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Study of Cardiovascular Complications in Long Term Diabetes Mellitus- An Indian Perspective

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Abstract

Background: Diabetes mellitus is a disorder in which the body is unable to metabolize carbohydrates properly. In view of the above facts the study was undertaken to know the incidence of cardiovascular complications, to establish its relationship with duration of disease; severity of diabetes mellitus; its state of control, the body weight and the type of treatment patient was receiving. An attempt was also taken to find out the interrelationship between different complications.

Materials & Methods: The present study includes adult cases of diabetics who were attended and /or admitted to Medicine and Cardiology wards of a tertiary care teaching hospital, Haldia, West Bengal. All the known cases of diabetics of more than 5 years duration on antidiabetic treatment were included in the study. Fasting blood sugar, post prandial blood sugar, serum cholesterol routine urine examination for reducing substances, albumin, ketone bodies and microalbuminuria were examined. Measurement of HbA1C done in all 106 cases and categorized into good controlled, moderately controlled and poorly controlled. The patients of more than 5 years duration with diabetes were taken as long term diabetics and the long diabetics were divided into two groups as diabetics <10 yrs and diabetics of >10 yrs.

Results: It was observed from table 4 that out of 106 cases, 25 (23.8%) were of severe variety, 35 cases (33%) were of moderate variety and 46 cases (43.2%) were of mild variety. In all instances males were outnumbered females. The incidence of hypertension in good, moderate and poor controlled groups was 12.5%, 18.85 and 66.75% respectively.

Conclusion: Good control of diabetes decreased the incidence of micro and macrovascular complications. Obesity, IHD and hypertension are interrelated. Severity of diabetes was not related to incidence of IHD, hypertension and PVD. CVA and cardiomyopathy showed a more incidence in severe diabetics with an incidence of 58% and 50% respectively.

Keywords: Diabetes Mellitus; Cardiovascular complications, Outcome.

Introduction

Diabetes mellitus, more simply called diabetes, is a chronic condition that occurs when there are raised levels of glucose in the blood because the body cannot produce any or enough of the hormone insulin or use insulin effectively.¹ The classification and diagnosis of diabetes is complex and have been the subject of much consultation, debate and revision stretching over many decades, but it is now widely accepted that there are three main types of diabetes, type 1 diabetes, type 2 diabetes and gestational diabetes (GDM). Type 2 diabetes is the most common type of diabetes, accounting for around 90% of all cases of diabetes.^[2-4]

In type 2 diabetes, hyperglycaemia is the result of an inadequate production of insulin and inability of the body to respond fully to insulin, defined as insulin resistance. Type 2 diabetes is most commonly seen in older adults, but it is increasingly seen in children, adolescents and younger adults due to rising levels of obesity, physical inactivity and poor diet. There are 425 million people with diabetes in the World. There will be 629 million people with diabetes in the World in 2045.⁵

Characteristics	2017	2045
Prevalence (20-79 years)	8.8% (7.2-	9.9% (7.5-
	11.3%)	12.7%)
Number of deaths due to	4.0 (3.2-5.0)	-
diabetes	million	
(20-79 years)		
India: Number of people	72.9 million	
with diabetes	(55.5-90.2)	
Number of people with	42.2 million	57.9%
undiagnosed diabetes	(32.1-52.2)	

Table 1: Diabetes global estimates⁵

Mauritius has the highest adult diabetes prevalence rate in this region (22.0%), followed by Sri Lanka (10.7%) and India (10.4%). India is home to the second largest number of adults living with diabetes worldwide, after China. People with diabetes in India, Bangladesh, and Sri Lanka make up 98.9% of the region's total adult diabetes population. Diabetes prevalence has been rising more rapidly in middle- and low-income countries. It is a major cause of blindness, kidney failure, heart attacks, stroke and lower limb amputation. In 2015, an estimated 1.6 million deaths were directly caused by diabetes.⁶ Diabetes is one of the largest global health emergencies of the 21st century. Diabetes is among the top 10 causes of death globally and together with the other three major non communicable diseases (NCDs) (cardiovascular disease, cancer and respiratory disease) account for over 80% of all premature NCD deaths. In 2015, 39.5 million of the 56.4 million deaths globally were due to NCDs.¹ A major contributor to the challenge of diabetes is that 30-80% of people with diabetes are undiagnosed.⁷

