REVIEW OF LITERATURE
The heart in the patients with diabetes mellitus may be affected by several different ways - firstly a large vessel disorder affecting the coronary vessels manifest in cardiac disease, secondly a subclinical involvement producing abnormality of functions, thirdly as a result of autonomic neuropathy presenting in the form of impaired vasomotor reflex response. Patients of diabetes mellitus are more prone for development of hypertension and hypertensive heart disease.

Diabetic microangiopathy is thought to be the sheet anchor in pathogenesis of diabetic complications (Williamson and Kite, 1980).

Shapiro et al. (1981) have depicted in their study that diabetics have increasing evidence of abnormalities of LV function in absence of clinical heart disease. Patients without microvascular disease have been shown to have normal (Rubler et al., 1978) and abnormal (Ahmed et al., 1975) systolic time intervals and those with severe microvascular disease (Proliferative retinopathy and nephropathy) have abnormal systolic time intervals (Seneviratine et al., 1977) and echocardiograms (Sanderson et al., 1978). Delia et al. (1979) reported that there is high prevalence of myocardial dysfunction among diabetic uremic patients. In this study 15 patients with diabetes of juvenile onset with severe renal insufficiency and no evidence of significant atherosclerotic large vessel coronary artery disease were taken.
59% patients had some evidence of myocardial dysfunction. 50% of these patients had severe abnormality. In this study LV function was assessed by echocardiography as well as cardiac catheterization with coronary angiography. The authors have enumerated following possible factors of myocardial dysfunction in patients of diabetes mellitus.
1. Diabetic cardiomyopathy due to small vessel disease.
2. Volume over load and salt retention, due to renal failure.
3. Hypertension.
4. Uremic myocardial dysfunction.
5. Deposition of calcium in myocardium due to associated hyperparathyroidism.
6. Increased atherosclerosis and type IV hyperlipidemia.
7. Anaemia.
8. Nutritional deficiency due to low protein diet and thiamine deficiency.
9. Accumulation of catecholamines due to a decrease in renal clearance.

CORONARY ARTERY DISEASE

Lewine gave the first suggestion that diabetics are excessively prone to ischemic heart disease as early as 1922. In Framingham prospective community study there was an excess mortality amongst diabetics from sudden death, myocardial infarction and cerebrovascular disease
(Garcia et al., 1973). Particularly striking was excess of death in diabetic women. Mortality statistics assembled by Hayward and Lucena (1975) for a cohort of diabetics attending the large Birmingham (England) diabetic clinic also showed an excess of deaths predominantly due to diseases of circulatory system. In the tecumecah community study (Ostrander et al., 1986) known diabetics were found to have at every age level, two or three times more vascular disease than would have been expected from population as a whole.

Incidence

Incidence of coronary artery disease in diabetics varies from 1.4 to 77% as reported by various authors. Cornet and associates (1959) found the incidence to be around 14%, while Bradley et al (1956) and Liebow and colleagues' (1949) reported an incidence of 40% to 67% of the diabetics and coronary artery disease in the study by Lundback et al (1954). Variations of similar magnitude has been described by Indian authors - the reported incidences vary from 16% (Vaishnava et al., 1968), 21% (Pathania et al., 1961) and 25–30% (Pathak et al., 1966; Banerjee et al., 1966).

Relation to age and sex

Incidence of ischemic heart disease in relation to age and sex is again controversial. Tridberg (1956) indicated that the coronary artery involvement in diabetic subjects develops at an early age. The incidence has been
found to be increasing with age (Pathania et al., 1964; Urs et al., 1966; Banerjee et al., 1966 and Shah et al., 1970) and peak incidence occurs in the sixth decade (Pathania et al., 1961). Males are involved more often under the age of 50 but beyond 5th decade usually the females out number them. Pathania et al (1961), Banerjee et al (1966), Urs et al (1966) and Shah et al (1970) found an excess of males while equal sex incidence was claimed by Root et al (1939).

Relation to duration of diabetes

Increased incidence of CAD is frequently encountered as the duration of diabetes lengthens (Pathania et al., 1961; Vytillingan et al., 1964; Pathak et al., 1966; Banerjee et al., 1966; Vaishnava et al., 1968 and Malhotra et al., 1968). Pathak (1966) concluded that the incidence of CAD hopped to 72% in diabetics of more than five years' duration in contrast to the general incidence of 25-30%. There are some reports to the contrary too (Bradly and Brytogle, 1956; Abukhatwa, 1963; and Urs et al., 1966).

Relation to severity of diabetes

The severity of diabetic illness was more often than not found to have no correlation with the prevalence of IHD among diabetic individuals (Banerjee et al., 1966; and Pathak et al., 1966). Differing from the Indian reports are few studies claiming increased incidence of IHD amongst subjects harbouring diabetes of greater severity (Leibow et al., 1949; Lundback, 1954; Bradley, 1956; Caridy et al., 1966 and Wilson et al., 1966).
Relation to the status of control of diabetes

Knowels (1964) reviewed this topic and analysed 300 papers from 85 different centres, 50 considered that there was a positive correlation between vascular disease and poor control of the diabetes, 25 thought that there was no relationship and 10 were undecided. Robinwitch (1944) in a prospective study (50 years follow up) showed an association between relatively low serum cholesterol and a higher index of diabetes control on one hand and decreased incidence of atherosclerosis on the other. Skouby (1956), Keiding and associates (1952) and Lundback (1953) drew an inference that a good control was comparable to low incidence of vascular, ocular and renal complic-a-tions. Schlisinger and colleagues (1960) stated that a good control could do nothing to already established vascular complication. White et al (1965) and Colwell et al (1966) in a UGDP (University group diabetes programme, 1970) study indicated that the severity of diabetic compli-ca-tion is related to the level of control. Some authors have claimed that the fate of a diabetic patient is sealed at the inception of the disease and that progress of the vascular disorder is largely independent of the blood sugar levels (Colwell et al, 1942). Raheja (1970) found increased frequency, more severity and greater deteriora-tion in better controlled diabetics than poorly controlled ones. Shah et al indicated an equal incidence of IHD
among poorly and nicely controlled diabetic patients. Luken and Franklin (1966) after a 20 years' follow up stated that out of 11 patients escaping cardiovascular disease, 10 had poor diabetic control. However, increased incidence running in parallel to the extent of poor control of diabetic state was described by Lawrence et al (1951), Root et al (1959), Pathak et al (1966) and Wilson et al (1966).

Relation to various risk factors

Incidence and severity of IHD in diabetics is related to various risk factors.

