Correlation between Mean Carotid Intima Media Thickness (CIMT) With Retinopathy in Diabetic Patients

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Abstract: *Vascular changes in the patients with the Diabetes mellitus had significant role to develop Diabetic retinopathy and higher mean Carotid intima media thickness (CIMT) value. Thus the main aim of this study was, to correlate the mean CIMT with Diabetic retinopathy. Total 158 patients with diabetic, were included in this cross sectional study which was conducted at out-patients department at MLB Medical College, Jhansi, (U.P.) from May 2018 to October 2019. Patients below 15 year of age group and patients with history of any retinal surgery were excluded from the study. All necessary information and investigations were noted. Ocular examination includes Visual acuity, slit lamp examination, direct/Indirect ophthalmoscopy, OCT and Fundus Fluorescein angiography (FFA) was done. Then all patients sent for CIMT measurement via B- mode ultrasound. In this study the male female ratio was 1.43:1. The diabetic male of study group had higher Mean CIMT (0.84±0.28 mm) as compare to diabetic female (0.72±0.22 mm). The older patients had higher Mean CIMT value as compare to younger patients, maximum mean CIMT was found in above 60 years of age group (0.86±0.30 mm) and minimum mean CIMT was found in 16-31 years of age group i.e. 0.57±0.11 mm. Patients with diabetic retinopathy had higher Mean CIMT (0.85±0.27 mm) value as compare patients with no sign of Diabetic retinopathy (0.72±0.20 mm). In this study, as severity of DR increases, the mean CIMT value also higher in those patients. Maximum mean CIMT was found in those patients who had PDR/Advance diabetic eye (i.e1.1± 0.31 mm) and minimum mean CIMT value founds in patients with no sign Diabetic retinopathy (0.67± 0.26 mm). Mean CIMT value also depend on Hypertension, Body mass index (BMI), Lipid profile, and addiction (Alcohol and smoking) of the patients. Thus the Mean CIMT value cannot be taken as a marker of Diabetic Retinopathy or vice versa, but it can be used as a screening purpose and need much more attention in future.*

Keyword: *B- mode ultrasound, CIMT, Diabetic retinopathy, Direct/Indirect Ophthalmoscopy, FFA, Lipid profile, OCT*

I. Introduction:

Diabetes mellitus (DM) is the most serious non communicable disease in recent time worldwide. It mostly affects the over middle aged peoples. Diabetes contributes many life threatening conditions as like atherosclerosis, nephropathy, neuropathy, diabetic coma etc. Diabetic retinopathy (DR) is a most common ocular complication in Diabetic patients. DR known as a one of most sight threatening condition in recent time after glaucoma. The basic pathology behind these complications is vascular (Macro and micro vascular) changes. The mechanism of vascular changes is rooted in chemical reactions between by-products of sugars and proteins which produce irreversible cross-linked protein derivatives called advance glycation end product (AGE).[1] These derivatives can exhibit a wide range of effects on surrounding tissues, including modification (eg, thickening) of collagen[2] and endothelium.[3] Specifically, in DR, AGE can induce growth inhibition and programmed cell death (ie, apoptosis) of retinal pericytes,[4] induce overproduction of endothelial growth factors [5,6] increase pathologic angiogenesis (neovascularization),[7] and increase vascular inflammation [8]; all of these actions lead to an increased risk for microthrombosis formation, capillary blockage, and retinal ischemia.[9] Neovascularization, vitreous hemorrhage, and increased levels of vascular endothelial growth factor can further lead to retinal fibrosis and detachment and loss of vision.[10] In addition, AGE can bind to immunoglobulin protein receptors for AGE and produce a cascade of signaling events that lead to endothelial cell dysfunction[10]

Diabetic Retinopathy (DR): Most sight threatening condition among diabetics, it classified into 4 stages according to ETDRS Classification that is

1.	No Diabetic retinopathy	3.	Proliferative Diabetic retinopathy (PDR)
2.	Non proliferative Diabetic retinopathy (NPDR)	4.	Advance diabetic eye

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NPDR further divided into early, intermediate, server form. Full disease classifications have developed from the original Airlie House classification that was modified by the Diabetic Retinopathy Study (DRS) [11] developed for the Early Treatment Diabetic Retinopathy Study (ETDRS)[12] aimed at grading retinopathy in the context of overall severity of ophthalmoscopic signs.

