

A STUDY OF 100 PATIENTS OF TYPE 2 DIABETES MELLITUS IN RELATION WITH CAROTID ARTERY INTIMA MEDIA THICKNESS AND DYSLIPIDAEMIA

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ABSTRACT

BACKGROUND

The Framingham study pointed out that diabetic individuals have dyslipidaemia and hypertension, obesity are more prone to metabolic syndrome and its sequelae namely coronary artery disease (CAD), cerebrovascular disease and vascular atherosclerosis.¹ Carotid intima media thickness (CIMT) is a relatively simple, non-invasive measurement that uses ultrasound to detect the presence of an extent of atherosclerosis. Normal CIMT is 0.9 mm.

Aims and Objectives:

1. To evaluate the carotid intima media thickness in 100 patients of type 2 diabetes mellitus with its duration, hypertension, age and sex distribution and also lipid profile abnormalities.
2. To study the correlation of carotid intima media thickness with dyslipidaemia.

MATERIALS AND METHODS

100 patients of type 2 diabetes mellitus getting admitted into medical wards of Anil Neerukonda Hospital of NRI Institute of Medical Sciences, Sangivalasa, Visakhapatnam District of Andhra Pradesh. The patients were divided into two groups based on CIMT thickness, group 1 with CIMT < 0.9 and group 2 with CIMT ≥ 0.9. The purpose of the study was to study the carotid intima media thickness in patients with type 2 diabetes mellitus and to correlate with lipid profile.

RESULTS

An observation was made in this study that of the 47 patients who had atherosclerosis risk factors like diabetes mellitus, majority (74.4%) had intima media thickness greater than 0.9 mm. At the same time, of the 53 patients who had only risk factors for atherosclerosis but no events, majority (60.3%) had IMT less than or equal to 0.9 mm.

CONCLUSION

The present study revealed that the CIMT in diabetic patients with atherosclerotic events was significantly higher as compared to carotid artery IMT in diabetic patients who had only risk factors for atherosclerosis, but no events with a P value < 0.01.

KEYWORDS

CIMT, Carotid Intima Media Thickness, Dyslipidaemia, IMT, Intima Media Thickness.

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BACKGROUND

Atherosclerosis, which is the major risk factor is accelerated in diabetes mellitus. The Framingham study¹ pointed out that diabetic individuals have dyslipidaemia and hypertension, obesity are more prone to metabolic syndrome and its sequelae namely coronary artery disease

(CAD), cerebrovascular disease and vascular atherosclerosis.¹

B mode ultrasonography of peripheral vessels such as carotid artery for intima media thickness was emerged during 1980s as an alternative to angiography to quantify atherosclerotic lesions and their progression.^{2,3}

There are few Indian studies where carotid intima media thickness (CIMT) has been measured in type 2 diabetics. Therefore, the present study was planned to generate more data on this subject with the aim of measuring the CIMT in type 2 diabetics and with lipid abnormalities, as these patients are more prone to develop macrovascular complications like coronary artery disease.

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Aims and Objectives

1. To evaluate the carotid intima media thickness in 100 patients of type 2 diabetes mellitus with its duration, hypertension, age and sex distribution and also lipid profile abnormalities.
2. To study the correlation of carotid intima media thickness with lipid abnormalities.

MATERIALS AND METHODS

Type of Study- Prospective study.

Source of Data- 100 patients of type 2 diabetes mellitus getting admitted into medical wards of Anil Neerukonda Hospital of NRI Institute of Medical Sciences, Sangivalasa, Visakhapatnam District of Andhra Pradesh.

For this study, permission was given by the Ethics Committee of the NRI Institute of Medical Sciences.

Study Period- 1st October 2016 to 30th September 2017.

Selection of Patients- Diabetic patients were divided into two groups based on CIMT values.

Group 1- This group includes Type 2 diabetics with CIMT <0.9 mm.

