Int J Biol Med Res. 2013; 4(2) : 3078- 3083

BioMedSciDirect Publications

Contents lists available at BioMedSciDirect Publications

International Journal of Biological & Medical Research

Journal homepage: www.biomedscidirect.com

Original Article

A study of Carotid Intima Medial thickness among Diabetic and non Diabetic patients and its association with the Vascular Complications – a Comparative Study.

ArunKumar.R[a], Lokesh.S[b]

ARTICLE INFO

Keywords:
HbA1C
SBP
DBP
TC
TG
HDL-C
LDL-C
CIMT

ABSTRACT

Introduction: the incidence and prevalence of diabetes mellitus is on a rise as a result of changing environmental and social factors, increased risk of metabolic syndrome and increased longevity. Survival of the diabetic patients has increased due to the advent of newer and effective drugs for managing diabetes mellitus. Diabetic patients are often seen suffering from micro and macro vascular complication which has become a major factor increasing mortality and morbidity. There is a need to have a sensitive and cost effective investigation which is capable of identifying the vascular complications at a much earlier stage. Carotid Intima Medial thickness is one such accessible structure which can be studied to risk stratify the patient with diabetes mellitus and an early effective therapy can be introduced to prevent further progression of the vascular insult. Material and methods: study was carried out by the Department of General Medicine, Sri LakshmiNarayana Institute of Medical Sciences, Puducherry. Patients attending medicine OPD were divided in to Diabetic group and Non Diabetic group after considering exclusion criteria. Both the groups were subjected to relevant biochemical and radiological investigations. Results were analysed with appropriate statistical methods. Results: hypertension was the common comorbid illness found in diabetic group. Diabetic group had significantly higher SBP, DBP, HbA1C, TC, TG, LDL-C and low HDL-C. The CIMT and the vascular complications was significantly higher in diabetic group. Conclusion: CIMT was positively associated with greater overall risk of vascular events in diabetic group .Vascular events of all forms were significantly seen in those patients with increased CIMT. Hence the detection of abnormal CIMT predicts the risk of vascular complications in diabetic patients.

1. Introduction

Diabetes mellitus comprises a group of metabolic disorders that share the phenotype of hyperglycemia. It is worldwide in distribution and the incidence of both Type 1 and type 2 Diabetes Mellitus is rising dramatically. It is estimated to have 150 million cases worldwide. It is expected that the number of adults with diabetes mellitus will rise to 300 million by the year 20251. India has nearly 44 million diabetic subjects today and is chiefly contributed by urban population2.

Diabetes is frequently associated with the development of premature atherosclerotic vascular disease. Macrovascular complications like coronary artery disease, cerebrovascular disease and peripheral vascular diseases are the major cause of morbidity and mortality in Type 2 diabetic patients. Cardiovascular mortality is twice as high in diabetic men and four times as high in diabetic women than non diabetics, the relative risk being 50% and 150% greater respectively. This increased risk has been attributed to the prevalence of multiple atherosclerotic risk factors among diabetic patients[3-6].

* Corresponding Author : **Dr.ArunKumar.R D.N.B (Gen Medicine)**
Senior Resident, Department of General Medicine,
Sri LakshmiNarayana Institute of Medical Sciences,
Ossudu, Kudapakkam Post, Villianur Commune,
Puducherry 605502.
Email Id–arun.dr.310379@gmail.com
Phone number – 09787084864.

Joslin in 1927 wrote "with an excess of fat, diabetes begins and from an excess of fat diabetes die". The most important components of this dyslipidemia are an elevated very low-density lipoproteins (VLDL), total triglycerides (TG's) and a decreased high-density lipoproteins (HDL) concentration in the serum.[7,8]

Atherosclerosis, unless in a severe form is often asymptomatic, so that a direct examination of the vessel wall is necessary to detect affected individuals in the early stages. It has been suggested by International atherosclerosis project that the atherosclerotic process occurs at the same time in carotid, cerebral and coronary arteries16. Measurement of the carotid intima-media thickness (CIMT) of the common carotid artery (CCA) by B-mode ultrasound was found to be a suitable noninvasive method to visualize the arterial walls and to monitor the early stages of the atherosclerotic process17-19. An increased CIMT was observed in type 2 diabetic patients. This increase in carotid intima-media thickness was associated with an increased risk of ischemic heart disease (IHD) and cerebrovascular disease (CVD) in diabetics[20].

