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A Study on Lipid Profile and Cardiovascular Manifestations in Type 2 Diabetes Mellitus Patients

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Abstract

Background and objective: This study outlines a comprehensive approach for exploring the interplay between lipid profile and cardiovascular manifestations in type 2 diabetes mellitus patients, aiming to provide actionable insights and contribute to the broader scientific understandings of these relationships. This approach provides a comprehensive evaluation of therapeutic effectiveness and helps in identifying factors that could impact treatment outcomes.

Methodology: This is prospective comparative study conducted from June 2018 to December 2019 in the Department of Medicine and Cardiology at Paras HMRI hospital Patna, included 165 patients who fulfilled the WHO criteria of type 2 Diabetes Mellitus were taken of any age group on the basis of random sampling. The study collected demographic and medical history data using a pre-designed proforma. The statistical analysis of this study was done by 'S PLUS'' Statistical software.

Result: We compared the lipid profile abnormality of < 10 years and > 10 years duration group, there is absence of difference between two groups which shows that lipid profile abnormality does not varies much with time.

We also found no significant relation with respect to lipid profile between the group of glycosylated haemoglobin level HbA1C < 10 and HbA1c > 10 group, this shows that there no significant relationship exists between severity of diabetes and lipoprotein abnormality.

Left ventricular abnormalities in type 2 diabetes patients, shows that more the duration of the disease lesser is the E/A ratio, i.e., greater is the diastolic dysfunction. It is found that diastolic dysfunction was more common than systolic in type 2 diabetes mellitus.

Conclusion: No significant change in lipid profile is found between the study group on the basis of duration >10 years and <10 year and severity of type 2 diabetes mellitus i.e. HbA1c >10 and <10.

Diabetic patients have cardiovascular dysfunction and it depends on the duration of the disease, also diastolic dysfunction precedes systolic dysfunction and there is no difference between both sexes with respect to diastolic dysfunction.

Also, we found that the fasting and post prandial blood glucose level gradually increase with increase duration of type 2 diabetes mellitus.

Keywords: lipid profile, type 2 diabetes mellitus, LV diastolic and LV systolic dysfunction

Introduction

Diabetes, a multi-system disease is a curse to the mankind both in terms of mortality and morbidity and is known from ancient civilizations.

Type 2 diabetes incidence is rising rapidly. It is now a common and serious health problem, which has evolved in association with rapid social and cultural changes, ageing population, dietary changes, reduced physical activity and other lifestyle and behavioural changes.

Cardiovascular disease accounts for the 50-80% death in diabetic people with acute myocardial infarction accounting for about 30%. Worldwide there is a vast potential for diabetes associated cardiovascular disease notably among 73 million people in India and 114 million in China estimated to have diabetes[1]. The survival rate in diabetic subjects with angiographically proven coronary artery disease has decreased by 30% as compared with their nondiabetic counterparts[2]. Overall, the cardiovascular risk conferred to diabetes is high. In one 7-year prospective study, this was comparable with the increased risk seen in non-diabetic people who have already suffered a myocardial infarction or stroke[3]. This fact needs no explanation as diabetes is associated with an earlier onset, faster development and greater density of atheromatous lesion. Most of the myocardial abnormalities in diabetes can be due to coronary artery disease and hypertension. However, post-mortem, experimental and observational studies also give evidence for a specific cardiomyopathy in diabetes which may contribute to the myocardial abnormalities in the absence of coronary artery atheroma[4].

Left ventricular hypertrophy has also been detected in non-hypertensive diabetic individuals particularly women[5]. The important effect of myocardial disease is cardiac failure, which is common in diabetic people and results in the complications of acute myocardial infarction more than that in non-diabetics. Diabetes is known for its autonomic neuropathy. In diabetic patients with cardiovascular autonomic neuropathy (CAN), there is a poor prognosis of cardiovascular disease. Most of the patients with CAN come to clinical attention when they develop resting tachycardia, postural hypotension, exercise intolerance or painless myocardial ischemia or infarction. The risk of CAN depends on the degree of glycaemic control as well as duration of diabetes. Symptoms of CAN often occur relatively late. Heart rate variability on 24 hours ambulatory ECG showed abnormalities in nearly 50% of diabetics for more than in controls[6.] Increased rate of mortality has been reported in diabetic patients with CAN[7,8]. CAN conferred excess mortality beyond that attributable to other risk factors[9].

Diabetic dyslipidaemia includes multiple lipoprotein disorders. Diabetic dyslipidaemia is characteristically known for raised triglyceride levels, low HDL level, and slightly elevated LDL-cholesterol with domination of atherogenic small dense LDL [10,11]. So, if we measure HDL level only, we may underestimate the risk related to the concentration of atherogenic lipoprotein particles in diabetes. Certainly, in some studies on patients with diabetes, total cholesterol and LDL level did not correlate with CVS risk, although, high triglyceride level or low HDL level were powerful predictors of CHD event [12,13]. Characteristically, there is mild hypertriglyceridemia accompanied by reduced HDL cholesterol level[14] , even though tightening glycaemic control reduce the initially high production rate of large triglyceride rich VLDL1, and increase the direct secretion of small VLDL2

particles, which have a lower triglyceride APO-B ratio. One of the actions of lipoprotein lipase (LPL) is to convert VLDL1 to VLDL2. This conversion of VLDL1 to VLDL2 explains the change in the triglyceride APO-B ratio[15]. The triglyceride rich lipoprotein resides in the circulation for a long time. This leads to bigger exchange of their triglyceride for cholesterol esters in HDL (as well as in LDL) by cholesteryl ester transferase protein (CETP). This exchange leads to comparatively cholesterol ester depleted LDL and HDL particles. These particles also become smaller by the hydrolysis of their unusually rich triglyceride core by hepatic lipase. Therefore, fasting triglyceride level is an accurate predictor of LDL size because of increased bi-directional triglyceride cholesterol ester exchange in hypertriglyceridemia patients with type 2 diabetes[16.] Triglyceride rich HDL and LDL are formed and are then hydrolysed by hepatic lipase to produce small dense HDL and LDL particle. The former is quickly cleared from the circulation, which leads to lower serum HDL concentration. In diabetes, the plasma triglyceride concentration is negatively correlated with that of large HDL2 and positively correlated with the level of small HDL3 – an indication of the impact of triglyceride enriched lipoprotein or HDL concentration and composition [17,18].

This exchange is also applicable to cardiovascular risk in diabetes as HDL2, which is comparatively depleted has greater anti-atherogenic effect. These metabolic inter-relationships complicate the evaluation of triglyceride HDL and LDL concentration and of LDL and HDL size as independent predictor of CHD risk in type 2 diabetes[19]. A low HDL cholesterol level in type 2 diabetes is most often an element of metabolic syndrome that is typically accompanied by moderate triglyceridemia[20.] Since, there is low concentration of HDL in metabolic syndrome, the ratio of total cholesterol to HDL cholesterol comes high, which was used as the best lipid index for forecasting cardiovascular events in prospective studies such as Framingham Heart Study and the Quebec Cardiovascular Study [21,22.]

Material and Methods

The present study is a prospective comparative study. The study was performed in type 2 diabetes mellitus patients with reference to lipid profile and cardiovascular abnormalities. It was performed in Paras HMRI Hospital, from June 2018 to December 2019 in the Department of Medicine and Cardiology. The study consisted of three parts:

1. Selection of cases
2. Measurement of variables
3. Comparison, Analysis, and Interpretation

Selection of Cases

Inclusion Criteria: A patient with undisputed diabetes mellitus was taken as a case. They were either known diabetics and controlled by antidiabetic therapy, or they fulfilled WHO criteria for diagnosis of diabetes without any therapy. ADA guidelines for diagnosing Diabetes Mellitus 2000: Venous plasma glucose (fasting) more than 126 mg/dl and/or post prandial more than 200 mg/dl on one or more occasions. Antidiabetic therapy meant either oral hypoglycaemic agents or insulin therapy. Cases who fulfilled the criteria of type 2 Diabetes Mellitus were taken of any age group on the basis of random sampling.

