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## Carotid artery Disease Assessed by Color Doppler Flow Imaging: Comparison Between Diabetic and Non-Diabetic Patients

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**Keywords:**

Ultrasonography; Carotid artery disease; Carotid artery stenosis; Carotid plaque; Vascular ultrasound; Diabetes

**Abstract**

**Background:** Carotid artery disease is most often seen in hypertensive patients and in patients with diabetes mellitus. More than 50% stenosis of extra cranial internal carotid arteries is linked with about 8–15% of ischemic strokes. The incidence of carotid artery stenosis (CAS) among diabetic patients is rising as compared to non-diabetic patients.

**Methods:** A cross-sectional study was performed on 120 patients, out of whom 60 were diabetic and 60 non-diabetics with clinically suspected carotid artery disease. The study was conducted at the university ultrasound clinic in Green Town by Doppler ultrasonography using the Toshiba XARIO XG, which features a linear probe of 5-7.5 MHz frequency. The data was analyzed with the help of SPSS version 25.0. Variables like age, gender, diabetes, and Intima-media thickness (IMT) were reported and the mean  $\pm$  standard deviation of Pulsatility Index, Resistive Index, Peak Systolic Velocity, and End Diastolic Velocity were calculated with a significant p-value, which is less than 0.05. An independent t-test was applied to compare Doppler indices in diabetic and non-diabetic subjects.

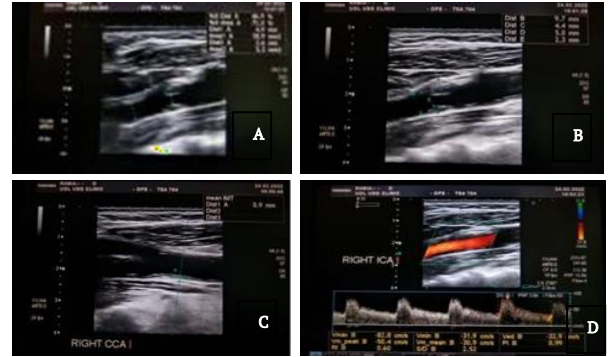
**Results:** Data was collected from 120 patients. IMT of right and left carotid artery, PI and RI of right carotid were observed to be statistically significant in diabetic and non-diabetic.

**Conclusions:** This study concluded that there is a significant correlation found between carotid artery disease and diabetes. Through ultrasonography, the presence of plaque and stenosis was found in more diabetic patients than in non-diabetic patients.

## Introduction

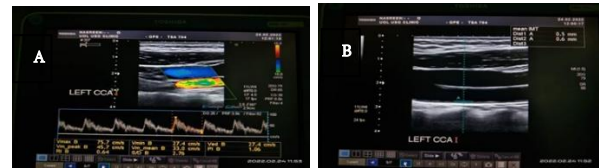
More than 50% stenosis of extra cranial internal carotid arteries is linked with about 8– 15% of ischemic strokes. Among diabetic patients, the incidence of carotid artery stenosis (CAS) is rising [1]. According to the Global Burden of Diseases, Injuries, and Risk Factors Study (2015), cardiovascular disease affected 422.7 million people and killed 17.9 million people worldwide in 2015, accounting for 31% of all global deaths. Annually, approximately 23.6 million people are expected to die from cardiovascular diseases by 2030 [2]. Any occlusion in the carotid arteries causes decreased blood supply to the brain, thus leading to significant permanent injury to the brain. Deposition of cholesterol or atherosclerosis causes narrowing of the carotid artery. The symptoms of carotid artery disease depend on the location of the blocked brain blood vessel. The symptoms of carotid artery disease include numbness in arms or legs; loss of vision in one eye; slurring of speech; and numbness on one side of the face [3]. With increasing age, the carotid arterial wall undergoes structural changes. The elasticity of the vessel decreases due to the assemblage of stiff substances like collagen and calcification. These changes are most often marked in hypertensive patients and in patients with renal failure [4]. Stroke occurs due to the occlusion of the main blood vessels. The non-modifiable risk factors that lead to stroke are age, family history, sex, and race. The modifiable risk factors include carotid stenosis, transient ischemic attack, cardiac disease, hypertension, diabetes mellitus, hyperlipidemia, alcohol abuse, physical inactivity, and cigarette smoking [5].