DM, whether type 1 or type 2, is a very strong risk factor for the development of coronary artery disease (CAD) and stroke.^{8,9} Two recent prospective epidemiologic studies, the Pittsburgh Epidemiology of Diabetes Complications (EDC) study¹⁰ and Eurodiab¹¹, a multicenter, clinic-based study in Europe, confirmed these earlier reports and reported an incidence of total coronary events (including electrocardiogram [ECG] changes) of 16% over 10 years and 9% over 7 years, respectively, of follow-up in type 1 diabetic patients. Eighty percent of all deaths among diabetic patients are due to atherosclerosis, and its complications compared with 30% among non-diabetic persons.¹²

Long standing diabetes mellitus is associated with an increased prevalence and incidence of microvascular and macrovascular diseases. Recent data from Chennai show that the prevalence of complications of type 2 diabetes are high; retinopathy 23.7%, nephropathy 5.5%, peripheral neuropathy 25.5%, CHD 11.4%, PVD 4% and stroke 0.9%. Prevalence of hypertension is also high 38.2%. Duration of diabetes had significant association with the complications other than CHD. Higher HbA1 increased the risk of retinopathy, neuropathy and nephropathy.¹³

Similar results also been published by Mohan et al and Lily John et al from India. There was a linear increase in prevalence of PVD with increasing duration of diabetes. Multiple logistic regression analyses showed that serum cholesterol, serum

creatinine, systolic BP, duration of diabetes and ishaemic heart disease is strong predictive factors for PVD.^{14, 15} One of the earliest discernible atherogenic changes in diabetes is endothelial dysfunction, which is characterized by inhibited vasodilatation, vascular smooth muscle proliferation, increased thrombogenesis and proatherogenic cellular process.¹⁶ Abnormal endothelium dependent vasodilatation also occurs in the microcirculation of patients with diabetes, where it may contribute to ischemia and its sequelae.¹⁷

A high prevalence of risk factors for cardiovascular diseases, such as diabetes, insulin resistance, upper body adiposity and increased levels of fibrinogen are reported in Asian Indians, both in their native country and abroad.^{18, 19}

In view of the above facts the study was undertaken to know the incidence of cardiovascular complications, to establish its relationship with duration of disease; severity of diabetes mellitus; its state of control, the body weight and the type of treatment patient was receiving. An attempt was also taken to find out interrelationship the between different complications.

Materials & Methods

The present study includes adult cases of diabetics who were attended and /or admitted to Medicine and Cardiology wards of a tertiary care teaching hospital, Haldia, West Bengal. All the known cases of diabetics of more than 5 years duration on antidiabetic treatment were included in the study. After selection, all cases were subjected to through clinical examination with detail history and relevant investigations were done in each case. One hundred and six cases of diabetes mellitus (80 males and 26 females) of different age groups (30-80 yrs) and disease of more than 5 years were taken up for the present study. Fasting blood sugar, post prandial blood sugar, routine urine examination for reducing substances, albumin, ketone bodies and microalbuminuria. Protein estimation was done by Esbach's albuminometer. Microalbuminuria (Albustix nehative) is urine albumin excretion of 30-300 mg/dl and macroalbuminuria (Albustix positive) is >300 mg/dl.²⁰ Serum cholesterol was estimated by Kings technique by modified Liberman Burchand reaction.²¹ Patients were divided into 2 groups; group I- serum cholesterol <240 mg% and group II- serum cholesterol >240 mg%. Measurement of HbA1C done in all 106 cases and categorized into good controlled, moderately controlled and poorly controlled. The patients of more than 5 years duration with diabetes were taken as long term diabetics and the long diabetics were divided into two groups as diabetics <10 yrs and diabetics of >10 yrs. Hypertensive was classified as per JNC7 guidelines. Opthalmoscopy was done in each case to note the evidence of diabetic retinopathy and divided accordingly.²² Chest X-ray, X-ray foot (AP & lateral view), ECG, and echocardiogram were done in each case. M mode 2D echo was done in all the 106 cases to find out RWMA and diastolic dysfunction. Diminished or absence of peripheral pulses, intermittent claudication, gangrene and previous history of amputation was taken as evidence of peripheral vascular disease.²³

Results

In the present study total 106 cases of diabetes mellitus with more than 5 years duration were studied which fulfilling the diagnostic criteria of DM and on antidiabetic therapy.