Exclusion Criteria (a) Patients with severe symptoms (like palpitation, dyspnoea, easy fatiguability) or critically ill were not taken. (b) Patients having diseases that can affect the left ventricular function (like high blood pressure, previously known cardiomyopathy of definite aetiology other than diabetes, rheumatic heart disease and congenital heart disease) were excluded from

the study after clinical evaluation and proper investigations. (c) Patients having known risk factors for coronary artery disease were also excluded from the study, as far as possible. We took non-smokers, non-hypertensive, and cases without positive family history. (d) Dyslipidaemias were taken as a part of our study and not the exclusion criteria. (e) The patients having the following diseases, which could adversely affect the outcome were excluded from the study. Patients with – I) Chronic liver disease ii) renal disease iii) Anaemia iv) C.O.P.D. All these were excluded after proper history, clinical examination and relevant investigations.

Measurement of Variables

After selection, the patients were subjected to the following procedures:

History taking

Detailed clinical examination

Investigation (I) Patients were subjected to history taking and thorough physical examination as outlined in the proforma. (ii) The body weight and height were measured and body mass index (BMI) was calculated by the following formula. Body weight in kgs/(Height in Meters)2 (iii) The Mean arterial pressure (MAP) was calculated as MAP = Diastolic pressure + 1/3rd pulse pressure. Blood pressure was measured in both supine and erect posture to detect any postural hypotension. (iv) Patients were subjected to detailed ophthalmoscopic examination after dilating the pupils. (v) The test to detect autonomic dysfunction was done as follows: (a) Resting pulse rate and variation with respiration, undue resting tachycardia or bradycardia, absence of slowing pulse rate with deep inspiration. (b) Postural change: Patients were asked to lie on a couch for 15 minutes with cuff and lead I ECG was attached. Then, blood pressure was measured. Patient was then asked to stand. ECG was taken and blood pressure was measured at the first minute and third minute after standing. Pulse rate was calculated at 15th and 30th beats after standing. Fall in systolic blood pressure 30 mm of Hg (Autonomic Neuropathy). 30th/15th pulse ratio = 1.03 (Normal) 30th/15th pulse ratio = 1 (Autonomic Neuropathy) (vi) Chest X-ray (PA view) was done and cardio thoracic ratio was noted. (vii) To confirm the inclusion and exclusion criteria and to know the duration of disease, the following investigations were done in all cases. (a) Venous plasma glucose estimation both fasting and postprandial. (b) Long term glycaemic control was assessed by the estimation of glycosylated haemoglobin (HbA1c) (Normal range – 4 to 6%). (c) Fasting serum cholesterol (Desirable 240 mg%). (d) Serum triglyceride (Desirable < 150 mg%; Borderline High 150- 199 mg%; High 200-499 mg%; Very High >500 mg%). (e) Serum HDL cholesterol (Normal 40 – 60 mg%). (f) Serum LDL cholesterol (Optimal < 100 mg%; Near Optimal 100- 129 mg%; Borderline High 130-159 mg%; High 160-189 mg%; Very High >190 mg%). (g) Serum urea estimation (Normal 19 – 43 mg%). (h) Serum creatinine estimation (Normal up to 1.5 mg%). (i) Urine protein estimation. (viii) In every case resting ECG was taken in usual 12 lead system and long strip of lead II was taken in deep inspiration and expiration. (ix) Echo Doppler Study: Non-invasive assessment of left ventricular function was done by using echo doppler machine in the Department of Cardiology, Paras HMRI Hospital. The echocardiographer was kept uninformed about the clinical details of the patients in order to eliminate the possibility of biased observations. All the patients were subjected to echocardiography at approximately the same time in the morning in order to minimize changes in the results due to diurnal variations of the sympathetic nervous system function. Each patient underwent two-dimensional, M-mode echocardiogram and doppler

examination. M-MODE After imaging the left ventricular chamber by 2-D echo in the parasternal short axis view, the M-Mode cursor was positioned through the centre of the cavity and M-Mode recordings were taken just beneath the mitral valve to determine left ventricular dimensions. The following parameters were derived from five consecutive cardiac cycles – (a) Left ventricular internal diameter in diastole (LVIDD). (b) Left ventricular internal diameter in systole (LVIDS). (c) Left ventricular posterior wall thickness (LVPWT). (d) Interventricular septal wall thickness (IVSWT). First three measurements were taken by „leading edge to leading edge" technique. Septal thickness was taken from the leading edge of the right septal echo to trailing edge of left septal echo. Amplitude of septal motion was noted, as it is related to the left ventricular filling. The M-Mode cursor was then positioned at the mitral valve for the following readings – Mitral E-point septal separation (EPSS): The EPSS is seen to correlate with angiographic ejection fraction fairly well. Left ventricular ejection fraction (EF%) was calculated as – (LVIDD)3 – (LVIDS)3 EF% = x 100 (LVIDD)3 .Fractional shortening of left ventricle was calculated as: LVIDD – LVIDS FS% = x 100 LVIDD Doppler Echocardiographic Study Mitral inflow velocities were recorded by pulse wave doppler from an apical four chamber view with the sample volume placed near the tips of mitral leaflets. The following were measured. E – Peak velocity of early (E) diastolic phase of rapid passive filling (cm/sec). A – Peak velocity of late (A) diastolic phase of active atrial contraction (cm/sec). Normally, peak velocity is greater with early diastolic flow. E/A ratio being about 1.6 + 0.5. In patients with impaired left ventricular relaxation, peak E velocity is reduced while peak A velocity is increased. Any ischaemic segment exhibiting regional wall motion abnormality was looked for in M-Mode and 2-D echo, in both long axis and short axis view, in all patients. (x) Clinical examination and investigations to exclude pertinent selected disease. (a) Liver disease: From history, clinical examination. (b) Renal disease: From history, clinical examination. - Urine for RE/ME - Blood for urea, creatinine (c) Cerebrovascular disease: By history and clinical examination (d) Anaemia: By clinical examination and blood for complete hemogram. (e) C.O.P.D.: By history, clinical examination, X-ray chest – PA view. 3. Comparison, Analysis and Interpretation Variables related to both case group i.e., (1) type 2 diabetes of 10 yrs. duration, (2) type 2 diabetes with HbA1c 10 were compared. The standard deviation and mean were calculated for each variable. The p value was calculated using S PLUS statistical software. (I) Evidence of dyslipidaemia (ii) Evidence of left ventricular dysfunction as evidenced by – (a) Systolic dysfunction by – EPSS – (E point septal separation) (cm) EF% - (Ejection fraction) FS% - (Fractional shortening) (b) Diastolic dysfunction by – E – Peak velocity of early diastole (cm/sec) A – Peak velocity of late diastole (cm/sec) E/A ratio (iii) Evidence of coronary artery disease: with Positive ECG changes for ischaemia – as evidenced by ST segment depression of 0.2 mv and persistent for 0.08 m sec. Either horizontal or down sloping.

Result

The study comprised of 165 patients with sex ratio male: female 3:1, lowest and highest age was 22 and 65 respectively.