Group 2- This group includes Type 2 diabetics with CIMT ≥0.9 mm.

Sampling Criteria

Inclusion Criteria- Patients with Type 2 diabetes mellitus admitted in medical wards of NRI Institute of Medical Sciences.

Exclusion Criteria- Patients with Type 1 diabetes mellitus and gestational diabetes mellitus were excluded from the study.

Data Collection

- All enrolled patients were informed about nature of the study and their rights to refuse. The informed written consent was taken before including them in the study.
- A detailed history was obtained in all cases through all available sources.
- All the patients were subjected to detailed clinical examination including anthropometric measurements and systemic examination.

- Biochemical parameters and other investigations recorded during study period.
 - Fasting, 2-hour postprandial blood sugars, HbA1c,
 - Fasting lipid profile,
 - Blood urea, serum creatinine,
 - Electrocardiograph,
 - B-Mode, two-dimensional ultrasound with frequency ranges between 5 to 15 MHz is used for carotid intima media thickness (CIMT).

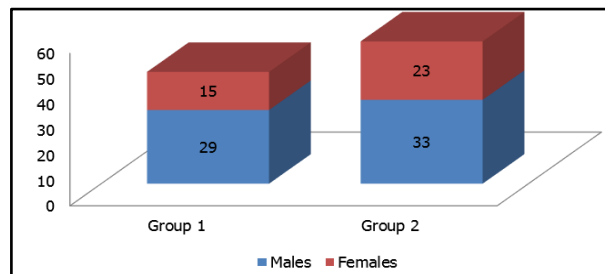
All the data were tabulated and the results were statistically analysed by using [http://graphpad.com/quickcalcs/ttest1/? Format=C](http://graphpad.com/quickcalcs/ttest1/?Format=C). Data were presented as mean ± SD values were called significant if p < 0.05. The correlation coefficient test and student t-test was used in most cases to compare frequency distribution.

OBSERVATIONS AND RESULTS

Sex	Group 1 (n= %)	Group 2 (n= %)	Total
Males	29	33	62
Females	15	23	38
Total	44	56	100

Table 1. Age and Sex Distribution

In the present study majority (62%) of cases were males, females constitute 38% of cases. Out of the 44% of group 1, majority (29%) were males and remaining 15% were females. Out of the 56% of group 2, majority (33%) were males and females were 23%.



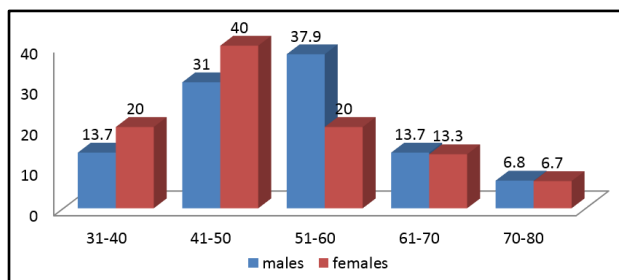
Graph 1. Comparing Males and Females in both Groups

Age (Years)	Males (n)	Percentage	Females	Percentage	Total	Percentage
31-40	4	13.7	3	20	7	15.9
41-50	8	31.0	6	40	14	31.8
51-60	11	37.9	3	20	14	31.8
61-70	4	13.7	2	13.3	6	13.6
71-80	2	6.8	1	6.7	3	6.8
Total	29	100	15	100	44	100
CIMT Mean ± S.D	0.75 ± 0.08		0.74 ± 0.07		0.75 ± 0.07	

Table 2. Age and Sex Distribution of Group 1

In group 1 there are totally 44 cases, of which males constitute 29 and females constitute 15 cases. Majority of the cases were in the 5th and 6th decade. Mean age in the

group 1 is 51.95 ± 11.38 years. The mean CIMT in males is 0.75 ± 0.08 mm and females is 0.74 ± 0.07 mm. The mean CIMT of this group is 0.75 ± 0.07 mm.