Table 2: Age and sex distribution of study participants with DM [n=106]

Age group in years	Male		Female	Female		Total	
	No	%	No	%	No	%	
31-40	9	11.25	2	7.69	11	10.3	
41-50	11	13.7	3	11.5	14	13.2	
51-60	50	62.5	15	57.69	65	61.3	
>60	10	12.5	6	23.07	16	15.09	
Total `	80	75.4	26	24.52	106	100	

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Table 2 showed that out of 106 cases with DM 80 cases (75.4%) were males and 26 cases (24.52%) were females. Majority of patients were found to be distributed in 51-60 years of age whereas minimum occurrence in the age group between 31-40 yrs (10.3%).

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Table 3: Distribution of cases by duration of disease and sex [n=106]

Duration of disease (Yrs)	No. of cases				Total		
	Male		Female		No	%	
	No	%	No	%			
5-10	32	40	16	61.53	48	45.2	
>10	40	60	10	38.47	58	54.8	
Total	80	100	26	100	106	100	

About 58 (54.8%) of diabetic patients having duration of disease was more than 10 years [Table 3]. About 96 (90.6%) cases were belonging to type 2 diabetes.

Table 4: Distribution of cases according to severity of diabetes [n=106]

Duration of disease (Yrs)		No	Total			
	Male		Female		No	%
	No	%	No	%		
Mild	30	37.5	16	61.6	46	43.2
Moderate	30	37.5	5	19.2	35	33
Severe	20	25	5	19.2	25	23.8
Total	80	100	26	100	106	100

It was observed from table 4 that out of 106 cases, 25 (23.8%) were of severe variety, 35 cases (33%) were of moderate variety and 46 cases (43.2%)

were of mild variety. In all instances males were outnumbered females.

Table 5: State of control of cases of diabetes on the basis of HbA1C [n=106]

Sex	Go	od	Moderate		Poor		Total	
	No.	%	No.	%	No.	%	No.	%
Male	10	12.5	5	6.25	65	81.25	80	75.4
Female	4	15.3	2	7.6	20	76.92	26	24.6
Total	14	13.2	7	6.6	85	80.18	106	100

The table 5 showed that out of 106 cases, 85 cases (80.18%) were in state of poor control whereas

only 14 cases (13.2%) were in good control of diabetic state.

Table 6: Distribution of cases to their body built [n=106]

Body built	Male	Female	Total
Obese	10 (12.5%)	14 (53.8%)	24 (22.6%)
Non obese	70 (87.5%)	12 (46.2%)	82 (77.4%)
Total	80 (100%)	26 (100%)	106 (100%)

Table 6 indicated that 10 cases (12.5%) were obese and 70 cases (87.5%) were nonobese among male subjects. The ratio of obese male and female

0.71:1. which showed females had was outnumbered the males.

Table 7: Showing the sex distribution of cardiovascular complications [n=106]

-		-	
Sex	With cardiovascular complications	Without cardiovascular complications	Total
Male	43 (40.6%)	37 (34.9%)	80
Female	19 (17.9%)	7 (6.6%)	26
Total	62 (58.49%)	44 (41.51%)	106
s evident from	the table 7 that 43 males	About 44 cases (41.51%) did	not suffe

It w cardiovascular (40.6%)suffered from complications along with 19 females (17.93%).

from cardiovascular complications.

Table 8: Showing the prevalence o	of complications among	g study participants with	DM [n=106]
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	U		L .
Complications	Male	Female	Total
Ischemic heart disease	30 (37.5%)	12 (46.15%)	42 (39.6%)
Hypertension	20 (25%)	12 (46.15%)	32 (30.1%)
Peripheral vascular disease	12 (15%)	3 (11.5%)	15 (14.1%)
Cardiomyopathy	4 (5%)	2 (7.6%)	6 (5.6%)
Cerebrovascular accident	5 (6.25%)	2 (7.6%)	7 (6.6%)
Retinopathy	30 (37.5%)	8 (30.7%)	38 (35.8%)
Nephropathy	4 (5%)	2 (7.6%)	6 (5.6%)
Neuropathy	20 (25%)	5 (19%)	25 (23.6%)

It was found from above table 8 that incidence of ischemic heart disease in 39.65 cases, hypertension in 39.1% and peripheral vascular disorders in 14.1% cases. Apart from these

complications retinopathy was found to be 35.8%, nephropathy in 5.6% and neuropathy in 23.6% along with cerebrovascular accident in 6.6% of diabetic cases.

