

## Assessment of the Prevalence and Clinical Significance of Asymptomatic Atherosclerotic Plaques in Lower Limb Vessels of Patients of Type 2 Diabetes Mellitus by Color Doppler Study

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**Abstract:** Diabetes Mellitus (DM) is a serious, chronic disease that occurs either when the pancreas does not produce enough insulin (a hormone that regulates blood sugar, or glucose), or when the body cannot effectively use the insulin it produces. Atherosclerosis involves a combination of fatty degeneration (atherosis) and of vessel stiffening (sclerosis) of the arterial wall. Peripheral vascular disease (PVD) of lower limb described as atherosclerosis below the bifurcation of abdominal aorta, The severity and duration of DM are important predictors of both the incidence and the extent of PVD, The aim of our study is to identify the prevalence of asymptomatic atherosclerotic plaques in type-II diabetes mellitus patients, using color doppler ultrasonography and to associate it with risk factors like hyperlipidemia, hypertension, obesity, smoking, coronary artery disease (CAD), family history and duration of diabetes. It is an observational study done on 100 cases of type 2 diabetes mellitus who presented at our centre during study period. The Pearson's Chi-Square test had used to demonstrate the associations of risk factors like, hyperlipidemia, hypertension, obesity, smoking, coronary artery disease (CAD), family history and duration of diabetes. The prevalence of asymptomatic atherosclerotic plaques in lower limb vessels of diabetic patients was found to be 52%. It showed significant association with hyperlipidemia, hypertension, obesity, smoking, coronary artery disease (CAD), family history and duration of diabetes. In our case study, the prevalence of asymptomatic atherosclerotic plaques was studied among patients with established type —II diabetic mellitus using Colour Doppler Ultrasonography and correlation of the Atherosclerotic Plaque morphology with risk factors was made. The study group comprised of 100 patients of type 2 diabetes mellitus.

**Keywords:** Type 2 diabetes mellitus, peripheral vascular disease, atherosclerotic plaques, colour Doppler study.

### INTRODUCTION

Diabetes Mellitus (DM) is a serious, chronic disease that occurs either when the pancreas does not produce enough insulin (a hormone that regulates blood sugar, or glucose), or when the body cannot effectively use the insulin it produces. Globally, an estimated 422 million adults were living with diabetes in 2014, compared to 108 million in 1980[1]. India had 69.2 million people living with diabetes (8.7%) as per the 2015 data. Type 2 Diabetes Mellitus i.e non-insulin dependent diabetes mellitus (NIDDM) accounts for over 85% of diabetics patients worldwide. This rise is seen mainly in developing countries like India. By year 2025, India will become the “Diabetic Capital of the world”[3]. Atherosclerosis involves a combination of fatty degeneration (atherosis) and of vessel stiffening

(sclerosis) of the arterial wall. Peripheral vascular disease (PVD) of lower limb described as atherosclerosis below the bifurcation of abdominal aorta, this could lead to progressive narrowing of the lower limb arteries leading to claudication, gangrene and amputation [2]. The risk of PVD increases substantially with age [3-4]. The prevalence of PVD is 4.8%, 12.0% and 22.0% for men and women aged 60-69 years, and >80 years, respectively [5]. PVD is also several times more common among diabetic subjects compared to non-diabetic subjects [6, 7]. The severity and duration of DM are important predictors of both the incidence and the extent of PAD, as observed in United Kingdom Prospective Diabetes Study, where each 1% increase in glycosylated hemoglobin (Hb1Ac) was correlated with a 28% increase in incidence of PAD,

and higher rates of death, microvascular complications and major amputation[8,9]. The gold standard for diagnosis of PVD is angiography. However, the use of this technique is limited due to its invasive nature, the use of contrast agents and the cost. The Color Doppler Ultrasound (CDU) is a non invasive technique. The aim of our study is to identify the prevalence of asymptomatic atherosclerotic plaques in type-II diabetes mellitus patients, using color Doppler ultrasonography and to associate it with risk factors like hyperlipidemia, hypertension, obesity, smoking, coronary artery disease (CAD), family history and duration of diabetes.

