SIGNIFICANCE OF SERUM HOMOCYSTEINE LEVELS IN TYPE 2 DIABETES MELLITUS IN MIDDLE AGED INDIVIDUALS

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ABSTRACT

BACKGROUND

Diabetes mellitus (DM) is a syndrome characterized by chronic hyperglycaemia and disturbances of carbohydrate, fat, and protein metabolism associated with absolute or relative deficiencies in insulin secretion and/or insulin action. Worldwide, approximately 200 million people currently have type II diabetes mellitus (DM), a prevalence that has been predicted to increase to 366 million by 2030.

MATERIALS AND METHODS

All participants are selected from those who visited Diabetes Clinic, in Al-Ameen Medical College Hospital and District Hospital, Bijapur between Dec 2013 - June 2015. 50 patients presenting with type 2 diabetes mellitus in middle age are included in the study. In our study, diabetic patients with cardiovascular complications had poor glycaemic status compared to diabetic patient without cardiovascular complications.

RESULTS

The results of this study confirm the hypothesis that hyperhomocysteinaemia is a risk factor for endothelial dysfunction and vascular diseases such as atherosclerosis and occlusive vascular disorders.

CONCLUSION

The homocysteine levels were comparatively more elevated in patients of diabetes with cardiovascular complications than the patients of diabetes alone, thus indicating that hyperhomocysteinaemia is an independent risk factor for CVD incidence in type 2 diabetic patients in middle age individuals.

KEYWORDS

Homocysteine (Hcys), Type 2 Diabetes Mellitus.

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BACKGROUND

Worldwide, approximately 200 million people currently have type II diabetes mellitus (DM), a prevalence that has been predicted to increase to 366 million by 2030.[1]

Rates of cardiovascular disease (CVD) mortality and morbidity are particularly high in this population; Acute myocardial infarction in diabetes carries twice the mortality of that in the general population and contributing factors may include coexistent diabetic cardiomyopathy, adverse cardiac and metabolic effects of increased non-esterified fatty acid levels.[2-6] Therefore, successful management of cardiovascular disease associated with diabetes represents a major challenge to the clinicians. Clinicians consider a risk factor–guided screening approach to early diagnosis of cardiovascular disease and to target treatment toward their improvement. Targeting hyperglycaemia alone does not reduce the excess risk in diabetes, highlighting the need for aggressive treatment of other risk factors.

Homocysteine (Hcys) has been implicated to be associated with diabetes and its complications,[7] is a major risk factor for myocardial infarction (MI) in patient with type 2 diabetes mellitus, however the role of increase serum homocysteine level in the development of coronary heart disease in patient with type 2 diabetes mellitus is still unknown and there is strong evidence suggesting that hyperhomocysteinaemia accelerates the process of atherogenesis.

Diabetes mellitus (DM) is a syndrome characterized by chronic hyperglycaemia and disturbances of carbohydrate, fat, and protein metabolism associated with absolute or relative deficiencies in insulin secretion and/or insulin action[8]. Type 2 diabetes mellitus is due to relative deficiency

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of insulin as a result of impaired secretion of insulin as well as insulin resistance 9. Cardiovascular disease (CVD) is a major cause of morbidity and mortality, and, in India, in the past 5 decades, its rate among urban population has risen rapidly.

As obesity, hypertension, and dyslipidaemia, which are known to be frequently associated with, type 2 diabetes mellitus, are insufficient in explaining the increase in risk, researchers are focusing on investigating new risk factors. Homocysteine (HCY) is a sulphur containing amino acid in the body, which is produced by conversion of methionine. The normal value ranges from 5-15 µmol/L. Recently, mild elevations of serum Homocysteine have been identified as an independent risk factor for early atherosclerotic vascular disease and thromboembolic disease. High circulating Homocysteine concentrations may increase the risk of cardiovascular diseases when present with other cardiovascular risk factors like hypercholesterolemia and diabetes. The study is, therefore, aimed to assess the correlation between hyper-homocysteinaemia as an associated risk factor for cardiovascular complications in type 2 diabetes mellitus in middle aged individuals.

The present study will be conducted a minimum of 50 patients presenting with type 2 diabetes mellitus in middle aged individuals are included in the study.

Aim of the Study

To study significance of serum homocysteine levels as associated risk factor for cardiovascular complications in type 2 diabetes mellitus in middle aged individuals.

MATERIALS AND METHODS

All participants are selected from those who visited Diabetes Clinic, in Al-Ameen Medical College Hospital and District Hospital, Bijapur between Dec 2013-June 2015. The present study will be conducted a minimum of 50 patients presenting with type 2 diabetes mellitus in middle aged individuals are included in the study. These diabetic mellitus patients are divided into 2 subgroups: Group 1 (n = 25), type 2 diabetes mellitus with cardiovascular complications; Group 2 (n = 25) type 2 diabetes mellitus without cardiovascular complications. Type 2 diabetes mellitus without cardiovascular complications are taken as control subjects.

Inclusion Criteria

1. Age should be between 40 and 65 years.
2. The diagnosis of DM are based on WHO criteria.
   A fasting plasma glucose of ≥ 126 mg/dL (7.0 mmol/L) after minimum 12-h fast, with symptoms of diabetes. 2 h of postprandial glucose level of ≥ 200 mg/dL (11.1 mmol/L) after 75 g oral glucose load. Participants suffering from diabetes are included in the study irrespective of their glycaemic status.
3. Diagnosis of cardiovascular complications is based on; History, Clinical findings, and Findings from serial tracings of 12 lead ECG.