Carotid artery disease was found in diabetics with unstable and susceptible plaques, which might result in thrombo-embolism. Compared to non-diabetics, patients with diabetes mellitus had a larger carotid intima-media thickness (CIMT). A cluster of metabolic variables, such as insulin resistance, hyperlipidemia, obesity, and arterial hypertension, have a role in the etiology of carotid artery disease in people with type 2 diabetes [6]. Carotid artery stenosis (CAS) is becoming more common in diabetes patients. Diabetic people are three times more likely than non-diabetics to develop cardiovascular illnesses (CVD), such as coronary and carotid artery problems, and stroke [7]. The carotid bifurcation, which is typically affected by atherosclerosis and is a source of both transient ischemic events and strokes, is an important site to investigate [8]. Diabetes complications can be divided into three categories: metabolic, microangiopathic, and macroangiopathic problems. It was discovered that 20% of the patients experienced a stroke within a year, and 37% experienced a stroke within five years [9].



**Figure 1:** A 40-year-old female diabetic has 2 plaques in RICA. The 1st and 2nd plaques measured 9.7 x 4.4mm and 5.0 x 2.3mm, respectively, causing 46.9% stenosis. IMT is slightly raised (0.9mm) but has no effect on flow pattern.

Doppler Ultrasonography (DU) is an accurate, well-recognized, and non-invasive method for evaluating carotid artery disease. Through this technique, various parameters like the presence of plaque, intima-media thickness (IMT), blood flow velocity, and arterial diameter are measured [10]. Intima media thickness (IMT) is considered an indicator of atherosclerotic changes in the vessel [11]. DU is used not only to determine the presence or absence of plaques, as well as the early and late manifestations of vascular disease in people with and without diabetes, but also to predict who is at risk of developing cardiovascular or cerebrovascular disease [12].



**Figure 2:** A non-diabetic female in her 30s has a normal IMT (0.6mm) and flow pattern.

This study benefits from the discovery of a significant correlation between carotid artery disease and diabetics and non-diabetics. Only a few studies are published in the literature, most of which are done only on diabetics, but our main objective is to focus on both groups [diabetics and non-diabetics]. This study contributes to the early detection of plaque or stenosis in the carotid artery in diabetic patients and non-diabetic subjects.

## Methods

The study was performed at the university ultrasound clinic in Green Town from October 2021 to June 2022 for duration of 8 months. Sample size was calculated by the prevalence of carotid artery stenosis in diabetic patients. The prevalence was 10% and the sample size was 138. We collected 120 cases (60 diabetic and 60 nondiabetic) due to limited time duration. We

considered any history of diabetes mellitus, hypertension, ischemic heart disease, and smoking. All patients clinically suspected of having carotid artery disease were included in this study. Males and females were included. Unwilling and non-cooperative patients were excluded from this study. A convenient sampling technique was preferred. All patients were examined by Doppler ultrasonography using the TOSHIBA XARIO XG, which features a linear probe of 5–7.5 MHz frequency. The data was analyzed with the help of SPSS version 25.0. The data was reported using descriptive statistics. The mean  $\pm$  standard deviation of age, PI, RI, PSV, EDV, and IMT were calculated. An independent t-test was applied to compare Doppler indices in diabetic and non-diabetic subjects. The p-value is less than 0.05, which is significant [13].

## Results

In this study, 120 patients at the University Ultrasound Clinic Green Town were enrolled. Patients were divided into 2 groups: Diabetic and non-diabetic. Minimum age of the patient was 13 and maximum was 80. The Mean of weight was  $= 68.21 \pm 14.17$ . Out of 120 patients, females were 78 and males were 42. The diabetic group consisted of 60 patients (47 females and 13 males). The non-diabetic group consisted of 60 patients (31 females and 29 males). Risk factors learned from the patient's history were considered, and no laboratory tests were performed to look for additional risk factors. Ischemic heart disease, hypertension, and diabetes were observed in 14.2%, 60.0%, and 50% of patients, respectively. 18.3% were smokers. The percentage of diabetic patients with plaque was 13.3%, but there was no plaque in non-diabetic patients.