The baseline data are as follow:

	Mean	Standard Deviation
Age	48.29	9.07
Body mass index (BMI)	24.47	1.86
Fasting blood sugar (FBS)	178.16	21.12
Post-prandial blood sugar (PPBS)	290.42	34.21
Glycosylated haemoglobin (HbA1c)	9.68	0.94
Mean arterial pressure (MAP)	90.73	3.95
Total cholesterol	203.79	12.37
Low density lipoprotein (LDL)	127.56	15.20
High density lipoprotein (HDL)	42.50	4.22
Triglyceride	184.61	33.40
Very low density lipoprotein (VLDL)	36.79	6.77
E-point septal separation (EPSS)	0.364	0.158
Ejection fraction (EF)	65.52	5.88
Fractional shortening (FS)	33.43	3.19
Ratio of E-flow/A-flow velocity (EA)	1.36	0.308
Duration of disease	9.47	5.44

The statistical analysis of this study was done by „S PLUS" Statistical software. Unpaired t test was used to test the association between different variables under study. In the process of statistical calculation following variables were taken as follows:

X5: Fasting blood sugar

X6: Post prandial blood sugar

X11: HDL concentration

X12: Triglyceride concentration

X14: E-point septal separation (EPSS)

X15: Ejection fraction

X16: Fractional shortening

X17: Ratio of E/A flow velocity etc.

The other variables were found non-significant. The above variables are compared with **X19 (i.e., duration of disease)** and **X7 (HbA1c i.e., severity of the disease)** and statistically analysed using "S PLUS" statistical software

A. Lipoprotein and Cardiovascular abnormalities in relation to the duration of diabetes.

While doing this we took 10 years as a limit. Cardiovascular and lipoprotein abnormality of diabetic patients above and less than equal to 10years duration was compared.

Table 1:

Fasting and Post-prandial Blood Sugar Level Abnormality Study

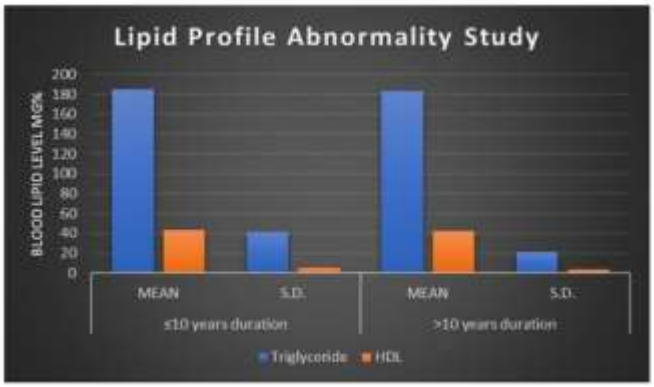
Parameters	Case group ≤ 10 years duration n = 93	Case group > 10 years duration n = 72	P Value
FBS	Mean 172.27 S.D. ± 17.94	Mean 185.81 S.D. ± 22.56	0.0001
PPBS	Mean 280.24 S.D. ± 27.89	Mean 303.58 S.D. ± 37.21	0.0001

So, the FBS and PPBS were significantly different in the group having duration of disease > 10 years rather than the population group having disease < 10 years, $P < 0.05$.

Table 2:

Lipid Profile Abnormality Study

Parameters	Case group ≤ 10 years duration n = 93	Case group > 10 years duration n = 72	P Value
Triglyceride	Mean 185.21 S.D. ± 41.32	Mean 183 S.D. ± 21.09	0.679
HDL	Mean 42.86 S.D. ± 4.92	Mean 42.18 S.D. ± 3.17	0.310

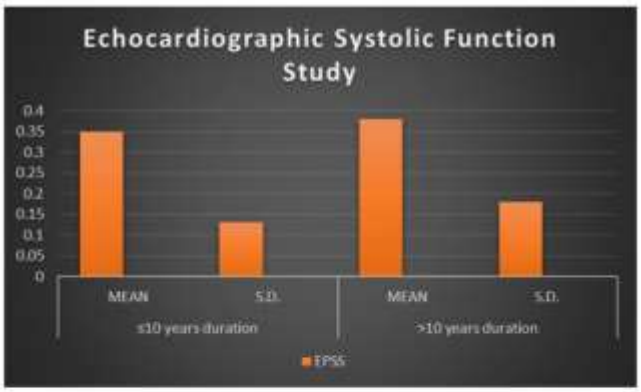


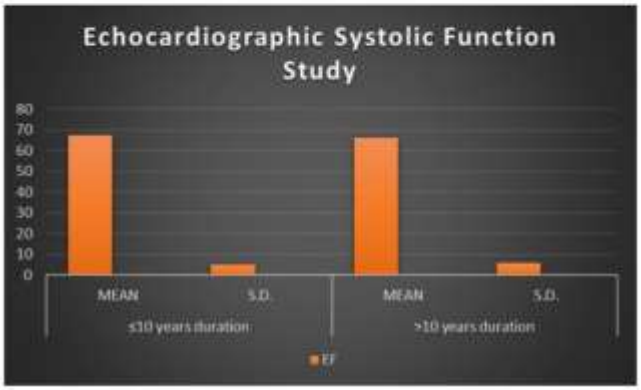
So, the two groups are not significantly different in the above-mentioned parameters of lipid profile (TG and HDL), $P > 0.05$

Table 3:

Echocardiographic Systolic Function Study

Parameters	Case group ≤ 10 years duration n = 93	Case group > 10 years duration n = 72	P Value
EPSS	Mean 0.35 S.D. ± 0.13	Mean 0.38 S.D. ± 0.18	0.184
EF	Mean 66.22 S.D. ± 5.44	Mean 64.49 S.D. ± 6.33	0.062



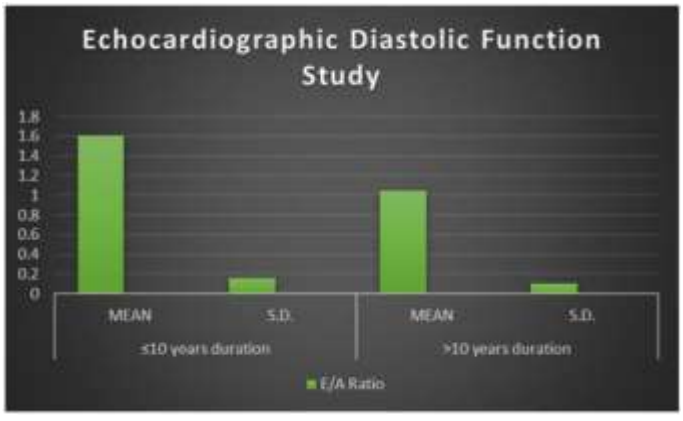


So, the two groups are not significantly different in the above-mentioned parameters of systolic function (EPSS, EF), P > 0.05

Table 4:

Echocardiographic Diastolic Function Study

Parameters	Case group ≤ 10 years duration n = 93	Case group > 10 years duration n = 72	P Value
E/A Ratio	Mean 1.6047 S.D. ± 0.1603	Mean 1.0493 S.D. ± 0.1025	0.0001



E/A ratio shows significantly different in the population group having duration of disease <10 year than population having disease >10 years duration, P = <0.05.

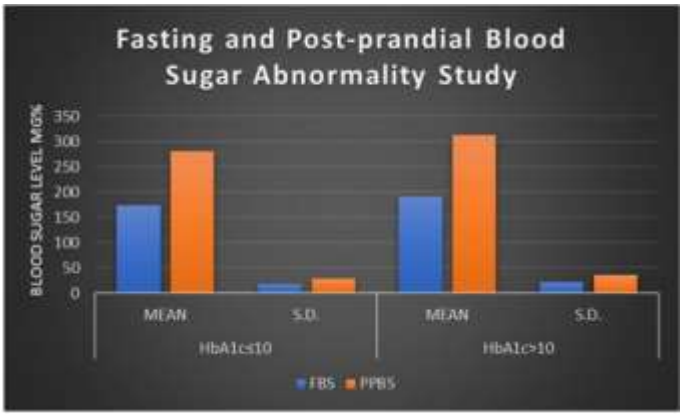
B. Lipoprotein and Cardiovascular abnormalities in relation to severity of disease.