Exclusion Criteria

Pregnancy, Severe renal impairment, Severe hepatic impairment, Cancer, Thyroid disease, Patient on lipid-lowering drugs, Patient on vitamin B supplements, Patient aged less than 40 and more than 65 years are excluded.

Statistical Analysis

The information collected regarding all the selected cases will be recorded in a Master Chart. Data analysis will be done with the help of computer using Epidemiological Information Package (EPI 2002). Using this software, frequencies, percentage, mean, standard deviation, x2 and 'p' values will be calculated.

RESULTS

Age in Years	Cases		Controls	
	No.	%	No.	%
40-50	6	12.0	14	28.0
51-60	11	22.0	27	54.0
61-65	33	66.0	9	18.0
Total	50	100.0	50	100.0
Mean ±SD	61.02±5.13		54.36±6.51	

Table 1. Age Distribution of Patients Studied

The mean age of the patients in both cases and controls were 61.02 and 54.36 years respectively. 51-60 in controls with P value <0.001 the highest numbers of patients were in the age group of 61-65 in cases and There is a significant difference in the age group between cases and controls with p value <0.001.

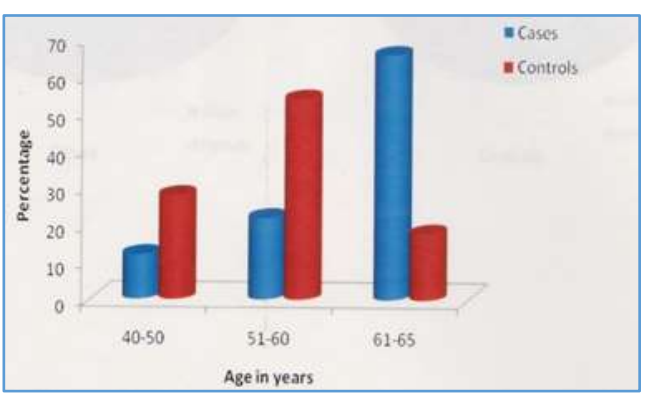


Figure 1

Gender	Cases		Controls	
	No.	%	No.	%
Male	31	62.0	28	56.0
Female	19	38.0	22	44.0
Total	50	100.0	50	100.0
Samples are gender matched with P= 0.542				

Table 2. Sex Distribution of Patients Studied

In present study we observed that, there were 62% males and 38% females in cases and 56% males and 44% females in controls in our study high prevalence of diabetes mellitus seen in males.

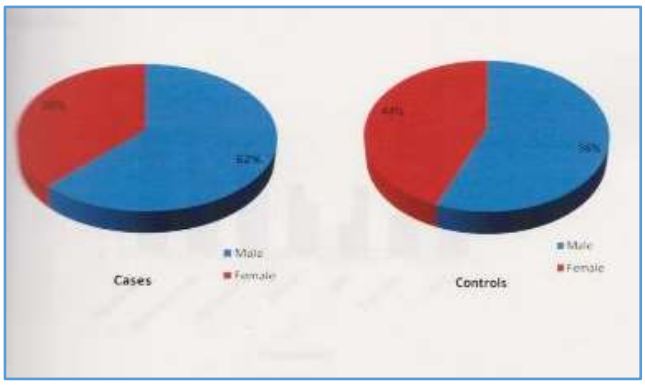


Figure 2

Occupation	Cases		Controls	
	No.	%	No.	%
House wife	13	26.0	12	24.0
Business men	10	20.0	8	16.0
Agriculture	9	18.0	8	16.0
Driver	7	14.0	5	10.0
Labour	3	6.0	7	14.0
Teacher	4	8.0	6	12.0
Govt. Employ	4	8.0	4	8.0
Total	50	100.0	50	100.0
P = 0.851, Not Significant, Fisher Exact test				

Table 3. Occupation Distribution in the Two Groups Studied

In our study, majority of patients were house wife, 26% in cases and 24% in control followed by business man (20% in cases and 8% in control) and other occupations.

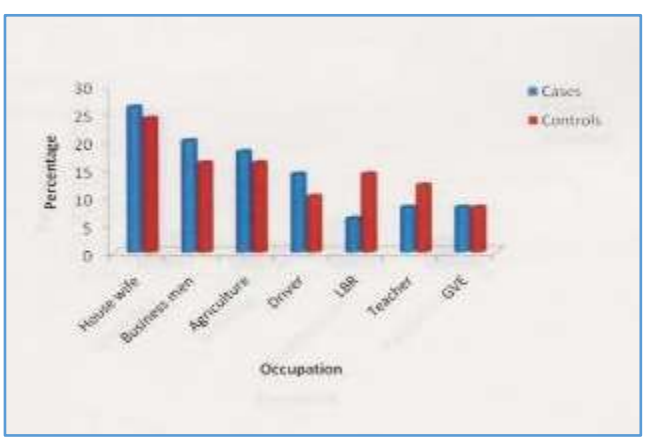


Figure 3

Symptoms	Cases		Controls		P Value
	No.	%	No.	%	
Chest Pain	42	84.0	9	18.0	<0.001**
Sweating	27	54.0	6	12.0	<0.001**
Breathlessness	12	24.0	2	4.0	<0.001**
Palpitation	8	16.0	1	2.0	<0.001*
Chi-Square test					

Table 4. Symptoms Distribution in the Two Groups Studied

Chest pain, sweating, breathlessness and palpitation were the common symptoms in our study. Among them, chest pain is the most common presentations, presented in 84% of cases and in 18% of controls, followed by other symptoms. Symptoms are significantly higher in cases as compared to controls with p value <0.001.

