolic heart failure as it does in systolic heart failure.

Left Ventricular Hypertrophy Regression :

Left ventricular hypertrophy regression (LVH) is thought to be one of the more reliable surrogate endpoints for diastolic heart failure[175-177]. Therefore, in terms of the left ventricular hypertrophy regression, ACEI, angiotensin receptor blockers, diuretics [178-180], calcium antagonists [181-182] and aldosterone antagonists [183-185] are useful agents.

Non-Drug Therapy :

It is important to recognise that weight loss, salt intake reduction and exercise can all help with left ventricular hypertrophy regression [186,187].

Cardiac rehabilitation programs are very helpful in the reconditioning of patients with diastolic heart failure [188].

Diabetic management :

Only proven treatment is long term good glycemic control and prevention of microvascular complications.

What treatment modality - insulin or OHA'S, and which OHA to be selected still needs further studies.

# MATERIALS AND METHODS

**PLACE OF STUDY** :

This study was conducted in Diabetology and Cardiac care unit GRH.

**PERIOD OF STUDY** :

From April 2009 to May 2010.

**DESIGN** :

A Prospective Case Control Study. A total of 50 Diabetic and 50 age matched Non-diabetic control were selected and ECHO-Doppler study done.

The study was reviewed and approved by the Institutional Ethical Committee, Kilpauk Medical College and Hospital, Chennai.

**METHODOLOGY** :

SUBJECT SELECTION :

A. INCLUSION CRITERIA :

Case : Diabetes mellitus patient

Control : Age-matched non Diabetic patients

B. EXCLUSION CRITERIA :

Patients with history of

1) Age more than 65 years

2) Systemic hypertension

3) Coronary artery disease

4) Valvular heart disease

5) Restrictive cardiomyopathy

6) Hypertrophic obstructive cardiomyopathy

7) Heart failure

8) Pericardial disease

9) Ejection Fraction less than 50%

10) Blood Urea >40mg/dl & Serum creatinine >0.9mg/dl for females and >1.2 mg/dl for males. Diastolic Dysfunction was diagnosed in all selected 50 DM patients and Age matched controls using M mode ECHO-Doppler – Transmitral and pulmonary vein flow pattern.

**Definition of Diabetes mellitus** :

Patients were considered to be Diabetic if,

- Individuals who are already on OHA'S or Insulin

(or)

- Symptoms of Diabetic mellitus and Random blood sugar $\geq$ 200mg/dl

(or)

- Fasting Plasma Glucose $\geq$ 126 mg/dl

(or)

- Two hour Plasma Glucose $\geq$ 200 mg/dl during an OGTT.

**Definition of Hypertension** :

Patients were considered to be Hypertensive when,

- They were already on anti – HT medications

(or)

- Documented BP of $\geq$ 140/90 mm of Hg on two or more occasions.

**Definition of Dyslipidemia** :

Values were considered to be abnormal if;

- Total Cholesterol $\geq$ 200 mg/dl
- LDL $\geq$ 100 mg/dl
- HDL $\leq$ 40 mg/dl
- TG' s $\geq$ 200 mg/dl

**Body Mass Index** :

BMI is considered abnormal if it is $\geq$ 25 $kg/m^2$

**Urine Proteinuria** :

Abnormal if Urine protein by dipstick 2+ or more

**STATISTICAL METHOD**:

Statistical Analysis was done by,

- Chi square.
- Two sample t test.
- Binary Logistic Regression.

# OBSERVATION AND ANALYSIS

Total of 50 Diabetic and 50 Non Diabetic control were subjected to ECHO-Doppler study. The mean Age group of Diabetic was 54.38 and for Non – Diabetic was 53. There were 32 and 33 males & 18 and 17 females in Diabetic and Non – Diabetic group respectively.

The variables in two groups were compared and various factors associated with Diastolic Dysfunction were analysed in Diabetic group.

The results are as follows,

## COMPARISON BETWEEN DM AND NON-DM GROUP WITH RESPECT TO:

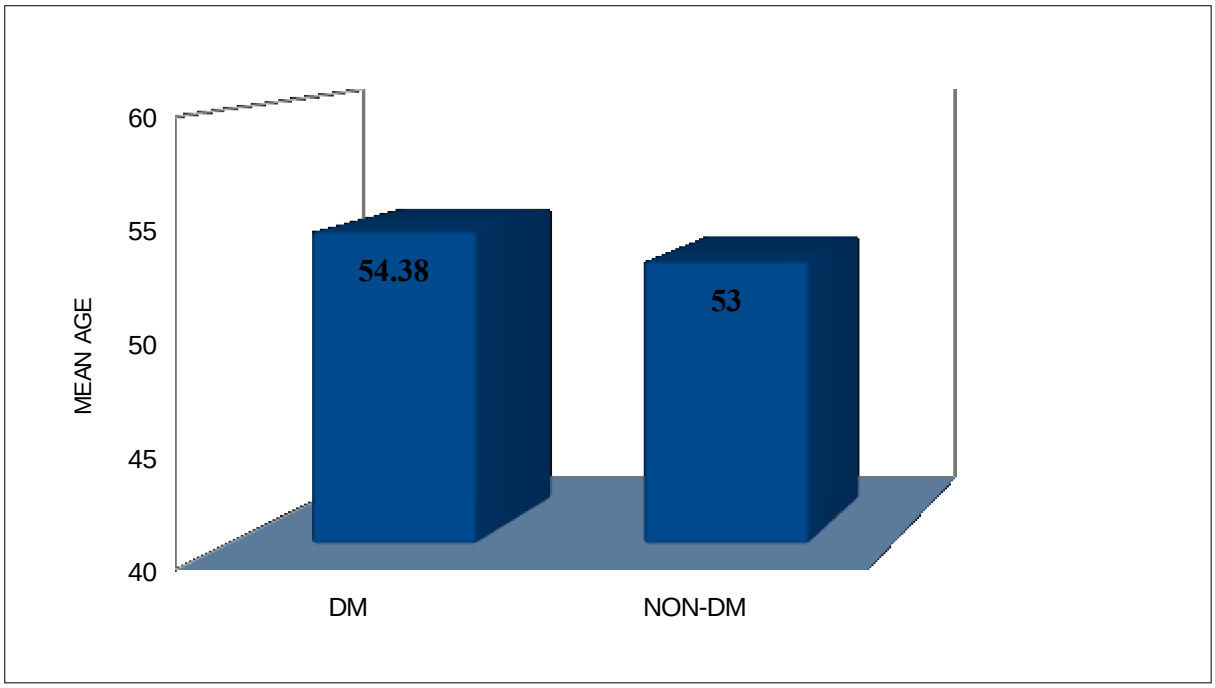
1. **AGE**
2. **SEX**
3. **ALCOHOL**
4. **SMOKING**
5. **BMI**
6. **DYSLIPIDEMIA**
7. **DIABETIC RETINOPATHY**
8. **URINE PROTEIN**
9. **ECHO DD**

# MEAN AGE

The mean age of the DM group is 54.38 and Non-DM group is 53, which is not statistically significant.

| | DIABETIC | NON-DIABETIC |
|---|---|---|
| **MEAN AGE** | 54.38 | 53 |

**p value : 0.176 ( >0.05 ) not significant**

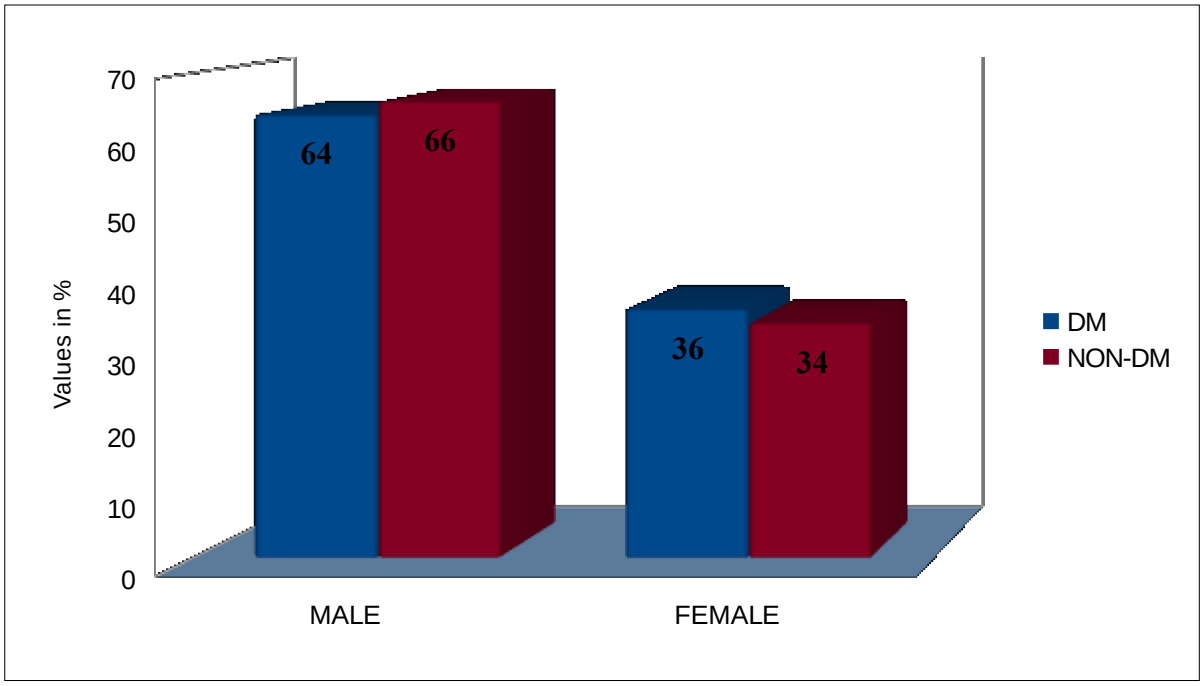


# SEX

The sex distribution between DM and Non-DM group is depicted below and not statistically significant.

| | DIABETIC | NON-DIABETIC |
|---|---|---|
| **MALE** | 64.00% | 66.00% |
| **FEMALE** | 36.00% | 34.00% |

**p value : 0.834 (>0.05 ) not significant**

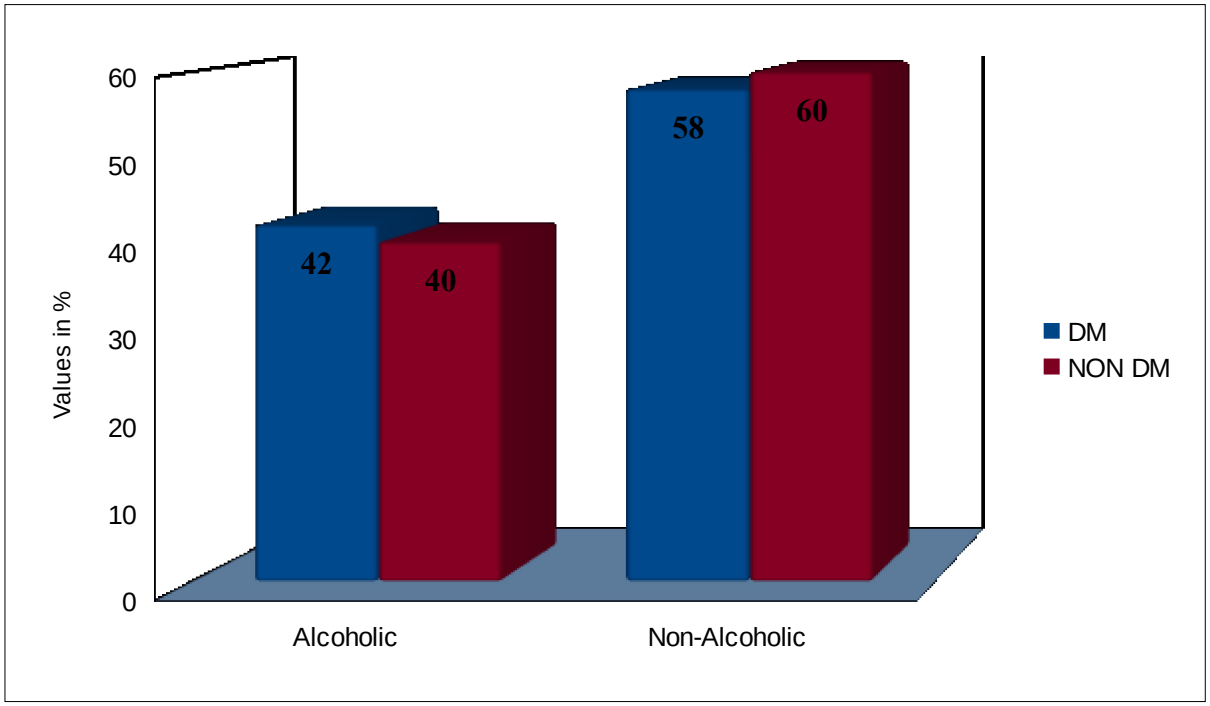


# ALCOHOL

The distribution of alcohol intake between DM and Non-DM group is depicted below and not statistically significant.