Aims and Objectives:

1. To compare the incidence of Carotid Intima Medial thickness between diabetic and non-diabetic population.

2. To assess the relation between carotid Intima Medial thickness in relation to microvascular and macrovascular morbidity in diabetic and non-diabetic population.

Material and Methods:

It was a Cross sectional analytical study conducted at Sri LakshmiNarayana Institute of Medical Sciences, Puducherry, between March 2011 to February 2013.

Diabetic group: All diabetic patients attending endocrine clinic of the hospital were evaluated and included in the study. Diabetic patients irrespective of the duration were included in this group (n=100)

Non Diabetic group: Age and sex matched non-diabetic population who underwent evaluation for other reasons in our hospital during this study period were included in the control group (n=100).

Both diabetic and non diabetic group were evaluated for presence of vascular complications like Retinopathy, Cerebrovascular disease, Cardiovascular disease and Nephropathy in association with CIMT.

Exclusion criteria: Patients with impaired fasting glucose or impaired glucose tolerance were excluded from both study and control group.

After obtaining ethical committee clearance from the institute, patients were subjected to a detailed history taking including intake of drugs that may influence the CIMT such as anti-diabetic drugs ,antiplatelets, statins and anti-hypertensives was also considered.

Both study and control group underwent the assessment for micro and macro vascular complications such as retinopathy, neuropathy, nephropathy, and CAD, cerebrovascular diseases and peripheral vascular diseases (PVD).

Both study and control group underwent assessement of CIMT by measuring the intima media thickness of common carotid artery (CCA) on both sides by using 2D ultrasound with a high frequency (10MHz) linear probe. The presence or absence of plaques was also studied .The imaging for all these patients were done by the same sinologist so as to prevent any inter-observer variation. The values of intima media thickness on both sides were obtained. The mean value was calculated and greater than 0.8 mm was considered to be abnormal.

STATISTICAL METHODS: Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean SD (Min-Max) and results on categorical measurements are presented in number (%). Significance is assessed at 5 % level of significance.

Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups Inter group analysis) on metric parameters. Leven1s test for homogeneity of variance has been performed to assess the homogeneity of variance.

Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups

Results of the t-test: If the p-value associated with the t-test is small (< 0.05), there is evidence to reject the null hypothesis in favour of the alternative. In other words, there is evidence that the means are significantly different at the significance level reported by the p-value. If the p-value associated with the t-test is not small (> 0.05), there is not enough evidence to reject the null hypothesis, and you conclude that there is evidence that the means are not different.

Significant figures

+ Suggestive significance (P value: 0.05<P<0.10)

* Moderately significant (P value:0.01<P 0.05)

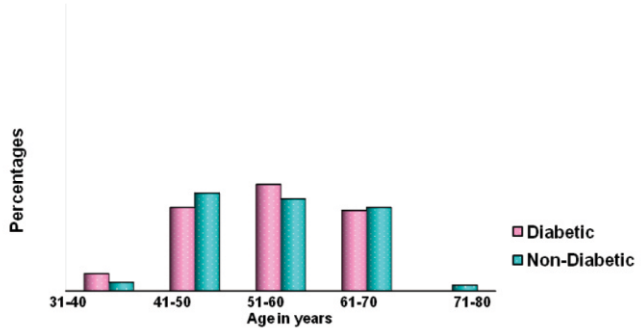
** Strongly significant (P value: P0.01)

Statistical software: The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1 ,Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Results:

Among the two groups studied, the mean age was 56.10±9.03 years in diabetic group and 55.28±7.56 years in non diabetic group. (Graph: 1)