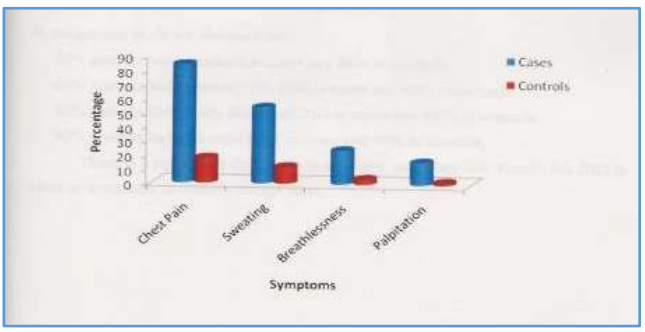


Figure 4

Risk Factors	Cases (n=50)		Controls (n=50)		P Value
	No	%	No	%	
Smoking					
• Negative	21	42.0	31	62.0	0.045*
• Positive	29	58.0	19	38.0	
Sedentary Life					
• Negative	19	38.0	30	60.0	0.028*
• Positive	31	62.0	20	40.0	
Family h/o IHD					
• Negative	20	40.0	30	60.0	0.046*
• Positive	30	60.0	20	40.0	
BMI (kg/m^2)					
• 18.5-25	4	8.0	5	10.0	0.914
• >25-30	26	52.0	27	54.0	
• >30	20	40.0	18	36.0	
Chi-Square test					

Table 5. Risk Factors Distribution in the Two Groups Studied

In the present study we observed that: 58% patients were smokers in cases and 38% in controls. 62% patients had sedentary life style in cases and 40% in controls 60% patients had family history of IHD in cases and 40% in controls 92% patients had abnormal BMI in cases and 90% in controls, there is a significant difference in smoking, sedentary life, Family h/o IHD in cases as compared to controls except BMI.

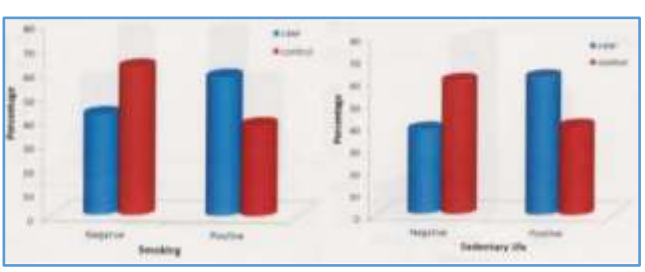


Figure 5a

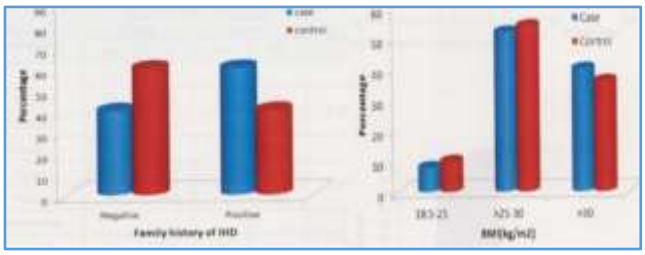


Figure 5b

Physical examinations	Cases (n=50)		Controls (n=50)		P Value
	No.	%	No.	%	
JVP					
• Negative	41	82.0	50	100.0	0.003**
• Positive	9	18.0	0	0.0	
Pedal Oedema					
• Negative	41	82.0	50	100.0	0.003**
• Positive	9	18.0	0	0.0	
Basal Crepitations					
• Negative	41	82.0	50	100.0	0.003**
• Positive	9	18.0	0	0.0	
Chi-Square test					

Table 6. Physical Examination Distribution in the Two Groups Studied

In present study we observed that, in cases 18% patients had increased JVP pedal oedema and basal crepitation.

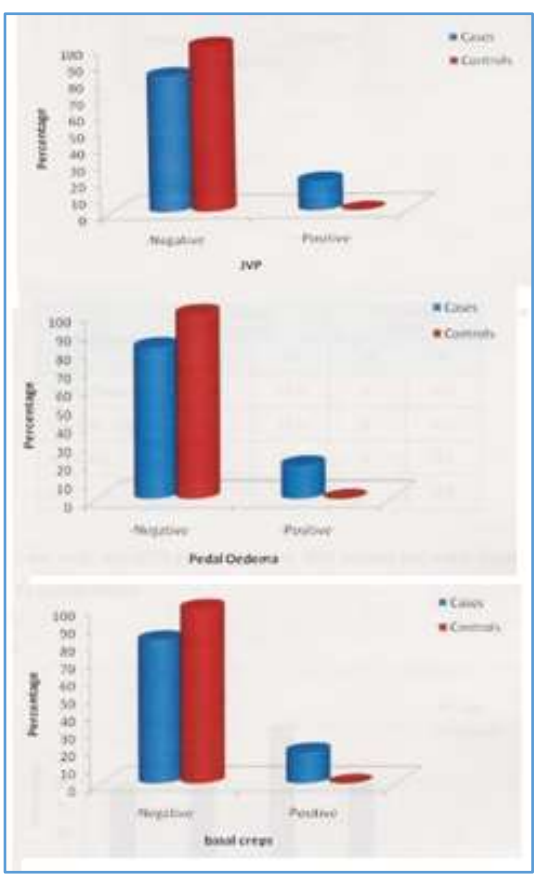


Figure 6

Diagnosis	Cases (n=50)		Controls (n=50)	
	No.	%	No.	%
Stable Angina	9	18.0	0	0.0
Unstable Angina	17	34.0	0	0.0
Acute MI	15	30.0	0	0.0
CCF	9	18.0	0	0.0

Table 7. Diagnosis Distribution in the Two Groups Studied

In our study, out of 50 patients in cases, 18% patients had stable angina, 34% patients had unstable angina, 30% patients had acute MI and 18% patient had congestive cardiac failure.