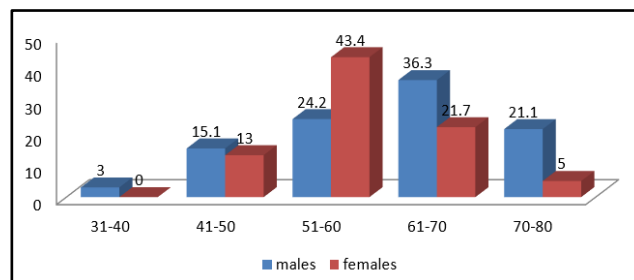


Graph 2. Comparing Male and Female in Group 1 with Respect to Age

Age (Years)	Males (n)	Percentage	Females	Percentage	Total	Percentage
31-40	1	3	0	0	1	1.7
41-50	5	15.1	3	13	8	14.2
51-60	8	24.2	10	43.4	18	32.1
61-70	12	36.3	5	21.7	17	30.3
71-80	7	21.1	5	21.7	12	21.4
Total	33	100	23	100	56	100
CIMT Mean ± SD	1.37 ± 0.21		1.13 ± 0.2		1.27±0.23	

Table 3. Age and Sex Distribution of Group 2

In group 2 there are totally 56 cases, of which males constitute 33 and females constitute 23 cases. Majority of cases were in the 6th and 7th decade. Mean age in this group is 59.64 ± 10.14 years. The mean CIMT in males is 1.37 ± 0.21 mm and females is 1.13 ± 0.2 mm. The mean CIMT of this group is 1.27 ± 0.23 mm.



Graph 3. Comparing Male and Female in Group 2 with Respect to Age

Duration (Years)	Group 1			Group 2		
	Numbers	Percentage	CIMT	Numbers	Percentage	CIMT
0-5	18	40.9	0.73 ± 0.07	10	17.8	1.14 ± 0.19
6-10	16	36.4	0.76 ± 0.08	26	46.4	1.29 ± 0.23
11-15	8	18.2	0.82 ± 0.02	14	25	1.38 ± 0.22
≥16	2	4.5	0.86 ± 0.02	6	10.7	1.57 ± 0.14

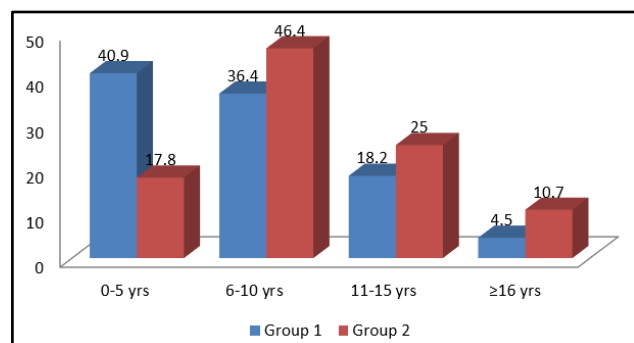
Table 4. Comparison of Duration of Diabetes with CIMT

In the present study, 18 out of 44 cases (40.9%) in group 1 had duration of diabetes less than 5 years; 26 cases (59.1%) had duration of diabetes more than 5 years.

In group 2, 10 cases out of 56 (17.86) had duration of diabetes less than 5 years, whereas 46 cases out of 56 (82.14%) had duration of diabetes more than 5 years.

As the duration of diabetes mellitus increases the mean CIMT also increases, which is very much evident from the data.

The mean duration of diabetes in group 1 and group 2 is 7.07 ± 4.9 years and 9.21 ± 4.98 years respectively, which is statistically significant (p < 0.03).