*Carotid intima media thickness [CIMT]:*Carotid artery intima media thickness was measured by B mode ultrasound having an electric transducer with a mid frequency of 7.5 MHz. Scans were performed on both the right and left extracranial carotid arteries (2-3 cm proximal to the bifurcation) by trained personnel. [13] Arterial diameter and mean CIMT measurements were done three times for each artery at each site. The average of three measurements of each carotid artery diameter or CIMT was taken. The average mean CIMT is 0.6 to 0.9 mm. Many other studies showed its wide range from 0.4 mm to 0.9 mm

II. Method And Material:

Total 158 patients with diabetic, were included in this cross sectional study. All patients were well known case diabetes irrespective of its duration. This study was conducted at out-patients department at MLB Medical College, Jhansi, (U.P.) in period of 18 month from May 2018 to October 2019. The procedures followed were in accordance with the ethical standards committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975, as revised in 2000. The necessary permission from the Ethical and Research Committee was obtained for the study. As our study, another parallel study was conducted in department of medicine to see the correlation of Mean CIMT in patients with Diabetes Mellitus (DM) and Metabolic Syndrome (MS).

EXCLUSION CRITERIA:
* Those patients with diabetic, who refuse to be included in the study,.
* Patients below 15 year of age group.
* Patients with history of any retinal surgery.
* Patients with diabetes, who had hazy media for direct or indirect ophthalmoscopy.

INCLUSION CRITERIA:
* Patients with diabetic irrespective sex of the patients, diabetic control, and duration of the diabetes.
Diabetes was diagnosed as per following criteria (any one of these):
Fasting blood sugar ≥126mg% on 2 occasions with classical symptoms (Polyphagia, polyphasia, polydipsia, polyuria).

Or

Post-prandial blood sugar ≥200mg% with classical symptoms

Or

HbA1c> 6.5%.

Initial workup start with patient's personal information, detailed diabetic history of the patient's (regarding duration, medication), and other medical or surgical history. Blood pressure and body mass index were noted. Blood investigation like complete heamogram, serum urea and cretinine, Hb1Ac and lipid profile were done.

Ocular examination includes Visual acuity, slit lamp examination, direct/Indirect ophthalmoscopy, OCT and Fundus Fluorescein angiography was done. After that, all 158 patients were classified into 2 groups.

Group A-Diabetic patients without DR ($N_{A=}$81)

Group B- Diabetic patients with DR ($N_{B=}$77)

Then all patients sent for CIMT measurement via B mode ultrasound and tabled accordingly.

III. Results

Table 1: Male and female diabetic patients with mean CIMT in study

	Male	Female
Numbers	93	65
Percentage	58.86%	41.14%
Mean CIMT (In mm) ± SD	0.84±0.28	0.72±0.22
P value	0.0044	

As table1, in this study the male female ratio was 1.43:1. Out of 158 patients, total 93 males were included in this study, while 65 females were included for study. The male diabetic patients had higher mean CIMT (0.84±0.28 mm) as compare to female diabetic patients (0.72±0.22 mm), which was statistically significant (P value 0.0044)

Table 2: Mean CIMT in various age groups (N=158)

Age group (In years)	Numbers	Mean CIMT (In mm) ± SD
16-30	11 (7%)	0.57±0.11
31-45	24 (15.19%)	0.72±0.17
46-60	66(41.77%)	0.79±0.24
Above 60	57(36.08%)	0.86±0.30
Total	158	0.79± 0.26

As table 2, it shows that the Mean CIMT was increases with increasing age. Maximum mean CIMT was found in above 60 years of age group (0.86±0.30 mm) followed by 46 to 60 years (0.79±0.24 mm), 31-45 years of age group had 0.72±0.17 mm mean CIMT. Minimum Mean CIMT was found in 16 to 30 years of age group (0.57±0.11 mm)

Table 3: Age and sex wise distribution of the diabetic patients and mean CIMT (N=158)

Age group (In years)	Group A (81)		Group B (77)		Total	Percentage
	Male	Female	Male	Female		
16-30	03	00	06	02	11	7 %
31-45	02	06	07	09	24	15.19%
46-60	19	14	21	12	66	41.77%
Above 60	24	13	11	09	57	36.08%
Total	48	33	45	32	158	100%
Mean CIMT (In mm) ± SD	0.90±0.30	0.78± 0.28	0.78±0.23	0.66±0.13	0.79± 0.26	
	0.85±0.27		0.72±0.20			
P value	0.9659					

Table 3 shows that the mean CIMT in Group A males (Male patients with Diabetic retinopathy) had 0.90±0.30 mm Mean CIMT value, where as females (Female patients with diabetic retinopathy) had 0.78± 0.28 mm.
Group B males (Male patients without sign of Diabetic retinopathy) had 0.78±0.23 mm, and females had 0.66±0.13 mm. Mean CIMT value.