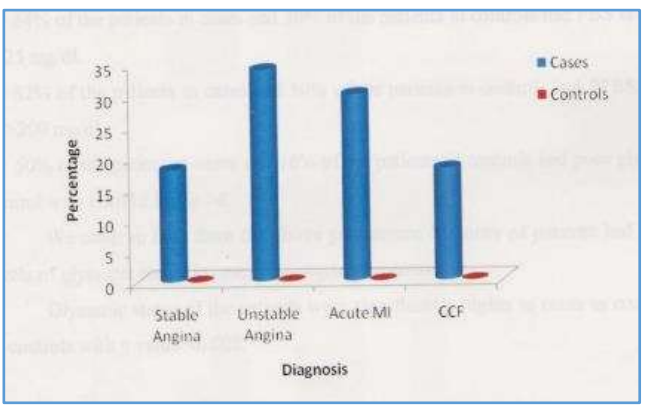


Figure 7

Investigations	Cases (n=50)		Controls (n=50)		P Value
	No.	%	No.	%	
FBS(mg/dL)					
• <125	8	16.0	32	64.0	<0.001**
• >125	42	84.0	18	36.0	
PPBS (mg/dL)					
• <200	9	18.0	25	50.0	<0.001**
• >200	41	82.0	25	50.0	
HbAlc					
• 6-7.5	10	20.0	25	50.0	<0.001**
• >7.5-8	15	30.0	17	34.0	
• >8	25	50.0	8	16.0	
Chi-Square test					

Table 8. Glycaemic Status Parameters In the Two Groups Studied

84% of the patients in cases and 36% of the patients in controls had FBS levels of >125 mg/dL. 82% of the patients in cases and 50% of the patients in controls had PPBS levels of >200 mg/dL. 50% of the patient in cases and 16% of the patients in controls had poor glycaemic control with HbA1c levels >8. We observe here from the above parameters; Majority of patients had higher levels of glycaemic status in cases as compared to controls Glycaemic status of the patients were significantly higher in cases as compared to controls with p value <0.001.

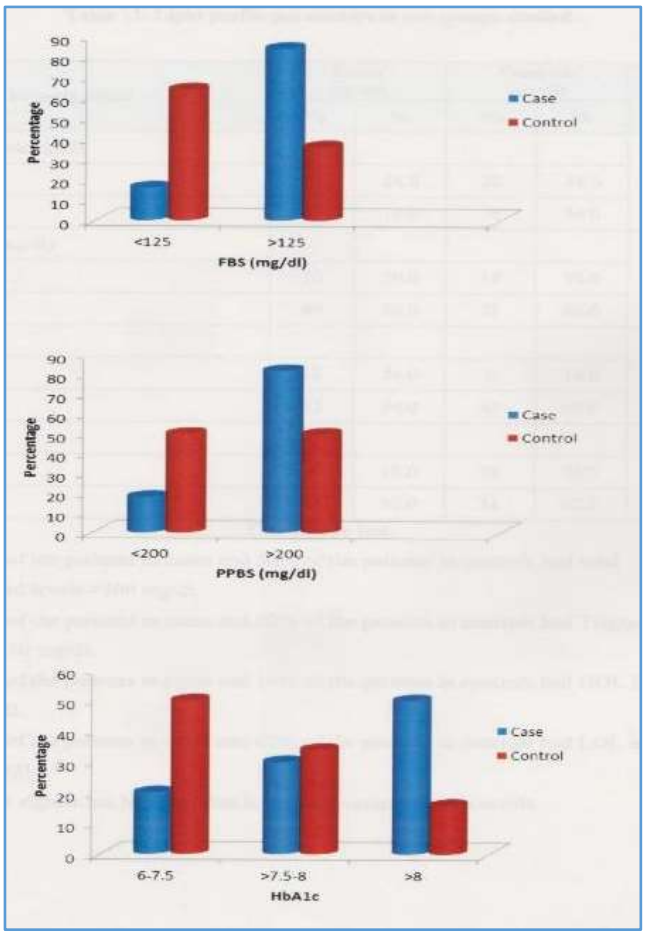


Figure 8

Investigations	Cases (n=50)		Controls (n=50)		P Value
	No.	%	No.	%	
Total Cholesterol (mg/dL)					
• <200	12	24.0	22	44.0	0.035*
• >200	38	76.0	28	56.0	
Triglycerides (mg/dL)					
• <150	10	20.0	19	38.0	0.047*
• >150	40	80.0	31	62.0	
HDL (mg/dL)					
• <40	18	36.0	7	14.0	0.011*
• >40	32	64.0	43	86.0	
LDL (mg/dL)					
• <100	9	18.0	19	38.0	0.026*
• >100	41	82.0	31	62.0	
Chi-Square test					

Table 9. Lipid Profile Parameters In the Two Groups Studied

76% of the patients in cases and 56% of the patients in controls had total cholesterol levels >200 mg/dL. 80% of the patients in cases and 62% of the patients in controls had Triglycerides levels >150 mg/dL. 36% of the patients in cases and 14% of the patients in controls had HDL levels <40 mg/dL. 82% of the patients in cases and 62% of the patients in controls had LDL levels >100 mg/dL. There is a significant hyperlipidaemia in cases compared to controls.