DIABETIC CARDIOMYOPATHY

The clinical condition

Diabetes mellitus was first linked to cardiomyopathy over 100 years ago by Leyder et al (1981). Diabetic cardiomyopathy was further characterized in 1972 by Rubler et al based on necropsy finding in four diabetic patients with Kimmelstiel Wilson disease and heart failure. Coronary atherosclerosis's and hypertension were not present in those patients. Severe renal disease and anemia may have played a role in production of the pathologic myocardial changes, the likelihood remained that the metabolic derangements of diabetes contributed to the cardiomyopathy. Hamby et al (1974) in their series of 73 patients with primary myocardial disease found that 16 were diabetics. Their coronary angiograms were normal, 3 of them showed
small vessel involvement. Regan et al (1977) and D'Elia et al (1979) have also concluded that diabetics can develop abnormalities of myocardial function with patent main coronary arteries, which may progress to cardiomyopathy and congestive heart failure. Kannel et al (1978) reported from the Framingham study showing the diabetic men had a 2.4 fold greater risk for developing heart failure, than non diabetic men over an 18 years period. The relative risk for diabetic women was 5.2 times higher. Zoneraich et al (1977) viewing this association from a different perspective reported an increased incidence of diabetes mellitus in patients with idiopathic cardiomyopathy. Senewirante et al (1977) proposed that the association of microangiopathy and impaired left ventricular function may explain high immediate mortality and the increase of cardiogenic shock and congestive cardiac failure after myocardial infarction in diabetes. Diabetic cardiomyopathy is reported in both type I and type II diabetics.

**Pathology of Diabetic Cardiomyopathy**

Gross pathologic changes found at necropsy in the cardiomyopathic hearts of diabetic patients include increased weight, pale appearance and firmness to palpation (Sandel et al, 1988 and Feim et al, 1985).

The firmness is associated with an increase in myocardial collagen. Light and electron microscopy
reveals thickening of capillary basement membranes and capillary microaneurysms.

**CLINICAL PRESENTATION**

Potential or latent cardiomyopathy exists in all persons with diabetes mellitus (Sander et al., 1988). One of the earliest manifestations is altered left ventricular diastolic function. Even before clinically apparent cardiac disease appears, left ventricular dysfunction may be detected by abnormalities of resting hemodynamic and left ventricular response to exercise as well as abnormal systolic time interval (Ahmed et al., 1975; Unsitupal et al., 1985; Shapiro et al., 1980). Left ventricular filling abnormalities were detected by pulse doppler echocardiography. These findings are similar to those previously recorded utilizing M-mode echocardiography (Sanderson et al., 1978; Unsitupal et al., 1985 and Seneviratne et al., 1977).

The early stage of clinically apparent diabetic cardiomyopathy results largely from clinical expression of those diastolic abnormalities and is dominated by a restrictive clinical picture, increased pulmonary and systemic venous pressure, audible fourth heart sound, increased left ventricular wall: cavity ratio with a normal heart size on chest radiographic examination. Decreased stroke volume and increased end diastolic pressure may occur in the absence of large coronary artery disease (Regan et al., 1977). Diabetic cardiomyo-
Pathy may progress to resemble typical dilated cardiomyopathy. Coronary atherosclerosis may be present in many but not all patients. Electrocardiographic TMT changes are common and include nonspecific ST segment and T wave changes. Conduction abnormalities, atrial abnormalities and left ventricular hypertrophy.

**Physiology of diabetic cardiomyopathy**

Multiple metabolic abnormalities resulting from diabetes may contribute to the development of cardiomyopathy.

- Genetic
  - Diabetes mellitus
  - Hyperglycemia

- Environmental
  - Decreased T<sub>3</sub>
  - Glycosylation pathway
  - Polyol pathway
  - Hyperlipidemia

  - Myosine isoenzyme shift from V<sub>1</sub> to V<sub>2</sub>
  - Depresses myosin ATPase

- Increased collagen
- Increased cross-linking

- Increased LCAC
- Increased cholesterol
- Increased phospholipid ratio

- Increased MVO<sub>2</sub>

**Fig. 1:** Numerous established or potential factors important for the development of diabetic cardiomyopathy (LCAC = long chain acyl carnitine; MVO<sub>2</sub> = myocardial oxygen consumption - modified from Tahiliani et al (1983).
Physiologic abnormalities

The structural physiologic abnormalities observed in experimental diabetic animal models are similar to those occurring in human. Increased collagen and interstitial accumulation of PAS material is present in alloxan induced diabetic rhesus monkeys (Haider et al, 1981).

Diabetic dogs treated with insulin may show partial reversal of abnormalities in left ventricular compliance. Decreased contractility and relaxation are seen in isolated papillary muscle obtained from diabetic rats (Fein et al, 1980; Miller et al, 1979; Heylinger et al, 1982). Those observed in dogs and these functional abnormalities may be improved with insulin (Tahiliani et al, 1983).

Role of Hypertension

A predilection of diabetes to raised blood pressure level has often been asserted but remained disputed. Keen et al (1974) showed that the mean blood pressure and the influence of age and sex upon them are strikingly similar among diabetics and non diabetics. So too severe the standard deviation about the mean providing no evidence of underly high or low pressure among younger diabetics compared with controls. There was a deficiency of higher level of blood pressure among the older diabetics presence of atherosclerosis and neuropathy accounting for it. Presence of proteinuria was accompanied by high mean pressure. Freedom et al, (1958) and
Pyket et al (1958) supported above general conclusion. No trend of increase in pressure with increasing duration of illness was noted. The strongest evidence for a special risk between diabetes and hypertension is that of Dell and D'Alouzo (1967). They studied 662 employees of Du Font Company (US) and asserted that as compared to non diabetics overall prevalence of hypertension (systolic 7160 and diastolic 795 mm Hg) was 54% higher in diabetics. They concluded that the increased susceptibility of diabetics to atherosclerotic heart disease (ASHD) can be explained almost entirely by the higher prevalence of hypertension. In Framingham study (Garcia et al, 1973) the mean systolic blood pressure of diabetics was significantly higher than in matched non diabetic, the excess being in women. Epidemiological study of inhabitants of tecumsch, Michigan (Epstein and colleagues, 1967) indicated that the frequency of clinically evident diabetes progressed with increasing level of blood pressure. In the Bedford diabetic survey (Sharp et al, 1962) systolic blood pressure are high in certain age groups in the diabetics, the excess being greater in males (Fowler et al, 1970).
Relation to age and sex

Relation of age and sex to prevalence of hypertension among diabetic population has its share of conflicting claims. Pathania et al (1961) and Vaishnava et al (1964) found higher incidence in males while a preponderance of females was witnessed by various other authors. Brytogle et al (1957), Friedman et al (1958), Tolloch et al (1962), Boas et al (1952, Brytogle et al (1957) and Banerjee et al (1966) asserted that females are more often involved than males above the age of 60. Tolloch et al (1962) noted the same trend even after the age of 30.

Relation to Duration of Diabetes

Duration of diabetes was shown to have a peculiar relationship by Banerjee et al (1966). Diabetics of less than 15 years duration have higher incidence of hypertension but those with more than 15 years' duration of illness presented with lower blood pressure level. Pathania et al (1961) and Vaishnava et al (1964) described a definite correlation between the duration of diabetes and severity of hypertension. Lewis and Simons (1958) however, denied any such correlation.