While doing this, we took HbA1c 10 as a limit. Cardiovascular and lipoprotein abnormalities with glycated haemoglobin values (HbA1c) above and less than equal to 10 were compared.

Table 5:

Fasting and Post-prandial Blood Sugar Abnormality Study

Parameters	Case group having HbA1c ≤ 10 n = 116	Case group having HbA1c > 10 n = 49	P Value
FBS	Mean 172.84 S.D. ± 18.15	Mean 190.78 S.D. ± 22.44	0.0001
PPBS	Mean 281.11 S.D. ± 28.55	Mean 312.88 S.D. ± 36.05	0.0001

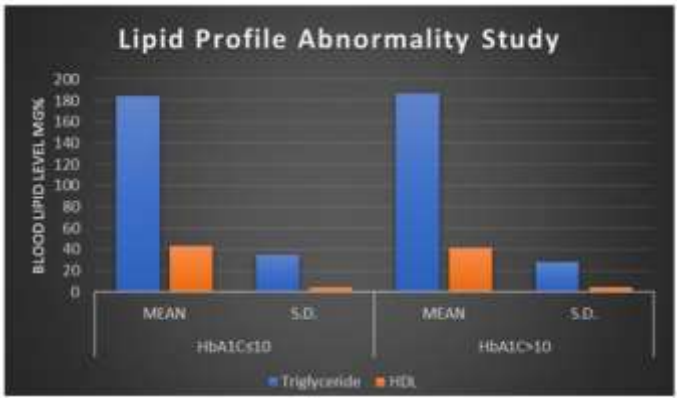


So, the FBS and PPBS show significant values in the population group having HbA1c > 10 than the population group having HbA1c < 10, P < 0.05.

Table 6:

Lipid Profile Abnormality Study

Parameters	Case group having HbA1c ≤ 10 n = 116	Case group having HbA1c > 10 n = 49	P Value
TG	Mean 184.47 S.D. ± 34.75	Mean 186.98 S.D. ± 27.87	0.655
HDL	Mean 42.85 S.D. ± 4.28	Mean 41.88 S.D. ± 4.32	0.184

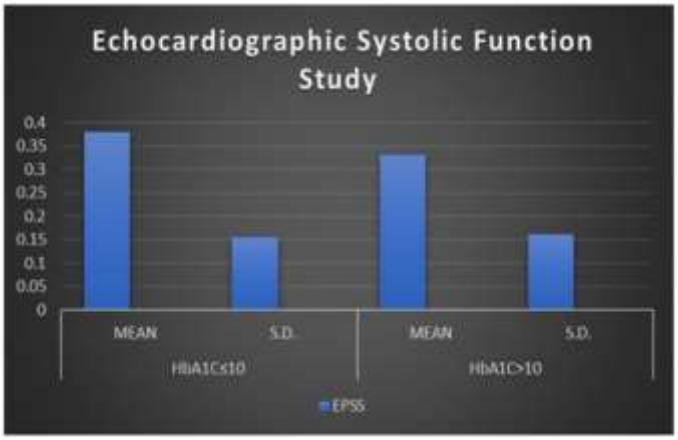


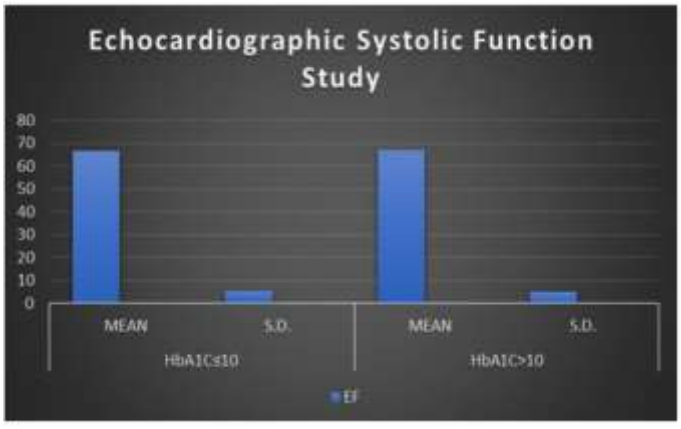
The two groups are not significantly different in the above-mentioned parameters of lipid profile (TG and HDL), P > 0.05.

Table 7:

Echocardiographic Systolic Function Study

Parameters	Case group having HbA1c ≤ 10 n = 116	Case group having HbA1c > 10 n = 49	P Value
EPSS	Mean 0.379 S.D. ± 0.1552	Mean 0.331 S.D. ± 0.1610	0.070
EF	Mean 65.78 S.D. ± 5.54	Mean 64.90 S.D. ± 5.13	0.379



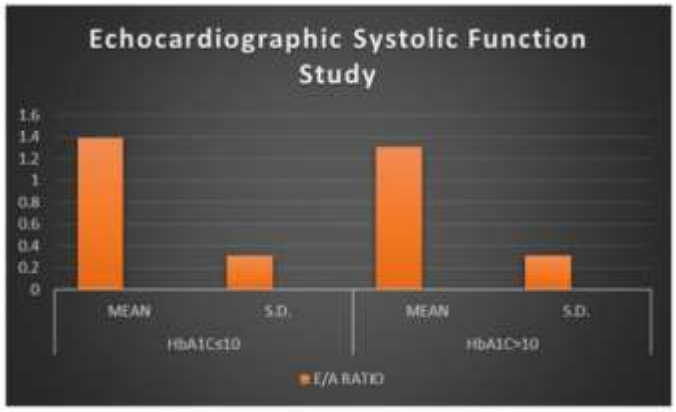


The two groups are not significantly different in the above-mentioned parameters of systolic function (EPSS, EF), P > 0.05.

Table 8:

Echocardiographic Diastolic Function Study

Parameters	Case group having HbA1c ≤ 10 n = 116	Case group having HbA1c > 10 n = 49	P Value
E/A	Mean 1.3870 S.D. ± 0.3098	Mean 1.3092 S.D. ± 0.3091	0.142

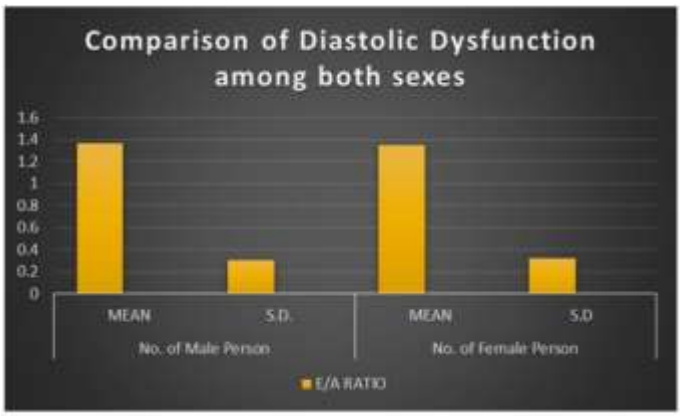


The two groups are not significantly different in the above-mentioned parameters of diastolic function (E/A), P > 0.05.

C. Comparison of Diastolic Dysfunction among both sexes.

Table 9:

Parameters	No. of Male Person n = 124	No. of Female Person n = 41	P Value
E/A ratio	Mean 1.366 S.D. ± 0.305	Mean 1.344 S.D. ± 0.322	0.2432



The two groups are not significantly different from the above-mentioned parameters (E/A), P > 0.05.