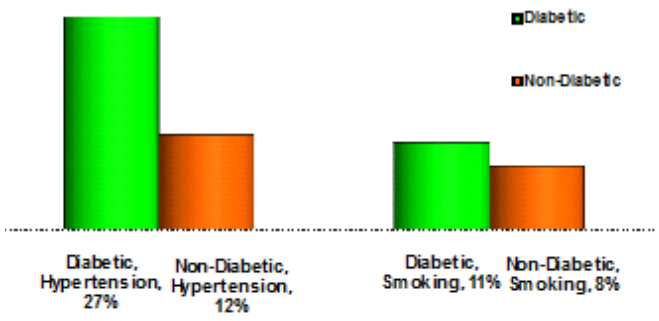
Graph: 1



The duration of diabetes was 1 to 5 years in 40 patients, 6 to 10 years in 43 patients, more than 10 years in 17 patients, with a mean duration of 7.65±4.78 years.

Body Mass Index between two groups did not reveal any statistical difference.

Graph: 2



Hypertension was the most common comorbid illness documented in diabetic patients (Graph: 2).

In diabetic group the mean systolic blood pressure was 133.14±9.25mmHg, as compared to non diabetic group who had a mean systolic blood pressure of 119.32±12.06mmHg (P<0.001**). (Graph: 3, Table: 1)

The diabetic group showed a significantly higher Diastolic Blood pressure of 82.84±6.83mmHg when compared to non diabetic group of 80.04±6.75mmHg (P<0.001**).

Graph: 3

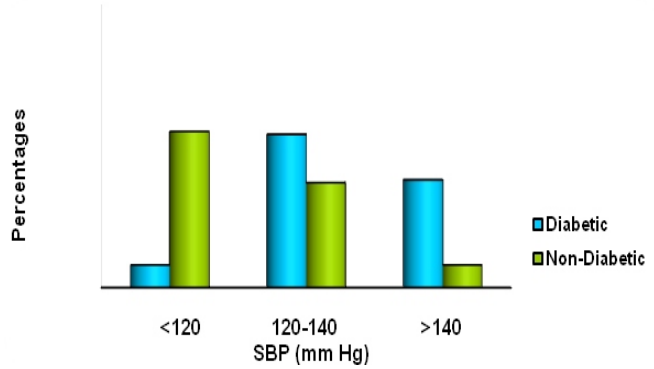
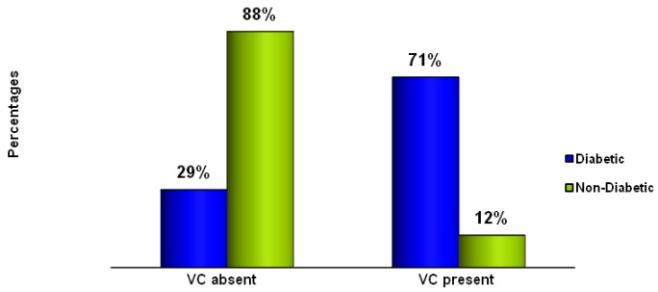