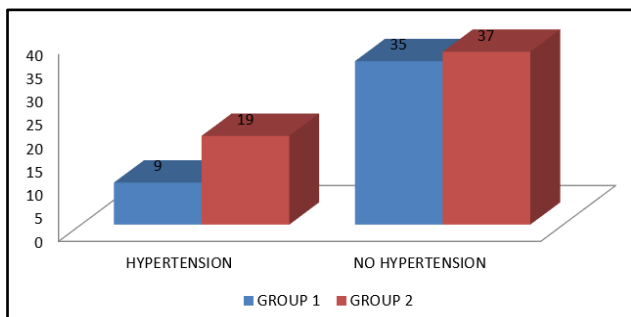


Graph 4. Comparison of Duration of Diabetes with CIMT

Hypertension	Group 1			Group 2			Total
	Numbers	Percentage	CIMT Mean ± SD	Numbers	Percentage	CIMT Mean ± SD	
HTN	9	20.5	0.83 ± 0.07	19	34.0	1.35 ± 0.12	28
Non-HTN	35	79.5	0.73 ± 0.08	37	66.0	1.23 ± 0.24	72

Table 5. Distribution of Hypertension Patients among both Groups and in Comparison with CIMT

In the study, majority (79.55%) of group 1 patients had no history of hypertension. In the group 2 patients, 66.07% had no history of hypertension. The mean CIMT in the group 1 is 0.83 ± 0.07 mm and 0.73 ± 0.08 mm in the hypertensive and non-hypertensive respectively, which is statistically significant ($p < 0.05$). The mean CIMT between the HTN and non-HTN groups in group 2 is 1.35 ± 0.12 and 1.23 ± 0.24 , which is statistically significant ($p < 0.05$).

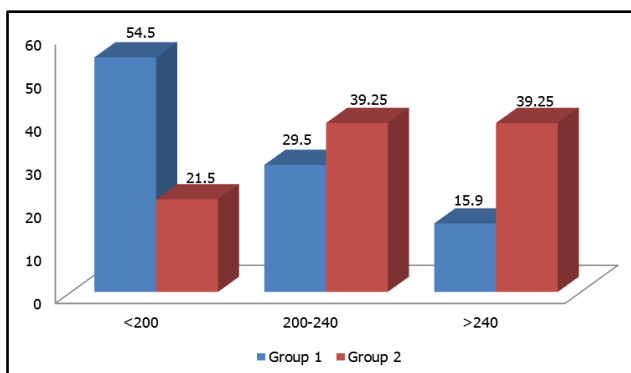


Graph 5. Distribution of Hypertension Patients among both Groups

Total Cholesterol mg/dL	Group 1		Group 2	
< 200	24	54.5%	12	21.4%
200-240	13	29.5%	22	39.3%
> 240	7	15.9%	22	39.3%
Total	44	100%	56	100%

Table 6. Comparison of Total Cholesterol in both Groups

In the study, majority of the patients (54.5%) in group 1 had total cholesterol less than 200 mg/dL, whereas in group 2 majority (78.6%) had total cholesterol above 200 mg/dL. In the present study, mean total cholesterol in group 1 and group 2 were found to be 195.33 ± 44.87 and 222 ± 40.57 respectively ($t= 3.20$, $p= 0.0018$ highly significant). Also in the group 1, comparison of total cholesterol with CIMT showed statistically positive correlation (correlation coefficient $r= 0.606$, $p < 0.01$). In group 2 also significant positive correlation was found between total cholesterol and CIMT (correlation coefficient $r= 0.676$, $p < 0.01$).



Graph 6. Comparison of Total Cholesterol in both Groups

LDL-C mg/dL	Group 1		Group 2	
100	15	34%	9	16%
101-130	13	29.5%	9	16%
131-159	10	22.7%	23	41%
160-189	4	9.5%	15	26.7%
>190	2	4%	0	0
Total	44	100	56	100

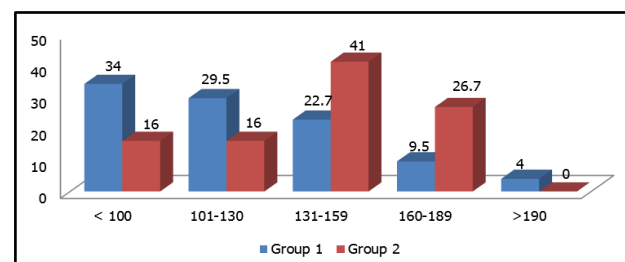
Table 7. Comparison of LDL Cholesterol in both Groups

In the study majority of the patients (63.5%) in group 1 had LDL cholesterol less than 130 mg/dL, whereas in group 2 majority (67.7%) had LDL greater than 130 mg/dL.