**MATERIALS & METHODS**

The present study was an observational study entitled “Assessment of the prevalence and clinical significance of asymptomatic atherosclerotic plaques in lower limb vessels of patients of type 2 diabetes mellitus by color doppler study” was conducted at Sri Aurobindo Medical College & PG Institute, Indore, a 1200 bedded a tertiary care and referral center situated in heart of the city with state of the art technology catering to all sections of the society.

**Duration of Study**

The study was conducted from December 2015 to June 2017 among the patients who presented as outdoor patient (OPD) and in patients at Sri Aurobindo Medical College & PG Institute, Indore.

**Sample Size**

100 patients with established diabetes mellitus without symptoms of peripheral vascular disease were enrolled for the study

**Inclusion Criteria**

- Age > 18 year and <60 year.
- Patients with type- II Diabetes Mellitus with no symptoms of peripheral vascular disease(rest pain, claudication and foot ulcers).

**Exclusion Criteria**

- All patient < 18 years and >60year.
- Patients with symptoms or history of peripheral vascular disease.
- Procedure Planned:- Colour Doppler, Blood Investigations

**Observations and Results**

The age of all patients of established type-II diabetes mellitus were obtained in the range from 24 to 60 years. The scatter for age (Mean ± Standard Deviation) of all subjects (N=100) was found to be 50.50±7.73 years.

The spread of mean age (mean ± standard deviation) of male patients with type-II diabetes mellitus was found to be (50.52±7.57) years as compared to age of female patients (50.46±8.11).

**Table No.1**

All these patients were planned to generate the prevalence and clinical significance of asymptomatic atherosclerotic plaques in lower limb vessels using color doppler ultrasonography for this observational study purpose.

The age distribution of studied patients with asymptomatic type-II diabetes mellitus is highlighted in table 1.

**Table-1:-Association of obesity, smoking history, hypertension and coronary artery disease history of patients of type 2 diabetes mellitus with atherosclerotic plaques in lower limb vessels**

Parameter/Variable		Atherosclerotic Plaque		Total patient	p-value (LOS)
		Absent	Present		
Obesity	No	31 64.6%	28 53.8%	59 59.0%	$\chi^2 = 1.19$ p>0.05 <sup>⊗</sup>
	Yes	17 35.4%	24 46.2%	41 41.0%	
Smoking History	No	29 60.4%	17 32.7%	46 46.0%	$\chi^2 = 7.72$ p<0.005 <sup>#</sup>
	Yes	19 39.6%	35 67.3%	54 54.0%	
Hypertension	No	26 54.2%	17 32.7%	43 43.0%	$\chi^2 = 4.70$ p<0.03 <sup>*</sup>
	Yes	22 45.8%	35 67.3%	57 57.0%	
Coronary Artery Disease History	No	35 72.9%	26 50.0%	61 61.0%	$\chi^2 = 5.51$ p<0.02 <sup>*</sup>
	Yes	13 27.1%	26 50.0%	39 39.0%	

\* The association is significant at the 0.03 and 0.02 level of significance. # The association is highly significant at the 0.005 level of significance. ⊗ The association isn't (Insignificant) significant at the 0.05 level of significance. [LOS- Level of Significance]

**Table-2:-Association of hyperlipidemia, urine sugar, urine ketone and family history of diabetes of patients of type 2 diabetes mellitus with atherosclerotic plaques in lower limb vessels**