D. ECG Abnormality

It was done in all cases taken for our study and the following table shows the abnormality detected.

Table 10:

ECG Changes	Percentage
RBBB	15.75
Sick Sinus Syndrome	1.21
Ischaemic Change	3.03
Intraventricular conduction defect	4.24

Discussion

Lipoprotein abnormalities and cardiovascular dysfunction remain the fundamental defect in type 2 diabetes mellitus patients and are the major cause of mortality and morbidity.

The goal of the present study

1. To observe diabetes mellitus cases with special reference to the cardiovascular system manifestations and lipid abnormality.

2. To find out a standard criterion for preventive and therapeutic guidelines for such patients for the reduction of mortality and morbidity in broader sense, by correlating cardiovascular manifestations and lipid profile with duration and severity of diabetes.

The present study is a hospital based prospective comparative study done in Paras HMRI Hospital from June 2018 to December 2019. The mean age of study population is 48.29 with total no. of cases being 165 and sex ratio male: female 3: 1 (Approx).

The relatively asymptomatic or mildly symptomatic patients are taken in our study. We tried to exclude other co-morbid conditions like essential hypertension, obesity, smoking, familial dyslipidaemia as far possible. We also tried to exclude other medical disorder like chronic liver disease, renal disease, thyroid disorder, anaemia and COPD, which may affect ventricular function. We also excluded all secondary causes of diabetes like pancreatitis, endocrinopathy, drug induced or other syndrome associated diabetes. Patients having any congenital, hypertensive, valvular heart disease were also carefully omitted.

The study bears some similarity with the study conducted by Mustonen et al. in 1988, to see left ventricular function in middle aged asymptomatic diabetic patients. But the BMI of our patients are quite lower than this study. The cause being probably racial variation and poor nutrition. Though the study group may be criticized not being truly representative of total population people of all categories and classes are included for this reason.

Depending upon the age of onset, clinical history, BMI, family history, H/O diabetic ketoacidosis and insulin requirement type 2 diabetic patients are taken. ADA 2000 criteria for diagnosing such patients are adopted. Glycosylated haemoglobin level in our study is found to be in the range of higher side. The reason for this is probably poor patient compliance, lack of knowledge and ignorance.

Microangiopathy and related complication

In our study, we found following other complications associated with diabetes. No patient in our study have got any evidence of nephropathy as documented by urine albumin estimation. A few patients have got traces of albumin, but these patients also have got evidence of infection of urinary tract. The other complications found are:

Table 11:

ECG Changes	Percentage
RBBB	15.75
Sick Sinus Syndrome	1.21
Ischaemic Change	3.03
Intraventricular conduction defect	4.24

Lipid profile abnormality

The classic lipid profile abnormality found in type 2 diabetes mellitus is increase in triglyceride and decrease in HDL cholesterol level. The LDL part being more small, dense and atherogenic.

In our study here, we compared the lipid profile abnormality of < 10 and > 10 years duration group, we found no significant difference of the same. But the average value of these parameters of both these groups are higher side of the normal range. The inference of this observation is that lipid profile abnormalities do persist in diabetic patients. It is reflected by the higher/below normal range of these parameters in all diabetic cases.

The absence of significant difference between two groups means the lipid profile abnormality does not change much with time. We also found no significant relation with respect to lipid profile between the group of HbA1C < 10 and > 10 group, this means that no significant relationship exists between severity of diabetes and lipoprotein abnormality.

Left ventricular abnormalities in type 2 diabetes patients

The left ventricular functions are assessed by echocardiography. The systolic and diastolic function are studied separately. The systolic functions are assessed with the following parameters: 1. E point septal separation (EPSS) 2. Ejection fraction (EF) 3. Fractional shortening (FS) .Diastolic abnormality is assessed by ratio of the E flow velocity and A flow velocity. Pulse doppler echocardiography is a simple reproducible method of assessing left ventricular function. It has got some important limitation. Measurement of mitral inflow velocity is dependent on sample volume location which move during cardiac cycle and respiration. We minimized these limitations by arranging at least five consecutive cycles.

1. In this study, we found the ratio of the E flow velocity and A flow velocity (E/A ratio) showed significant reduction in the disease duration group > 10 years than those having duration < 10 years. This simply means that more the duration of the disease lesser is the E/A ratio, i.e., greater is the diastolic dysfunction.
2. In this study, it is evident that diastolic dysfunction of heart can occur in an asymptomatic diabetic patient. Shapiro[105] also found that diastolic dysfunction was more common than systolic in NIDDM subjects.
3. The same is confirmed by other corroborative study that the abnormalities in left ventricular diastolic function may be an earlier sign of diabetic heart disease than impaired systolic function at rest. Even young patient with diabetes mellitus suffers from diastolic dysfunction while systolic ventricular function is normal. Therefore, echocardiography with measurement of diastolic functional parameters appears to be the sensitive method for evaluating the manifestation and course of early diabetic cardiomyopathy[62].
4. It is observed that E/A ratio is not significantly reduced in female as compared to male. The famous Framingham Heart Study showed that the increased cardiovascular risk was particularly striking in female. The lack of significance probably due to small study sample and uneven sex ratio comparison (male: female = 3: 1).

In our study the parameters of the systolic functions of heart like EPSS, EF, FS are studied in two groups both in respect to duration and severity of diabetes. We found no relationship between these two groups. The contributory factor may be a small study group, selection bias etc. but

we should also keep this fact in mind that diastolic function abnormality precedes systolic dysfunction.

So, the systolic abnormality appears in the later part of the disease. Patel et al. [108] showed reduced ejection fraction in type 2 patients. But Shapiro et al. [104] found no significant change in systolic function in diabetics.

Fasting and post prandial blood glucose showed significantly greater values in the age group of duration > 10 years than < 10 years group. Probable explanation of this fact is as follows: With increase of duration and age, the control of blood sugar may become more difficult due to insulin resistance and increased obesity. This is attributed to the various combination of insulin resistance and impaired insulin secretion that results in a progressive age-related decline in glucose tolerance, which begin in the 3rd decade and continues throughout adulthood[109]. Perhaps the most important factor contributing to age related glucose intolerance is impairment of insulin mediated glucose disposal, especially in skeletal muscle[110] which is particularly marked in obese subjects[111]. Obesity is also associated with increasing age.

The limitation of the present study is that it consists of small number of patients and the study period is short. Many patients are from a poor socio-economic class with cultural taboos and dependence on indigenous medicine. Cardiovascular symptom manifestations do not seem to be very reliable so also the treatment history and patient compliance. So, it is often difficult to access the cardiovascular manifestations in these category of patients

Summary And Conclusion

The following facts are evident from the present study: Diabetic patients have cardiovascular dysfunction. The dysfunction becomes more evident as the disease progresses i.e.; it depends on the duration of the disease. Diastolic dysfunction precedes systolic dysfunction. Systolic dysfunction in our study does not show any correlation with duration or severity of disease between the study group mentioned. No significant change in lipid profile is found between the study group of duration 10 years and glycosylated haemoglobin level (HbA1c) 10. Here, we found that the fasting and post prandial blood glucose level gradually increase with increased duration of the disease. The established fact that glycosylated haemoglobin (HbA1c) varies directly with fasting and post prandial blood glucose level i.e., it denotes the control of diabetes is once again shown. There is no difference between both sexes with respect to diastolic dysfunction.