| | DIABETIC | NON-DIABETIC |
|---|---|---|
| **ALCOHOL** | 42.00% | 40.00% |
| **NON-ALCOHOL** | 58.00% | 60.00% |

**p value : 0.839 (>0.05) not significant.**

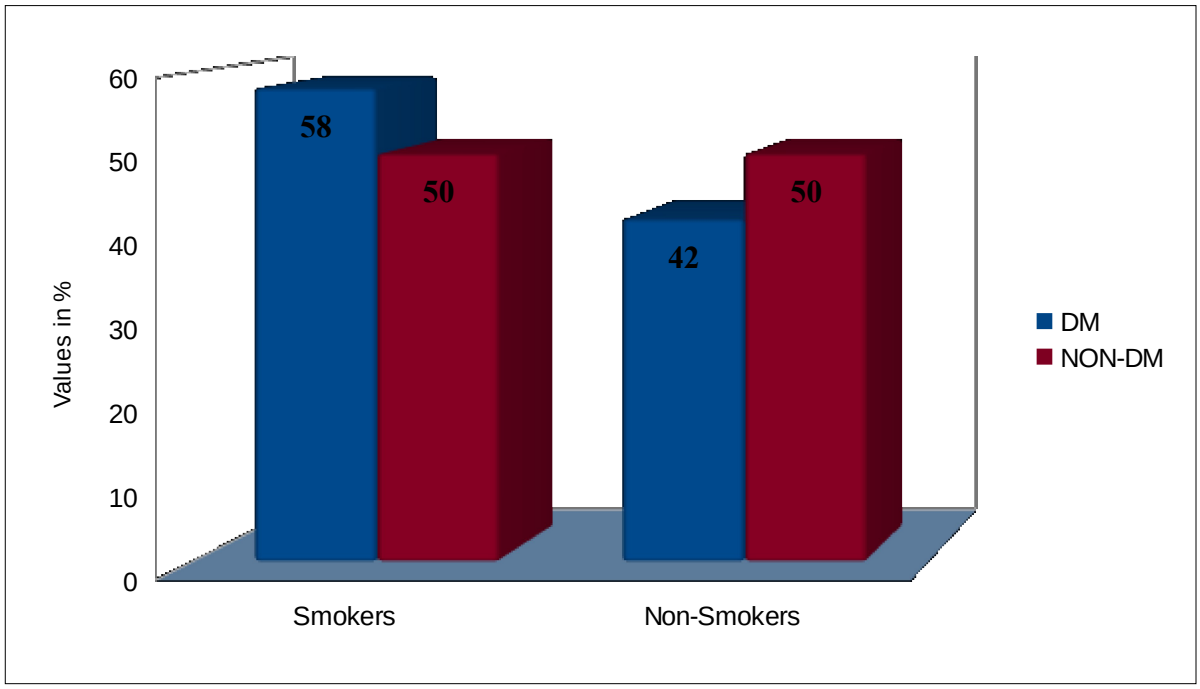


# SMOKING

The distribution of tobacco smoking between DM and Non-DM group is depicted below and not statistically significant.

| | DIABETIC | NON-DIABETIC |
|---|---|---|
| **SMOKERS** | 58.00% | 50.00% |
| **NON-SMOKERS** | 42.00% | 50.00% |

**p value : 0.422 (>0.05) not significant**

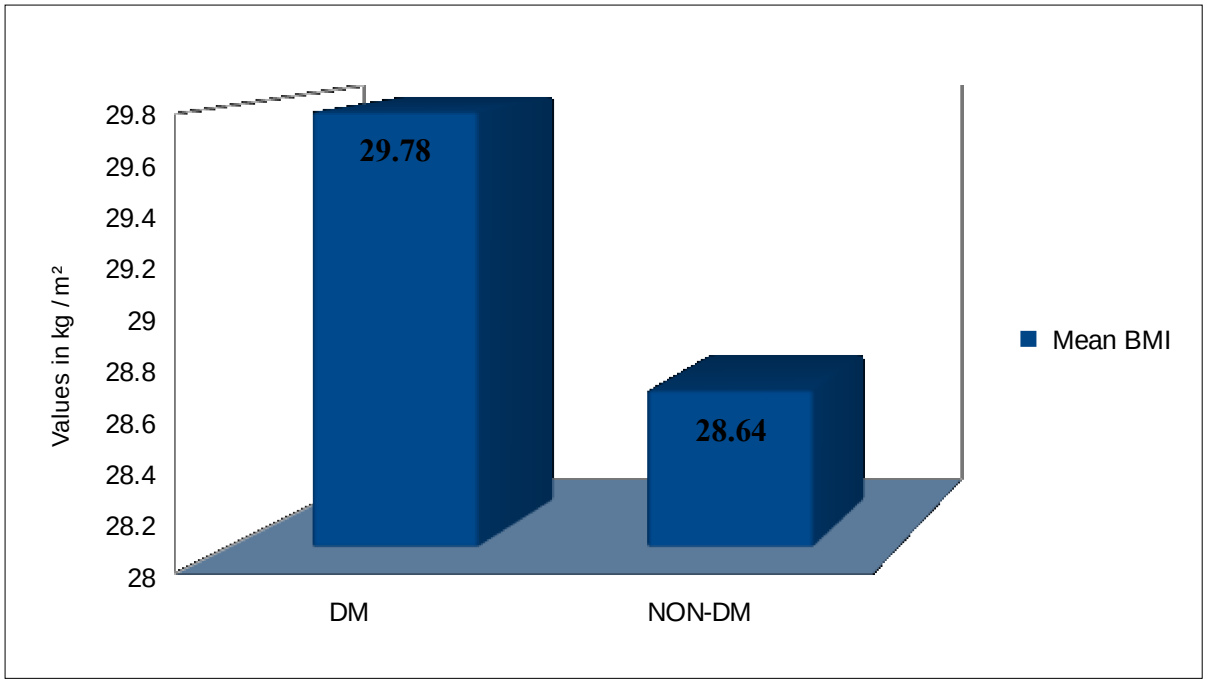


# BMI

The Body mass index (mean value) of the DM and Non-DM group is 29.78 and 28.64 respectively. It is statistically significant.

| | DIABETIC | NON-DIABETIC |
|---|---|---|
| **BMI (mean value)** | 29.78 | 28.64 |

**p value : 0.030 (<0.05) significant**



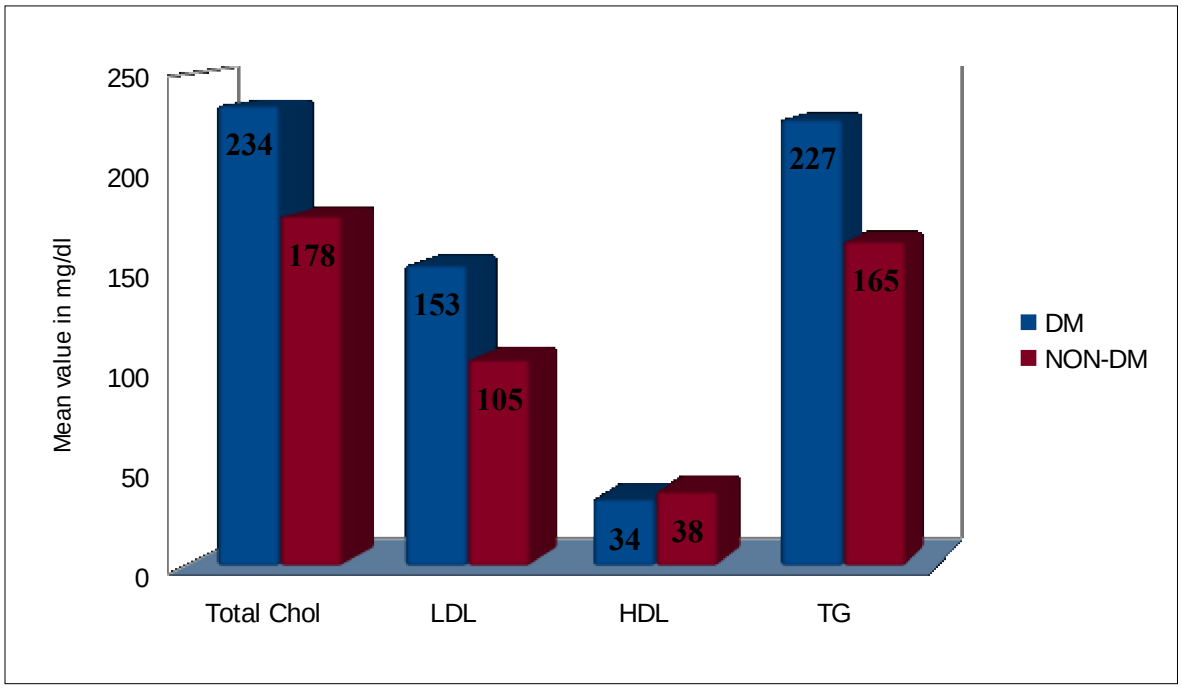

## t-test

| | | t-test for Equality of Means | | |
|---|---|---|---|---|
| | | P value | | |
| **BMI** | Equal variances assumed | .030 | | |

# DYSLIPIDEMIA (mean value)

The difference between mean value of TC, LDL and TG were statistically significant, and not so for HDL.

| | DIABETIC | NON-DIABETIC |
|---|---|---|
| **TOTAL CHOLESTEROL** | 234 | 178 |
| **LDL** | 153 | 105 |
| **HDL** | 34 | 38 |
| **TG** | 227 | 165 |



# t-test

| | | F | P value |
|---|---|---|---|
| **TOTAL CHOLESTEROL** | Equal variances assumed | 6.489 | .012 |
| **HDL** | Equal variances assumed | 2.755 | .100 |
| **LDL** | Equal variances assumed | 10.274 | .002 |
| **TG** | Equal variances assumed | 5.990 | 0.02 |