Relation to Severity

Severity of diabetes had a striking relation, Vaishnava et al (1964) and Banerjee et al (1966) explained
that with increasing severity, the incidence of hypertension mounts but it crumbles down in very severe diabetes.

ROLE OF HYPERLIPIDEMIA

Hypertriglyceridemia is associated with uncontrolled insulin dependent diabetes. Enzyme system lipoprotein lipase responsible for the hydrolysis of circulating triglycerides and which is partly controlled by insulin. When diabetes is well controlled lipid levels lie in normal range (Kaiding et al., 1952; Wolff and Salt, 1958). In Framingham study mean serum cholesterol levels were not higher in diabetic men while it was so in the diabetic women. Diabetes mellitus progressing to cause diminution of coronary flow either by microangiopathic affection or vasa vasorum of coronary arteries (Herman and Gorlin, 1965) or by producing hyperlipidemia and thereby producing coronary atherosclerosis. Increase in lipid has been consistently reported by various investigators (Albrink et al., 1963; Aldersberg and Eisler, 1959; Gofman et al., 1959; Fukui and Yoshida, 1964; Koshy et al., 1965; Hatch et al., 1966, Shaefer et al., 1968 and Talwalkar et al., 1971). Epstein et al (1971) asserted that diabetics with hyperlipidemia have premature susceptibility to coronary artery disease. Guttler and White (1954) indicated that serum cholesterol level was most sensitive indicator for prediction of development of ischemic heart disease.
A positive correlation with increased incidence of IHD and hypertriglyceridemia has been described (Albrink et al., 1963; Brown et al., 1965, Carlson et al., 1966; Hemile et al., 1969; and Chaudhry et al., 1971).

Sharde (1963) reported consistently higher level despite good control of diabetes in patients with long term disease. A positive correlation between the duration of illness and presence of hyperlipidemia was indicated by Gossin and Ahuja (1967). They found the lipid levels to be normal in those with a less than 1 year duration, esterified fatty acid were observed as the severity of diabetes disease increased. Gossain and Ahuja (1966) stated increase levels of total cholesterol and triglyceride in patients with fasting blood sugar levels higher than 130 mg/dl. However, Mathur and colleagues (1961) failed to find any such definite relationship. Sandberg and colleagues (1960) observed abnormal fat tolerance among uncomplicated diabetics.

ROLE OF OBESITY

Any group of maturity onset diabetics, even on dietary therapy is likely to contain more obese people than a comparable non diabetic group from the same population. Increased prevalence of obesity of the diabetics could account for part of the augmented arterial disease risk. Keys (1972) using multivariate analysis of data in large population found that no measure of relative body weight
or obesity made a significant contribution to the prediction of coronary heart disease when age, presence of blood pressure, serum cholesterol levels and smoking were taken into account. In the Bedford borderline trial (Keen et al., 1974) dividing subjects into tertiles of ponderal index (HT/WT$^{-1/3}$) distribution, there was a clear excess of new complaints of angina pectoris in the most overweight group. There is thus little justification for the widely held view that obesity is a special risk for arterial disease in diabetics (Keen and Jarrett, 1975).

**METABOLIC ABNORMALITIES**

Data from studies of metabolic derangements in experimental animal models of diabetes have yielded a myriad of possibilities for pathophysiology of diabetic cardiomyopathy (Figure 1). Biochemical abnormalities reported in rat model include diminished myocardial membrane actomyosin and myoosin adenosine triphosphatase (ATPase) activity, altered myoosin isoenzyme distribution, and decreased calcium binding and uptake by sarcoplasmic reticulum (Billman et al., 1986; Ganguly et al., 1983; Malhotra et al., 1981) and Pierce et al., 1981). These changes are decreased by controlling hyperglycemia with insulin. Electron microscopic changes in such rats include condensation of nuclear chromatin folding of nuclear membranes, mitochondrial matrix (Seoeger et al., 1984). These structural changes occurred independently of vascular occlusion.
The metabolic disorders in diabetes are, of course, hyperglycemia, which results in non-enzymatic glycosylation of proteins. Although non enzymatic glycosylation may affect the myocardium in many ways (Brown Lee et al, 1984; 1988), the resultant collagen cross linking might provide the basis for the previously described decreased LV compliance in diabetic dog and monkeys, which is associated with the interstitial accumulation of PAS positive material and increased content of collagen resistant to proteolysis. Such structural changes could result in increased ventricular stiffness and thus be partially responsible for the delayed relaxation and decreased velocity of shortening of pupillary muscle from diabetic animal models.

**ROLE OF AUTONOMIC DYSFUNCTION**

Derangement of autonomic nervous system due to abnormalities of the polyol pathway may also contribute to the development of diabetic cardiomyopathy. Both the parasympathetic and sympathetic nervous systems are affected in diabetes, resulting in an increased heart rate and abnormal baroreceptor reflex responses (Tehili et al, 1983). The data clearly indicate that diabetic individuals with an intact cardiovascular autonomic nervous system respond more normally to exercise RR variation as a marker prevalence of cardiac autonomic neuropathy in asymptomatic diabetic patients is approximately 35% but can increase to 82% in those of diabetic patients with signs of symptoms of
neuropathy (Freiber et al, 1934). Recent studies by Khan et al (1987) and Bellavere et al (1988) have suggested that diabetic patients with impaired cardiac autonomic nervous system are at greater risk for sudden death and arrhythmias.

**ROLE OF MICROVASCULAR DISEASE**

Small vessel coronary artery disease frequently occurs in diabetics (Sander et al, 1988; Fein et al, 1985). However, the pathophysiologic role of these vascular lesions has not been convincingly demonstrated. In fact in some diabetics with cardiomyopathy, both large and small coronary arteries are minimally diseased or are normal (Regan et al, 1977). It has been suggested that increased sensitivity to catecholamine occurs which may result in myocardial ischemia mediated by focal small coronary artery vasoconstriction. Fein et al (1985) observed LV ejection fraction in response to exercise in diabetics did not correlate with the degree of metabolic control of diabetes. Presence of microangiopathy or abnormalities in autonomic nervous system function, myocardial perfusion scintigraphy revealed evidence for ischemia in only 28% of such patients (Mustonen et al, 1988).

**ROLE OF HYPERTENSION IN MYOCARDIAL DISEASE IN DIABETICS**

Thomas et al (1989) have concluded that potential mechanism for development of diabetic cardiomyopathy are complex but hyperglycemia and hyperlipidemia play an important role. Primary hypertension is also associated
with the development of myocardial abnormalities. Many of these changes are similar to those seen in diabetic cardiomyopathy. It is clear that coexistence of hypertension and diabetic mellitus produce a more severe cardiomyopathy than that produced by hypertension and diabetes mellitus alone.

**Hypertensive Cardiomyopathy**

Increase in arterial pressure may be of major importance in myocardial disease. Other factors such as catecholamines the renin angiotensin system genetic factors and obesity are also important as in diabetes early cardiac findings in hypertensive patients consists of abnormal left ventricular diastolic function and abnormal systolic response to stress with few associated symptoms (Dunn et al., 1977).