Mean LDL in group 1 and 2 were 118.6 ± 33.83 and 138.5 ± 30.94 respectively, which is statistically significant ($p= 0.0028$).

TG mg/dL	Group 1		Group 2	
< 150	31	70.4%	28	50%
151-199	7	15.9%	15	26.7%
200-499	6	13.6%	12	21.4%
> 500	0	0	1	1.7%
Total	44	100	56	100

Table 8. Comparison of Triglycerides in both Groups

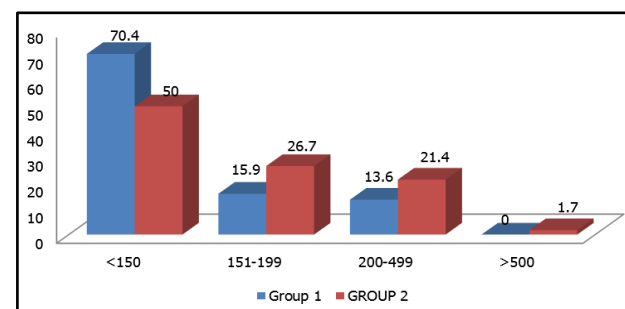


Graph 7. Comparison of LDL Cholesterol in both Groups

In the present study 70.4% of the patients in group 1 had triglycerides less than 150 mg/dL and 29.5% of them had above 150 mg/dL.

In group 2, 50% of the patients had triglycerides above 150 mg/dL and 50% of them below that level.

A very high triglyceride level above 500 mg/dL was found in one patient of group 2 in the entire study population. The mean triglyceride value in group 1 was 149.4 ± 66.82 and in group 2 it was 184.6 ± 98.48 , which is statistically significant ($p= 0.0452$).



Graph 8. Comparison of Triglycerides in both Groups

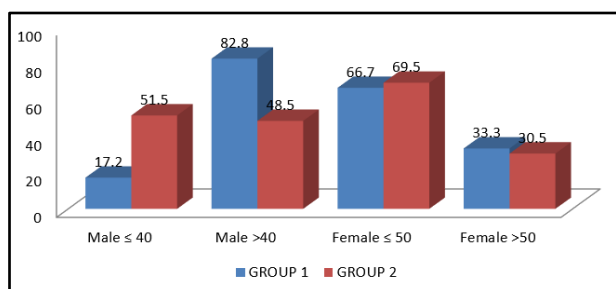
HDL-C in mg/dL		Group 1		Group 2	
Male	< 40	5	17.2%	17	51.5%
	> 40	24	85.8%	16	48.5%
Female	< 50	10	66.7%	16	69.5%
	> 50	5	33.3%	7	30.5%
Total		44		56	

Table 9. Comparison of HDL Cholesterol in both Groups

HDL-Cholesterol of > 40 was observed in 85.8% and 48.5% of male patients in group 1 and group 2 respectively.

In the present study, 66.7% and 69.5% female patients in group 1 and group 2 respectively had HDL cholesterol level less than 50 mg/dL.

The mean HDL cholesterol in group 1 and group 2 were 47.9 ± 7.75 and 41.59 ± 8.69 respectively, which was statistically significant ($p = 0.0003$).



Graph 9. Comparison of HDL Cholesterol in both Groups

DISCUSSION

The patients were divided into two groups based on CIMT thickness, group 1 with CIMT < 0.9 mm and group 2 with CIMT ≥ 0.9 mm. The purpose of the study was to study the carotid intima media thickness in patients with type 2 diabetes mellitus and in relation with lipid abnormalities.