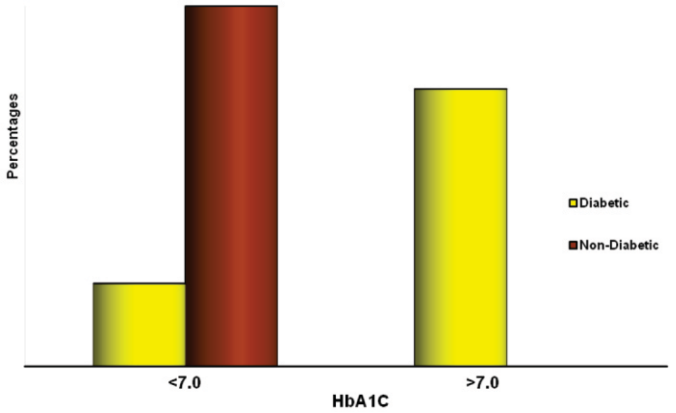
Table: 1

Blood pressure	Diabetic (n=100)	Non-Diabetic (n=100)	Significance
SBP (mm Hg)			
·<120	8(8.0%)	55(55.0%)	x^2=57.800
·120-140	54(54.0%)	37(37.0%)	P<0.001**
·>140	38(38.0%)	8(8.0%)	
·Mean ±SD	133.14±9.25	119.32±12.06	
DBP(mm Hg)			
·<80	16(16.0%)	36(36.0%)	2=18.000
·80-90	57(57.0%)	56(56.0%)	P<0.001**
·>90	27(27.0%)	8(8.0%)	
·Mean ±SD	82.84±6.83	80.04±6.75	

The incidence of vascular complication was higher among diabetic group when compared to non diabetic group (p<0.001**) (Graph: 4). Among the diabetic group 45 patients had retinopathy, 32 had CAD, 17 had CVD, 14 had Nephropathy.



The mean HbA1C among diabetic group was 7.79±0.79 when compared to non diabetic group with 6.47±0.30 (P<0.001). In diabetic group 77% patients had HbA1C >7.0. None of the non diabetic group showed HbA1C >7.0 (Graph: 5).

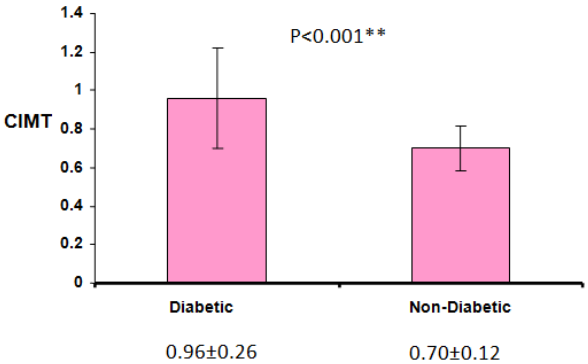


The mean Total cholesterol (194.95±46.36mg%), Triglycerides (140.28±56.12mg%), HDL-C(35.55±7.25mg%) and LDL-C(105.06±29.11mg%) was significantly higher among diabetic group (Table: 2).

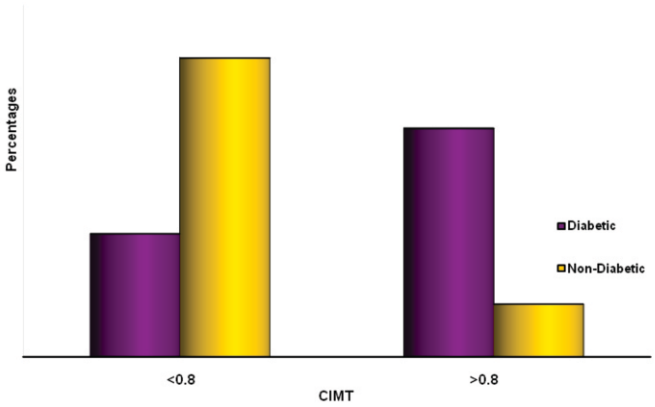
Lipid parameters	Diabetic (n=100)	Non-Diabetic (n=100)	P value
Total cholesterol (mg/dl)	194.95±46.36	184.17±17.94	0.031*
HDL	35.55±7.25	38.78±3.69	<0.001**
LDL	105.06±29.11	89.88±10.14	<0.001**
Triglycerides	140.28±56.12	91.28±9.89	<0.001**

On comparing the lipid parameters in both groups, 38 (38%) diabetics had TC of more than 200mg% as compared to just 12 non diabetics. A similar finding of low HDL-D (76%), high LDL-C (13%) and high TG (24%) was observed in diabetics when compared to non diabetic group.

The mean CIMT value among diabetic group was 0.96±0.26 as compared to non diabetic group with CIMT of 0.70±0.12 (P<0.001**).