The mean and standard deviation of PSV of the right carotid artery were  $-71.41 \pm 22.09$  in non-diabetic patients while  $-64.56 \pm 39.53$  in diabetic respectively. The mean and standard deviation of EDV of the right carotid artery were  $-27.04 \pm 13.02$  in non-diabetic patients while  $-31.95 \pm 28.41$  in diabetic respectively. The mean and standard deviation of PSV of the left carotid artery were  $-67.10 \pm 20.99$  in non-diabetic patients while  $-64.75 \pm 29.20$  in diabetic respectively. In non-diabetic patients, the mean and standard deviation of EDV of the left carotid artery were  $-22.76 \pm 13.84$  while  $-25.10 \pm 15.17$  respectively (Table 1).

Right peak systolic velocity (R.PSV), Right end diastolic velocity (R.EDV), Left peak systolic velocity (L.PSV), Left end diastolic velocity (L.EDV) Mean peak systolic velocities of right and left carotid artery were compared in two groups (diabetic and non-diabetic). No statistically significant difference found between means of PSV of right carotid artery and left carotid artery in two groups as the mean difference between

PSV of right and left carotid artery were  $-6.84$  with p-value  $= 0.244 > 0.05$  and  $-2.35$  with p-value  $= 0.613 > 0.05$  respectively. Mean end diastolic velocities of right and left carotid artery were compared in two groups (diabetic and non-diabetic). No statistically significant difference found between means of EDV of right carotid artery and left carotid artery in two groups as the mean difference between EDV of right and left carotid artery were  $4.91$  with p-value  $= 0.227 > 0.05$  and  $2.34$  with p-value  $= 0.379 > 0.05$  respectively (Table 2).

Mean and standard deviation of IMT of right carotid artery was  $0.57 \pm 0.14$  in non-diabetic while  $0.63$  and  $0.17$  in diabetic patients respectively. Mean and standard deviation of RI of right carotid artery was  $0.63 \pm 0.18$  in non-diabetic while  $0.63 \pm 0.18$  in diabetic patients respectively. Mean and standard deviation of PI of right carotid artery was  $1.33 \pm 0.84$  in non-diabetic while  $1.02 \pm 0.48$  in diabetic patients respectively. Mean and standard deviation of IMT of left carotid artery was  $0.56 \pm 0.15$  in non-diabetic while  $0.64 \pm 0.13$  in diabetic patients respectively. Mean and standard deviation of RI of left carotid artery was  $0.64 \pm 0.14$  in non-diabetic while  $0.60 \pm 0.15$  in diabetic patients respectively. Mean and standard deviation of PI of left carotid artery was  $3.22 \pm 14.94$  in non-diabetic while  $1.11 \pm 0.42$  in diabetic patients respectively (Table 3).

Right intima media thickness (R.IMT), Right resistive index (R.RI), Right pulsatility index (R.PI), Left resistive index (L.RI), Left intima media thickness (L.IMT), Left pulsatility index (L.PI) IMT of right and left carotid artery was observed statistically significant in diabetic and non-diabetic as the mean difference between the right and left IMT was  $-0.063$  with p-value  $= 0.027 < \mu=0.05$  and  $-0.078$  with p-value  $= 0.003 < 0.05$ . A statistically significant difference found between mean PI of carotid artery of right side as p-value  $= 0.017 < 0.05$ . No statistically significant difference found between mean PI of carotid artery of left side as p-value  $= 0.277 > 0.05$ . A statistically significant difference found between mean RI of carotid artery of right side as p-value  $= 0.007 < 0.05$ . No statistically significant difference found between mean RI of carotid artery of left side as p-value  $= 0.120 > 0.05$  (Table 4).