Distribution of Age and Sex and its Correlation with CIMT-

In the present study, total number of cases in group 1 were 44 out of which 29 were males, 15 were females; whereas in group 2 out of 56 cases 33 were males and 23 were females. Majority of cases in group 1 were in 5th and 6th decade, whereas in group 2 majority of cases were in 6th and 7th decade. Overall, mean age of patients was 56.26 ± 11.32 and in group 1 and group 2 was 51.95 ± 11.38 years and 59.64 ± 10.14 years respectively. On comparison of age in group 1 and group 2, t-value is 3.56 and $p = 0.0006$ (significant). Mean age of the patients in the present study was comparable with R Gayathri et al,⁴ in which mean age was 55.79 years. Mean age in group 2 is comparable to study conducted by A K Agarwal et al⁵ (2008), in which mean age was 59.78 ± 8.81 . Mean age in group 2 is comparable with studies conducted by Davidson et al,⁶ which was 58.9 ± 7.8 . In the present study, as the age increased a gradual increase in mean CIMT was noted in both groups.

Comparing age and CIMT, the present study revealed correlation coefficient "r" = 0.94, $p < 0.05$ (significant) in group 1 and correlation coefficient "t" = 0.94, $p < 0.05$ (significant) in group 2. Therefore, as age increases CIMT

increases, which has positive correlation and was statistically significant. In Cardiovascular Health Study, Daniel H O'Leary et al (1992)⁷ studied 5201 patients and concluded that prevalence and severity of carotid atherosclerosis continued to increase with age even in late decades of life. Sang Su Chang et al observed 535 Korean type 2 diabetic patients and found that mean CIMT was positively correlating with age. Robin et al⁸ reported that IMT was independently and positively related to age. The present study is very much comparable to the above studies.

Out of 100 diabetic cases, 62% were males and 38% were females. The bias in sex was in concordance with the admission statistics of hospital. On comparing males and females higher values of CIMT was found in males than in females in both groups, possibly due to protective effect of female hormones and/or male gender being at a higher risk of atherosclerosis. Similar results have been reported by Kraml et al,⁹ who also observed significant higher IMT in men than women and a study conducted by Sunil Kumar Kota et al¹⁰ concluded that males are more prone for high CIMT.

	Mean Age (Years)
Present study	56.26 ± 11.32
R Gayathri et al ⁴	55.79
AK Agarwal et al ⁵	59.78 ± 8.81
Davidson et al ⁶	58.9 ± 7.8

Table 10. Comparison of Mean Age with other Studies

Relation of Diabetes Mellitus and its duration with CIMT-

Diabetes mellitus and its duration play a significant role in carotid atherosclerosis. The mean duration of diabetes in both group 1 and group 2 is 7.07 ± 4.9 and 9.21 ± 4.98 respectively, which is statistically significant ($p < 0.03$). A positive correlation that is statistically significant in both groups (correlation coefficient 'r' = 0.823, $p < 0.01$ (significant) when duration of diabetes mellitus is compared with progression of CIMT.

Bonoro et al¹¹ have studied carotid intima media thickness (CIMT) in a total of 114 patients and concluded that diabetes is characterised by a greater thickness of carotid artery independent of other established risk factors of atherosclerosis. AK Agarwal et al⁵ (2008) observed duration of diabetes as a predictor of CIMT, which was statistically proved in his study ($p < 0.002$). In the Chennai Urban Population Study (CUPS) done by V Mohan et al¹² in 2000 proved that diabetic subjects have higher intima media thickness values. Butt MU et al¹³ showed a significant association of duration of diabetes and CIMT ($p < 0.05$). The present study is very much comparable to above studies.