Left ventricular hypertrophy is the hallmark of hypertensive heart disease and its presence is correlated with the level of blood pressure, particularly with 24 hours mean systolic blood pressure (Rowlands et al., 1982). In the offspring of hypertensive parents, eccentric hypertrophy, increased left ventricular mass with normal wall thickness may occur prior to obvious development of hypertension or increase in ventricular wall thickness (Savage et al., 1982). The late stages of hypertensive cardiomyopathy are associated with progressive left ventricular chamber dilatation and decreased left ventricular systolic function (Murson et al., 1962; and Karliner et al., 1977).
Thus there are similar architectural and metabolic changes in the heart occurring in hypertension which provide multiple common ground for an interaction with diabetes. Moreover, there is a depression of calcium binding to sarcoplasmic reticulum associated with abnormal calcium ATPase action (Linas et al, 1977). Thus the factors that may be important in the development of hypertensive cardiomyopathy are similar to those contributing to diabetic cardiomyopathy.

![Diagram](https://via.placeholder.com/150)

**Fig. 2:** Development of hypertensive cardiomyopathy may depend upon any pathophysiologic factors.

Increased arterial blood pressure is very common in patients with diabetes mellitus (Soueirs et al, 1988). Because of increasing population, hypertensive and diabetics are increasing in country like India, primary hypertension and diabetes frequently co-exist, when diabetes mellitus and hypertension occur together a more serious cardiomyopathy results than when each is present alone (Sauder et al, 1988; Fein et al, 1985, Factor et al, 1980).
The heart of diabetics appear to be particularly sensitive to increased levels of blood pressure (Domilsen et al., 1988). An echocardiographic evaluation of 32 patients with type I diabetes and a wide range of systemic arterial blood pressure revealed subclinical diastolic dysfunction that correlated positively with systolic blood pressure and left ventricular mass. When compared with 32 normotensive non-diabetic persons. Thus even mild hypertension should be treated in diabetics to delay the onset of cardiomyopathy.

In a study conducted in I.M.S., B.H.U., Dhillon (1982) had evaluated LV function by echocardiography in 25 cases of essential hypertension and concluded that thickness of interventricular septum and its ratio to posterior wall were considerably increased in patients of hypertension compared to control. The left atrial diameter was also significantly increased. The EF Vcf and % PD were significantly depressed and LV mass was markedly increased. The echocardiographic abnormalities were more marked in cases who had clinical cardiac involvement.

TREATMENT OF HYPERTENSIVE DIABETIC CARDIOMYOPATHY

Following factors must be considered in the pharmacologic management of hypertensive diabetic patients to prevent or treat cardiomyopathy. Control of diabetes, reduction of blood pressure, reduction or prevention of left ventricular hypertrophy and avoidance of drugs that increases cardiac risk factors.
Insulin therapy is beneficial for preventing or treating the cardiomyopathy associated with diabetes. (Feuvarg et al, 1979). However, in alloxon induced diabetic dogs tolbutamide treatment resulted in an even further reduction of left ventricular function and myocardial pathology, despite improved glucose tolerance (Wucf et al, 1977). Thus insulin may be more efficacious than orally administered hypoglycemic drugs in treating diabetic cardiomyopathy.

The choice of an antihypertensive must be based on the therapeutic goal and avoidance of side effects. Thiazide and loop diuretics worsen glucose tolerance, an effect that is showed by beta adrenoceptor antagonists without significant intrinsic sympathomimetic activity (Struthers et al, 1985). The effect is additive when these classes of drugs used together(Doruhrst et al,1985).

Worsening of lipid profile by thiazides is well known and is dose related (Weinberger et al, 1985). Regression of left ventricular hypertrophy occurs in both hypertensive animal models and hypertensive humans following treatment with sympatholytics (Senekal, 1974; Fouad et al, 1982; Wallan et al, 1983; Hill et al, 1979), angiotensin converting enzyme inhibitors (Pfeffer et al, 1982; Richis et al, 1978) and calcium antagonists (Draycs et al, 1984; Sziachic et al, 1989). Left ventricular hypertrophy may remain unchanged or worsen after treatment with diuretics (Lombardo et al, 1983) or direct vasodilators such as
hydralazine and minoxidil (See et al, 1983). Sympatholytic agents must be used with caution in diabetic patients due to presence of autonomic dysfunction. So ACE inhibitors and calcium channel antagonist are two class of drugs of most desirable pharmacologic profile for treatment of hypertension in diabetics. Weight reduction is often a good treatment for both obese NIDDM and hypertensive and have beneficial effects in regressing LV hypertrophy and improving diastolic dysfunction (Mack Mohan et al, 1986; Sowers et al, 1988).

**DIABETIC RETINOPATHY**

Diabetic retinopathy is now-a-days considered as single most common cause of blindness between the age group 32-64 years. The retina is the only vascular bed in the body which can be studied directly and repeatedly. All elements of vascular tree are affected in many diabetic patients. New vessels developed. There are extravascular lesions also such as hemorrhages, hard exudate and cotton wool spots.

In juvenile diabetics these lesions are rare before duration of five years of illness. Thereafter occurs a steep rise in diabetics with 5-15 years duration of illness (Keen and Jarret, 1975). In maturity onset diabetics it appears after even a short duration of illness (Lundback et al, 1955; Kornerup et al, 1958).
Incidence of diabetic retinopathy is reported to be between 4 to 63% (Western studies) and 7-40% (Indian studies). Incidence has been reported to increase with age (Vaishnava et al., 1964; Johnmalins et al., 1968). In children there is no difference in sex incidence but females outnumber males beyond 40 years (Joslin, 1971). Male dominance has been reported by Indian investigators (Urs et al., 1966; Gaur et al., 1966). Severity of diabetes is well correlated to severity of retinopathy (Lundback, 1953; Kazima et al., 1963; Vaishnava et al., 1964).

The severity and progression of retinopathy is highly correlated with diabetic myocardial microangiopathy (Shapiro et al., 1980; 1981; 1982).

SUBCLINICAL CARDIAC DISEASE IN DIABETES MELLITUS

There is increasing evidence that diabetics can develop abnormality of myocardial function with patent main coronary arteries (Regan et al., 1977; D'Elia et al., 1979) which may progress to cardiomyopathy and congestive heart failure. This has been suggested to be part of generalized microvascular disease which may result in retinopathy, nephropathy and neuropathy (Ahmed et al., 1975; Serevirante, 1977; Sanderson et al., 1973; Rubler et al., 1978 and Hamby, 1974). Kannal et al. (1979) while analysing the role of diabetes in congestive cardiac failure in the Framingham's study found that the incidence of congestive cardiac failure was higher in diabetics and that excessive
risk seemed to be independent of hypertension and large CAD. Some form of cardiomyopathy was associated with diabetes. Senevirante (1977) proposed that the association of microangiopathy and impaired left ventricular function may explain the high immediate mortality and the increased incidence of cardiogenic shock and congestive cardiac failure after myocardial infarction.