Among diabetic group the incidence of CIMT of more than 0.8 was 65% when compared to 15% among non diabetic group (2=52.083 P<0.001**).This shows that there was significant association between diabetes and an increased incidence of abnormal CIMT (> 0.8) (Graph: 6).



The diabetic group had significantly higher vascular complications (73.2%) in association with abnormal CIMT.

In the diabetic group those who had CIMT of >0.8 had 95.9% incidence of carotid plaque (2=40.372,P<0.001**).

In the diabetic group those who had a Serum TG level of >150mg% had a CIMT of >0.8.This shows the association of increased TG with abnormal CIMT in diabetic group.

Higher HbA1c was positively associated with CIMT >0.8(P<0.001**).

Discussion:

The mean age of distribution among diabetic group was 56.10±9.03 years. A similar association was found by Agarwal et al in which the mean age distribution among study group was 59.78 ± 8.81 years.

The mean duration of diabetes mellitus was 7.65±4.78 years in our study. The mean duration of diabetes among the study group was 11.23±6.89 years as per Agarwal et al.

Hypertension was the most commonest co-morbid illness found among the diabetic group.The mean SBP studied among diabetic population was 133.14±9.25 mmHg , and the mean DBP was 82.84±6.83 mm Hg. A similar association of high blood pressure was found by Agarwal et al, in which the mean SBP was 140.07±15.28 mm Hg and the DBP was 86.67±10.45 mm Hg.J Ahmed et al in their study revealed that the mean SBP was 135.42±18.28 mm Hg, and the DBP was 85.20±10.30 mm Hg.

In our study, the mean HbA1c was 7.79±0.79 % among diabetic group. Agarwal et al and J Ahmed et al in their study found a mean HbA1C of 7.64±1.42% and 8.63±0.55% respectively.

Serum lipid profile: In our study, the mean total cholesterol was 194.95±46.36 mg%, triglyceride was 140.28±56.12 mg%, HDL-C was 35.55±7.2 mg%, LDL-C was 105.06±29.11mg% among diabetic group. Agarwal et al – in their study found a mean Total cholesterol of 182.08 ± 41.61 mg %, triglyceride of 155.17 ±82.557 mg %, HDL of 42.46 ±9.00 mg%, LDL of 110.16 ±34.69 mg% among diabetic group. V kumar et al- in their study found a mean Total cholesterol of 186.3 ± 42.2 mg %, triglyceride of 145.0 ±85.3 mg %, HDL of 34 ±3.5 mg%, LDL of 123.2 ±40.8 mg% among diabetic group.

Carotid Intima Media Thickness: In our study, the mean CIMT was 0.96±0.26 among diabetics as compared to 0.70±0.12 of non diabetic group (p<0.001). V. Mohan et al: (CUPS) In their study on intima-medial thickness of carotid artery in the south Indian diabetic and non-diabetic group have shown that the mean intimal-media thickness of 0.95±0.31 mm among the diabetic subjects which was significantly higher than those of non-diabetic subjects with 0.74±0.14 mm (p<0.001)20. Agarwal et al; in their study, the mean CIMT among diabetic group was 0.840 ±0.20. J.Ahmed et al – in their study, the mean CIMT among diabetic group was 0.93±0.34 as compared to non diabetics who had CIMT of 0.77 ±0.22 (p<0.01).

CIMT AND ITS ASSOCIATION WITH VASCULAR COMPLICATIONS:Among diabetic patients with high CIMT, vascular complications were noted in 71% cases as compared to only 12% of non diabetic group. Of these 71% complications, 45% had retinopathy, 32% had CAD, 17% had CVD, and 14% had nephropathy. Snichi Teno et al documented diabetic retinopathy in 19 patients (31.6%), diabetic nephropathy in 7 patients (11.6%). Agarwal et al documented increased CIMT in 63% diabetic patients with CAD. Mohan Rema et al documented diabetic retinopathy in 19.6% patients and CAD in 21.6% patients with increased CIMT.