Parameter/Variable		Atherosclerotic Plaque		Total patient	p-value (LOS)
		Absent	Present		
Hyperlipidemia	No	24 50.0%	38 73.1%	62 62.0%	$\chi^2 = 5.64$ p<0.02 *
	Yes	24 50.0%	14 26.9%	38 38.0%	
Urine sugar	No	36 47.4%	40 52.6%	76 76.0%	$\chi^2 = 0.05$ p>0.05 <sup>⊗</sup>
	Yes	12 50.0%	12 50.0%	24 24.0%	
Urine ketone	No	44 91.7%	50 96.2%	94 94.0%	$\chi^2 = 0.89$ p>0.05 <sup>⊗</sup>
	Yes	4 8.3%	2 3.8%	6 6.0%	
Family history of diabetes	No	38 79.2%	22 42.3%	60 60.0%	$\chi^2 = 14.13$ p<0.001 #
	Yes	10 20.8%	30 57.7%	40 40.0%	

\* The association is significant at the 0.02 level of significance. # The association is highly significant at the 0.001 level of significance. <sup>⊗</sup> The association isn't (Insignificant) significant at the 0.05 level of significance. [LOS-Level of Significance]

## DISCUSSION

Peripheral artery disease (PAD) is defined as atherosclerotic occlusive disease of lower extremities. It involves a combination of fatty degeneration (atherosis) and vessel stiffening (sclerosis) of the arterial wall. Compromise of arterial flow due to the stenosis and occlusions can result in limb ischemia, which may manifest as claudication, rest pain, local tissue loss (ulceration) and potentially amputation. Patients with PAD may or may not be symptomatic. The most common cause of lower limb arterial occlusive disease is atherosclerosis. Since diabetes itself is a risk factor for atherosclerosis, PAD is also several times more common amongst the diabetes patients compared to non-diabetics[10]. It is stated that foot related disorders are one of the commonest causes of hospitalization among patients with DM and are responsible for a substantial proportion of morbidity in diabetic patients. Since doppler ultrasound, has been proved to be popular, non-invasive, accurate and cost effective means of assessing peripheral vascular disease, we included this modality of diagnosis in our study. Our study also aimed at associating the atherosclerotic plaques with other various risk factors like hyperlipidemia, hypertension, obesity, smoking, CAD, and family history of diabetes. On studying age distribution, we found the scatter for age (Mean  $\pm$  Standard Deviation) of all subjects to be 50.50 $\pm$ 7.73 years with a male female ratio of 1.7:1. The prevalence of asymptomatic atherosclerotic plaques in lower limb vessels among total patients was found to be 52.0% and was more prevalent (58.73%) among male patients as compared to female patients (40.54%). A study of Greek Hospitalized patients by Antonopoulos S *et al.* also supports our study and stated that male sex has a higher

prevalence of PVD (P=<0.001)[11]. The predisposing factors for PVD are the same as those for coronary heart disease. Smoking is considered to be one of the most significant risk factors for PVD and is related to a three times greater risk of limb amputation and death for patients with intermittent claudication [12]. The 5 year mortality rate for such patients, who continue smoking, is 40-50 % [12]. In our study, smokers appear at a 3 times higher risk of developing PVD than non-smokers. A study done by Jue li ET (4126) concluded, duration of smoking was an independent risk factor for low Ankle brachial index.

With regards to the Lipid profile in our study group, patients with asymptomatic PVD have higher mean total cholesterol (230.08 mg/dl), higher mean serum triglyceride (173.0 mg/dl), lower serum mean HDL (37.69 mg /dl) and higher mean LDL (133.15 mg/dl). The mean VLDL level is 59.15 mg/dl. Since PVD is an atherosclerotic disease, dyslipidemia represents a significant contributing factor. Patients with high Total cholesterol, Triglycerides, LDL as well as those with high levels of VLDL have been found to be at an increased risk of developing PVD. This type of association was not demonstrated with low levels of HDL cholesterol. Subjects with high Total cholesterol levels had a 6.075-fold greater risk for PVD than those with normal levels, as did the patients with elevated levels of LDL. Patients with elevated levels-of triglycerides showed a 4.9 times greater risk of developing PVD compared to normal subjects. Undoubtedly, we would expect an association between dyslipidemia and the development of PVD. A similar type of association was also found by Criqui MH *et al.* [13] with high LDL, triglyceride and low HDL. One