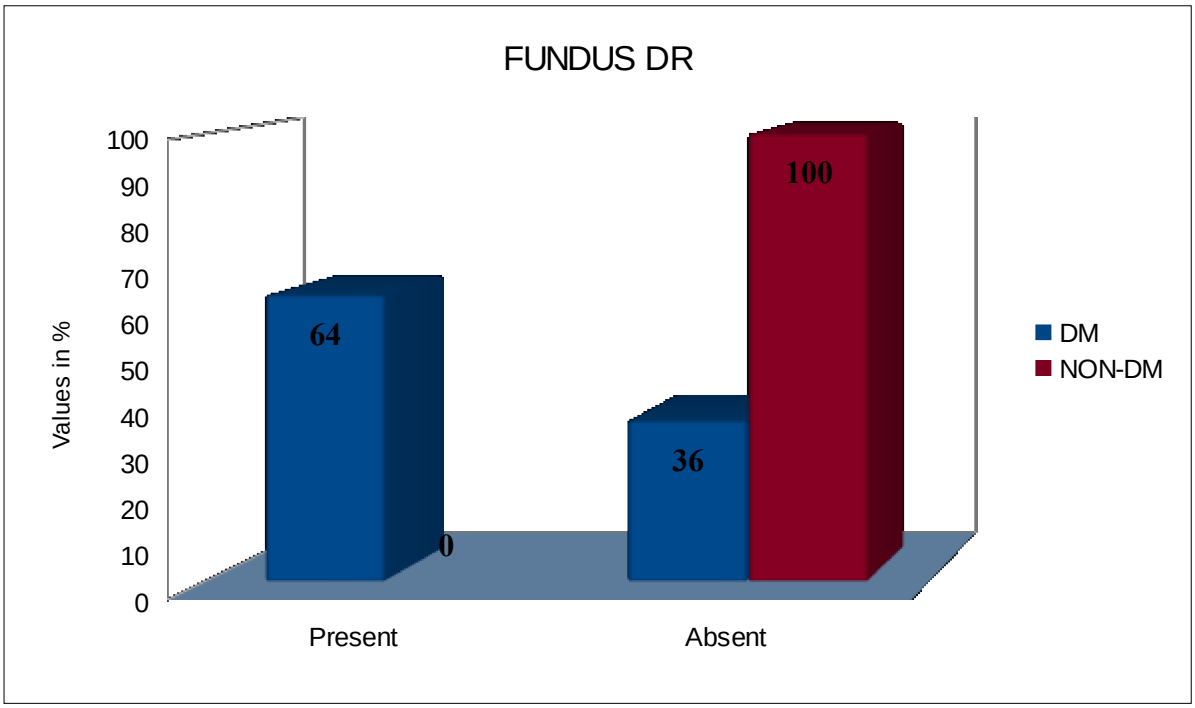
| | GROUP | N | Mean | Std. Deviation | Std. Error Mean |
|---|---|---|---|---|---|
| **TOTAL CHOLESTEROL** | DM | 50 | 234.50 | 24.337 | 3.442 |
| | NON-DM | 50 | 176.80 | 17.643 | 2.495 |
| **HDL** | DM | 50 | 34.96 | 2.432 | .344 |
| | NON-DM | 50 | 38.28 | 2.061 | .291 |
| **LDL** | DM | 50 | 153.48 | 23.907 | 3.381 |
| | NON-DM | 50 | 105.44 | 15.450 | 2.185 |
| **TG** | DM | 50 | 227.60 | 24.963 | 3.530 |
| | NON-DM | 50 | 165.04 | 36.850 | 5.21 |

# FUNDUS DR

In the DM group 32 had DR i.e. 64%, where as none had in Non-DM group. It is statistically significant.

| DIABETIC RETINOPATHY | DIABETIC | NON-DIABETIC |
|---|---|---|
| **PRESENT** | 64.00% | 0.00% |
| **ABSENT** | 36.00% | 100.00% |

**p value: 0.000 (< 0.05 ) significant**




## CHI-SQUARE TEST

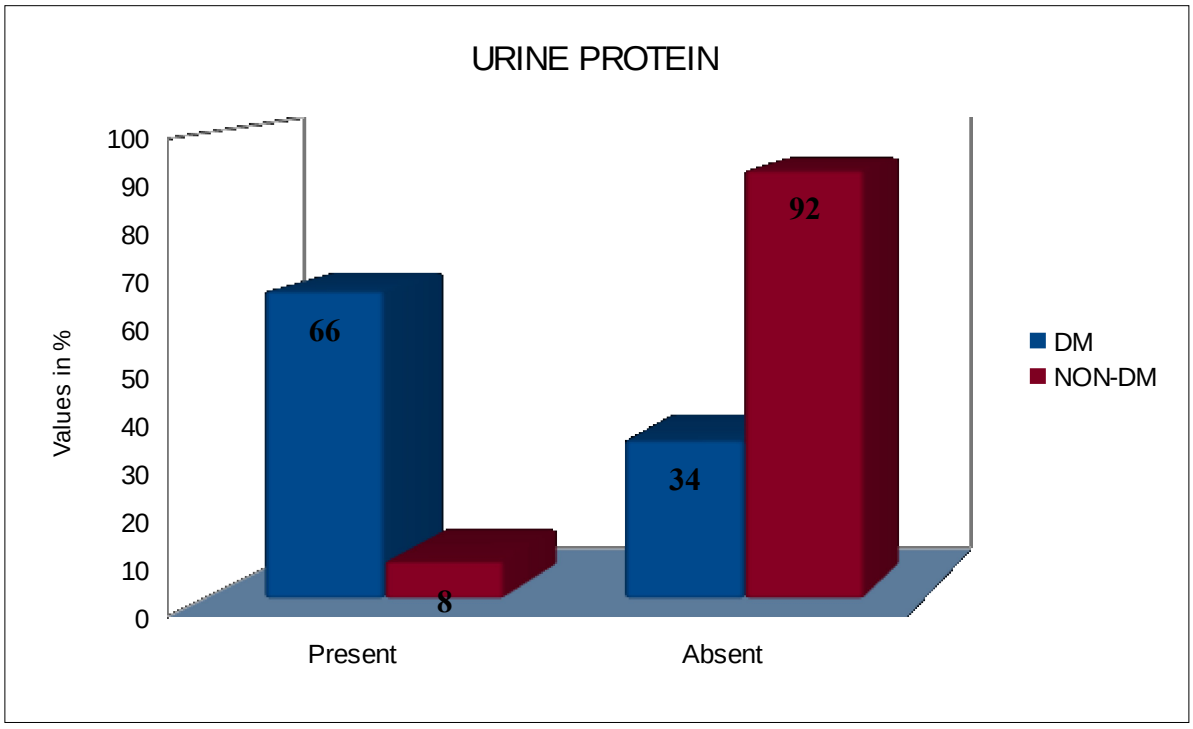
| | Value | df | P value |
|---|---|---|---|
| **Pearson Chi-Square** | 47.06 | 1 | 0 |

# URINE PROTEIN

In DM group 33 i.e. 66% had significant proteinuria where as in Non-DM group 4 i.e. 8% had which is statistically significant.

| URINE PROTEIN | DIABETIC | NON-DIABETIC |
|---|---|---|
| **PRESENT** | 66.00% | 8.00% |
| **ABSENT** | 34.00% | 92.00% |

**p value : 0.000 (<0.05) significant**




## CHI-SQUARE TEST

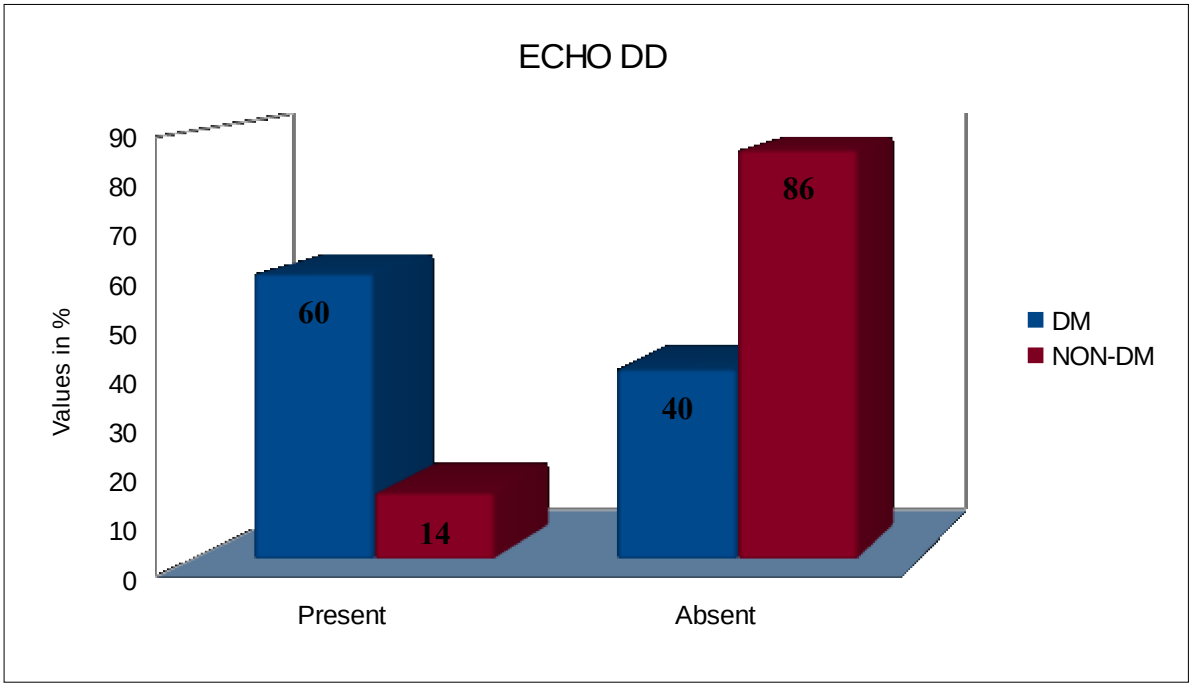
| | Value | df | P value |
|---|---|---|---|
| **Pearson Chi-Square** | 36.08 | 1 | 0 |

## ECHO DD

In the DM group 30 i.e. 60% had Diastolic Dysfunction where as Non-DM 7 i.e. 14% had DD, which is statistically significant.

| ECHO DD | DIABETIC | NON-DIABETIC |
|---|---|---|
| **PRESENT** | 60.00% | 14.00% |
| **ABSENT** | 40.00% | 86.00% |

**p value : 0.000 (<0.05) significant**




## CHI-SQUARE TEST

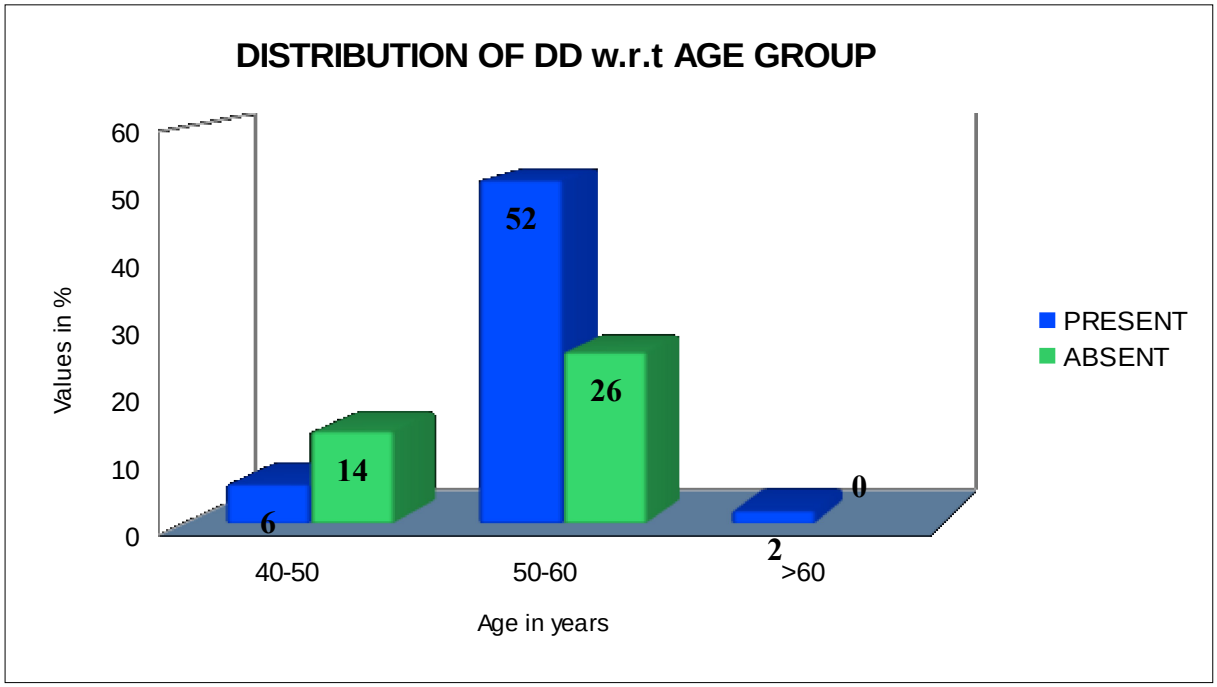
| | Value | df | P value |
|---|---|---|---|
| **Pearson Chi-Square** | 22.69 | 1 | 0 |