References

1. Gan D. ed. Diabetes Atlas 2017: the Rising Global Burden of Diabetes International Diabetes Federation, 2017: 9-13.
2. Barzilay JI, Kronmal RA, Bittner V et al. coronary artery disease and coronary artery bypass grafting in diabetic patients aged > 65 years Am.J. Cardiol 1994; 74: 334-9.
3. Haffner SM, Lehto S, Ronnemaa T, Pyolora K, Laakso M. Mortality from coronary heart disease in subjects with type-2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. NEngl J Med 1998; 339: 229-34.
4. Fisher BM, Gillen G, Lindop GBM, Dargie HJ, Frier B M. Cardiac function and coronary arteriography in asymptomatic type-1 (insulin-dependent) diabetic patients; evidence for a specific diabetic heart disease. Diabetologia 1986; 29: 706-12.
5. Pham I, Cosson E, Nguyen MT, et al. Evidence for a Specific Diabetic Cardiomyopathy: An Observational Retrospective Echocardiographic Study in 656

Asymptomatic Type 2 Diabetic Patients. Int J Endocrinol. 2015; 2015: 743503.

6. Ewing DJ, Neilson JM, Shapiro CM, et al.: Twenty four hour heart rate variability: Effects of posture, sleep, and time of day in healthy controls and comparison with bedside tests of autonomic function in diabetic patients. Br Heart J. 1991;65(5):239-44.
7. Lozano T, Ena J. Cardiovascular autonomic neuropathy in patients with diabetes mellitus. Neuropatia autonomica cardiovascular in pacientes con diabetes mellitus. Rev Clin Esp. 2017; 217(1): 46-54.
8. Liu Y, Liu SX, Zheng F, Cai Y, Xie KL, Zhang WL. Cardiovascular autonomic neuropathy in patients with type 2 diabetes. J Diabetes Investig. 2016; 7(4):615- 21.
9. Maser RE, Mitchell BD, Vinik AI, Freeman R. The association between cardiovascular autonomic neuropathy and mortality in individuals with diabetes: a meta-analysis. Diabetes Care. 2003; 26(6): 1895-1901.
10. Hirano T. Pathophysiology of Diabetic Dyslipidemia. J Atheroscler Thromb. 2018; 25(9): 771-82.
11. Mark L, Dani G. Diabeteses dyslipidaemia es atherosclerosis [Diabetic dyslipidaemia and the atherosclerosis]. Orv Hetil. 2016; 157(19): 746-52.
12. Welty FK. How do elevated triglycerides and low HDL-Cholesterol affect inflammation and atherothrombosis? Curr Cardiol Rep. 2013; 15(9): 400.
13. Ye X, Kong W, Zafar MI, Chen LL. Serum triglycerides as a risk factor for cardiovascular diseases in type 2 diabetes mellitus: a systematic review and meta-analysis of prospective studies. Cardiovasc Diabetol. 2019; 18(1): 48.
14. Steiner G. Dyslipoproteinemias in diabetes. Clin Invest Med. 1995;18(4):282-87.
15. Taskinen MR, Packard CI, Shepherd J. Effect of insulin therapy of metabolic fate of apolipoprotein B-containing lipoproteins in NIDDM Diabetes 1990; 39: 1017- 27.
16. Siegel RD, Cupples A, Schaefer EJ, Wilson PW. Lipoproteins, apolipoproteins, and low-density lipoprotein size among diabetics in the Framingham offspring study. Metabolism. 1996; 45 (10): 1267-72.
17. Yang Y, Yan B, Fu M, Xu Y, Tian Y. Relationship between plasma lipid concentrations and HDL subclasses. Clin Chim Acta. 2005; 354 (1-2): 49-58.
18. Tian L, Fu M. The relationship between high density lipoprotein subclass profile and plasma lipid concentrations. Lipids Health Dis. 2010; 9: 118.
19. Betteridge DJ. Diabetic dyslipidaemia Diabetes Obes Metab 2000; 2 (Suppl 1) S31-S36.
20. Bo S, Cavallo-Perin P, Gentile L, Repetti E, Pagano G. Low HDL cholesterol a component of the metabolic syndrome only in the presence of fasting hypertriglyceridemia in type 2 diabetic patients. Diabetes Metab 2001; 27: 31-5.
21. Wam BH, Kennel WB, D‟ Agostino. Search for an optimal atherogenic lipid risk profile: from the Framingham Study. Am J Cardiol. 2006; 97 (3): 372-75.
22. Lamarche B, Moorjani S, Cantin B et al. Associations of HDL2 and HDL3 subfractions with ischemic heart disease in men prospective result from the Quebec Cardiovascular Study Arterioscler Thromb Vasc Biol 1997; 17: 1098- 105
23. Alvin C. Power, Diabetes Mellitus, Harrison's Principle of Internal Medicine 20th Edition.
24. Ahmed AM. History of diabetes mellitus. Saudi Med J. 2002; 23 (4): 373-78.

25. Garcia MJ, McNamara PM, Gordon T et al: Morbidity and mortality in diabetes in the Framingham population. Sixteen years follow up study. Diabetes, 1974, 23: 105-11.
26. Rivellese AA, Riccardi G, Voccaro O. Cardiovascular risk in women with diabetes. Nutr Metab Cardiovasc Dis. 2010; 20 (6): 474-80.
27. Levitzky YS, Pencina MJ, D‟ Agostino RB, et al. Impact of impaired fasting glucose on cardiovascular disease: the Framingham Heart Study. J Am Coll Cardiol. 2008; 51 (3): 264-70
28. Setacci C, de Donato G, Setacci F, Chisci E. Diabetic patients: epidemiology and global impact. J cardiovasc Surg (Trrino) 2009; 50: 263-73.
29. Thiruvoipati T, Kielhorn CE, Armstrong EJ. Peripheral artery disease in patients with diabetes: Epidemiology, mechanisms and outcomes. World J Diabetes, 2015; 6 (7): 961-69.
30. Mensah GA, Wei GS, Sorlie PD, et al. Decline in Cardiovascular Mortality : Possible Causes and Implications. Circ Res. 2017; 120 (2): 366-80.
31. Burchfiel CM, Reed DM, Marcus EB, Strong JP, Hayashi T. Association of diabetes mellitus with coronary atherosclerosis and myocardial lesions: an autopsy study from Honolulu Heart program. Am J Epidemiology 1993, 137: 1328- 40.
32. Hubbard BL, Gibbons RJ, Lapeyre AC III, Clements IP. Identification of severe coronary artery disease using simple clinical parameters. Arch Intern Med 1992, 152: 309-12.
33. Singh VP, Bali A, Singh N, Jaggi AS, Advanced glycation end products and diabetic complications. Korean J Physiol Pharmacol. 2014; 18 (1): 1-14
34. Reaven GM. the role on insulin resistance and hyperinsulinemia in coronary heart disease. Metabolism, 1992; 41 (5 Suppl 1): 16-19.
35. Pankow JS, Kwan DK, Duncan BB, et al. Cardiometabolic risk in impaired fasting glucose and impaired glucose tolerance: the Atherosclerosis Risk in Communities Study. Diabetes Care. 2007; 30 (2): 325-31.
36. Amini M, Horri N, Zare M, et al. People with impaired glucose tolerance and impaired fasting glucose are similarly susceptible to cardiovascular disease: a study in first degree relatives of type 2 diabetic patients. Ann Nutr Metab. 2010; 56 (4): 267-72.
37. Raynauld E, Perez-Martin A, Brun J, Aissa-Benhaddad, Fedou C, Mercier J. Relationship between fibrinogen and insulin resistance. Atherosclerosis. 2000; 150 (2): 365-70.
38. Yarmolinsky J, Bordin Barbieri N, Weinmann T, Ziegelmann PK, Duncan BB, Ines Schmidt M. Plasminogen activator inhibitor-1 and type 2 diabetes: a systematic review and metaanalysis of observational studies. Sci Rep. 2016; 6 : 17714.
39. Reaven GM. Syndrome x : a short history. Ochsner J. 2001; 3 (3) : 124-25.
40. Espinosa RA; Grupo FRICVE. El fibrnogeno: factor de riesgo cardiovascular[Fibrinogen ; Cardiovascular risk factor] Invest Clin. 2003 Jun; 44 (2) : 165.
41. Gragnano F, Golia E, Natale F et al. Von Willebrand Factor and Cardiovascular Disease: From a Biochemical Marker to an Attractive Therapeutic Target. Curr Vasc Pharmacol. 2017; 15 (5) : 404-15.
42. Heller FR, Jamart J, Honore P et al. Serum Lipoprotein(a) in patients with diabetes mellitus. Diabetes Care 1993, 16 : 819-23.
43. Sulikowska B, Manitius J. Bialkomocz jako wskaznik ryzyka powiklan sercowoneczyniowych--nowe dane [Proteinuria as a predictor of risk of

cardiovascular disease: a new insight]. Pol Arch Med Wewn. 2007; 117 (9) : 411-14.