Gibson and Brown (1973) noted that CHF and cardiomegaly occur in diabetics, many a times without accompanying coronary artery disease.

**ELECTROCARDIOGRAPHIC ABNORMALITIES**

Electrocardiographic abnormalities have been reported by many authors. The findings are the changes suggesting myocardial ischemia or infarction. ST-T changes are commonly seen.

Banerjee and Ray (1959) stated that diabetics have a special predilection for anteroseptal infarction. Other changes that may be encountered are those suggesting chamber hypertrophy, conduction defect, premature beats and voltage changes.

Changes are the result of myocardial ionic derangements and ischemia due to compromised oxygen supply (Raheja et al., 1972). Changes in small calibre vessels (Osterele, 1970) or their narrowing or occlusion (James, 1967; Ladet, 1968) have also been held responsible.

Presence of diabetic cardiomyopathy may form another contributory factor (James, 1967; Varenoskas,
Rost and Brodley (1959) noted presence of unexplained congestive cardiac failure, arrhythmias and conduction defects more frequently in diabetics. Pathania et al (1961) described many changes in electrocardiographic tracings from his diabetic patients. Karlefors et al (1966) described number of alterations in ECG of diabetic individuals. Banerjee and associates found 90 ECGs suggesting ischemia among 172 recordings from diabetic patients. 54 of these had no history suggestive of ischemic heart disease.

Wada and Schigeta (1966) showed higher incidence of abnormal electrocardiogram in diabetic subjects. Raheja (1972) described his abnormal ECG findings among two groups, B (63 patients asymptomatic) in whom abnormalities were detected on routine ECG and C (6 patients presenting with congestive cardiac failure).

GROUP B: Asymptomatic (Subdivision, 3:2:4:1) of WHO study group, 1962).

1. Smaller R waves in left sided leads, QS pattern in L2, L3 and avF.
2. Notching or slurring of QRS.
3. Progressive widening of QRS - RBBB or LBBB.
4. Prolonged P-R intervals.
5. Premature beats, one patient had atrial fibrillation.

GROUP C: Presenting with CCF (Subdivision 3:2:4:2 of WHO study group, 1962).

1. Biphasic p in V1 (4 cases).
2. ST changes, low voltage QRS complex in left sided leads (all died).
3. T inversion.
4. Left ventricular hypertrophy.

**Exercise ECG in Diabetics**

The significance of exercise ECG test in diabetics is further increased because of higher incidence and atypical presentation or even absence of alarming symptoms inspite of myocardial infarction.

Katz and Landt (1935) proposed that lead V5 was best lead to bring out the ischemic changes.

By continuous monitoring Roseman and co-workers (1940) described for the first time that ST segment depression usually appeared before the onset of anginal pain and usually persisted for a time after the chest pain subsided.

Johnson and co-workers (1942) developed Harvard step test which was very similar to the original Master's test. It was used widely in athletic circles to assess physical fitness.

Wood and co-workers (1950) described their experience with an effort test at the National Heart Hospital, London. They asked their patients to run the maximal level to their capacity. They concluded that sensitivity of their test was 88%, as compared to 39% of Master's test. They further emphasized that the amount of exercise should not be fixed but rather adjusted to the
patients' capacity in order to bring out a higher percentage of positive tests in patients with coronary artery disease by giving the maximal exercise.

According to Master's test following points are in the favour of myocardial ischemia by continuous monitoring:

1. ST segment depression of 1.0 mm or more.

2. Alteration of the T wave direction from upright to inverted or inverted to upright.

3. 50% or more increase in T wave amplitude as compared to resting.

4. Prolongation of Q-T: T Q to more than two, during exercise.

Feil and Brofman (1953) observed the effect of exercise on ECG in bundle branch block and also reported false positive exercise ECG tests in his patient with WPW syndrome.

**PATHOPHYSIOLOGY OF EXERCISE**

The basic aim of exercise testing is to increase myocardial oxygen requirements to unmask a reduced and relatively fixed coronary blood flow. The resultant myocardial ischemia may then be detected through electrocardiographic abnormalities, usually in the form of ST segment changes. Exercise ECG has two major roles - one is to determine whether the coronary circulation is capable to increase the oxygen supply to the myocardium in response to increased demands.
During physical exercise, myocardial oxygen demand is increased by increment of systolic blood pressure, the contractile state of the myocardium and the heart rate. The other role of exercise ECG test is to assess the exercise capacity. The decrease in total peripheral vascular resistance results from marked local vasodilatation in exercising muscles, a response, which overcomes the opposing effects of a generalised inactivity of sympathetic noradrenergic fibres to both resistance and capacitance vessels.

Mechanism responsible for augmenting oxygen delivery to cardiac versus skeletal muscle has two important differences.

1. Myocardium depends almost entirely upon increase in coronary artery blood flow, for oxygen extraction is nearly complete about 7% even at rest, with coronary sinus blood containing only 2 to 5 volumes percent of oxygen. It indicates that myocardium is a flow dependent tissue. Skeletal muscles on the other hand, are capable of three fold increase in oxygen extraction above resting volumes.

2. Skeletal muscle is able to continue contracting in the absence of oxygen, where as cardiac muscle is strictly aerobic. During exercise a fall in coronary vascular resistance accounts for increase in coronary blood flow despite a decrease in diastolic time per minute.

The coronary blood flow during exercise is significantly reduced when there is at least 50% narrowing of the
coronary blood vessels although a significant reduction at rest occurs only when the stenosis is 85%.

**PROTOCOLS FOR TREADMILL ECG TEST**

As far as the ideal exercise ECG test is concerned the initial work load should be well within the individual's anticipated physical working capacity. The work load should be increased gradually.

In Bruce protocol the work load is increased by changing speed and grade. For progressive increment of work load at least three minutes' intervals are preferable so that steady state blood pressure and heart rate responses can be achieved.

It is important to look for the symptoms and signs, like chest pain, dizziness, dyspnoea, extreme fatigue, blood pressure, heart rate and ECG changes during the entire procedure and throughout at least six to eight minutes of post exercise period. The exercise should be terminated when significant symptoms, abnormal signs, marked ST segment changes or serious arrhythmias are appreciated or when a predetermined heart rate is reached.

Many authorities usually prefer submaximal exercise test because many patients with coronary heart disease are unable to perform the exercise upto maximum limit. The percentage of maximal predicted heart rate that a patient achieves at peak exercise can provide an estimate of efficacy of the test.
The percentage of maximum heart rate at which symptoms or electrocardiographic changes occur may be helpful in assessing a person's degree of disability.

**Lead System**

When two channel recording are available, an additional inferior lead (II, III or avF) with a modified lead V₃ can increase the diagnostic yield of exercise ECG test. When a multichannel recording is available, six leads consisting of leads II, avF, and V₃, V₄, V₅ and V₆ are said to be ideal to detect more ECG abnormalities.

In most of the institutions now 12 leads ECG recording is done before/during exercise and during recovery period with simultaneous 3 lead recording for continuous monitoring.