## COMPARISON OF THE VARIABLES WITHIN DIABETIC GROUP :

## (1) WITH RESPECT TO AGE GROUP

| | | | ECHO DD | | |
|---|---|---|---|---|---|
| | **In yrs** | | **ABSENT** | **PRESENT** | **Total** |
| **AGE GROUP** | 40 -50 | Count | 7 | 3 | 10 |
| | | % of Total | 14.0% | 6.0% | 20.0% |
| | 50 -60 | Count | 13 | 26 | 39 |
| | | % of Total | 26.0% | 52.0% | 78.0% |
| | >60 | Count | 0 | 1 | 1 |
| | | % of Total | .0% | 2.0% | 2.0% |
| | Total | Count | 20 | 30 | 50 |
| | | % of Total | 40.0% | 60.0% | 100.0% |

**p value : 0.077 ( >0.05) not significant**




## CHI-SQUARE TEST

| | Value | df | P value |
|---|---|---|---|
| **Pearson Chi-Square** | 5.14 | 2 | .077 |

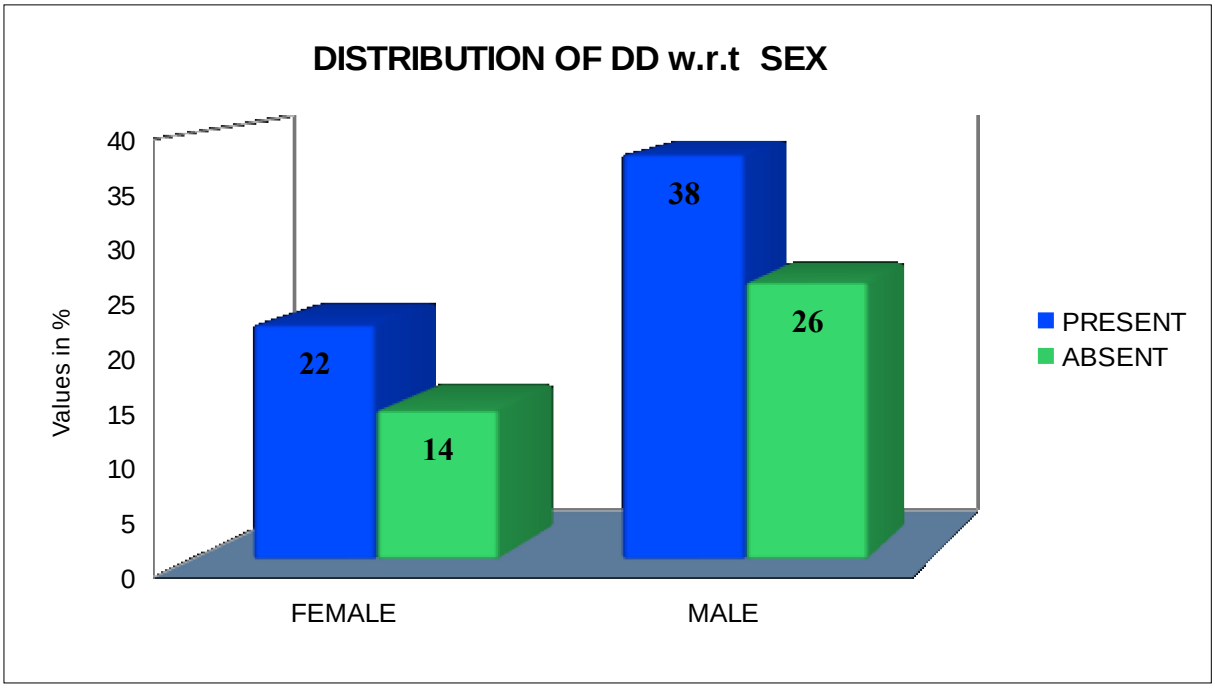
## (2) WITH RESPECT TO SEX

| | | | ECHO DD | | |
|---|---|---|---|---|---|
| | | | **ABSENT** | **PRESENT** | **Total** |
| **SEX** | Female | Count | 7 | 11 | 18 |
| | | % of Total | 14.0% | 22.0% | 36.0% |
| | Male | Count | 13 | 19 | 32 |
| | | % of Total | 26.0% | 38.0% | 64.0% |
| | Total | Count | 20 | 30 | 50 |
| | | % of Total | 40.0% | 60.0% | 100.0% |

**p value 0.904 (>0.05) not significant**

### CHI-SQUARE TEST

| | **Value** | **df** | **P value** |
|---|---|---|---|
| **Pearson Chi-Square** | 0.01 | 1 | .904 |



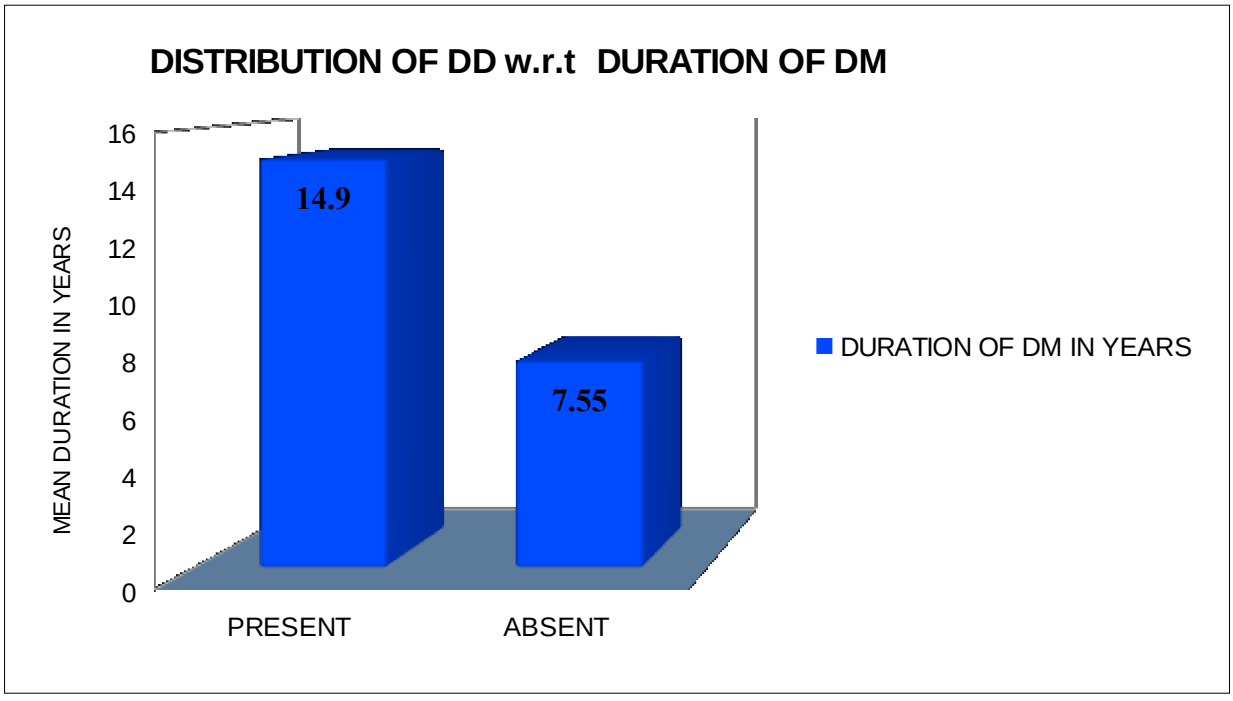
## (3) WITH RESPECT TO DURATION OF DM

| | ECHO DD | N | Mean | Std. Deviation | Std. Error Mean |
|---|---|---|---|---|---|
| **DURATION OF DIABETES** | PRESENT | 30 | 14.90 | 2.524 | .461 |
| | ABSENT | 20 | 7.55 | 1.432 | 0.32 |

**p value : 0.000 ( <0.05 ) significant**

### CHI-SQUARE TEST

| | | t-test for Equality of Means | | |
|---|---|---|---|---|
| | | df | P value | Mean difference |
| **DURATION OF DIABETES** | Equal variances assumed | 48 | .000 | 7.35 |



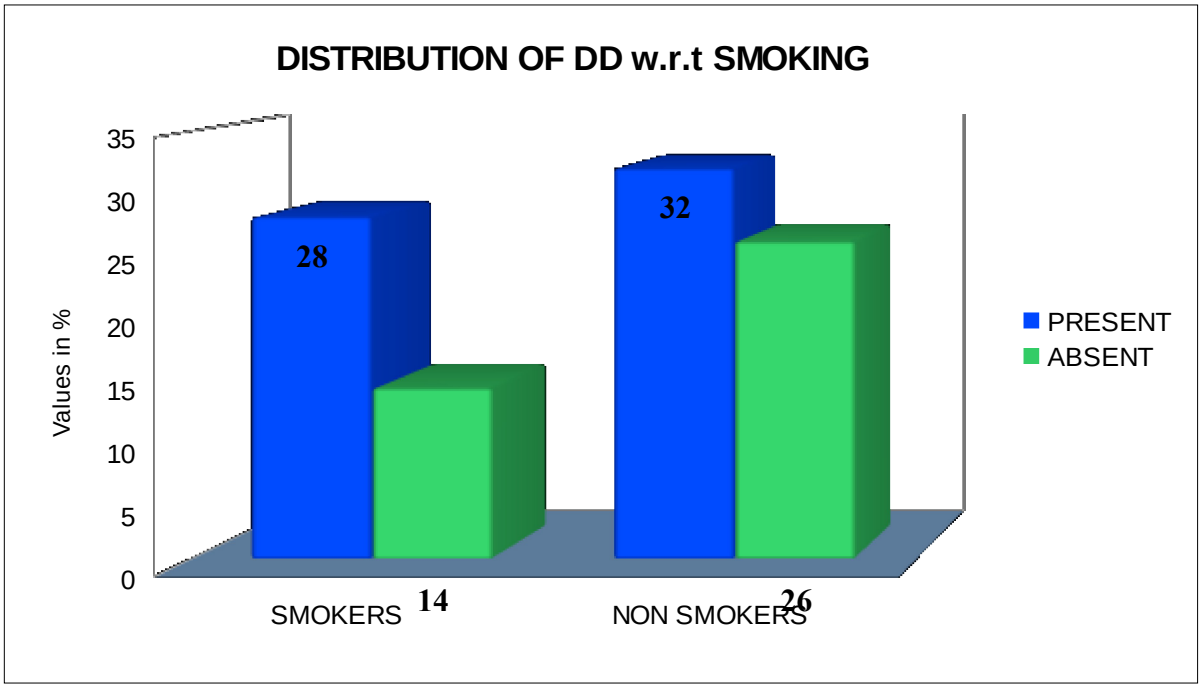
# (4)WITH RESPECT TO SMOKING

| | | | ECHO DD | | |
|---|---|---|---|---|---|
| | | | **ABSENT** | **PRESENT** | **Total** |
| **SMOKERS** | | Count | 7 | 14 | 21 |
| | | % of Total | 14.0% | 28.0% | 42.0% |
| **NON SMOKERS** | | Count | 13 | 16 | 29 |
| | | % of Total | 26.0% | 32.0% | 58.0% |
| | Total | Count | 20 | 30 | 50 |
| | | % of Total | 40.0% | 60.0% | 100.0% |

**p value : 0.413 (>0.05) not significant**

## CHI-SQUARE TEST

| | **Value** | **df** | **P value** |
|---|---|---|---|
| **Pearson Chi-Square** | 0.67 | 1 | .413 |