Relation of Total Cholesterol with CIMT-

In the present study, mean total cholesterol in group 1 and group 2 were found to be 195.33 ± 44.87 mg/dL and 222 ± 40.57 mg/dL respectively ($t = 3.20$, $p = 0.0018$ highly significant). Also in the group 1, comparison of total cholesterol with CIMT showed statistically positive correlation (correlation coefficient 'r' = 0.606, $p < 0.01$). In group 2 also significant

positive correlation is found between total cholesterol and CIMT (correlation coefficient $r = 0.676$, $p < 0.01$). The study conducted by R Gayathri et al⁴ reported the mean total cholesterol in group 1 and group 2 were 175.5 ± 34.8 and 188.9 ± 39.7 respectively. The study conducted by Shinichi Teno et al¹⁴ correlated lipid profile in type 2 diabetic patients with CIMT and concluded that total cholesterol was significantly associated with CIMT. Yamasaki Yoshimitsu et al¹⁵ concluded that total cholesterol was significantly related to progress of CIMT. In Muscatine study, there was a significant association of total cholesterol and CIMT. Magyar MT suggested increase in total cholesterol has an important role in early onset of IMT changes. Therefore, the present study is comparable to above studies.

	Group 1 Mean T-Cholesterol	Group 2 Mean T-Cholesterol
Present study	195.33 ± 44.87	222 ± 40.57
R Gayathri et al ⁴	175.5 ± 34.8	188.9 ± 39.7

Table 11. Comparison of Mean Total Cholesterol with other Studies

Relation of LDL Cholesterol with CIMT- In the present study mean LDL in group 1 and 2 were 118.6 ± 33.83 and 138.5 ± 30.94 respectively, which were statistically significant ($p = 0.0028$). Anath Oren et al¹⁶ in the ARYA study demonstrated that LDL-C was positively associated with significant increase in CIMT. Similar association between LDL-C and CIMT was seen in The Cardiovascular Risk in Young Finns' study done by OT Raitakari et al.¹⁷ The study conducted by R Gayathri et al⁴ reported the mean LDL-Cholesterol of group 1 and group 1 patients were 112.4 ± 28.1 and 121.1 ± 34.6 respectively. N Bhalla et al¹⁸ showed significant association between LDL-Cholesterol and CIMT ($p < 0.01$). In the Muscatine study, there is a significant correlation with the LDL-Cholesterol. UM Jadhav¹⁹ showed LDL-Cholesterol had significant association with increase in CIMT. J Ahmad²⁰ reported CIMT is significantly associated with LDL-Cholesterol. The present study showed significant positive correlation ($p < 0.01$) between LDL-C and CIMT is very much comparable to above studies.

	Group 1 Mean LDL-Cholesterol	Group 2 Mean LDL-Cholesterol
Present study	118.6 ± 33.83	138.5 ± 30.94
R Gayathri et al ⁴	112.4 ± 28.1	121.1 ± 34.6

Table 12. Comparison of Mean LDL-Cholesterol with other Studies

Relation of Triglycerides and CIMT- In the present study 70.4% of the patients in group 1 and 50% of patients in group 2 had triglycerides less than 150 mg/dL, 29.5% of patients in group 1 and 50% of patients in group 2 had triglycerides above 150 mg/dL. The correlation coefficient $r = 0.838$, which was statistically significant ($p < 0.01$). In the present study the mean triglyceride value in group 1 was 149.4 ± 66.82 and in group 2 was 184.6 ± 98.48 , which was statistically significant ($p = 0.0452$). The mean triglycerides

in a study conducted by R Gayathri et al⁴ in group 1 and group 2 were 112.5 ± 27.7 and 132.9 ± 53.5 respectively. Shinichi Teno et al¹⁴ showed a positive correlation between triglycerides and CIMT ($p < 0.05$). AK Agarwal et al (2008)¹¹ showed that triglycerides are strong predictors of increase in CIMT. In the Muscatine study,²¹ there is a significant association between triglycerides and CIMT. Therefore, the present study is comparable to above study group. A positive correlation is found between triglycerides and progression of CIMT.