**Normal Response to Exercise**

1. Progressive increment of blood pressure and heart rate during exercise.
2. Shortening of QT interval with increase QT,R-R ratio.
3. Physiological ST segment alterations:
   a. Junctional (J point) ST segment depression of 2 mm with duration of ≥0.06 sec.
   b. Vasoregulatory asthenia.
   c. Orthostatic ECG changes.
   d. Lebile T wave changes.
   e. ST segment depression only in the post exercise period.
4. Alteration of T wave direction or morphology.
5. Slight reduction of R wave amplitude.
7. Downward displacement of P–R segment due to prominent Ta wave amplitude.
8. Peaking and tall P wave during very rapid heart rate.
9. Minor symptoms such as dyspnoea, fatigue, sweating etc.

INTERPRETATION OF THE EXERCISE ECG TEST

As the various ST segment changes have been described the horizontal or downsloping ST segment depression of 1 mm or more is the most reliable criteria for the positive exercise ECG test. The ST segment elevation is only occasionally observed and in most cases it is found in patients with previous myocardial infarction.

ST segment depression of 1.0 mm or more after J point with a horizontal or downsloping ST segment is said to be positive test. The incidence of true positive responses in patients with coronary artery disease varies from 60–89% by using this criteria.

Goldschlazer et al (1976) reported his series of 330 patients referred for diagnostic evaluation of chest pain with or without prior infarction who had both maximal treadmill exercise testing and selective coronary angiography. Sensitivity of ST segment changes was 64% to 76% and specificity was 83 to 93%. Downsloping ST segment was associated with only 1% false positive results while horizontal depression was associated with a 15% false positive test.
The following table compiles the results of four studies in which the extent of ischemic depression is compared with the incidence and extent of coronary occlusion. Study shows that patients in whom 2 mm or greater ischemic ST depression occurs have a 57% incidence of two or three vessels disease. Incidence of single vessel disease in patients having 2 mm or more ST depression is only 17%.

<table>
<thead>
<tr>
<th>S-T depression (mm)</th>
<th>Single vessel (%)</th>
<th>Double vessel (%)</th>
<th>Triple vessel (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 2</td>
<td>17</td>
<td>28</td>
<td>57</td>
</tr>
<tr>
<td>1.0 - 1.9</td>
<td>21</td>
<td>30</td>
<td>42</td>
</tr>
<tr>
<td>&lt; 1</td>
<td>19</td>
<td>16</td>
<td>21</td>
</tr>
</tbody>
</table>

The patient with atypical angina has 50% chances of having angiographic coronary disease, while in ischemic exercise response it increases to 88%, and a normal treadmill test reduces it to 25%. In asymptomatic subjects a negative exercise test reduces the probability of an individual having coronary artery disease to 4% while an ischemic S-T response increases upto 44%.

<table>
<thead>
<tr>
<th>Clinical presentation</th>
<th>Pretest odds/ probability</th>
<th>Positive test post test odds/ probability</th>
<th>Negative test post test odds/ probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical angina</td>
<td>9:1/90%</td>
<td>63:1/98%</td>
<td>9:3/75%</td>
</tr>
<tr>
<td>Atypical angina</td>
<td>1:1/50%</td>
<td>7:1/88%</td>
<td>1:3/25%</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>1:9/10%</td>
<td>7:9/44%</td>
<td>1:27/4%</td>
</tr>
</tbody>
</table>
NON ELECTROCARDIOGRAPHIC CRITERIA

- Low achieved heart rate (≤120/minute).
- Hypotension (≤10 mm Hg rise in systolic pressure at any time during the test).
- Rise in diastolic blood pressure (≤110-120 mm Hg).
- Low achieved rate pressure product (≤15,000).
- Inability to exercise beyond 3 minutes.

ST segment response of an individual with known left main coronary disease is shown below in the table III. In these studies 100% patients had S-T segment depression ≥2 mm, while Ellested noted only 67% of such patients with 2 mm or more S-T depression and 20% with negative tests. In the study of ST segment patients with greater than 50% left main obstruction, Salem et al (1978) found that 89% had ischemic S-T depression and in 70% S-T depression was greater than 2 mm. Further more of 23 patients with left main obstruction greater than 75%, 19 (83%) had ≥2 mm S-T segment depression.

| TABLE III |
| S-T segment depression in subjects with left main obstruction. |

<table>
<thead>
<tr>
<th>No.</th>
<th>Name of author</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Cheitlin et al (1975)</td>
<td>100.0</td>
</tr>
<tr>
<td>2.</td>
<td>Kliener et al (1976)</td>
<td>100.0</td>
</tr>
<tr>
<td>3.</td>
<td>Levitas et al (1976)</td>
<td>100.0</td>
</tr>
<tr>
<td>4.</td>
<td>Salem et al (1978)</td>
<td>70.0</td>
</tr>
<tr>
<td>5.</td>
<td>Ellested et al (1975)</td>
<td>67.0</td>
</tr>
</tbody>
</table>
Case et al (1969) demonstrated that in early myocardial ischemia, the onset of anaerobic metabolism is manifested first by J point depression and followed later by ST depression. When S-T response is limited to J point depression it is generally interpreted as normal finding.

Kurita et al (1977) evaluated the relationship of isolated junctional ST depression, induced during treadmill exercise testing, with coronary angiographic findings in 230 patients. Of 75% patients with junctional depression of less than 1.5 mm only 10 had 50% or greater stenosis of at least one major coronary artery. Only two patients had multivessel disease., 42 patients had junctional depression of 1.5 mm or more. Of these 23 had significant stenosis and 12 of this group had multivessel disease.

Exercise induced ST segment elevation is rarely normal and is commonly associated with severe localised coronary artery obstruction or with left ventricular aneurysm. Chahine and co-workers (1976) reported 86% incidence of left ventricular dyskinesia or aneurysm in their patients who developed S-T segment elevation with exercise. They also noted that exercise ST elevation is related more to the wall motion abnormality than to myocardial ischemia.

In contrast Fortium and Friessinger and Heege et al (1970) reported that exercise S-T elevation was a
manifestation of severe myocardial ischemia. Stress and co-workers (1975) supported the theory that in the absence of previous myocardial infarction, severe ischemia alone can produce ST segment elevation.

Ekmekei et al (1961) gave their opinion that the lead in which ST segment depression occurs is poor predictors of the anatomic location of myocardial ischemia. However, ST segment elevation seems to be a fairly good localiser of the site of coronary stenosis.

R WAVE AMPLITUDE (RWA)

R wave amplitude was proportionate to left ventricular valves because of the radial orientation of left ventricular electromechanical forces (Brody, 1956). Monoach et al (1971) confirmed the Brody's hypothesis: "Exercise in normal subjects could result in an increase in stroke volume, resulting in a decrease left ventricular volume and a decrease in R wave amplitude, while subjects with coronary artery disease particularly with impaired left ventricular function, might show the opposite effect."