44. Naidoo DP. The link between microalbumimuria , endothelial dysfunction and cardiovascular disease in diabetes. Cardiovasc I S Afr. 2002; 13 (4) : 194-99.
45. Aronson D. and Rayfield EJ : Diabetes and obesity. In Fuster V, Ross R. Ropol : Atherosclerosis and coronary artery disease. Philadelphia, Lippin Cott-Raven 1996.
46. Stone PH, Muller JW, Hartwell T et al. The effect of diabetes mellitus on prognosis and serial left ventricular function after acute myocardial infarction, contribution of both CAD and diastolic left ventricular dysfunction to the adverse prognosis. J. Am. Coll. Cardiol. 1989, 14 : 49.
47. Nesto RW, Phillips RT, Kett KG et al. Angina and exertional myocardial ischaemia in diabetic and non-diabetic patients, assessment by exercise thallium scintigraphy. Ann Intern Med 1998, 108 : 170-5.
48. Scheidt-Nave C, Barret-Connor E, Wingard DL. Resting heart disease associated with NIDDM in a defined population. Circulation 1990, 81 : 899-906.
49. Weiner DA, Ryan TJ, Parsons L et al. Significance of silent myocardial ischaemia during exercise testing in patients with diabetes mellitus : a report from CASS registry. Am. J. Cardiol 1991, 68 : 729-34.
50. Yudkin J, Hendra TJ, Vascular events and diabetes : Acute myocardial infarction and stroke. In, Alberti KGMM, Keen HA, De Franzo RA, eds. International text book of diabetes. Chichester, John Wiley and Sons Ltd. 1992 : 1185-212.
51. Einarson TR, Acs A, Ludwig C, Phanton UH. Prevalence of cardiovascular disease in type 2 diabetes: a systematic literature review of scientific evidence from across the world in 2007-2017. Cardiovasc Diabetol. 2018; 17 (1) : 83.
52. Dhingra R, Vasan RS, Diabetes and the risk of heart failure. Heart Fail Clin. 2012; 8 (1) : 125-33.
53. Aronson D, Edelman ER. Coronary artery disease and diabetes mellitus. Cardiol Clin. 2014; 32 (3) : 439-55.
54. Haffner SM. Coronary heart disease in patients with diabetes. N Eng J Med. 2002; 342 (14) : 1040-42.
55. Kawano Y, Takemoto M, Mito T, et al. Silent myocardial ischemia in asymptomatic patients with type 2 diabetes mellitus without previous histories of cardiovascular disease. Int J Cardiol. 2016; 216 : 151-55.
56. Cornelia Junghans, Neha Sekhri, M. Justin Zaman, Harry Hemingway, Gene S. Feder, Adam Timmis, Atypical chest pain in diabetic patients with suspected stable angina : Impact on diagnosis and coronary outcomes, European Heart Journal-Quality of care & clinical outcomes, Volume 1, Issue 1, 2015; 37-43.
57. Hamby RI, Zoneriach S, Sherman L. Diabetic cardiomyopathy JAMA 1974; 229 (13) : 1749-54.
58. Paolillo S, Marsico F, Prastaro M, et al. Diabetic Cardiomyopathy: Definition, Diagnosis and Therapeutic Implications. Heart Fail Clin. 2019; 15 (3): 341-47.
59. Law B, Fowlkes, Goldsmith JG, Carver W, Goldsmith EC. Diabetes-induced alterations in the extracellular matrix and their impact on myocardial function. Microsc Microanal. 2012; 18(1): 22-34.
60. Berridge BR, Mowat V, Nagai H et al. Non-proliferative and Proliferative Lesions of the Cardiovascular System of the Rat and Mouse. J Toxicol Pathol. 2016; 29 (3 Suppl) : 1S-47S.
61. Shapiro LM. A prospective study of heart disease in diabetes mellitus. Q J Med. 1984; 53 (209): 55-68.

62. Paillole C, Dahan M, Paycha F, Cohen A, Gourgon R. Prevalence and significance of left ventricular filling abnormalities determined by Doppler echocardiography in young type 1 diabetic patients. Am J. Cardiol, 1990,64: 1010-16.
63. Cosson S, Kevorkian JP. Left ventricular diastolic dysfunction : an early sign of diabetic cardiomyopathy? . Diabetes Metab. 2003; 29(5) : 455-66.
64. Mishra TK, Rath PK, Mohanty NK, Mishra SK. Left ventricular systolic and diastolic dysfunction and their relationship with microvascular complications in normotensive, asymptomatic patients with type 2 diabetes mellitus. India Hear J. 2008; 60 (6): 548-53.
65. Schannwell CM, Schneppenheim M, Perings S, Plehn G, Strauer BE. Left ventricular diastolic dysfunction as an early manifestation of diabetic cardiomyopathy. Cardiology. 2002; 29 (5): 455-66.
66. Redfield MM, Jacobsen SJ, Burnett JC Jr, Mahoney DW, Bailey KR, Rodeheffer RJ. Burden of systolic and diastolic ventricular dysfunction in the community: appreciating the scope of the heart failure epidemic. JAMA. 2003; 289 (2) : 194- 202.
67. Poirier P, Bogaty P, Garneau C, Marois L, Dumesnil JG. Diastolic dysfunction in normotensive men with well-controlled type 2 diabetes : importance of maneuvers in echocardiographic screening for preclinical diabetic cardiomyopathy. Diabetes Care. 2001; 24 (1) : 5-10.
68. Bertoni AG, Tsai A, Kasper EK, Brancati FL. Diabetes and idiopathic cardiomyopathy: a nationwise case-control study. Diabetes Care. 2003; 26 (10): 2791-95.
69. Galderisi M, Anderson KM, Wilson PW, Levy D. Echocardiographic evidence for the existence of a distinct diabetic cardiomyopathy (the Framingham Heart Study). Am J Cardiol. 1991; 68(1) : 85-89.
70. Struthers AD, Morris AD. Screening for and treating left-ventricular abnormalities in diabetes mellitus: a new way of reducing cardiac deaths. Lancet. 2002; 359 (9315) : 1430-32.
71. Fishman SL, Sonmez H, Basman C, Singh V, Poretsky L. The role of advanced glycation end-products in the development of coronary artery disease in patients with and without diabetes mellitus: a review. Mol Med. 2018; 24 (1) : 59
72. Ziegelhöffer A, Ravingerová T, Styk J, et al. Mechanisms that may be involved in calcium tolerance of the diabetic heart. Mol Cell Biochem. 1997;176(1- 2):191-98.
73. Das Evcimen N, King GL. The role of protein kinase C activation and the vascular complications of diabetes. Pharmacol Res. 2007;55(6):498-510.
74. Henning RJ, Bourgeois M, Harbison RD. Poly(ADP-ribose) Polymerase (PARP) and PARP Inhibitors: Mechanisms of Action and Role in Cardiovascular Disorders. Cardiovasc Toxicol. 2018;18(6):493-506.
75. Young ME, McNulty P, Taegtmeyer H. Adaptation and maladaptation of the heart in diabetes: Part II: potential mechanisms. Circulation. 2002;105(15):1861-70.
76. Liu JE, Robbins DC, Palmieri V, et al. Association of albuminuria with systolic and diastolic left ventricular dysfunction in type 2 diabetes: the Strong Heart Study. J Am Coll Cardiol. 2003;41(11):2022-28.
77. Arnold JM, Yusuf S, Young J, et al. Prevention of Heart Failure in Patients in the Heart Outcomes Prevention Evaluation (HOPE) Study. Circulation. 2003;107(9):1284-90.