Severity of CIMT with vascular complications: In our study, 73% of diabetic patients with CIMT of more than 0.8 had vascular complications. Agarwal et al in their study found 63.3% of diabetic CAD patients had CIMT of more than 0.8. Lorenz MW et al found that every 0.1mm increase in CIMT, the odd risk of stroke increased by 1.18 for CAD. Matsumoto K et al found that every 0.1 mm increase in CIMT, the odd risk of stroke increased by 1.80.

In our study, 49% of diabetics had plaques as compared to just 06% of non diabetics which was statistically significant (p<0.001). Satoshi Hirayama et al found that 80% of diabetics had plaques compared to non diabetic group.

In our study there was a statistically significant increase in CIMT with duration of diabetes, the similar finding was also observed by Lynne E Wgenknecht et al.

Conclusion

At any age point, carotid intima medial thickness values of the diabetic patients are significantly higher than that of the non diabetic patients irrespective of the co-morbid conditions. There exists a strong linear association between the duration of diabetes and the carotid intima medial thickness. Hypertension remains the most common comorbid illness associated with diabetes mellitus. Dyslipidaemia co exists often in diabetic patients which tend to worsen the vascular insult.

CIMT was positively associated with greater overall risk of vascular events in diabetic group .Vascular events of all forms i.e. retinopathy, CAD, CVD, Nephropathy and PVD were significantly seen in those patients with increased CIMT. Hence the detection of abnormal CIMT predicts the risk of vascular complications in diabetics.

Diabetic patients with higher CIMT associated with plaques had higher chances of vascular complications.

Diabetes mellitus is regarded as vascular disease and by measuring the carotid intima medial thickness, the diabetic vascular complications can be predicted. Hence ultrasound screening of carotid intima medial thickness is mandatory in diabetic subjects so as to detect the early atherosclerosis and hence the preventive measures or therapeutic options can be intiated early and thus preventing the development of further acceleration of both micro and macro vascular complications.

References

[1] King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: Prevalence, numerical estimates and projections. Diabetes Care 1998;21:1414-1431

[2] Diabetes atlas: 2006.

[3] Fagan TC, Sowers J. Type 2 diabetes mellitus: greater cardiovascular risks and greater benefits of therapy. Arch Intern Med 1999;159: 1033-1034,

[4] Haffner SM, Lehto S, Ronnemaa T, Pyorala K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. N Eng J Med 1998;339: 229-234.

[5] Davis TM, Millns H, Stratton IM, Holman RR, Turner RC. Risk factors of stroke in type 2 diabetes mellitus: UKPDS 29. Arch Intern Med 1999;159: 1097-1103.

[6] Kannel W, McGee D. Diabetes and glucose tolerance as risk factor for cardiovascular disease. The Framingham study. Diabetes Care 1979; 2: 120-126

[7] Madhu SV et al. "Post prandial lipemia in Diabetic Atherosclerotic Heart Disease". Medicine Update (Vol-1) 2004:114-118.

[8] Teno S, Uto Y, Nagashima H. Association of Postprandial hypertriglyceridemia and carotid intima-medial thickness in patients with type 2 diabetes. Diabetes Care Sept 2000;23(9):1401-1406.

[9] Haffner SM, D'Agostino R Jr, Mykkanen L, Tracy R, Howard B, Rewers M, Selby J, Savage PJ, Saad MF. Insulin sensitivity in subjects with type 2 diabetes: relationship to cardiovascular risk factors: the Insulin Resistance Atherosclerosis Study. Diabetes Care 1992;22: 556-568.

[10] Patsch JR, Meisenbock G, Hopferwieser T, Muhlberger V, Knapp E, Dunn JK, Gotto AM Jr, Patsch W. Relation of triglyceride metabolism and coronary artery disease. Studies in the postprandial state. Arterioscler Thromb 1992;12:1336-1354.

[11] Miller M, Seidler A, Moalemi A, Pearson TA. Normal triglyceride levels and coronary artery disease events: The Baltimore Coronary Observational Long-Term Study. J Am Coll Cardiol 1998;31: 1252-1257.