Table 9: Distribution of cardiovascular complication to types of diabetes

Cardiovascular complications	Type 1	Type 2	Total
IHD	2 (4.9%)	40 (95.1%)	42 (100%)
Hypertension	2 (6.2%)	30 (93.8%)	32 (100%)
PVD	-	15 (100%)	15 (100%)
CVA	-	7 (100%)	7 (100%)
Cardiomyopathy	-	6 (100%)	6 (100%)
Retinopathy	10 (26%)	28 (74%0	38 (100%)
Nephropathy	2 (33.3%)	4 (66.7%)	6 (100%)

The table 9 clearly shows that incidence of retinopathy 10 cases (26%) and nephropathy 2 case (33.3%) clearly outnumbers the **Table 10:** Distribution of macrovascular complication

macrovascular complications in type 1 DM whereas in type 2 DM both microvascular and macrovascular complications predominant.

 Table 10: Distribution of macrovascular complications in relation to age

Age [Yrs]	Complications						
	IHD	Hypertension	PVD	CVA	Cardiomyopathy		
31-40	4 (9.5%)	-	1 (6.6%)	-	-		
41-50	8 (19%)	8 (25%)	2 (13.3%)	-	-		
51-60	20 (47.6%)	20 (62.5%)	10 (66.5%)	2 (29%)	2 (33.3%)		
>60	10 (23.8%)	4 (12.5%0	2 (13.3%)	5 (71%)	4 (66.7%)		
Total	42 (39.6%)	32 (30.1%)	15 (14.1%)	7 (6.6%)	6 (5.6%)		

It is evident from table 10 that IHD was more prevalent in 51-60 yrs age group. Hypertension also was most prevalent in same age group whereas 31-40 yrs age group show no evidence of hypertension. Both CVA and cardiomayopathy were most prevalent in the age group >60 yrs. The age group of 31-40 yrs was having low prevalence of cardiovascular complications.

Severity	Complications				
	IHD	HTN	PVD	CVA	Cardiomyopathy
Mild	13 (30.9%)	5 (15.6%)	3 (20%)	1 (14%)	1 (16.7%)
Moderate	12 (28.7%)	11 (34.4%)	4 (26.6%)	2 (28%)	2 (33.3%)
Severe	17 (40.4%)	16 (50%)	8 (53.3%)	4 (58%)	3 (50%)
Total	42 (100%)	32	15	7	6

The table 11 showed that out of 42 cases having IHD, 17 cases (40.4%) were with severe diabetes,

12 cases (28.7%) were with moderate diabetics and 13 cases (30.9%) were with mild diabetics.

Cardiovascular	Diabetes status				
complications	Good	Moderate	Poor		
IHD	2 (4.7%)	4 (9.5%)	36 (85.8%)		
Hypertension	4 (12.5%)	6 (18.8%)	22 (66.75%)		
PVD	1 (6.6%)	2 (13.4%)	12 (80%)		
CVA	1 (14%)	2 (28%)	4 (58%)		
Cardiomyopathy	-	2 (33.3%)	4 (66.7%)		
Retinopathy	10 (26%)	12 (31%)	16 (43%)		
Nephropathy	-	2 (33.3%)	4 (66.7%)		

Table 12: Showing the relationship of cardiovascular complications to the state of control of diabetics

The table 12 showed that 2 cases (4.7%) of good controlled group, 4 cases of (9.5%) of moderate group and 36 cases (85.8%) of poor control were having IHD. The incidence of hypertension in good, moderate and poor controlled groups was 12.5%, 18.85 and 66.75% respectively. Poorly controlled group had an incidence of 80% PVD in comparison to 6.6% and 13.4% in good and moderate control groups respectively.