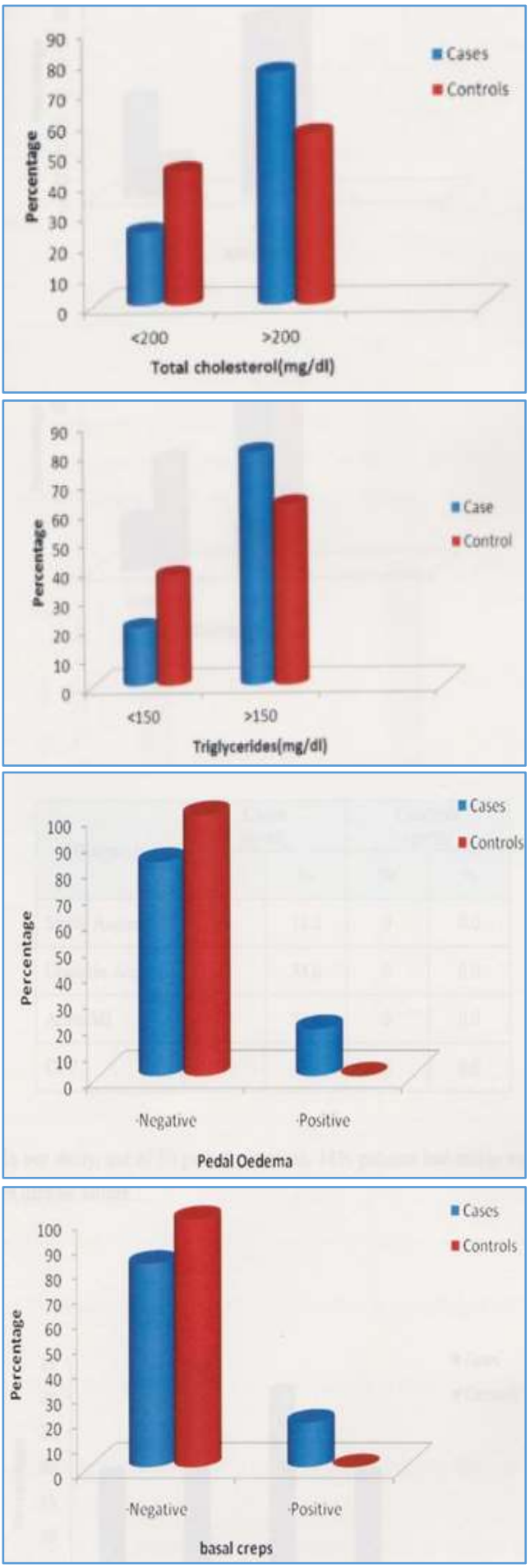


Figure 9

Investigations	Cases (n=50)		Controls (n=50)		p-Value
	No.	%	No.	%	
ECG					
• Ischemic Changes	38	76.0	0	0.0	<0.001**
• Non-Specific ST Changes	7	14.0	0	0.0	
• Within Normal Limits	5	10.0	50	100.0	
TROP 1					
• Negative	20	40.0	50	100.0	<0.001**
• Positive	30	60.0	0	0.0	
Echo					
• Normal	19	38.0	50	100.0	<0.001**
• Abnormal	31	62.0	0	0.0	
Chi-Square test					

Table 10. Cardiac Parameters in the Two Groups Studied

Among the cases, 76% patients had ischemic changes, 14% patients had non-specific ST changes and 10% had normal ECGs. 60% of the patients had positive TROP-I levels. 62% of the patients had abnormal 2D-Echo reports.

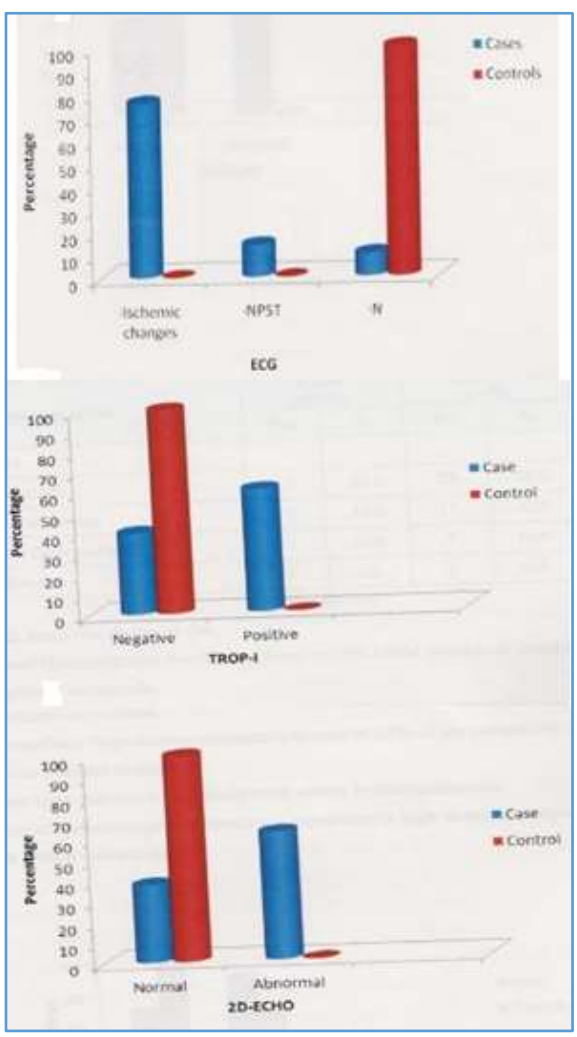


Figure 10

Investigations	Cases (n=50)		Controls (n=50)		P Value
	No.	%	No.	%	
Hcy (mic.mol/L)					
• 5-15 (Normal)	17	34.0	29	58.0	0.042*
• >15-30 (Moderate)	22	44.0	16	32.0	
• >30-100 (Intermediate)	11	22.0	5	10.0	
• >100 (Severe)	0	0.0	0	0.0	
Chi-Square test					