In several studies, Borories et al (1978) noted R wave amplitude changes during T.M.T.. They found that patients with decreased RWA after exercise had less severe coronary artery disease and fewer wall motion abnormalities.

Oillerpie et al (1978) studied 75 subjects with bicycle ergometry and coronary angiography. They found that the sensitivity for ST change alone was 64%. 
Greenburg and Ellested (1979) suggested that in normals the R wave increase until the patient reaches a heart rate of 120-130 at which point it begins to decrease suggesting that measurement would have less significance in patients who step early in the protocol before their heart rates reach a significant level.

**T-WAVE VECTOR**

Aravindakshan et al (1977) evaluated the results of submaximal exercise tests in two groups of patients with T wave abnormalities. Group I consisted of patients with documented ischemic heart disease and group II consisted 28 individuals in whom ischemic heart disease appeared unlikely. T wave normalization occurred frequently in both groups and was unrelated to changes in ST segment. ST segment changes occurred in 88% of the patients with ischemic disease and in only 4% of group II subjects indicating that the S-T segment response to exercise was not influenced by the T wave vector. Thus T wave normalization is thought to be independent of S-T segment changes. The appearance of isolated T wave inversion is of no diagnostic significance as it is commonly seen in patients without disease.

**U WAVE**

Exercise induced U wave inversion in patients with a normal resting ECG and in the absence of left ventricular hypertrophy strongly suggest myocardial ischemia.
it may occur in the absence of ST segment abnormalities and is usually indicative of significant stenosis of left anterior descending coronary artery. The T wave inversion is difficult to detect during exercise especially at high heart rates and often becomes apparent in the immediate recovery period when the heart rate is slowing.

ECHOCARDIOGRAPHY

It has been a long time since echocardiography was invented by Elder and Hertz from Sweden in early 1950s. A ceramic compound such as barium tetanate is excited by short high frequency (1.6 to 2.5 MHz) electrical signals to provide inaudible ultrasonic pulses in the commonly used 'M-mode technique'. Reflection of the ultrasonic pulses occurs at an interface between two media of different densities. Only those interfaces which are relatively perpendicular to the sound are being sampled. The electromechanical transducer serves as emitter and the receiver both of ultrasound at a repetition rate of 1000 impulses per second. The amplified echoes are displayed on oscilloscope. A 'time motion' presentation is commonly used which plots distance from chest wall against elapsed time and displays moving structures as undulating lines for recording the echoes. The tracings are recorded on a strip chart recorder. On the recorded tracing the ECG and time distance markers are used as reference signals.

Tilting the ultrasound transducer
towards head or feet in the 4th left intercostal space permits the echocardiographic demonstration of a number of cardiac structures between the aortic root and LA superiorly and the LV apex inferiorly. During the echocardiographic sweep the anterior wall of aortic root is normally continuous with the interventricular septum (IVS) and the posterior aortic root with the anterior leaflet of the mitral valve (ALM).

In two dimensional echocardiography ultrasonic beam is moved in a sector so that a pie-shaped slice of the heart is interrogated. By oscillating a single transducer or by rotating a series of transducers the ultrasound beam can be moved mechanically. To control the firing of the element and the direction of the beam a computer or microprocessor is necessary.

MEASUREMENT OF LV FUNCTIONS

Echocardiography has always been enticed by its ability to demonstrate sluggish wall motion of failing heart compared with vigorous wall motion of normal and volume overloaded heart. To demonstrate LV function many methods have been employed during recent years. These efforts have been frustrated by inability to draw conclusion for whole left ventricle (Jos, 1981) since only a part of LV can be visualised. Considering above problem, methods used to determine LV function such as cine-angiocardiography, systolic time intervals and more recently
nuclear cardiac imaging are limited to same extent. Echocardiography does not solve these problems, nor is unique enough to be employed as sole method. However, it provides additional data sometimes not otherwise available which is obtained in a simple manner non-invasively.

**M-mode**: Echocardiograms are recorded in a resting subject and the transducer placed in 3rd, 4th or 5th left intercostal space, is angled down from aortic root through LV until echoes are obtained simultaneously from septum (IVS) and posterior wall. AML measurements include EF slope of mitral valve (diastolic function), systolic diameter of LV (LVESD), and diastolic LV diameter (LVEDD). To estimate the ventricular volume these dimensions are used. Various indices of LV function such as ejection fraction (EF), percentage fractional shortening are calculated. Fractional shortening i.e. the difference between the end diastolic and end systolic dimensions divided by end diastolic dimension (McDonald et al, 1972) provide information about LV systolic function. The quotient of fractional shortening and ejection time provides the mean fractional or circumferential shortening (Quinones et al, 1974). Another M-mode echocardiographic technique for assessing the status of the LV is to measure the distance between the point of mitral valve and the left side of the IVS (Roffet al, 1985). Normally, the mitral E point and the left side of the septum are within few millimeters of each other. The upper limit of normal of
the mitral E point septal separation (EPSS) is approximately 8 mm. As the LV ejection fraction decreases, the EPSS increases. The opening of mitral valve is largely dependent upon the volume of blood passing through that orifice. The amplitude of the E point decreases as mitral valve flow or LV status volume decreases i.e. with decreased stroke volume and/or LV dilatation, the septum and AML would move in opposite directions.

2-D: For assessing cardiac chambers, there has been increasing interest in using two dimensional echocardiography. Akinesia or hypokinesia of particular segment of LV depicts ischemia of that particular zone. There have been numerous attempts to use two dimensional echocardiography to calculate LV volumes (Striller et al., 1979; Gordon et al., 1983). Several geometric formulae have been suggested among them Simpson's rule formula (Guret et al., 1980) and bullet formulae are important.

**Dysfunction Reported in Diabetic Ventricles**

Impaired LV function is commonly detected in diabetes even when they don't have any evidence of cardiac disease. Significantly higher values of PEP/LVET ratio and reduced ejection fraction and fractional shortening (p < 0.001) were found by Senewirante (1977). Sanderson and associates (1978), focussed attention towards diastolic events which are more significantly affected by diabetic microangiopathic process. Early diastole is a part of
cardiac cycle that has received scanty attention but recent echocardiographic (Upton et al., 1976; Sanderson et al., 1978; Shapiro et al., 1980; 1981) and angiographic studies (Gibson et al., 1976 and Ruttley, 1974), have emphasized the importance of this period on overall function and showed that relaxation and filling of the ventricle is a precisely timed and coordinated process. Echocardiography has two advantages in the study of myocardial function. Firstly, it is noninvasive and secondly the endocardium can be recognised throughout the diastole unequivocally and the pattern of MV cusp movement can be observed and compared with it.

Shapiro and associates (1981) asserted that the impairment of LV function was related to the presence and extent of other diabetic microvascular complications and the duration of diabetes. Higher incidence and degree of abnormalities in insulin dependent diabetics were noticed by him. STT's are abnormal in some diabetics (Ahmed et al., 1978; D'Elies et al., 1978). They have a complex underlying mechanism and are more frequently abnormal in diabetics with associated disorder such as hypertension, coronary artery disease and heart failure (Ahmed et al., 1975).

