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ORIGINAL ARTICLE

Frequency of Peripheral Arterial Disease among Diabetic Patients

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ABSTRACT

Background: Peripheral artery disease, or PAD, is among the significant macro-vascular problems of diabetes mellitus and is connected with the cardio death rate and a higher rate of impairment after extremity amputation in people with diabetes. For that reason, the present research is targeted at figuring out the frequency as well as corresponding elements of Peripheral artery disease among diabetic patients at Hayatabad Medical Complex MTI, Peshawar.

Place and Duration of study: Hayatabad Medical Complex MTI, Peshawar, Pakistan. The duration of the study was 6 months from 5th September 2021 to 5th March 2022.

Methods: An institution based cross sectional research had been carried out among diabetes mellitus patients. A pre-tested interviewer administered a survey had been utilized to gather the information. The existence of stenosis, as well as its grading, had been influenced by color Doppler ultra-sonography. Adjusted odds ratios, along with their confidence interval (CI), were calculated for possible predictors within the ultimate model. P = 0.05 had been utilized to declare mathematical significance.

Results: The mean chronological age of the research respondents was 60.5 ± 8.4 years. Two hundred fifty (55.5 %) sufferers were men, and two hundred (44.4%) were women. Sixty-seven (63.4%) sufferers were symptomatic. Age (adjusted odds ratio = 2.11 (2.45-3.11), high Glycated Hemoglobin (adjusted odds ratio = 3.87 (3.53-6.98)), as an ex-smoker (adjusted odds ratio = 5.78 (3.73-22.12), and present cigarette smoker (adjusted odds ratio = 10.12 (3.90-38.34)) were considerably connected with peripheral artery disease.

Conclusion: The frequency of peripheral artery disease between people with diabetes was higher. Growing age, higher Glycated Hemoglobin, and smokers boost the probability of developing peripheral artery disease. Physicians must protect against peripheral artery disease, screen diabetic sufferers aged with higher Glycated Hemoglobin and people who smoke and treat them on time.

INTRODUCTION

Diabetes can be described as a complicated, serious metabolic condition needing consistent health care with multi-factorial risk decline techniques, illustrated as prolonged hyperglycemia due to insufficient insulin release, insulin reluctance, or even both (American Diabetes Association, 2017). Its frequency is continuously rising globally, most substantially within the lower- and middle-income areas (World Health Organization, 2018), just like Pakistan, which is the 1st between the top locations for many individuals with diabetic issues. Over time, diabetes results in early micro-complications, mononeuropathy, diabetic eye disease (DED), as well as peripheral kidney disease, and later macro-complications that are due to vascular diseases of the arterial blood vessels, such as peripheral arterial disease (PAD), heart disease, and cerebrovascular event that all are possibly deadly (Bekele, 2019). Of these, peripheral artery disease is among the severe problems of diabetes. PAD is described as an atherosclerotic thinning of peripheral arterial blood vessels of the lower limbs, belly, arms, as well as head, mainly including arterial blood vessels of lower limbs (Saeedi et al., 2019). It's a severe issue of vascular disease and a symbol of the hardening of the arteries in major bloodstreams such as the heart and cerebral veins (Munger and Hawkins, 2004). It leads to wide spread atherothrombosis that results in a cerebrovascular accidents, such as myocardial infarction (MI), heart stroke, severe long-term impairment, and loss of life. Diabetics with peripheral artery disease are at higher risk of elevated deaths and fatality rates from heart diseases, along with a higher rate of transfemoral amputation. This elevated threat of amputation in diabetic patients is a result of gangrenous necrosis, end stage demonstration of peripheral artery disease, and feet ulcer secondary to peripheral artery disease. Nearly 2/3rds of people with diabetes with foot ulcers have peripheral artery disease, that is connected with a significant amputation rate as well as fatality rate (American Diabetes Association, 2010).

The frequency of peripheral artery disease is 3-4 times higher and more severe in diabetic people than non-diabetic people. The worldwide frequency of peripheral artery disease is approximated to be 201 million. 12 % of the grownup population has peripheral artery disease. Earlier treatment and diagnosis of peripheral artery disease in diabetic patients are significantly important for risk factor customization, decrease in its frequency, development, and advancement of the consequence, bettering the standard of living, stopping cardio events, and reducing the potential risk of long-term impairment along with other problems connected with it (Mohamed et al., 2019). Although, most sufferers with peripheral artery disease are asymptomatic and don't complain of intermittent claudication because of reduced discomfort perception secondary to mononeuropathy (Olin and Sealove, 2010). Of people who are symptomatic, merely a small percentage of the diabetes population reports it as a result of a lack of knowledge regarding the signs of peripheral artery disease. This, consequently, setbacks the identification as well as diagnosis of peripheral artery disease. This asymptomatic nature, lack of knowledge, and underutilization of testing methods made peripheral artery disease untreated and underestimated. Although diabetic issues are extremely common in Pakistan, to cause serious problems just like peripheral artery disease, there is nothing acknowledged about the frequency and related aspects of peripheral artery disease among diabetics in Pakistan. Thus, this research aims to fill this gap by identifying the frequency and related elements of peripheral artery disease among diabetic patients at Hayatabad Medical Complex MTI, Peshawar. Moreover, this research provides info to the medical community and will be the base line for future experts (Nygaard et al., 2003).