Table 11. Comparison of Homocysteine Levels in the Two Groups Studied

In our study we observed that, Normal Homocysteine levels were seen in 34% of the patients in cases of the patients in controls. Moderate hyperhomocysteinaemia is seen in 44% of the patients in cases and 32% of the patients in controls Intermediate hyperhomocysteinaemia is seen in 22% of the patients in cases and 10% of the patients in controls. There is no patients in our study with severe homocysteinaemia. In my study homocysteine levels are significantly high in cases compared to controls with p value 0.042

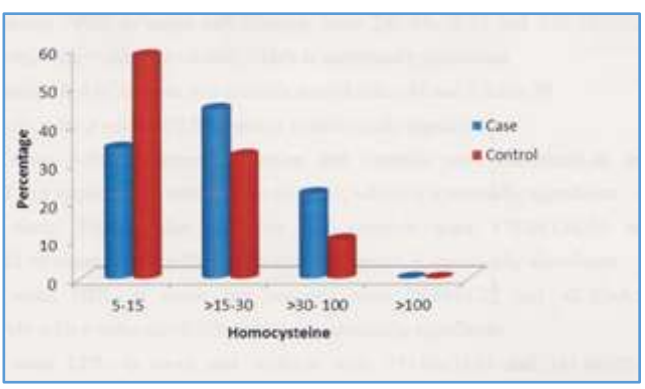


Figure 11

Variables	Cases	Controls	P value
Age in Years	61.02±5.13	54.36±6.51	<0.001**
BMI (Kg/m2)	28.71±2.70	27.88±2.54	0.117
FBS (mg/dL)	146.08±22.68	116.04±22.13	<0.001**
PPBS (mg/dL)	243.44±35.32	192.76±32.29	<0.001**
HbA1c	8.62±1.44	7.35±0.79	<0.001**
Total Cholesterol (mg/dL)	225.20±26.46	214.28±23.24	0.031*
TGL (mg/dL)	175.08±26.56	158.98±23.99	0.002**
HDL (mg/dL)	38.64±5.22	42.42±4.59	<0.001**
LDL (mg/dL)	157.04±34.03	141.64±37.89	0.035*
HCY (mic.mol/L)	24.14±9.51	15.17±7.96	<0.001**

Table 12. Comparison of Clinical/study Variables in the Two Groups Studied

In present study we observed that: The mean age in cases and controls were 61.02±5.13 and 54.36 ± 6.5 respectively with p value of <0.001, which is statistically significant. The mean BMI in cases and controls were

28.71±2.70 and 27.88±2.54 respectively, with p value of 0.117, which is statistically not significant. The mean FBS in cases and controls were 146.08±22.68 and 116.04±22.13 respectively, with p value of<0.001, which is statistically significant. The mean PPBS in cases and controls were 243.44±35.32 and 192.76±32.29 respectively, with P value of <0.001, which is statistically significant. The mean HbA1c in cases and controls were 8.62±1.44 and 7.35±0.79 respectively, with p value of 0.002, which is statistically significant. The mean Total cholesterol in cases and controls were 225.20±26.46 and 214.28±23.24 respectively, with p value of 0.031, which is statistically significant. The mean Triglycerides in cases and controls were 175.08±26.56 and 158.98±23.99 respectively, with p value of 0.002, which is statistically significant. The mean DL in cases and controls were 38.64±5.22 and 42.42±4.59 respectively with p value of<0.001, which is statistically significant. The mean LDL in cases and controls were 157.04±34.03 and 141.64±37.89 respectively, with p value of 0.035, which is statistically significant. The mean homocysteine level in cases and controls were 24.14±9.51 and 15.17±7.96 respectively, with p value of <0.001, which is statistically significant.