Studies of Sanderson (1978) and Shapiro (1980; 1981) suggested that impairment of some aspects of diastolic function is common and may be the primary abnormality in diabetics. Shapiro (1982) stated that diabetics with severe microvascular complications have more derangement
of LV function. If the diabetic patients develop hypertension LV functions are more deranged because a different type of cardiomyopathy sets in i.e. Diabetic hypertensive cardiomyopathy (Thomas et al, 1989). Interventricular septal thickness, LVPW thickness and diastolic function impairment is commonly seen in hypertensive patients (Lehner et al, 1979), which adds to impairment of LV function in diabetics.

Kasturi and Gupta et al (1991) studied 72 patients of diabetes mellitus without any clinical and electrocardiographic evidence of cardiovascular dysfunction and features of cardiomyopathy were studied by echocardiography. Other causes of cardiomyopathy were excluded. LV ejection fraction and fractional fibre shortening were measured using LV internal diameter in systole and diastole. Ejection fraction below 0.5 was considered to indicate impaired left ventricular function. In 66 patients the left ventricular EF was normal and in 6 (8.3%) it was less than 0.5. They were middle aged with equal sex distribution. The duration of diabetes mellitus averaged 12 years. Five of them were cases of IDDM with poor metabolic control. Microangiopathy in the form of proteinuria (2 cases), retinopathy (4 cases) and autonomic neuropathy (5 cases) were detected in them (6 cases). It was concluded from the study that diabetic cardiomyopathy tends to occur in middle aged more in insulin dependent diabetics with long duration of disease and in patients with poor metabolic
control. Microangiopathy may be a contributory factor in causing muscle dysfunction.

Bouchard et al (1989) studied a group of 88 asymptomatic normotensive diabetic patients between 20 and 50 years of age. Two dimensional echocardiography and stress myocardial perfusion scintigraphy were performed to detect and characterize the cardiac abnormalities in this study group and 65 volunteers control subjects are used. Diabetic patients were shown to have a mildly reduced LV end diastolic volume indices (50 ± 8.2 and 52.1 ± 14.7 ml/m² for patients with type I and type II diabetes respectively, versus 58.9 ± 11.7 ml/m² for control subjects). The left ventricular diastolic filling was also impaired in diabetic patients as reflected by a lower atrial emptying index 0.73 ± 0.24 and 0.76 ± 0.3 for type I and type II diabetics respectively as compared with 1.14 ± 0.24 for control subjects. Exercise tolerance was normal in subjects with type I diabetes. Only one patient developed regional ischemia on thallium exercise testing. They have concluded that asymptomatic normotensive diabetic patients between 20-50 years age group had a restrictive cardiomyopathy characterized by mildly reduced EDV and altered LV compliance independent of coronary artery disease.

Dash et al (1977) concluded in their study that there is an increased prevalence of cardiomyopathy syndrome in diabetics with coronary artery disease as compared to non diabetic patients with coronary artery disease. Coronary angiography was done in both groups of patients
and this difference exists independently of hypertension and hyperlipidemia.

Grandi et al (1992) studied cardiac and autonomic functions in diabetics. They had performed M-mode echocardiogram and autonomic function tests in 21 patients (mean age 38±11 years; range 18-55 years; 16 males and 5 females). In patients and 21 age matched controls the echocardiogram was also performed before and during handgrip. At rest ventricular function abnormalities were found only in 4 subjects and no significant correlation was found between echocardiographic parameters and autonomic function tests. Unlike controls, during handgrip diabetic subjects failed to increase peak VCF and peak filling rate and increased their LVESD.

Changes in LV parameters during handgrip are significantly correlated with resting autonomic function tests (p < 0.025). Authors have suggested that resting cardiac function may be normal in diabetics despite high incidence of abnormal autonomic tests. Later abnormalities are unmasked by acute haemodynamic challenges such as handgrip and are correlated with autonomic dysfunction. Other important study was conducted by Mustonen et al (1992) about autonomic nervous dysfunction and its relation to cardiac performance in middle aged diabetics without clinically evident cardiovascular disease. They have evaluated autonomic nervous function in 36 patients of IDDM, 39 patients of NIDDM and 48 control subjects, all without clinically evident cardiovascular disease.
Valsalva ratio and heart rate variation during deep breathing were lower in both diabetic groups than in the control group. Autonomic nervous function score (ANFS) was more abnormal in patients with IDDM than in control subjects, but was not significantly increased in patients with NIDDM. There was negative correlation between ANFS and LV diastolic filling evaluated by echocardiography or peak heart rate during exercise in both diabetic groups. There was no correlation between ANFS and LV systolic function at rest or during exercise in both diabetic groups. They have concluded that autonomic dysfunction was present in middle aged diabetic patients and it was associated with impaired LV diastolic filling at rest and decreased heart rate response to exercise but not with LV systolic function.

Watchinger et al (1991) studied left and right ventricular functions in normotensive type I diabetics and concluded that the high incidence of cardiac mortality in type I diabetics is further increased when diabetic nephropathy is present. Systolic and diastolic abnormalities have been found using echocardiography as diagnostic tool and the latter preceding the former. The pathophysiological substrate for these changes of diastolic LV performance leading to altered LV compliance could be microvascular disease within myocardium. This could explain why type I diabetics with nephropathy, who comprise about one third of all type I diabetics are predisposed to a high incidence
of cardiac complications throughout their disease while diabetic patients without renal complications are not at high risk. Vanni et al (1992) assessed LV function and dimension in newly diagnosed NIDDM patients and found that diabetic men had increased LV mass and decreased fractional shortening compared to controls. These diabetics were re-examined after 3 months and 15 months intervals. They have found that with decreasing blood glucose levels fractional shortening improved mainly during first 3 months and was significantly higher in both diabetic men and women after 15 months from the base line values. At 15 months, peak filling rate was correlated with autonomic nervous function assessed as heart rate variability during deep breathing test in diabetic men who also showed an inverse correlation between LV hypertrophy and heart rate variability throughout the follow up.

Other studies (Pailloe et al, 1989; Spirito et al, 1986) have done the echocardiographic evaluation of LV function and reported that diastolic functions are more detectable as compared to systolic functions. Margonato et al (1986) and Uchimoto et al (1991) have also concluded that there is impaired systolic functions during exercise in middle aged IDDM and NIDDM patients without clinically evident cardiovascular disease. Weinrauch et al (1992) have studied a group of stable patients on maintenance dialysis with diabetic mellitus up to 135 months to identify high risk of sudden death in these patients. They have concluded that although echocardiographic abnormalities
predicted cardiac mortality at 6 and 12 months, the combination of an abnormal ECG at base line, clinical history of angina and prior documented MI or congestive heart failure do not. When the study group was divided by duration of diabetes or use of cardioactive drugs, echocardiographic LV wall motion abnormalities remained the most important determinant of survival.