	Group 1 Mean Triglycerides	Group 2 Mean Triglycerides
Present study	149.4 ± 66.82	184.6 ± 98.48
R Gayathri et al ⁴	112.5 ± 27.7	132.9 ± 53.5

Table 13. Comparison of Mean Triglycerides with other Studies

Relation of HDL Cholesterol with CIMT- In the present study, 85.8% of the male patients in group 1 had HDL cholesterol more than 40 mg/dL. In group 2, 51.5% of the male patients had HDL cholesterol less than 40 mg/dL; 66.7% and 69.5% female patients in group 1 and group 2 respectively had HDL cholesterol level less than 50 mg/dL. The mean HDL cholesterol in group 1 and group 2 were 47.9 ± 7.75 and 41.59 ± 8.69 respectively, which was statistically significant ($p = 0.0003$). In group 2, progression of CIMT had negative correlation with HDL-C (correlation coefficient $r = -0.689$, $p < 0.01$), which was statistically significant. The study conducted by R Gayathri et al⁴ reported the mean HDL-Cholesterol in group 1 and group 2 were 41.3 ± 8.6 and 40.7 ± 8.2 respectively. Butt MU et al¹³ showed a statistical significant inverse relation with HDL-Cholesterol and CIMT ($P < 0.05$). Therefore, the present study is comparable to previous studies.

	Group 1 Mean HDL-Cholesterol	Group 2 Mean HDL-Cholesterol
Present study	47.9 ± 7.75	41.59 ± 8.69
R Gayathri et al ⁴	41.3 ± 8.6	40.7 ± 8.2

Table 14. Comparison of Mean HDL-Cholesterol with other Studies

The present study revealed that the CIMT in diabetic patients with atherosclerotic events was significantly higher as compared to carotid artery IMT in diabetic patients who had only risk factors for atherosclerosis, but no events with a P value < 0.01 .

An observation was made in this study that of the 47 patients who had atherosclerotic events, majority (74.4%) had intima media thickness greater than 0.9 mm. At the same time of the 53 patients who had only risk factors for atherosclerosis but no events, majority (60.3%) had IMT less than or equal to 0.9 mm.

Summary- To summarise the observations in the present study- The present study shows that Carotid Intima Media Thickness (CIMT) increases with age, which is a non-modifiable risk factor for atherosclerosis and the correlation was statistically significant.

Higher values of CIMT are found predominantly in male patients than female patients.

The present study emphasised that as duration of diabetes increases, there is progression of CIMT which is statistically significant.

- Hypertension, an established risk factor for atherosclerosis is found to have a positive correlation with progression of CIMT, which is statistically significant in the present study.
- The present study had demonstrated the role of traditional risk factors like total cholesterol, LDL-cholesterol and triglycerides in the progression of atherosclerosis as statistically highly significant between both the groups. There was also positive correlation between these risk factors with progression of CIMT in both the groups. But HDL-Cholesterol had a negative correlation with CIMT, which had statistical significance in both the groups.
- The present study revealed that the CIMT in diabetic patients with atherosclerotic events was significantly higher as compared to carotid artery intima media thickness in diabetic patients, who had only risk factors for atherosclerosis but no events.

CONCLUSION

There has been a steady rise in the prevalence of atherosclerotic events among diabetics and the problem is more marked in those with Type 2 Diabetes Mellitus. Assessment of carotid artery intima media thickness by B-mode ultrasound is a relatively inexpensive means of measuring subclinical atherosclerosis. The present study had demonstrated the significant role of total cholesterol, LDL-Cholesterol, HDL-Cholesterol and triglycerides in the progression of atherosclerosis and showed that carotid artery intima media thickness is significantly higher in those type 2 diabetic patients who had atherosclerotic events than in those type 2 diabetic patients who had only risk factors for atherosclerosis but no events.

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