possible explanation for this could be that the adoption of a Mediterranean diet by the Greek people may reduce the impact of dyslipidemia on PVD [13]. In 2006 Agrawal RP *et al.* [14] had done a Population based cross sectional study included 4067 diabetic patients. They concluded that the prevalence of dyslipidemia is high in diabetic population. Patients with type 2 diabetes generally have an atherogenic lipid pattern characterized by high triglyceride and low HDL cholesterol concentrations. However, the atherogenic influence of lipids in patients with diabetes is not necessarily linked to the degree of dyslipidemia only, but also to altered, particularly atherogenic, particles in patients with type-2 diabetes.

In our study group, 12 patients had a history of heart disease. Atherosclerotic plaques were detected in 7 patients. Presence of atherosclerotic plaques in heart disease patient is statistically significant ( $p=0.003$ ). However, it was seen that HbA1c is not an independent risk factor. Similar significant data were also found in a Chinese study of 2006 [15]. In 2005 Elizabeth Selvin *et al.* [16] conducted a prospective case-cohort study of 1321 adults without diabetes and a cohort study of 1626 adults with diabetes from the Atherosclerosis Risk in Communities Study and assessed the relation between HbA1c level and incident CHD during 8 to 10 years of follow-up. They concluded that elevated HbA1c level is an independent risk factor for CHD in persons with and without diabetes.

Guan h *et al.* [16] concluded that the duration of diabetes course was positively correlated with the prevalence of PVD ( $\chi^2 = 11.9$ ,  $P = 0.0026$ ). The ABI abnormality rate was 15.78% among those with a diabetic course of 5 years and was 23.84% among those with a diabetic course of 10 years. The HbA1c value of the PVD patients was significantly higher than that of the patients without PVD ( $\chi^2 = 5.10$ ,  $P = 0.0239$ ).

## CONCLUSIONS

In our case study, the prevalence of asymptomatic atherosclerotic plaques was studied among patients with established type —II diabetic mellitus using Colour Doppler Ultrasonography and correlation of the Atherosclerotic Plaque morphology with risk factors was made. The study group comprised of seventy two patients [17] of type II diabetes, out of which 50 were taken into study.

- Height, Weight, Waist circumference and Blood Pressure were measured according to fixed criteria.
- Haematological & biochemical parameters like haemoglobin, fasting and post prandial blood sugar, HbA1c, lipid profile, serum BUN and serum creatinine were done
- Persons fulfilling the criteria of Diabetes Mellitus according to the National Diabetes group and World Health Organization criteria were identified and compared.
- Mean age among the study group comprising of 50 patients was  $59.22 \pm 13.9$  years.

- Female: Male sex distribution was in the ratio of 1: 1 (Females = 50 %, males = 50 %).
- 26 % (females = 3, males = 10) subjects had Atherosclerotic plaques.
- Out of 50 subjects, 58 were % hypertensive, 26 % were smokers, 68% were obese, 24% had heart disease, 60% were found to be dyslipidaemic while 42% had family history of diabetes.
- Mean BMI of the study group was  $27.49 \pm 26.72$  Kg/m<sup>2</sup> and the corresponding waist circumference value was  $95.48 \pm 14.91$  cm. • A large subset of study population on basis of BMI was overweight (14 %) and obese (68 %). (According to Consensus Statement for Diagnosis of Obesity, abdominal Obesity and the Metabolic Syndrome for Asian Indians)[17]
- Patients with Atherosclerotic plaque had mean systolic blood pressure of  $139.07 \pm 22.29$  mm Hg and mean diastolic blood pressure of  $87.08 \pm 15.74$  mm Hg.

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