METHODS AND MATERIALS

Research Area: An institution based cross sectional research had been carried out at Hayatabad Medical Complex MTI, Peshawar, Pakistan.

The population of the Study: All diabetes sufferers going to the diabetic follow-up at Hayatabad Medical Complex MTI, Peshawar had been the study's population source. This research involved all diabetes sufferers aged equal to fifty years who went to the

diabetes follow-up center at Hayatabad Medical Complex MTI, Peshawar, throughout the research period.

Exclusion and Inclusion Criteria: Almost all diabetic sufferers aged equal to and more than fifty years present throughout the research time had been involved. However, diabetic sufferers who have been seriously ill; sufferers with lower limb inflammation because of filariasis, swelling, and other factors that damage the Doppler picture quality; sufferers having a history of coronary disease such as cerebrovascular accident; as well as sufferers having a history of high blood pressure before a diagnosis of diabetes had been omitted from the research.

Sampling Procedure and Sample Size: The specified sample size for the research had been approximated with a single human population percentage method through a twenty-four percent percentage of peripheral artery disease between diabetics of the selected population, 0.05 significance level (a), and a five percent margin of error. Appropriately, the ultimate sample size for the research was 450. We uninterruptedly enrolled as many as 450 diabetic patients.

Data Collection Method: A pre-tested, interviewer administered survey had been utilized to gather information. The survey had been modified from earlier published content articles (Sigvant et al., 2017). To evaluate the signs of peripheral artery disease and intermittent claudication (Arora et al., 2019). Data collectors, as well as a supervisor, took part in information collection. Data had also been obtained from patient files. Anthropometric specifications were taken by using standard methods and adjusted tools. Bodyweight (kilograms) and height (centimeters) had been calculated in barefoot topics wearing light clothes. Body mass index had been determined as body weight divided by height squared (kilograms meter per square). Blood pressure level (BP) had been noted using the correct size, which covers 2/3 of the arm with the subject within the resting position. The arm used for Blood pressure measurement had been supported on the event table. Individuals had been inspired to rest for around five minutes, and when they got any caffeinated drinks, they relaxed for half an hour before dimension. A couple of continuous measurements had been taken five minutes aside, as well as the mean value had been utilized. Glycated hemoglobin was assessed by using a 902 Automated Analyzer.

Proper Diagnosis of Peripheral Artery Disease: Diagnosis of peripheral artery disease was developed by utilizing color Doppler sonography with a sensitivity of ninety-seven percent, specificity of eighty-one percent, as well as diagnostic precision of eighty-five percent (Shammas et al., 2017). To remove interobserver variance, a single expert radiologist carried out all Doppler research using color Doppler ultrasound.

Functional Explanations: Peripheral artery disease had been understood to be Grade-3 (fifty percent to ninety-nine percent stenosis) or four stenosis (hundred percent stenosis) by color Doppler ultrasound (Forouhi et al., 2007). Grade 1 is one percent to nineteen percent stenosis: average triphasic circulation with regular top systolic velocity along with spectral widening. Grade 2 is twenty percent to forty-nine percent stenosis: a triphasic waveform with a rise in peak systolic velocity = thirty percent in the proximal recording-site marked spectral broadening (ultrasound). Grade 3 is fifty percent to ninety-nine percent stenosis: a monophasic waveform with the rise in peak systolic velocity = hundred percent and noted spectral broadening. The distal-waveform is disproportionate. Grade 4 is a hundred percent stenosis: no onward flow recognized with modified flow patterns, both distal and proximal to the abnormal narrowing in a blood vessel (Hur et al., 2018). High blood pressure is systolic bp, and Diastolic BP of 140/90 mmHg or higher (Natsuaki et al., 2014). Common claudication had been thought of as the inclusion of leg pain, no matter if there was a problem in other areas. Atypical claudication was thought of as discomfort within the leg or butt without leg pain. No claudication had been thought of as discomfort within the hamstrings, legs, foot, or joints; any leg, upper leg, or butt ache that seems to expand; or even no pain in any way in different parts of the calf (Marks et al., 2003). For BMI, an individual with a Body mass index of 18.5-24.9 kg/m2, 25-30 kg/m2, and greater than 30 kg/m2 is recognized as normal, over weight, and obesity, correspondingly. Ex-smokers had been individuals who didn't presently smoke however had a history of smoking cigarettes within their life span. Present smokers were considered individuals who smoked a cigarette at least once within the last month prior to the research.