## Discussion

Our objective was to assess carotid artery plaque or stenosis, which is a major cause of stroke and an early warning sign in both diabetic and non-diabetic patients. This is the only study conducted in Pakistan which explains the relation of Carotid artery disease in

	Group	N	Mean	Std. Deviation	Std. Error Mean
R.PSV	Non-Diabetic	60	-71.4117	22.08924	2.85171
	Diabetic	60	-64.5633	39.53445	5.10388
R.EDV	Non-Diabetic	60	-27.0417	13.02467	1.68148
	Diabetic	60	-31.9533	28.40635	3.66724
L.PSV	Non-Diabetic	60	-67.1033	20.99316	2.71021
	Diabetic	60	-64.7517	29.19512	3.76907
L.EDV	Non-Diabetic	60	-22.7583	13.83648	1.78628
	Diabetic	60	-25.1000	15.16539	1.95784

Table 1: Mean and Standard deviation between Doppler indices and diabetic/non-diabetic patients

		Levene's Test for Equality of Variances		t-test for Equality of Means							
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference		
										Lower	Upper
R.PSV	Equal variances assumed	2.652	.106	-1.171	118	.244	-6.84833	5.84652	-18.42603	4.72937	
	Equal variances not assumed	-	-	-1.171	92.566	.244	-6.84833	5.84652	-18.45908	4.76241	
R.EDV	Equal variances assumed	6.534	.012	1.217	118	.226	4.91167	4.03436	-3.07746	12.90080	
	Equal variances not assumed	-	-	1.217	82.758	.227	4.91167	4.03436	-3.11286	12.93619	
L.PSV	Equal variances assumed	.559	.456	-.507	118	.613	-2.35167	4.64232	-11.54472	6.84139	
	Equal variances not assumed	-	-	-.507	107.142	.613	-2.35167	4.64232	-11.55438	6.85105	
L.EDV	Equal variances assumed	.320	.573	.884	118	.379	2.34167	2.65027	-2.90660	7.58993	
	Equal variances not assumed	-	-	.884	117.021	.379	2.34167	2.65027	-2.90705	7.59039	

Table 2: Independent Samples Test between Doppler indices and diabetic/non-diabetic patients

	Group	N	Mean	Std. Deviation	Std. Error Mean
R.IMT	Non-Diabetic	60	.5700	.14297	.01846
	Diabetic	60	.6333	.16536	.02135
R.RI	Non-Diabetic	60	.6335	.17545	.02265
	Diabetic	60	.5373	.20691	.02671
R.PI	Non-Diabetic	60	1.3252	.84077	.10854
	Diabetic	60	1.0202	.48483	.06259
L.RI	Non-Diabetic	60	.6440	.14168	.01829
	Diabetic	60	.6022	.15051	.01943
L.IMT	Non-Diabetic	60	.5617	.14968	.01932
	Diabetic	60	.6400	.13045	.01684
L.PI	Non-Diabetic	60	3.2282	14.94931	1.92995
	Diabetic	60	1.1113	.41843	.05402

Table 3: Mean and Standard deviation between Doppler indices and diabetic/nondiabetic patients

		Levene's Test for Equality of Variances		t-test for Equality of Means							
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference		
										Lower	Upper
R.IMT	Equal variances assumed	.179	.673	-2.244	118	.027	-.06333	.02822	-1.1922	-.00745	
	Equal variances not assumed	-	-	-2.244	115.587	.027	-.06333	.02822	-1.1923	-.00744	
R.RI	Equal variances assumed	6.431	.013	2.746	118	.007	.09617	.03502	.02681	.16552	
	Equal variances not assumed	-	-	2.746	114.929	.007	.09617	.03502	.02679	.16554	
R.PI	Equal variances assumed	.811	.370	2.434	118	.016	.30500	.12530	.05688	.55312	
	Equal variances not assumed	-	-	2.434	94.331	.017	.30500	.12530	.05623	.55377	
L.RI	Equal variances assumed	.488	.486	1.568	118	.120	.04183	.02669	-.01101	.09468	
	Equal variances not assumed	-	-	1.568	117.570	.120	.04183	.02669	-.01101	.09468	
L.IMT	Equal variances assumed	.065	.800	-3.056	118	.003	-.07833	.02563	-1.2909	-.02757	
	Equal variances not assumed	-	-	-3.056	115.837	.003	-.07833	.02563	-1.2910	-.02756	
L.PI	Equal variances assumed	3.612	.060	1.096	118	.275	2.11683	1.93070	-1.70649	5.94015	
	Equal variances not assumed	-	-	1.096	59.092	.277	2.11683	1.93070	-1.74637	5.98004	

Table 4: Independent Samples Test between Doppler indices and diabetic/non-diabetic patients

both diabetics and non-diabetics. This study emphasizes the importance of doppler ultrasonography in the evaluation of carotid artery stenosis.