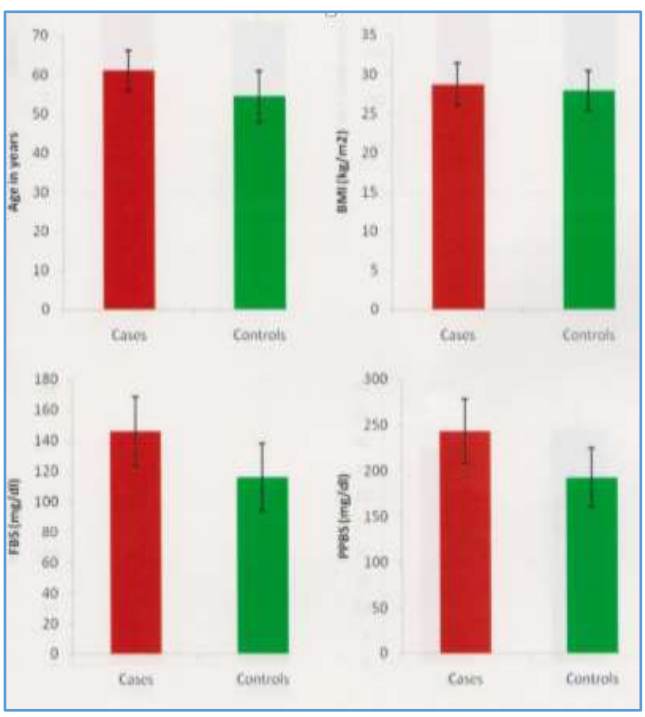
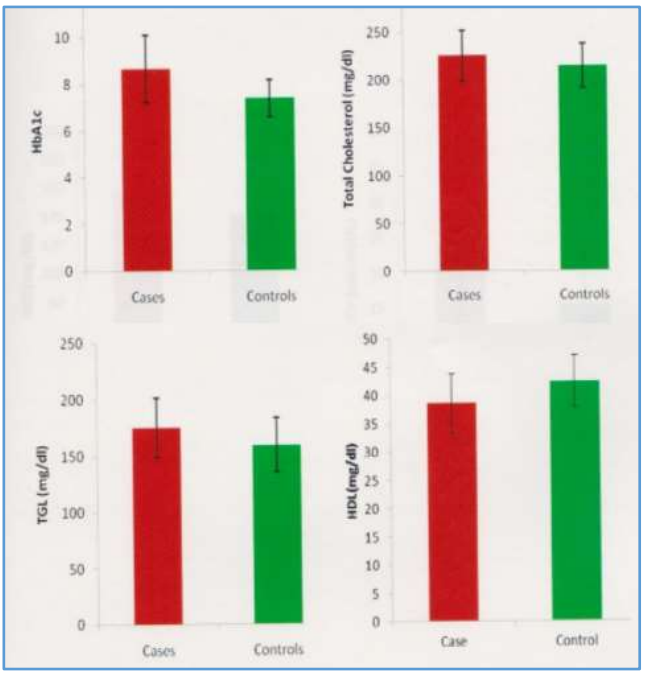


Figure 12a and 12b



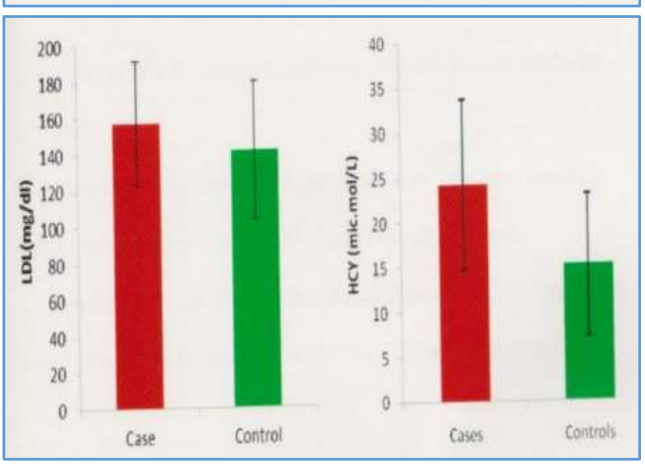


Figure 12c, 12d and 12e

DISCUSSION

Age

In our study we observed that, t mean age in cases and controls were 61.02±5.13 and 54.36±6.51 respectively. Most of the patients in my study group were 61 to 65 years. In the similar study carried out by Kangabam et al,[8] the mean age of the patients in cases and controls were 64.53±7.70 and 57.63±9.64 respectively.

In another study carried out by Ashok Kumar Behera et al,"[9] the mean age of the patients in cases and controls were 64.0±5.14 and 58.0±6.24 respectively.

Sex

In our study, we observed that, there were 62% of males and 32% of females in cases and 56% of males and 44% of females in controls. Males were predominant in our study.

In the similar study carried out by, Kangabam et al"[8], there were 77% males and 23% of females, which also showed male predominance

In another study carried out by Ho et al and Ashok Kumar Behera[9] et al who also reported the occurrence of DM more in males than in females.

BMI of study patients: In the present study, we observed that the mean BMI in cases was 28.71±2.70 and in controls was 27.88±2.54 and there is no significant difference in BMI between cases and controls with the p value 0.117

In the similar study carried out by Ashok Kumar Behera et al"[9], mean BMI in cases was 29.8±4.5 and in controls was 30.2±5.5, where there is no significant difference in BMI between cases and controls with p value >0.05. Thus, our study correlates with the above study.

Glycaemic Status Data of Study Patients

In present study, we observed that the mean fasting blood sugar in cases and controls were 146.08±22.68 and 116.04±22.13 respectively, mean post prandial sugar in cases and controls were 243.44±35.32 and 192.76±32.29 respectively and HbA1c in cases and controls were 8.62±1.44 and 7.35±0.79 respectively, with significant p value <0.001

In the similar study carried out by Kangabam et al,[8] the mean fasting blood sugar in cases and controls were 151.33±52.59 and 112.46±26.81 respectively, mean post prandial blood sugar in cases and controls were 246.37±54.64 and 195.23±37.46 respectively and mean HbAlc in cases and controls were 8.24±2.4 and 7.08±2.01 respectively, with significant p value.

In our study diabetic patients with cardiovascular complications had poor glycaemic status compared to diabetic patient without cardiovascular complications which correlates with the study done by Kangabam et al.[8]

In another study carried out by Gabbay et al[10] who also made similar observations, and observed the glycosylated haemoglobin concentrations was elevated as much as two fold in diabetes and decreased with improvement of glycaemic control.

Higher glucose concentrations and increased glycosylated haemoglobin might accelerate atherosclerotic process through several possible mechanisms such as oxidative stress and protein glycation of vessel walls

Another study done by Klein et al,[11] demonstrated the strong consistent relationship between hyperglycaemia and the incidence and progression of microvascular and macrovascular complications including cardiovascular mortality.