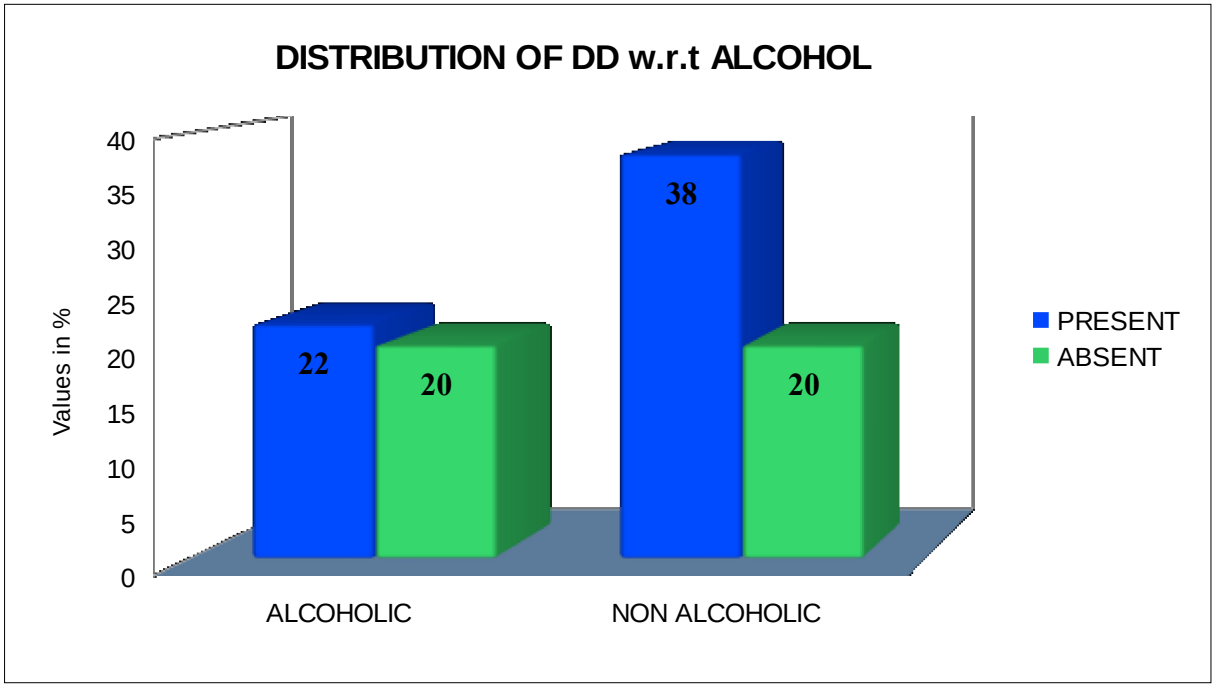
## (5)WITH RESPECT TO ALCOHOL

| | | | ECHO DD | | |
|---|---|---|---|---|---|
| | | | ABSENT | PRESENT | Total |
| ALCOHOL | _ | Count | 10 | 19 | 29 |
| | | % of Total | 20.0% | 38.0% | 58.0% |
| | + | Count | 10 | 11 | 21 |
| | | % of Total | 20.0% | 22.0% | 42.0% |
| | Total | Count | 20 | 30 | 50 |
| | | % of Total | 40.0% | 60.0% | 100.0% |

**p value : 0.349 (>0.05) not significant**

### CHI-SQUARE TEST

| | Value | df | P value |
|---|---|---|---|
| **Pearson Chi-Square** | 0.88 | 1 | .349 |



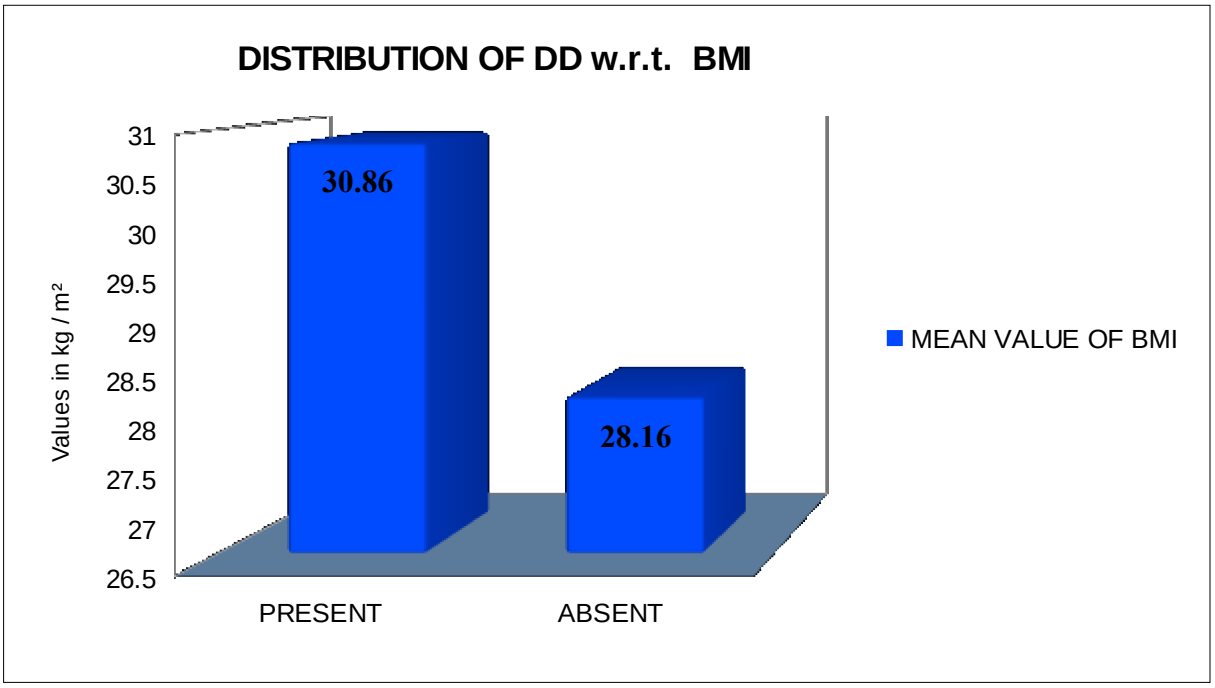
# (6)WITH RESPECT TO BODY MASS INDEX (BMI)

| | ECHO DD | N | Mean | Std. Deviation | Std. Error Mean |
|---|---|---|---|---|---|
| **BMI** | PRESENT | 30 | 30.8560 | 1.44123 | .26313 |
| | ABSENT | 20 | 28.1605 | 2.55091 | .57040 |

**p value : 0.000 ( < 0.05 ) significant**

## t-test

| | | P value |
|---|---|---|
| **BMI** | Equal variances assumed | .000 |
| | Equal variances not assumed | .000 |



# (7) WITH RESPECT TO DYSLIPIDEMIA

| | ECHO DD | N | Mean | Std. Deviation | Std. Error Mean |
|---|---|---|---|---|---|
| **TOTAL CHOLESTEROL** | PRESENT | 30 | 245.50 | 20.953 | 3.825 |
| | ABSENT | 20 | 218.00 | 19.488 | 4.358 |
| **HDL** | PRESENT | 30 | 34.80 | 2.265 | .414 |
| | ABSENT | 20 | 35.20 | 2.707 | .605 |
| **LDL** | PRESENT | 30 | 164.93 | 21.635 | 3.950 |
| | ABSENT | 20 | 136.30 | 15.550 | 3.477 |
| **TG** | PRESENT | 30 | 232.53 | 23.825 | 4.350 |
| | ABSENT | 20 | 220.20 | 25.389 | 5.68 |

## t-test

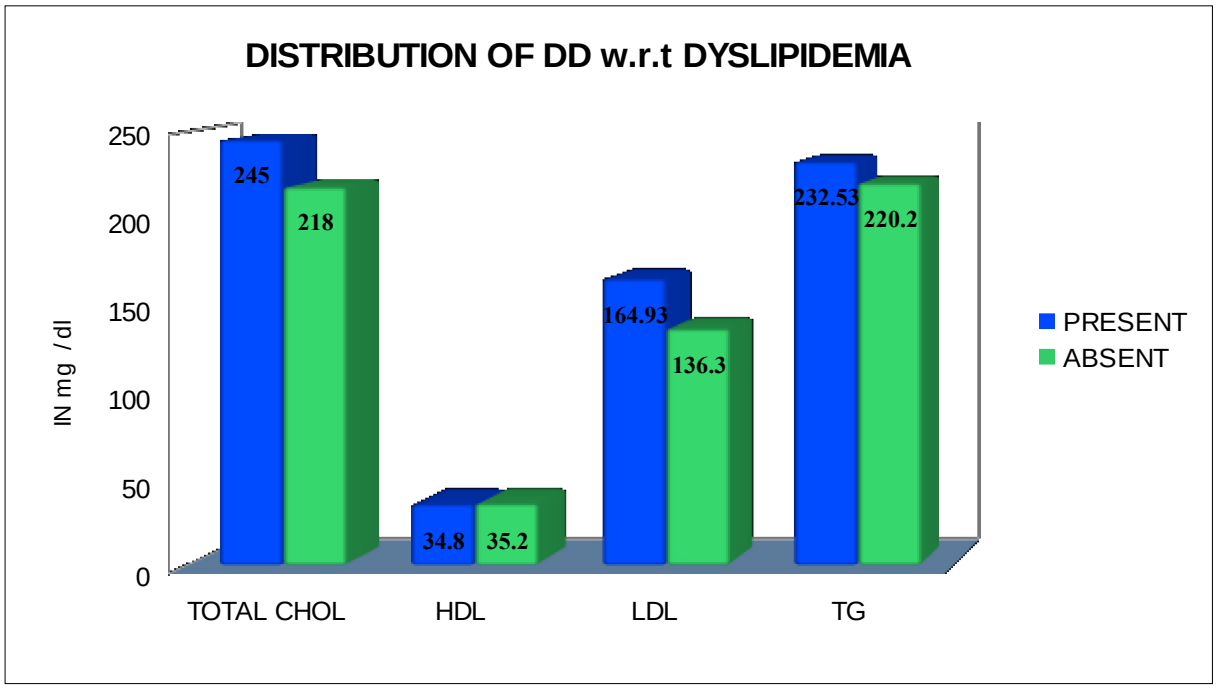
| | | t-test for Equality of Means | | |
|---|---|---|---|---|
| | | df | P value | Mean Difference |
| **TOTAL CHOLESTEROL** | Equal variances assumed | 48 | .000 | 27.500 |
| **HDL** | Equal variances assumed | 48 | .574 | -.400 |
| **LDL** | Equal variances assumed | 48 | .000 | 28.633 |
| **TG** | Equal variances assumed | 48 | .087 | 12.333 |