Data Analysis and Processing: Information had been accessed using an excel sheet. We indicated consistent information through the mean, standard deviation, and specific factors by proportions. After looking at its presumption, the Chi-square test had been utilized to look at the main difference among specific variables. Both multivariable and binary logistic regression analysis were carried out to discover risks for peripheral artery disease. Variables in bi-variable evaluation with P less than 0.2 had been entered into multi-variable logistic regression. In multi-variable logistic regression, parameters with P = 0.05 had been announced mathematically significant. Moreover, the connection of independent variables, which had been an applicant for the multi-variable logistic regression model, had been inspected. The effectiveness of the connection of risks with peripheral artery disease had been shown by calculating the crude odds ratio as well as the AOR with a ninety-five percent confidence interval.

Ethical Concern: Ethical authorization for the research had been acquired from the Hayatabad Medical Complex MTI, Peshawar. Written informed consent had been obtained from all research members, and confidentiality had been maintained. All the research subjects responded to the given pretested surveys willingly and confidently.

RESULTS:

Socio-demographic and Clinical Features of Research Participants: The research had been carried out on 450 diabetic sufferers. The mean age of the research individuals was 60.5 ± 8.4, which ranges from 45 to 90 years. Two hundred fifty (55.5 %) patients were male, and two hundred (44.4%) were female. The majority (66.6%) of the research participants reside in a major city. And one hundred and fifty (33.3%) lived in non-urban areas. Relating to academic status, 180 (40%) research participants can't write and read. One hundred and fifty (33.2%) research individuals were public employees. Ninety (20%) individuals have an education level of the middle, and 70 (15.5%) have an education level of metric and above. 189 (42%) of the research participants were diabetic for longer than ten years, 191 (42.2%) had diabetes from 10 to 19 years, and 70 (15.5%) had a history of diabetes from 20 years. The majority (63.3%) of the research participants had been over weight. Three hundred and fifteen (70%) participants use an OH agent as a cure alternative for diabetes. The mean Glycated Hemoglobin participants were 11.1 ± 4.11. Ninety (20%) and forty (8.8%) participants were ex-smoker and present smokers, correspondingly, although the remaining were non-smokers. Regarding high blood pressure status, 240 (53.3%) participants were presently hypertensive, while 250 (55.5%) had a history of high blood pressure (Table no. 1).

Table 1: Socio-demographic and medical features of diabetic sufferers, Hayatabad Medical Complex MTI Peshawar.

Variables	Categorizations	Frequency - Mean and Standard Deviation	Percentage
Age of the Participants		60.5 ± 8.4	
Gender	Male	250	55.5
	Female	200	44.4
Location	Urban	300	66.6
	Rural	150	33.3
Education	Cannot read and write	180	40
	Read and write	110	24.4

	Middle	90	20
	Metric and Above	70	15.5
Occupation	Cultivator	70	15.5
	Public Employee	150	33.2
	Buyer and Seller	120	26.6
	Housewife	100	22.2
	Others	10	2.2
Diabetes (year)	More than ten years	189	42
	10 to 19	191	42.2
	More than 20 years	70	15.5
Body Mass Index (kg/m^2)	Normal	101	22.4
	Over-weight	285	63.3
	Obesity	64	14.2
Types of anti-diabetic Medication	Oral Hypoglycemic	315	70
	Insulin	79	17.5
	Both insulin Oral Hypoglycemic	56	12.4
Glycated Hemoglobin (Percentage)		11.1 ± 4.11	
Smoking	Non-smoker	320	71.1
	Ex-smoker	90	20
	Smoking Currently	40	8.8
H/O Hypertension	NO	200	44.4
	YES	250	55.5
Current HTN Status	NO	210	46.7
	YES	240	53.3

Frequency of Peripheral Artery Disease and Standard of Stenosis in Diabetic Sufferers: Sixty-seven (63.4 %) patients have symptoms. Of people with symptoms, 50 (66.6%) had common irregular claudication (Table no. 2).

Table 2: Evaluation of peripheral artery disease symptoms among PAD positive and negative diabetic sufferers, Hayatabad Medical Complex MTI Peshawar.