We had two patient groups—60 diabetic and 60 non-diabetic—each with risk indicators that could be detected by Doppler ultrasound. Our results suggest

that the main risk factors for carotid plaque or stenosis are diabetes, hypertension, smoking, and increasing age. In one of our literature studies, IMT has been described as an early signal for plaque formation in the carotid system, and it was proven to be a significant variable for carotid stenosis in our study [14], Age,

hypertension, diabetes, hyperlipidemia, and ischemic heart disease are some of the risk factors linked to carotid atherosclerosis [15]. In some studies, the location of plaque and the diameter of carotid arteries that can be affected by plaque have been different [16]. Risk variables, such as smoking and hypertension, were shown to be strongly related to carotid stenosis, as shown above in the analysis [17]. Hypertension was found to have a significant association with carotid atherosclerosis [18]. In most studies, it has a significant association with stroke, ischemic heart disease, peripheral vascular disease, cerebral infarction, and death [19, 20]. Only one study was found in our review that has shown a no association between hypertension and carotid stenosis [21].

Cigarette smoking has been found as a significant predictor for carotid stenosis in many studies [22]. In only 1 study, there was no link found between smoking and carotid stenosis [14]. Increasing age has been reported as a contributor to carotid artery stenosis in many studies [23].

Many studies have reported that males at all ages have a high prevalence of developing carotid atherosclerosis. However, postmenopausal females are also at high risk of developing carotid plaque [24]. Several studies have been reported that obesity (high BMI) may increase the risk of carotid atherosclerosis, which further acts as a greater risk factor for developing stroke and cerebrovascular disease [25, 26].

The right pulsatility index (PI) of ICA, which was found to be significantly associated with carotid artery stenosis in our study, has been found as a strong indicator for developing cerebrovascular and cardiovascular disease in various studies [27, 28]. The Right Resistive Index (RI) of ICA, which was found to be strongly correlated with carotid stenosis in our research, has been linked to carotid atherosclerosis and stroke [29, 30].

The most important variable that was discovered to be linked with carotid artery atherosclerosis was diabetes. Although it may not affect the development of atherosclerosis it acts as a risk element for atherosclerosis [25]. The pathophysiology of carotid atherosclerosis in diabetic patients depends upon multiple factors. The hallmark of diabetes is hyperglycemia. Hyperglycemia causes plenty of changes at the cellular level of vascular tissue that may help to speed up the atherosclerotic process. Diabetes causes cerebrovascular disease and cardiac embolism, which lead to stroke [31].

Diabetes was identified as a modifiable risk factor associated with high-grade carotid artery stenosis in a study by Baki Go ksan et al [14]. Doppler ultrasonography is a credible, precise, and noninvasive

method for evaluating carotid artery stenosis that is widely available. DU should be the best option for the follow-up of patients with carotid atherosclerosis, especially those over 65 or those with other risk factors such as hypertension, diabetes, etc.

In conclusion, diabetes is considered as one of the most important risk factors that shows a significant association with carotid artery disease. The most common complication of carotid atherosclerosis is stroke. For the prevention of stroke, the main steps are early detection and management of diabetes and modifying other risk factors. Current study had some limitations. The sample size was limited and the results cannot be generalized on a larger population. Most of the participants were females.

## Competing Interest

The authors declare that there is no conflict of interest.

## Author Contributions

Samira Shokri: Data analysis

Kourosh Saki: Monitoring of research

Yeganeh mazaheri and Samira Shokri: Drafting

Gholamreza Jahed khaniki: Manuscript scanning

Samira Shokri: Data evaluation

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