**p value for Total chol : 0.000 ( <0.05 ) significant**

**p value for HDL : 0.574 (>0.05 ) not significant**

**p value for LDL: 0.000 ( <0.05 ) significant**

**p value for TG : 0.087 (>0.05 ) not significant**



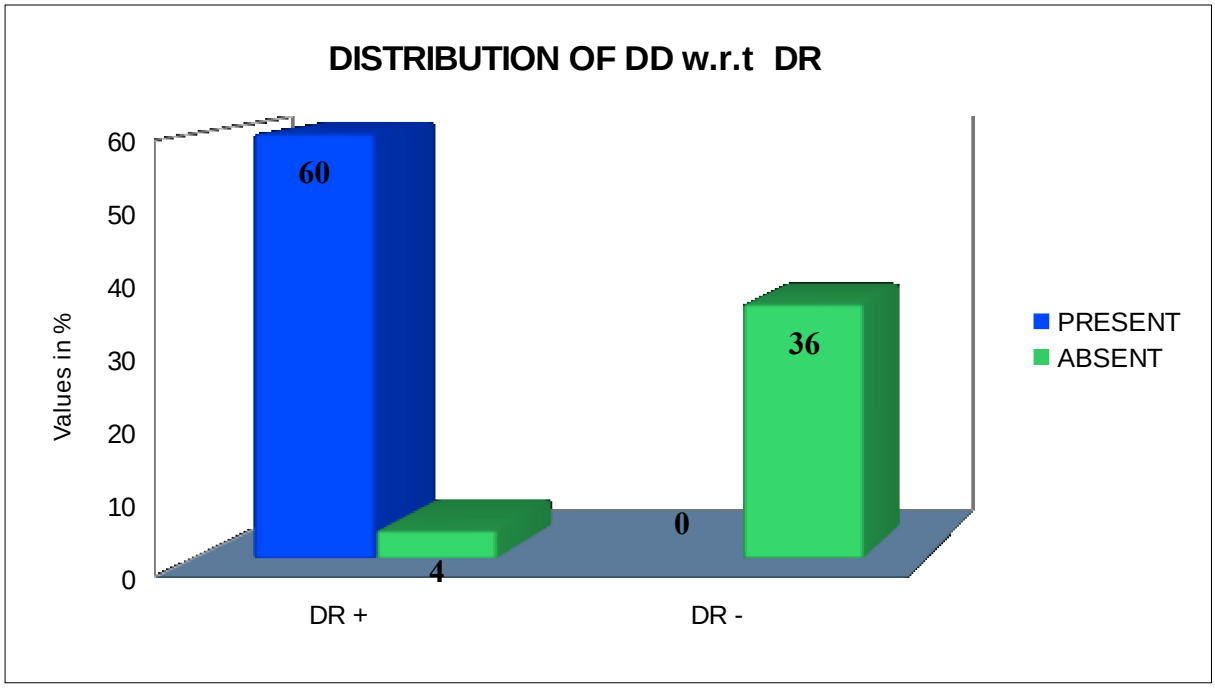
## (8)WITH RESPECT TO DIABETIC RETINOPATHY

| | | | ECHO DD | | |
|---|---|---|---|---|---|
| | | | **ABSENT** | **PRESENT** | **Total** |
| **FUNDUS DR** | _ | Count | 18 | 0 | 18 |
| | | % of Total | 36.0% | .0% | 36.0% |
| | + | Count | 2 | 30 | 32 |
| | | % of Total | 4.0% | 60.0% | 64.0% |
| | Total | Count | 20 | 30 | 50 |
| | | % of Total | 40.0% | 60.0% | 100.0% |

**p value : 0.000 ( <0.05 ) significant**

### CHI-SQUARE TEST

| | **Value** | **df** | **P value** |
|---|---|---|---|
| **Pearson Chi-Square** | 42.19 | 1 | .000 |



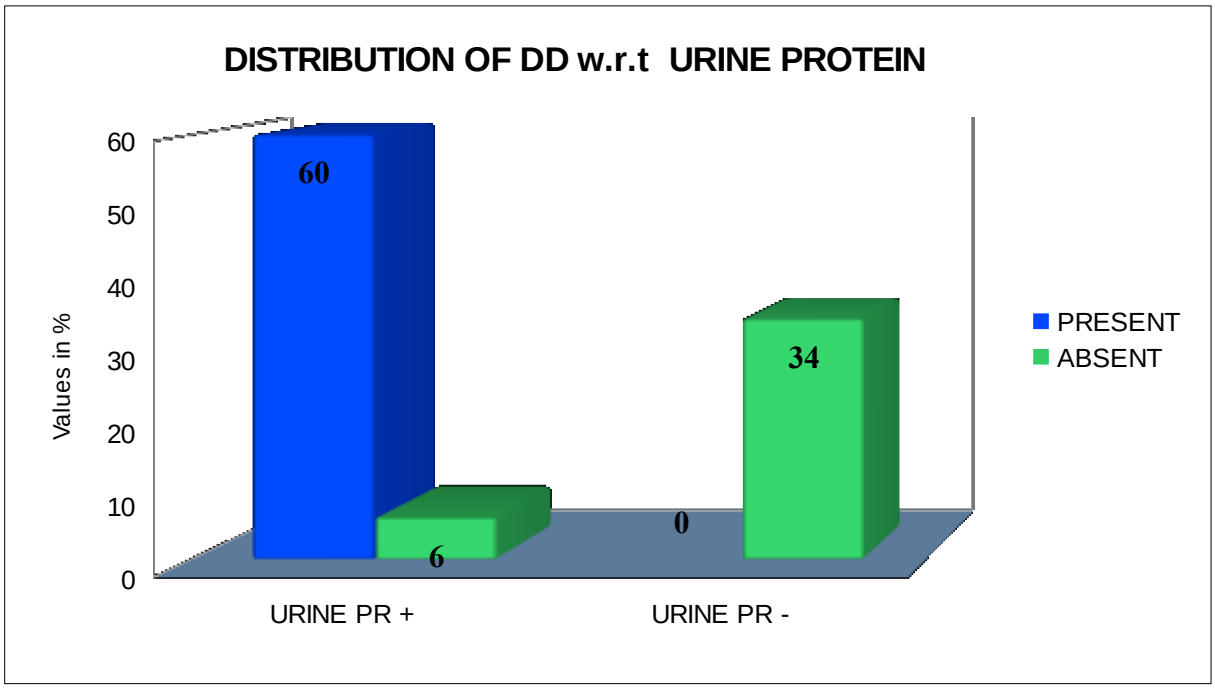
## (9) RESPECT TO URINE PROTEIN

| | | | ECHO DD | | |
|---|---|---|---|---|---|
| | | | ABSENT | PRESENT | Total |
| URINE PROTEIN | – | Count | 17 | 0 | 17 |
| | | % of Total | 34.0% | .0% | 34.0% |
| | + | Count | 3 | 30 | 33 |
| | | % of Total | 6.0% | 60.0% | 66.0% |
| | Total | Count | 20 | 30 | 50 |
| | | % of Total | 40.0% | 60.0% | 100.00% |

**p value : 0.000 ( <0.05 ) significant**

### CHI-SQUARE TEST

| | Value | df | P value |
|---|---|---|---|
| **Pearson Chi-Square** | 38.64 | 1 | .000 |



In the Diabetic group, the following variables were significantly different from ECHO DD present and absent group. By using Binary Logistic regression, we came to know that all the following variables are not associated risk factors with respect to Diastolic Dysfunction. Even though the variables were significant with respect to Diastolic Dysfunction, they are not significant associated risk factors with respect to Diastolic Dysfunction. So “ Diabetic itself, a risk factor for DD ”.

AGE GROUP

DURATION OF DIABETES

WEIGHT

BMI

FUNDUS DR

URINE PROTEIN

TOTAL CHOLESTEROL

# DISCUSSION

This study was conducted in individuals without HT, CAD and Heart failure, in 50 DM patients and 50 Age matched Non-DM controls. It was found that 30 of 50 DM patients had Diastolic Dysfunction whereas in Non-DM group, 7 out of 50 had DD. Age, Sex, Smoking and Alcohol were comparable between the two groups but Dyslipidemia, high BMI, Retinopathy, Proteinuria found to be more in the Diabetic group. From this study it was found that there was high prevalance of (60%) Diastolic Dysfunction in the diabetic individuals. This observation of high prevalence of DD in DM is consistent with several studies. In a community based study[165], 48% prevalence was found; Poirier et al,[119]found 60% prevalence and Zabalgoitia et al [120] found 47% prevalence. In one another study a prevalence of 60% was found.[189]

COMPARISON OF THE INDIVIDUAL VARIABLES WITH DD WITHIN THE DM GROUP

1. Influence of Age on DD :

The individuals were divided into three age groups of 40-50, 50-60, >60, with 3/10, 26/39 and 1/1 [DD+ / total number in that group]. At first look, it appears that DD incidence increases with age but this is not statistically significant.

2. Gender :

There were totally 32 males of whom 19 (59.35%) had DD and in females 11(61.11%) had DD of total 18, which is not statistically significant. Hence DD is equally distributed between both sexes.

3. Duration of DM :

The DM group was divided into two groups based on the presence and absence of DD. The mean duration of DM in individuals with DD was 14.90 years and for those without DD was 7.55 years which is statistically significant. This study shows that with increase in duration of DM there is more chance of developing DD. Many studies done in past have come to a similar conclusion [190 – 196]. Further it was also shown in studies that screening for DD after four years of diagnosing DM will increase its sensitivity. [197-199]

4. Smoking and Alcohol :

Among 21smokers 14 (66.67) had DD and in 29 non smokers 16(55.17) had DD which is not statistically significant. Similarly in 21 alcoholics 11 had DD and in 29 non alcoholics 19 had DD which is also not significant. Hence Smoking and Alcohol does not influence the development of DD in DM patients.

5. Body mass Index :

The mean value of BMI in patients with diastolic dysfunction is 30.86 and that of patients without diastolic dysfunction is 28.16. Hence it is statistically significant. Several previous studies have shown that there is higher incidence of DD in obese individuals. [200-202]

6. Association of Dyslipidemia with diastolic dysfunction :

In this study a significant association of DD with Total Cholesterol and LDL was found and not with HDL and TG's. Hence dyslipidemia particularly LDL cholesterol has been associated with DD in DM. Similar association was also found in previous studies [203].

7. Diabetic Retinopathy :

In this study, 32 individuals had DR of which 30 had diastolic dysfunction. It was found that no individual in the study population had DD in the absence of DR. Hence presence of diabetic retinopathy is strongly correlated to diastolic dysfunction. Studies performed in diabetic patients free of coronary artery disease, have demonstrated that patients with mild to severe retinopathy exhibited LV diastolic dysfunction (lower E/A values) compared to age-matched controls [114,127] or patients without retinopathy [123,128]. In the most recent report [129], a higher prevalence of retinopathy (49%) was encountered in patients with abnormal mitral filling pattern (E/A ratio < 1) compared to

patients with a normal diastolic function (20%). This relation with retinopathy was however not constantly found [118,130].

8. Association between Proteinuria and DD :

In this study, 33 individuals had significant proteinuria of which 30 had DD. It is highly significant. In a study done by Sampson et al [131], found that gradual decrease in E/A ratio in type 1 DM patients according to the presence of microalbuminuria and proteinuria. In another study conducted by Perez et al, [123] also observed similar finding. In type DM 1 patient with microalbuminuria demonstrated LV DD, whereas LV DD was not seen in patients without microalbuminuria in study done by Watschinger et al [131] and Guglielmi et al. [133]

**Binary Logistic Regression** :

Eventhough, Duration of DM, BMI, dyslipidemia, DR and Proteinuria were significantly associated with DD, by BINARY LOGISTIC REGRESSION method it was found that they were not significant risk factors and DIABETES itself, a risk factor for DD.

# SUMMARY

- In this study, diastolic dysfunction had 60% prevalence in Diabetic patients and 14% in case of Non-diabetic individuals.
- It was seen that with increasing age, there was an increase in incidence of DD but it was found to be statistically insignificant.
- Gender, alcohol and smoking does not play any role in diastolic dysfunction.
- Duration of diabetes is a significant factor. With increasing duration of DM, there is increase in incidence of DD.
- Body Mass Index is a significant factor. There is higher incidence of DD in individuals with elevated BMI.
- Dyslipidemia especially Total Cholesterol, LDL and Triglycerides were found to be associated with Diastolic dysfunction.
- Diabetic Retinopathy was found to be strongly correlated with diastolic dysfunction. No individual had DD in the absence of Diabetic retinopathy in the study population.
- Significant Proteinuria was also found to be associated with diastolic dysfunction. It was statistically significant.

From Binary logistic regression, it was found that, eventhough, most of the variables were significant in relation to DD, they are not significant risk factors for DD. Hence Diabetes, itself a risk factor for Diastolic dysfunction.

# CONCLUSION

The study was conducted to find out Diastolic dysfunction in diabetic patients and to find out the variables associated with it. It was done by prospective case control study in Diabetology and cardiac care unit of GRH.