78. Klein LW, Nathan S. Coronary artery disease in young adults. J Am Coll Cardiol. 2003;41(4):529-31.
79. Ferrario CM. Cardiac remodelling and RAS inhibition. Ther Adv Cardiovasc Dis. 2016;10(3):162-71.
80. Serhiyenko VA, Serhiyenko AA. Cardiac autonomic neuropathy: Risk factors, diagnosis and treatment. World J Diabetes. 2018;9(1):1-24.
81. Balcıoğlu AS, Müderrisoğlu H. Diabetes and cardiac autonomic neuropathy: Clinical manifestations, cardiovascular consequences, diagnosis and treatment. World J Diabetes. 2015;6(1):80-91.
82. Ewing DJ, Campbell IW, Cherke BF : The natural history of diabetic autonomic neuropathy. Quarterly Journal of Medicine, 1990, 35 : 193.
83. Neubauer B, Christensen NJ. Norepinephrine, epinephrine, and dopamine contents of the cardiovascular system in long-term diabetics. Diabetes. 1976;25(1):6-10.
84. Ganguly PK, Dhalla KS, Innes IR, Beamish RE, Dhalla NS. Altered norepinephrine turnover and metabolism in diabetic cardiomyopathy. Circ Res. 1986;59(6):684-93.
85. O‟Brien T, Nguyen TT, Zimmerman BR. Hyperlipidemia and diabetes mellitus. Mayo Clin Proc 1998; 73 : 969-76.
86. Laitinen T, Vauhkonen IK, Niskanen LK, et al. Power spectral analysis of heart rate variability during hyperinsulinemia in nondiabetic offspring of type 2 diabetic patients: evidence for possible early autonomic dysfunction in insulinresistant subjects. Diabetes. 1999;48(6):1295-99.
87. Wheelock KM, Jaiswal M, Martin CL, et al. Cardiovascular autonomic neuropathy associates with nephropathy lesions in American Indians with type 2 diabetes. J Diabetes Complications. 2016;30(5):873-79.
88. Beijers HJ, Ferreira I, Bravenboer B, et al. Microalbuminuria and cardiovascular autonomic dysfunction are independently associated with cardiovascular mortality: evidence for distinct pathways: the Hoorn Study. Diabetes Care. 2009;32(9):1698-1703.
89. Maqbool M, Cooper ME, Jandeleit-Dahm KAM. Cardiovascular Disease and Diabetic Kidney Disease. Semin Nephrol. 2018;38(3):217-32.
90. Bissinger, A. (2017). Cardiac Autonomic Neuropathy: Why Should Cardiologists Care about That? Journal of Diabetes Research, 2017, 1–9.
91. Vinik AI, Erbas T, Casellini CM. Diabetic cardiac autonomic neuropathy, inflammation and cardiovascular disease. J Diabetes Investig. 2013;4(1):4-18.
92. Lopaschuk G. Regulation of carbohydrate metabolism in ischemia and reperfusion. Am Heart J. 2000;139(2 Pt 3):S115-S119.
93. Feingold KR, Grunfeld C. Diabetes and Dyslipidemia. In: Feingold KR, Anawalt B, Boyce A, et al., eds. Endotext. South Dartmouth (MA): MDText.com, Inc.; 2000.
94. Rizzo M, Berneis K. Lipid triad or atherogenic lipoprotein phenotype: a role in cardiovascular prevention?. J Atheroscler Thromb. 2005;12(5):237-39.
95. McGarry JD. Banting lecture 2001: dysregulation of fatty acid metabolism in the etiology of type 2 diabetes. Diabetes. 2002;51(1):7-18.
96. Coppack SW, Jensen MD, Miles JM. In vivo regulation of lipolysis in humans. J Lipid Res. 1994;35(2):177-93.

97. Ginsberg HN. Diabetic dyslipidemia: basic mechanisms underlying the common hypertriglyceridemia and low HDL cholesterol levels. Diabetes. 1996;45 Suppl 3:S27-S30.
98. Durrington PN, Mackness B, Mackness MI. Paraoxonase and atherosclerosis. Arterioscler Thromb Vasc Biol. 2001;21(4):473-80.
99. Sniderman AD, Scantlebury T, Cianflone K. Hypertriglyceridemic hyperapob: the unappreciated atherogenic dyslipoproteinemia in type 2 diabetes mellitus. Ann Intern Med. 2001;135(6):447-59.
100. Proctor SD, Pabla CK, Mamo JC. Arterial intimal retention of pro-atherogenic lipoproteins in insulin deficient rabbits and rats. Atherosclerosis. 2000;149(2):315-22.
101. Mahley RW, Huang Y, Rall SC Jr. Pathogenesis of type III hyperlipoproteinemia (dysbetalipoproteinemia). Questions, quandaries, and paradoxes. J Lipid Res. 1999;40(11):1933-49.
102. Roche HM, Gibney MJ. The impact of postprandial lipemia in accelerating atherothrombosis. J Cardiovasc Risk. 2000;7(5):317-24.
103. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). JAMA. 2001;285(19):2486-97.
104. Mandal M,Kumari R,Mukherjee A.Prevalence of dyslipidemia in patients with type 2 diabetes mellitus patients:a hospital based study in kishanganj,India.Int J Res Med Sci 2015;3:3691-7
105. Shapiro LM, Leatherdale BA, Coyne ME, Fletcher RF, Mackinnon J. Prospective study of heart disease in untreated maturity onset diabetics. Br Heart J. 1980;44(3):342-48.
106. Rubler S, Dlugas h J, Yuceoglu YZ, Kumral T, Branwood AW, Grishman A. New type of cardiomyopathy associated with diabetic glomerulosclerosis. Am J Cardiol. 1972;30(6):595-602.
107. Russo C, Jin Z, Homma S, et al. Effect of diabetes and hypertension on left ventricular diastolic function in a high-risk population without evidence of heart disease. Eur J Heart Fail. 2010;12(5):454-61.
108. Patel TM, Mathur VS, Dave SH, Kothari SS, Patel TK. Noninvasive assessment of left ventricular function in asymptomatic diabetics and its relation to metabolic control and microangiopathy. Panminerva Med. 1991;33(1):6-10.
109. Stout RW. Glucose tolerance and ageing. J R Soc Med. 1994;87(10):608-9.
110. Muller DC, Elahi D, Tobin JD, Andres R. The effect of age on insulin resistance and secretion: a review. Semin Nephrol. 1996;16(4):289-98.
111. Meneilly GS, Elliott T, Tessier D, Hards L, Tildesley H. NIDDM in the elderly. Diabetes Care. 1996;19(12):1320-25