Table 4: Severity of Diabetic retinopathy (ETDR classification) and Mean CIMT

Severity of DR	Number of patients	Mean CIMT (In mm) ± SD
No Diabetic Retinopathy	77 (48.73%)	0.67± 0.26
Early to mod. NPDR	41(25.95%)	0.79± 0.26
Severe NPDR	26 (16.46%)	0.88± 0.26
Proliferative DR to advance Diabetic eye	14(8.86%)	1.1± 0.31
Total	158	0.79± 0.26

As table 4, with increasing of severity of DR, there is significant increment in mean CIMT value. Maximum mean CIMT was found in those patients who had PDR/Advance diabetic eye (i.e1.1± 0.31 mm) followed by patients with severe NPDR (0.88± 0.26 mm) and patients with early to moderate NPDR (0.79± 0.26 mm). Minimum Mean CIMT value founds in patients with no sign Diabetic retinopathy in fundus examination.

IV. Discussion:

Severity of Diabetic retinopathy basically depends on blood glycemic control. In this study the male :female ratio was 1.43:1, which actually depended on the sample selection. The diabetic male of study group had higher Mean CIMT (0.84±0.28 mm) as compare to diabetic female (0.72±0.22 mm) which was statistically significant in this study (P value 0.0044). Some study mentioned that the male had higher Mean CIMT as compare to female irrespective of diabetes and its duration. Similar results have been reported by Kramal*et al.,* who had also observed significantly higher CIMT in men (0.626 mm) than women (0.524 mm). In a study of healthy Taiwan population, mean CIMT again was significantly higher in men (0.558 mm) than women (0.527), beside these study also included normal healthy individual.

In this study, the older patients had higher Mean CIMT value as compare to younger patients, maximum mean CIMT was found in above 60 years of age group (0.86±0.30 mm) and minimum mean CIMT was found in 16-31 years of age group i.e. 0.57±0.11 mm. Few study say that the age factors individually affects the mean CIMT value. Robin et al reported that the mean CIMT was independently and positively related to the age. Pujia*et al.,* in Chennai Urban Population study studied mean CIMT of carotid artery in South Indian diabetic and non diabetic subjects and observed higher mean CIMT value with increasing age. Kwamori*et al.*in their study and concluded the same.

Group A patients (patients with diabetic retinopathy) had higher Mean CIMT (0.85±0.27 mm) value as compare Group B (Patients with no sign of Diabetic retinopathy) (0.72±0.20 mm). It is well known that the

Diabetic retinopathy strongly depends on the duration of diabetes and blood glycemic control. Patients had long duration of Diabetes had more chances to developed Diabetic retinopathy and increases its severity and it seems that the Mean CIMT value had also depends on the duration on Diabetes.

In this study, as severity of DR increases, the mean CIMT value also higher in those patients. Maximum mean CIMT was found in those patients who had PDR/Advance diabetic eye (i.e1.1± 0.31 mm) and minimum mean CIMT value founds in patients with no sign Diabetic retinopathy (0.67± 0.26 mm).Miyamoto in evaluation of 102 diabetic patients showed the significant correlation between retinopathy and common carotid artery thickness. [14]

V. Conclusion:

The study shows that the mean CIMT value also depend on Hypertension , Body mass index (BMI), Lipid profile, and addiction (Alcohol and smoking) of the patients.[15,16,17] So, the CIMT cannot be used as a marker of Diabetic retinopathy or vice versa but in current time the developing countries like India, cost-effectiveness and awareness to fundus examination (in diabetic patients) can be also used as a screening tool for the cerebral and coronary atherosclerosis in diabetic patients in future. To study the correlation between Diabetic retinopathy and Mean CIMT and their dependency in other factors need much more specific attention in future.

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