The Statistical Analysis was done by

- Chi-square test
- Student t-test
- Binary Logistic Regression

Among the 50 Diabetic patients, 30 (60%) had Diastolic dysfunction and in Non-diabetic group, 7(14%) had DD, which was statistically significant. Hence diabetes mellitus is associated with diastolic dysfunction.

Among the other variables, diabetic retinopathy, proteinuria, dyslipidemia, elevated BMI were found to be associated with DM.

By comparing the presence and absence of DD within diabetic group, the following variables were found to be statistically significant and associated:

- Duration of Diabetes
- Body Mass Index
- Diabetic retinopathy
- Proteinuria
- Dyslipidemia

By Binary Logistic Regression method, **“**DIABETES, itself a risk factor for diastolic Dysfunction.**”**

# PROFORMA

Name Diabetic OP number

Age Occupation

Sex

Personal Data

1. Smoking
2. Alcohol
3. Life style
4. Duration of DM

   on OHA's or on Insulin
5. Systemic hypertension
6. Dyslipidemia
7. Coronary Artery Disease
8. Congestive Cardiac Failure
9. Valvular Heart Disease
10. Pericardial Disease / RCM / HOCM

Physical Examination:

Height

Weight

BMI

Pulse Rate

Blood Pressure Systolic & Diastolic

JVP

CVS Heart Sounds & Murmurs Rub

RS

Diabetic Retinopathy

Lab Data:

Recent Blood Sugar Fasting/ PP / RBS

Fasting Lipid Profile

ECG

Urine Protein

ECHO

# ABBREVATIONS

| | | |
|---|---|---|
| LV | - | Left Ventricle |
| DP | - | Diastolic Pressure |
| DV | - | Diastolic Volume |
| ECM | - | Extra Cellular Matrix |
| BNP | - | Brain Natriuretic Peptide |
| HF | - | Heart Failure |
| NYHA | - | New York Heart Association |
| LVH | - | Left Ventricular Hypertrophy |
| DD | - | Diastolic Dysfunction |
| Vp | - | Propagation velocity |
| EF | - | Ejection Fraction |
| IN-CHF | - | Italian Network on Congestive Heart Failure |
| CHARM | - | Candesartan in Heart Failure Assessment of Reduction in Mortality |
| CHF | - | Congestive Heart Failure |
| OHA | - | Oral Hypoglycemic Agents |
| DM | - | Diabetes Mellitus |
| GRH | - | Government Royapettah Hospital |

| | | |
|---|---|---|
| OGTT | - | Oral Glucose Tolerance Test |
| TC | - | Total Cholesterol |
| LDL | - | Low Density Cholesterol |
| HDL | - | High Density Cholesterol |
| TG | - | Triglycerides |
| w.r.t | - | with respect to |
| DR | - | Diabetic Retinopathy |
| RCM | - | Restrictive Cardiomyopathy |
| HOCM | - | Hypertrophic Obstructive Cardiomyopathy |
| ECHO | - | Echocardiography |
| ECG | - | Electrocardiography |
| PP | - | Post Prandial |
| RBS | - | Random Blood Sugar |
| DHF | - | Diastolic Heart Failure |
| OPD | - | Out Patient Department |
| BP | - | Blood Pressure |
| CAD | - | Coronary Artery Disease |
| JVP | - | Jugular Venous Pressure |
| PAS | - | Periodic Acid Schiff |
| HT | - | Hypertension |

| | | |
|---|---|---|
| ACEI | - | Angiotensin Converting Enzyme Inhibitors |
| AGE | - | Advanced-Glycated End products |
| BMI | - | Body Mass Index |

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**MASTER CHART - CASES**

| Sl.No | Name | Age | Sex | Duration of DM | Smoking | Alcohol | Pulse rate | Systolic BP | Diastolic BP | Height | Weight | BMI |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Munnusawmy | 56 | Male | 18 | + | + | 98 | 130 | 80 | 163 | 83 | 31.32 |
| 2 | Samapath kumar | 58 | Male | 16 | + | - | 96 | 126 | 84 | 165 | 85 | 31.25 |
| 3 | Kumari | 60 | Female | 20 | - | - | 90 | 124 | 80 | 155 | 80 | 33.33 |
| 4 | Nagammal | 53 | Female | 14 | - | - | 86 | 114 | 70 | 151 | 78 | 34.21 |
| 5 | Kanagavalli | 48 | Female | 7 | - | - | 80 | 110 | 70 | 158 | 72 | 28.8 |
| 6 | Senguttuvan | 50 | Male | 10 | + | + | 82 | 124 | 80 | 170 | 88 | 30.45 |
| 7 | Mohamed haseem | 52 | Male | 9 | + | + | 82 | 130 | 80 | 157 | 78 | 31.58 |
| 8 | Rafi | 58 | Male | 17 | + | + | 90 | 132 | 80 | 166 | 82 | 29.71 |
| 9 | Ravi | 56 | Male | 15 | + | - | 86 | 130 | 80 | 170 | 88 | 30.45 |
| 10 | Irshad | 53 | Male | 8 | + | + | 80 | 130 | 80 | 167 | 85 | 30.47 |
| 11 | Lakshmi | 50 | Female | 13 | - | - | 80 | 118 | 72 | 156 | 76 | 31.28 |
| 12 | Gangabhai | 59 | Female | 16 | - | - | 82 | 130 | 80 | 154 | 75 | 31.65 |
| 13 | Selvam | 51 | Male | 8 | + | + | 90 | 124 | 70 | 168 | 87 | 30.85 |
| 14 | Thangadurai | 57 | Male | 14 | + | - | 80 | 130 | 80 | 172 | 80 | 30.41 |
| 15 | Saraswathi | 48 | Female | 6 | - | - | 82 | 110 | 70 | 152 | 72 | 31.17 |
| 16 | Mathivanan | 50 | Male | 7 | + | - | 84 | 130 | 80 | 156 | 76 | 31.28 |
| 17 | Senthilkumar | 47 | Male | 6 | + | + | 80 | 130 | 80 | 160 | 80 | 31.25 |
| 18 | Kasi | 56 | Male | 15 | + | - | 78 | 128 | 80 | 157 | 80 | 32.39 |
| 19 | Paneerselvam | 60 | Male | 16 | + | + | 82 | 130 | 80 | 162 | 82 | 31.29 |
| 20 | Nagaraj | 58 | Male | 15 | - | - | 72 | 124 | 80 | 159 | 80 | 31.62 |
| 21 | Meenakshi | 55 | Female | 13 | - | - | 88 | 130 | 84 | 154 | 72 | 30.37 |
| 22 | Shankar | 56 | Male | 18 | + | + | 86 | 126 | 80 | 164 | 80 | 29.74 |
| 23 | Ganesan | 54 | Male | 12 | + | + | 82 | 110 | 80 | 164 | 83 | 30.85 |
| 24 | Parameshwari | 50 | Female | 14 | - | - | 84 | 110 | 70 | 153 | 77 | 32.89 |
| 25 | Balasundharam | 52 | Male | 15 | + | + | 86 | 126 | 80 | 165 | 80 | 29.38 |
| 26 | Maheshwari | 52 | Female | 8 | - | - | 90 | 120 | 70 | 160 | 65 | 25.39 |
| 27 | Murugan | 52 | Male | 6 | + | + | 86 | 124 | 80 | 165 | 70 | 25.7 |
| 28 | Rajeshwari | 50 | Female | 13 | - | - | 86 | 126 | 84 | 155 | 68 | 28.3 |
| 29 | Palani | 54 | Male | 15 | + | + | 90 | 120 | 80 | 169 | 85 | 29.76 |
| 30 | Ramesh | 48 | Male | 4 | + | + | 84 | 116 | 80 | 172 | 78 | 26.12 |
| 31 | Amsa | 54 | Female | 8 | - | - | 82 | 110 | 84 | 157 | 62 | 25.15 |
| 32 | Sivaprakasam | 58 | Male | 16 | + | - | 82 | 120 | 76 | 162 | 80 | 30.48 |
| 33 | Thangavel | 60 | Male | 19 | - | - | 76 | 126 | 80 | 166 | 86 | 31.2 |
| 34 | Bhargavi | 58 | Female | 9 | - | - | 80 | 110 | 80 | 157 | 68 | 27.59 |
| 35 | Vadivel | 60 | Male | 17 | + | + | 74 | 120 | 76 | 171 | 90 | 31.14 |
| 36 | Chellamal | 54 | Female | 13 | - | - | 80 | 116 | 80 | 151 | 67 | 29.38 |
| 37 | Prakasam | 58 | Male | 7 | + | + | 76 | 120 | 80 | 169 | 76 | 26.61 |
| 38 | Dhanapal | 62 | Male | 20 | + | + | 76 | 126 | 80 | 170 | 88 | 30.45 |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 39 | Samundeshwari | 56 | Female | 14 | - | - | 84 | 130 | 78 | 158 | 78 | 31.25 |
| 40 | Sivakumar | 56 | Male | 6 | + | - | 82 | 126 | 84 | 178 | 89 | 28.09 |
| 41 | Kuppamal | 54 | Female | 12 | - | - | 80 | 130 | 82 | 157 | 78 | 31.64 |
| 42 | Ismael | 46 | Male | 8 | + | + | 84 | 126 | 80 | 169 | 87 | 30.46 |
| 43 | Subramaniam | 53 | Male | 12 | - | - | 86 | 120 | 84 | 174 | 95 | 31.38 |
| 44 | Kotteshwari | 55 | Female | 11 | - | - | 80 | 130 | 80 | 155 | 77 | 32.05 |
| 45 | Lakshmanan | 56 | Male | 9 | + | + | 78 | 124 | 76 | 172 | 75 | 25.35 |
| 46 | Shankaran | 53 | Male | 10 | + | + | 86 | 116 | 80 | 175 | 83 | 27.1 |
| 47 | Jansirani | 58 | Female | 9 | - | - | 76 | 110 | 76 | 153 | 60 | 25.63 |
| 48 | Shajahan | 56 | Male | 8 | + | - | 80 | 126 | 76 | 168 | 76 | 26.93 |
| 49 | Amudha | 53 | Female | 8 | - | - | 82 | 120 | 74 | 157 | 60 | 24.34 |
| 50 | Bhaskar | 56 | Male | 14 | + | + | 84 | 124 | 80 | 170 | 85 | 29.41 |

| Fundus DR | Urine albumin | Total Cholesterol | HDL | LDL | TG | ECHO DD |
|---|---|---|---|---|---|---|
| + | 2+ | 244 | 32 | 180 | 260 | Present |
| + | 2+ | 234 | 32 | 150 | 260 | Present |
| + | 2+ | 235 | 30 | 152 | 265 | Present |
| + | 2+ | 229 | 30 | 152 | 236 | Present |
| - | trace | 207 | 30 | 130 | 236 | Absent |
| + | Nil | 219 | 38 | 130 | 254 | Absent |
| - | 1+ | 220 | 32 | 140 | 240 | Absent |
| + | 2+ | 233 | 36 | 148 | 245 | Present |
| + | 2+ | 232 | 36 | 146 | 252 | Present |
| - | Nil | 224 | 34 | 140 | 252 | Absent |
| + | 2+ | 231 | 34 | 148 | 245 | Present |
| + | 2+ | 228 | 36 | 144 | 240 | Present |
| - | Nil | 219 | 34 | 136 | 244 | Absent |
| + | 2+ | 229 | 34 | 144 | 254 | Present |
| - | 2+ | 218 | 32 | 138 | 238 | Absent |
| - | Nil | 221 | 30 | 140 | 256 | Absent |
| - | 2+ | 260 | 32 | 138 | 222 | Absent |
| + | 2+ | 228 | 34 | 144 | 250 | Present |
| + | 2+ | 229 | 34 | 144 | 255 | Present |
| + | 2+ | 227 | 32 | 146 | 246 | Present |
| + | 2+ | 285 | 36 | 202 | 236 | Present |
| + | 2+ | 272 | 36 | 188 | 240 | Present |
| + | 2+ | 233 | 38 | 156 | 195 | Present |
| + | 2+ | 285 | 34 | 208 | 216 | Present |
| + | 2+ | 242 | 40 | 160 | 210 | Present |
| - | Nil | 200 | 36 | 124 | 198 | Absent |
| - | Nil | 208 | 36 | 128 | 218 | Absent |
| + | 2+ | 264 | 36 | 186 | 212 | Present |
| + | 2+ | 256 | 34 | 180 | 210 | Present |
| - | Nil | 214 | 38 | 134 | 208 | Absent |
| - | Nil | 202 | 38 | 128 | 178 | Absent |
| + | 2+ | 268 | 34 | 190 | 220 | Present |
| + | 2+ | 275 | 34 | 198 | 214 | Present |
| - | Nil | 222 | 36 | 146 | 200 | Absent |
| + | 2+ | 276 | 36 | 192 | 242 | Present |
| + | 2+ | 264 | 36 | 178 | 252 | Present |
| - | 1+ | 220 | 36 | 146 | 188 | Absent |
| + | 2+ | 257 | 34 | 172 | 256 | Present |