In another study carried out by Kuldip Singh et al[12] who reported the levels of HbA1c is proportional to the micro and macro vascular complications, in which cardiovascular complications are the leading cause of mortality and morbidity in diabetics.

Lipid Profiles of Study Patients

In our study we observed that, the mean Total cholesterol levels in Cases and controls were 225.20±26.46 and 214.28±23.24 respectively, the mean Triglycerides in cases and controls were 175.08±26.56 and 158.98±23.99 respectively, mean HDL in cases and controls were 38.64±5.22 and 42.42±4.59 respectively and mean LDL in cases and controls were 157.04±34.03 and 141.64±37.89 respectively, with significant p value <0.05.

In the similar study carried out by Kangabam et al[8] the mean Total cholesterol levels in cases and controls were 229.17±16.03 and 218.37±16.29 respectively, mean Triglycerides in cases and controls were 170.53±17.36 and 153.86±20.13 respectively, mean HDL in cases and controls were 34.62±6.42 and 35.09±7.28 respectively, mean LDL in cases and controls were 160.26±18.81 and 152.34±17.28 respectively, with significant p value <0.05.

The pattern of lipid abnormalities observed in a Multidisciplinary Study carried out by Khursheed Muhammad et al[13] was, high triglyceride in 31% patients, high LDL in 19%, low HDL in 11%, high cholesterol in 14% and combined hyperlipidaemia in 25% diabetic patients and he concluded hyperlipidaemia is the commonest complication of diabetes mellitus and it predisposes them to premature atherosclerosis, micro and macro vascular complications.

In another study carried out by Wexler et al[14] he observed; LDL, HDL, TC and TG were significantly higher in type 2 diabetics.

High prevalence of hypercholesterolemia, hypertriglyceridemia and high LDL and low HDL was found in type 2 diabetics in this study which are well known risk factors for cardiovascular diseases.

In another study carried out by Shivanand, et al[15] noted the increase in total and low-density lipoprotein cholesterol and decreases in high density lipoprotein cholesterol are more prevalent in diabetics with coronary artery disease than those without coronary artery diseases

In our study, Diabetic patients with cardiovascular complications had higher hyperlipidaemia compared to diabetic patients without cardiovascular complications and our study correlates with the above studies

Serum Homocysteine Levels

In our study, we observed that the mean Homocysteine levels in cases and controls were 24.14±9.51 and 15.17±7.96 respectively, with significant p value <0.001.

In the similar study carried out by Kangabam et al[8] the mean Homocysteine levels in cases and controls were 27.20±6.02 and 18.03±4.61 respectively, observed that the Hcys levels were significantly elevated in patients with diabetes and cardiovascular complications compared to the patients with only diabetes with the significant p value < 0.001.

Another similar study carried out by Ashok Kumar Behera et al,[9] the mean homocysteine levels in cases and controls were 19.4±7.5 and 12.75±4.2 respectively, which also shows significant difference with p value <0.01.

Another study carried out by Jayakrishnan et al[16] reported that homocysteine elevates the diabetic complications and progression of cardiovascular diseases.

The cohort study carried out by Soinio et al[17] also concluded that, in patients with type 2 diabetes mellitus the plasma homocysteine level was a strong and Independent risk factor for coronary heart disease events.

Hence our study correlates with the above studies, indicating that hyperhomocysteinaemia is an independent risk factor for cardiovascular incidence in type 2 diabetes mellitus.

Homocysteine and Atherothrombogenic Effects

Several studies suggest that elevated plasma Hcy level has both atherogenic and thrombogenic effects. Hyperhomocysteinaemia causes endothelial dysfunction by increasing oxidant stress and decreases the release of nitric oxide, impairing vasodilation.

Excess of Hcys stimulates smooth muscle cell proliferation and collagen synthesis promoting intima media thickening.

Hyperhomocysteinaemia is also considered to have thrombogenic activity by increasing platelet aggregation and causing abnormalities in the coagulation system.

High plasma Hcy level is also shown to be associated with increased lipid peroxidation.[18,19]

An alternative route of Hcy metabolism in hyperhomocysteinaemia is the formation of Hcy-thiolactone, which then reacts with LDL to form LDL-Hcy-thiolactone aggregates. These are taken up by macrophages and are subsequently incorporated into foam cells in early atherosclerotic plaques. Within these plaques, Hcy-thiolactone acylates proteins and modifies oxidative processes of the vessels, thereby promoting atherothrombosis.[16,20]

In our study, the association between elevated plasma Hcy level and increased rate of cardiovascular complications in diabetes patients were statistically significant as compared to those diabetes patients without cardiovascular complications.

Thus, our study shows strong association of hyperhomocysteinaemia in patients of type 2 diabetes with cardiovascular complications.

CONCLUSION

Homocysteine levels were comparatively more elevated in patients of diabetes with cardiovascular complications than the patients of diabetes alone, thus indicating that hyperhomocysteinaemia is an independent risk factor for CVD incidence in type 2 diabetic patients in middle aged individuals.

The results of this study confirm the hypothesis that hyperhomocysteinaemia a risk factor for endothelial dysfunction and vascular diseases such as atherosclerosis and occlusive vascular disorders.

There is very limited number of studies of hyperhomocysteinaemia cardiovascular risk factor in type 2 diabetes mellitus.

However, further studies are required to determine whether genetic, nutritional deficiencies, or diseases related metabolism account for hyperhomocysteinaemia observed in patients of type 2 DM with and without cardiovascular complications. Effective assessment of the role of lipid fractions and glycaemic control in coronary heart disease will be more useful if the sample size is large.

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