Symptoms	Total	Peripheral	No Peripheral	Statistical
		Artery Disease (N= 140)	Artery Disease (n = 310)	Measure
		N (%)	N (%)	P-value
No Symptoms	310 (79.3%)	65 (20.9)	245 (79.03)	P < 0.0005
Symptoms	98 (20.7%)	67 (63.4)	31 (36.6)	
Typical Presentation of Illness	75 (12.5%)	50 (66.6)	25 (33.3)	P < 0.0005
Atypical Presentation of Illness	53 (8.0%)	19 (35.8)	34 (64.1)	

Aspects Related to Peripheral Artery Disease between Diabetic Sufferers: Crude association of dependent variables with the independent variable peripheral artery disease had been examined by binary logistic regression. Hence, age group, academic status, diabetes duration, Body mass index, kind of anti-diabetic drug used by the patient, glycated hemoglobin, smoking cigarettes, history of high blood pressure, and present hypertension was a prospect for the ultimate model. After modifying for possible confounders in the multi-variable evaluation, age group, glycated hemoglobin, and smoking were considerably related to peripheral artery disease. A one year rise in chronological age of diabetic patients was connected with a nine percent high odds (Adjusted Odds Ratio = 1.09, 95 % CI,11 (2.45-3.11) of peripheral artery disease. Each 1-3 % rise in glycated hemoglobin was related to 2.1 times (Adjusted Odds Ratio = 1.97, 95 % CI (1.03-3.40)) high odds of getting peripheral artery disease.

The odd ratio of peripheral artery disease among diabetic sufferers was 4.7 times greater (adjusted odds ratio = 4.68, 95 % CI (1.93-11.30)) in ex-smokers compared to non-smokers. Likewise, the odd ratios of odd peripheral ratios between diabetic sufferers were 5.8 times (adjusted odd ratios = 5.84, 95 % confidence interval (1.79-19.04)) high in present smokers compared to non-smokers (Table no. 3).

Table 3: Elements related to Peripheral Artery Disease between diabetes patients in multivariable and bivariable logistic regression explanations, Hayatabad Medical Complex MTI Peshawar.

Variables	Peripheral Artery Disease		OR (95% CI)	
	Yes (n = 140)	No (n = 310)	Crudes Odd Ratio	Adjusted Odd Ratio
Age	60.7 ± 9.1	55.7 ± 6.6	2.15 (1.15-2.01)	2.11 (2.45-3.11)**
Gender				
Male	65 (46.6)	210 (67.7)	2.75 (1.90-3.45)	
Female	75 (53.5)	100 (32.3)	3	
Location				
Urban	69 (49.2)	220 (70.9)	2.56 (1.75-3.25)	
Rural	71 (50.8)	90 (29.1)	3	3
Education				
Illiterate	44 (31.4)	113 (36.4)	2.98 (2.39-3.11)	2.67 (2.66-3.11)
Literate	38 (27.1)	79 (25.4)	3.11 (2.66-3.98)	2.15 (2.14-3.14)
Middle	22 (15.7)	66 (21.3)	3.98 (3.03-5.89)	2.98 (1.89-4.78)
Metric	36 (25.7	52 (16.7)	3	
Profession				
Cultivator	55 (39.2)	62 (20)	3	
Public Servant	39 (27.8)	104 (33.5)	2.9 (2.55-3.98)	
Buyer and Seller	26 (18.5)	90 (29.1)	2.7 (1.96-6.12)	
Housewife	27 (19.2)	26 (8.4)	2.00 (1.92-3.70)	
Others	3 (2.1)	28 (9.1)	1.96 (1.34-5.30)	
Duration of Diabetes				
Less than 10 Years	62 (44.3)	157 (50.6)	3	
10 to 19 years	51 (36.4)	120 (38.7)	3.70 (3.10-5.95)	
Greater than equal to 20 years	27 (19.3)	33 (10.6)	8.29 (4.52-39.99)	
Body Mass Index (kg/m2)				
Normal Weight	29 (20.7)	26 (8.4)	3	
Over-weight	62 (44.3)	250 (80.6)	2.20 (2.53-2.53)	2.94 (2.37-3.91)
Obesity	49 (35)	34 (10.9)	20.56 (2.50-2.67)	2.90 (2.44-7.99)
Anti-diabetic Medication in use				
Oral Hypoglycemic	79 (56.4)	166 (53.5)	2.69 (2.91-3.91)	2.87 (3.23-3.15)
Both Insulin & Oral Hypoglycemic	38 (27.1)	106 (34.2)	4.19 (3.61-10.98)	3.68 (3.66-4.96)
Insulin	23 (16.4)	38 (12.3)	3	
Glycated Hemoglobin (%)	9.9 ± 2.2	8.9 ± 2.1	4.14 (2.98-4.99)	3.87 (3.53-6.98)*
Smoking				