| | | | | | | |
|---|---|---|---|---|---|---|
| + | 2+ | 237 | 38 | 158 | 206 | Present |
| - | Nil | 266 | 38 | 184 | 222 | Absent |
| + | 2+ | 262 | 34 | 182 | 228 | Present |
| + | 2+ | 240 | 36 | 160 | 218 | Absent |
| + | 2+ | 255 | 36 | 180 | 195 | Present |
| + | 2+ | 232 | 34 | 146 | 260 | Present |
| - | Nil | 184 | 38 | 110 | 180 | Absent |
| + | 2+ | 209 | 38 | 132 | 196 | Present |
| - | Nil | 208 | 36 | 130 | 210 | Absent |
| - | Nil | 212 | 36 | 124 | 250 | Absent |
| - | Nil | 196 | 38 | 120 | 192 | Absent |
| + | 2+ | 214 | 36 | 142 | 180 | Present |

**MASTER CHART - CONTROL**

| Sl. No | Name | Age | Sex | Smoking | Alcohol | Pulse rate | Systolic BP | Diastolic BP | Height | Weight | BMI | Fundus retinopathy |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Lakshmi | 48 | Female | - | - | 86 | 120 | 80 | 155 | 58 | 24.17 | - |
| 2 | Mahalakshmi | 51 | Female | - | - | 88 | 130 | 90 | 152 | 54 | 23.38 | - |
| 3 | Kesavan | 56 | Male | + | + | 78 | 124 | 82 | 158 | 74 | 29.6 | - |
| 4 | Murugan | 47 | Male | - | - | 84 | 136 | 74 | 160 | 78 | 30.47 | - |
| 5 | Sundharam | 55 | Male | + | + | 88 | 132 | 82 | 156 | 80 | 32.92 | - |
| 6 | Fatima | 52 | Female | - | - | 90 | 130 | 80 | 153 | 62 | 26.5 | - |
| 7 | Vimalakumari | 46 | Female | - | - | 86 | 120 | 80 | 149 | 56 | 25.23 | - |
| 8 | Gopal | 58 | Male | + | + | 84 | 130 | 86 | 158 | 80 | 32.13 | - |
| 9 | Mariammal | 49 | Female | - | - | 78 | 110 | 70 | 150 | 61 | 27.11 | - |
| 10 | Kathiravan | 44 | Male | + | + | 82 | 130 | 80 | 158 | 78 | 31.2 | - |
| 11 | Manivannan | 58 | Male | + | - | 76 | 134 | 86 | 160 | 75 | 29.3 | - |
| 12 | Selvam | 54 | Male | - | - | 78 | 128 | 80 | 153 | 80 | 34.19 | - |
| 13 | Manimeghalai | 47 | Female | - | - | 84 | 110 | 70 | 152 | 60 | 25.97 | - |
| 14 | Govindhaswamy | 48 | Male | + | - | 88 | 130 | 80 | 162 | 82 | 31.29 | - |
| 15 | Perumal | 53 | Male | + | + | 86 | 130 | 80 | 168 | 85 | 30.14 | - |
| 16 | Sasikala | 56 | Female | - | - | 76 | 120 | 70 | 154 | 58 | 24.47 | - |
| 17 | Ahmed | 60 | Male | - | - | 74 | 130 | 84 | 175 | 88 | 28.76 | - |
| 18 | Rani | 45 | Female | - | - | 86 | 110 | 70 | 150 | 56 | 24.89 | - |
| 19 | Sundharavadivel | 46 | Male | + | + | 80 | 134 | 80 | 156 | 82 | 33.74 | - |
| 20 | Gandhimathy | 52 | Female | - | - | 90 | 130 | 80 | 148 | 68 | 31.05 | - |
| 21 | Velu | 44 | Male | + | + | 76 | 130 | 86 | 150 | 72 | 32 | - |
| 22 | Marimuthu | 49 | Male | + | + | 76 | 126 | 80 | 158 | 80 | 32 | - |
| 23 | Kumar | 51 | Male | + | + | 82 | 120 | 80 | 165 | 77 | 28.31 | - |
| 24 | Pushpa | 62 | Female | - | - | 80 | 110 | 70 | 153 | 58 | 24.79 | - |
| 25 | Latha | 65 | Female | - | - | 84 | 110 | 70 | 152 | 56 | 24.24 | - |
| 26 | Sundhramoorthy | 63 | Male | - | - | 80 | 130 | 80 | 157 | 68 | 27.64 | + |
| 27 | Kumaravel | 58 | Male | + | + | 82 | 120 | 80 | 162 | 75 | 28.62 | - |
| 28 | Hussain | 56 | Male | + | - | 78 | 130 | 80 | 166 | 84 | 30.43 | - |
| 29 | Nazar | 49 | Male | + | + | 78 | 136 | 84 | 174 | 88 | 29.04 | - |
| 30 | Natesan | 54 | Male | - | + | 80 | 120 | 76 | 165 | 76 | 27.94 | - |
| 31 | Ponnuswamy | 58 | Male | - | - | 76 | 130 | 82 | 158 | 72 | 28.8 | - |
| 32 | Muthuvadivel | 45 | Male | + | + | 76 | 130 | 80 | 155 | 74 | 30.83 | - |
| 33 | Ravikumar | 49 | Male | + | - | 82 | 134 | 84 | 162 | 75 | 28.63 | - |
| 34 | Sultan | 53 | Male | + | - | 80 | 128 | 80 | 175 | 91 | 29.74 | - |
| 35 | Deepak | 57 | Male | + | + | 80 | 120 | 80 | 171 | 80 | 27.4 | - |
| 36 | Selvaraj | 48 | Male | + | + | 74 | 120 | 70 | 158 | 78 | 31.2 | - |
| 37 | Palani | 61 | Male | - | - | 78 | 130 | 80 | 155 | 76 | 31.67 | - |
| 38 | Anbu | 58 | Male | + | + | 78 | 130 | 82 | 158 | 75 | 30 | - |
| 39 | Padmavathy | 64 | Female | - | - | 92 | 110 | 80 | 149 | 56 | 25.23 | - |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 40 | Zaheer | 46 | Male | - | - | 84 | 120 | 80 | 166 | 76 | 27.54 | - |
| 41 | Palaniswamy | 43 | Male | + | + | 80 | 130 | 80 | 164 | 80 | 29.74 | - |
| 42 | Balakrishnan | 55 | Male | + | + | 74 | 130 | 82 | 158 | 72 | 28.8 | - |
| 43 | Vasanthi | 49 | Female | - | - | 76 | 110 | 80 | 151 | 56 | 24.56 | - |
| 44 | Kannnayiram | 50 | Male | + | + | 84 | 134 | 82 | 159 | 75 | 29.64 | - |
| 45 | Suseela | 59 | Female | - | - | 88 | 128 | 80 | 152 | 74 | 32.03 | - |
| 46 | Narayanan | 52 | Male | + | - | 72 | 130 | 80 | 163 | 72 | 27.07 | - |
| 47 | Savithri | 60 | Female | - | - | 80 | 110 | 70 | 152 | 60 | 25.97 | - |
| 48 | Devanantham | 57 | Male | + | + | 78 | 120 | 80 | 160 | 73 | 28.52 | - |
| 49 | Madhini | 46 | Female | - | - | 78 | 120 | 70 | 153 | 69 | 29.49 | - |
| 50 | Kuppammal | 64 | Female | - | - | 86 | 130 | 80 | 148 | 52 | 23.74 | - |

| Urine albumin | Total Cholesterol | HDL | LDL | TG | ECHO DD |
|---|---|---|---|---|---|
| Nil | 189 | 38 | 120 | 156 | Absent |
| Nil | 176 | 40 | 100 | 180 | Absent |
| Nil | 184 | 38 | 110 | 180 | Absent |
| 1+ | 240 | 36 | 160 | 218 | Absent |
| Nil | 208 | 36 | 130 | 210 | Absent |
| Nil | 184 | 38 | 126 | 98 | Absent |
| Nil | 174 | 40 | 108 | 128 | Absent |
| Nil | 212 | 36 | 124 | 250 | Present |
| Nil | 156 | 34 | 98 | 122 | Absent |
| 1+ | 196 | 38 | 120 | 192 | Absent |
| Nil | 214 | 38 | 134 | 208 | Absent |
| Nil | 169 | 36 | 98 | 176 | Absent |
| Nil | 172 | 38 | 102 | 162 | Absent |
| Nil | 177 | 40 | 110 | 133 | Absent |
| Nil | 198 | 40 | 122 | 180 | Absent |
| 1+ | 194 | 36 | 120 | 188 | Absent |
| Nil | 162 | 34 | 88 | 200 | Present |
| Nil | 158 | 38 | 96 | 122 | Absent |
| Nil | 177 | 34 | 96 | 235 | Absent |
| 2+ | 172 | 36 | 100 | 182 | Absent |
| Nil | 179 | 40 | 108 | 155 | Absent |
| Nil | 162 | 40 | 94 | 142 | Absent |
| Nil | 190 | 38 | 128 | 118 | Absent |
| Nil | 180 | 38 | 112 | 148 | Absent |
| Nil | 166 | 40 | 86 | 198 | Present |
| Nil | 157 | 38 | 92 | 135 | Present |
| 2+ | 158 | 38 | 88 | 162 | Absent |
| Nil | 178 | 40 | 98 | 200 | Absent |
| Nil | 172 | 36 | 100 | 182 | Absent |
| Nil | 180 | 38 | 110 | 160 | Absent |
| Nil | 168 | 38 | 96 | 168 | Absent |
| 1+ | 163 | 36 | 98 | 144 | Absent |
| Nil | 164 | 40 | 100 | 118 | Absent |
| Nil | 146 | 38 | 88 | 100 | Absent |
| Nil | 167 | 38 | 92 | 184 | Absent |
| Nil | 166 | 36 | 98 | 158 | Absent |
| Nil | 174 | 40 | 112 | 110 | Present |
| 2+ | 180 | 40 | 104 | 178 | Absent |
| Nil | 169 | 38 | 94 | 184 | Present |

| | | | | | |
|---|---|---|---|---|---|
| Nil | 178 | 38 | 118 | 112 | Absent |
| Nil | 210 | 40 | 128 | 210 | Absent |
| Nil | 167 | 42 | 106 | 96 | Absent |
| Nil | 168 | 40 | 90 | 192 | Absent |
| 1+ | 168 | 40 | 92 | 178 | Absent |
| Nil | 166 | 38 | 84 | 220 | Absent |
| Nil | 158 | 38 | 84 | 180 | Absent |
| Nil | 175 | 44 | 98 | 166 | Absent |
| Nil | 184 | 38 | 112 | 170 | Absent |
| 2+ | 176 | 40 | 110 | 128 | Absent |
| Nil | 159 | 42 | 90 | 136 | Present |