Discussion

In the present series, 106 cases of DM of more than 5 years duration were taken up for study to determine their cardiovascular status. Out of 106 cases, 10 cases were of type 1 diabetes and 96 were of type 2 diabetes. Majority of the present study series were in the age group 51-60 yrs. The present incidence was in agreement with the studies of Bahl et al $(1966)^{24}$; Pathania et al $(1961)^{25}$; Chakravarty et al $(1949)^{26}$; Banerjee JC $(1966)^{27}$ and Agrawal $(1977)^{28}$. Out of 106 cases in present series, 80 were male and 26 cases were females, with the ratio of 3.1:1. The sex ratio in the present series was similar to the study of Bahl et al $(1966)^{24}$; Banerjee JC $(1966)^{27}$ and Agrawal et al $(1966)^{27}$ and Agrawal et al $(1977)^{28}$.

In 48 cases (46%) of diabetes the duration of disease was less than 10 years and in 58 cases

(54%) the duration was less than 10 years, thus signifying an increased number of cases with long duration of the disease. This study was in agreement with that of Agrawal et al $(1977)^{28}$, the series showing 55.2% of cases with duration of more than 10 years. From the present study it was evident that 80% of the diabetics were having poor control of the diabetic state whereas 13.2% had only good control of disease. Majority of the cases 76.2% in the present series were having mild and moderate diabetes. Only 23.8% had severe diabetes.

In the present series 62 cases (58.49%) had cardiovascular complications and male were predominantly affected in comparison to females. Most of the Indian study reported an incidence of 40-56.7% (Vaishnava et al, 1973)²⁹. Mathew et al (1964)³⁰ had got an incidence of 53%, Bahl et al (1966)²⁴ reported 64% incidence and Agrawal et al (1967)²⁸ had an incidence of 62.3% of the diabetics having cardiovascular complications.

Among the macrovascular complications 39.6% were suffering from IHD, 30.1% from hypertension, 14.1% from PVD, 5.6% from diabetic cardiomyopathy and 6.6% from CVA.

Name of the authors	Year of study	IHD	PVD	HTN	CVA	Cardiomyopathy
Pathania et al ²⁵	1961	21.7	-	27.8	5.7	-
Bahl et al ²⁴	1966	25	29	44	-	-
Raheja et al ³¹	1970	24	-	64.8	-	-
Vaishnava et al ²⁹	1973	33.3	13.7	45.3	-	-
Agrawal et al ²⁸	1977	39.7	49.1	30.1	-	-
Mohan et al ¹⁴	1995	17.9	3.9	-	-	-
Ramachandran et al ¹³	1998	11.4	4	38	0.9	-
Present study	2010	39.6	14.1	30.1	6.6	5.6

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The incidence of IHD in the present study was significantly higher than other complications but majority of the workers had got a higher incidence of hypertension. Among microvascular complications 35.8% cases were suffering from retinopathy, 5.6% cases from nephropathy and 23.6% cases neuropathy.

Name of the authors	Year of study	Retinopathy	Neuropathy	Nephropathy
Pathania et al ²⁵	1961	-	-	5.7
John et al ¹⁵	1991	-	-	8.9
Samanta et al ³²	1991		-	
Asian Indian		11.6	-	22.3
White		32.3	-	12.6
Mohan et al ¹⁴	1995	34.1	-	-
Ramachandran et al ¹³	1998	23.7	27.5	5.5
Present study	2010	35.8	23.6	5.6

The incidence of retinopathy in present study 35.8% is similar to majority of the workers. The incidence of nephropathy was also similar 5.6% to majority of workers. The incidence of neuropathy 23.6% is similar to incidence of 27.5% shown by Ramachandran et al^{13} . In the present study 6 cases of diabetes had congestive heart failure without ECG evidence of IHD and the etiology was attributed to diabetic cardiomyopathy. The different complications found in this study were not isolated complication. IHD patients had hypertension, retinopathy, evidence of nephropathy, neuropathy and PVD also. Thus it was obvious that such complications were frequent association of diabetes.