[12] Koskinen P, Manttari M, Manninen V, Hultunen JK, et al., Coronary Heart disease incidence in NIDDM patients. Diabetes Care 1992;15:820-825.

[13] Bjorkegren J, Karpe F, Milne RW, Hamsten A. Differences in apolipoprotein and lipid composition between human chylomicron remnants and very low density lipoproteins isolated from fasting and postprandial plasma. J Lipid Res 1998;39: 1412-1420.

[14] Karpe F, de Faire U, Mercuri M. Bond MG, Hellenius ML, Hamsten A. Magnitude of alimentary lipemia is related to intima-media thickness of the common carotid artery in middle aged men. Atherosclerosis 1998;141: 307-314.

[15] Boquist S, Ruotolo G, Tang R, Bjorkegren J, Bond MG, de Faire U, Karpe F, Hamsten A. Alimentary lipemia, postprandial triglyceride rich lipoproteins, and common carotid intima-media thickness in healthy, middle aged men. Circulation 1986;74: 1399-1406.

[16] McGarry, McMohan CA, Montenegro MR at al. General findings of the International Atherosclerosis Project. Lab Invest 1968;18:498-502.

[17] Pignoli P, Tremoli E, Poli A, Oreste P, Paoletti R: Intimal plus medial thickness of the arterial wall. A direct measurement with ultrasound imaging. Circulation 1986;74:1399-1406.

[18] Salonen R, Salonen JT. Progression of carotid atherosclerosis and its determinants: a population-based ultrasonography study. Atherosclerosis 1990;81:33-40

[19] Handa N, Matsumoto M, Maeda H, Hougaka H, Ogawa S, Fukunaga R, Yoneda S, Kimura K, Kamada T. Ultrasonic evaluation of early carotid atherosclerosis. Stroke 1990;21: 1567-1572.

[20. O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson SK Jr. Carotid artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults: Cardiovascular Health Study Collaborative Research Group. N Engl J Med 1999;340:14-22

[21] The diabetes Control And Complication Trail Research Group. "The effect of intensive treatment of diabetes on the development and progression of long term complications in insulin –dependent Diabetes Mellitus .NEJM 1993;329(14):977-86.

[22] The UKPDS Group.Intensive blood-glucose control with sulhonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes(UKPDS 33).Lancet 1998;352:837-853.

[23] AK Agarwal et al – carotid intima medial thickness in Type2 diabetic patients and its co-relation with coronary risk factors,orginal article,vol 56,JAPI August 2008.

[24] J Ahmad, Faiz Ahmad et al: Insulin resistance and CIMT in Type 2 DM subjects JAPI October 2007 vol 55.

[25] V kumar et al: prandial hypertryglyceridemia in patients with type 2 diabetes melitius with and without macrovascular diseases. JAPI October 2010 vol 58,post

[26] Mohan Rema associates et al (CURES-2) ADA, association of CIMT with Diabetic retinopathy, DIABETES CARE 27:2004 August 1962-1967,

[27] Lynne E wagenknecht et al- duration of DM and CIMT,Insulin resistance atherosclerosis study(IRAS)AHA/ASA STROKE 1997,28:999-1005

[28] Mary J Roman et al clinical application of CIMT in cardiovascular risk stratification – VASCULAR MEDICINE 2006,11,201-211

[29] Lorenz MW et al- prediction of clinical cardiovascular events with CIMT : a systematic review and metaanalysis CIRCULATION -2007 JAN 30:115(4)

[30] Matsumoto k et al: correlation between CCAIMT & Ischemic Stroke in patients with Type 2 Diabetes melitius Metabolism -2002 Feb51(2)244-7

[31] Masoume sadeghi et al: Is CIMT an independent predictor for CAD?: ARYA journal (spring) 2005,5-8

[32] Satoshi Hirayama et al pre beta 1 HDL is a predictor of CIMT in Type 2 DM ADA –DIABETES CARE MAY2007 vol 30,1289-1291