About 42 cases of DM had the evidence of IHD, giving an incidence of 39.6% in the present study. Vaishnava et al $(1973)^{29}$ had an incidence of 33%, and Agrawal et al (1978)²⁸ had 39.7% which was similar to the present study. But Pathania et al $(1961)^{25}$, Mohan et al $(1995)^{14}$ and Ramachandran et al (1998)¹³ had lower incidence of IHD such as 14%, 21.7%, 17.9% and 11.4% respectively. In the present study distribution of IHD among diabetics was maximum in 51-60 yrs age group. This observation was similar to Sowers JR (2001); Lal and Bahl $(1967)^{34}$; Banerjee et al $(1966)^{26}$ but Raheja et al $(1970)^{31}$ had highest incidence in a relatively younger age group (41-50 yrs). Present study showed the incidence of IHD was more in males than females with a sex ratio of M: F 2.5:1, but sex ratio determined by Bryfogle and Bradley

 $(1957)^{35}$ was 1.6:1 and Pathania and Sachar²⁵ 1.7:1.

From the present study it was evident that 30.9% of the mild diabetics had IHD whereas only 40.4% of the severe diabetics had evidence of IHD. Thus the incidence of IHD was not influenced by the severity of disease. Bahl et al (1966)²⁴, Shah et al (1999)³⁶ and Raheja et al (1980)³¹ could not detect any relation between the incidence of IHD and severity of DM. Shah et al (1968)³⁷, Bahl et al (1967)³⁴ and Vaishnava et al (1968)²⁹ found out that the incidence of IHD increase with increase duration of diabetes which was in agreement with the present observations.

About 30.1% cases in DM of the present study had evidence of hypertension. Males predominated the incidence with a ratio of 1.6:1. Incidences of hypertension noted by previous Indian workers are as follows- Pathania et al (1961)²⁵ 27.8%, Shah et al (1968)³⁷, Vaishnava $(1968)^{29}$ 34.3%, Lal $(1967)^{34}$ 39.7%. Ramchandran et al (1998)¹³ 38%. The incidence of hypertension was more in the age group of 51-60 yrs showing a figure of 62.5%. Pathania et al $(1961)^{25}$ showed increased incidence of hypertension in 60-69 yrs age group whereas Raheja et al concluded no age specificity.

Most cardiovascular risk factors are affected directly by an acute increase of glycemia in individuals with diabetes and are modified in the postprandial phase. LDL oxidation in diabetes is related to metabolic control (Tsai et al., 1994)³⁸ and it has been shown in type 2 diabetic patients

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that after meals, LDL oxidation increases (Tsai et al., 1994)³⁸ and that this phenomenon is in strict relationship with the degree of hyperglycemia (Enkins et al., 1996).³⁹ Endothelial function is altered early in diabetes.⁴⁰ People with type 1 and type 2 diabetes are at significantly increased risk of developing atherosclerotic cardiovascular disease. Diabetes is associated with microvascular and macrovascular complications, and is a major and independent risk factor for CVD. The lifetime risk for CVD in people with diabetes is high, about 67% in men and 57% in women at age 50 years.⁴¹

One possible explanation for the onset of CVD risk in people with prediabetes and/or increased cardiometabolic risk is the development of atherogenic diabetic dyslipidemia. The pathophys-iology and emerging therapeutic strategies targeting the abnormal lipoprotein metabolic pathways are reviewed by Dominic Ng.⁴²

Conclusion

One hundred and six cases of diabetes mellitus studied with special reference were to cardiovascular complications. About 58.49% suffered from cardiovascular complications. The macrovascular complications like IHD, HTN, PVD, CVA and diabetic cardiomyopathy were met with microvascular complications like diabetic nephropathy, retinopathy and neuropathy. IHD was found in 39.6% cases, hypertension in 30.1%, PVD in 14.1%, cardiomyopathy in 5.6%, CVA in 6.6%, retinopathy in 35.8%, nephropathy in 5.6%, CVA in 6.6%, retinopathy in 35.8%, nephropathy in 5.6% and neuropathy in 23.6% cases.

Good control of diabetes decreased the incidence of micro and macrovascular complications. Obesity, IHD and hypertension are interrelated. Severity of diabetes was not related to incidence of IHD, hypertension and PVD. CVA and cardiomyopathy showed a more incidence in severe diabetics with an incidence of 58% and 50% respectively. Resumption to an ideal weight in the obese diabetic will further improve the mortality and morbidity arising out of the cardiovascular complications. Control of hypertension with suitable antihypertensive is necessary. Lifestyle modifications like avoidance smoking, and sedentary habit are also necessary. Life style modification and strict metabolic control will help to reduce the cardiovascular complications in long-term diabetics.

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