Non-smoker	47 (33.6)	231 (74.5)	3	
Ex-smoker	83 (59.3)	51 (16.5)	10.12 (4.65-20.53)	5.78 (3.73-22.12)**
Current smoker	10 (7.1)	28 (9.03)	11.99 (4.98-36.50)	10.12 (3.90-38.34)**
H/O Hypertension				
Yes	96 (68.6)	200 (64.5)	3.28 (2.98-3.90)	
No	44 (31.4)	110 (35.5)	1	
Current HTN				
Yes	94 (67.1)	198 (63.8)	4.99 (3.99-10.40)	3.99 (3.98-8.35)
No	46 (32.8)	112 (36.1)	3	

DISCUSSION

Total of 450 people with diabetes had been involved in the research. Color Doppler ultrasound proven frequency of peripheral artery disease between diabetes sufferers was 30.7 %.

This higher frequency is because of dyslipidemia, hyperglycemia, as well as insulin reluctance, secondary to diabetes, that all cause advancement as well as the advancement of peripheral artery disease or vascular disease by interfering with the vessel wall via promotion of general swelling and cell disorder, derangements of several cell types just like platelets in the general wall, promotion of coagulation, as well as inhibition of fibrinolysis (Williams et al., 2003).

Color Doppler sonography was utilized in the present study; that's the best diagnostic method in comparison with some other diagnostic techniques, such as the brachial ankle index, that can undervalue the frequency of peripheral artery disease (Piscaglia et al., 2012). Another possible reason behind the distinction might be a variance in the chronological age of research members, drug adherence, as well as treatments for diabetes. In the present research, age group, glycated hemoglobin, current smoker, and ex-smoker were considerably related to peripheral artery disease. Each one year rise in the age of diabetic sufferers was related to nine percent high odd ratios of developing peripheral artery disease. The reason behind a surge in the frequency of peripheral artery disease with a rise in age is that as we grow older, each layer of the bloodstream alters in complicated methods and activates arterial stiffening as well as thickening. Thickening of the intima because of getting older compromises endothelium-integrity and reduces the accessibility of nitric-oxide, a known vasodilator. Stiffening of the artery walls affects normal blood circulation, which makes it simpler for fatty debris to develop inside arterial blood vessels, which results in more fatty build-up as well as thinning of the vessels causing peripheral artery disease (Calcagno et al., 2013).

Each one percent rise in glycated hemoglobin was related to 1.9 times high odd ratios of building peripheral artery disease. These findings were similar to the results of other scientific studies (Norgren et al., 2007). This is due to the result of the procedure for glycation. Since glycated hemoglobin is a substance produced in the non-enzymatic glycation response of glucose as well as hemoglobin, particularly in inadequately managed diabetes (Marso and Hiatt, 2006), a boost in glycated hemoglobin is related to elevated glycation, non-enzymatic inclusion of glucose to amino-groups of proteins, because of hyperglycemia. Glycation improves the covalent holding of lipoproteins to vascular walls, promoting sequestration and causing irritation that all result in the introduction of vascular disease and peripheral artery disease. Antithrombin 3 might also be glycated, leading to disability of the function while increasing the thrombotic inclination that consequently activates vascular disease (Jude, 2004).

Regarding smoking cigarettes, the present research demonstrated that the odds ratios of peripheral artery disease among diabetic sufferers were 5.8 as well as 4.7 times high in the present cigarette smoker and ex-smokers, correspondingly than non-smokers. Research carried out in the USA demonstrated that current people who smoke have Four times more likelihood of peripheral artery disease than nonsmokers (Eraso et al., 2014). Likewise, research in the UK indicated that smoking cigarettes could lead to a sevenfold rise in the potential risk of peripheral artery disease (Soyoye et al., 2016). People who smoke tend to be more vulnerable to peripheral artery disease because of the poisonous aftereffect of nicotine, deadly carbon monoxide, and other components inside in bloodstream. Nicotine affects endothelium dependent vasodilatation by decreasing NO manufacturing (Hiatt, 2001). Nicotine energizes the launch of catecholamine that raises platelet aggregability. Platelets give rise to the development of build-up throughout the accumulation of thrombus. Nicotine also causes insulin reluctance and dyslipidemia, vascular irritation, disproportionate vascular development, and lack of endothelial homeostatic and restorative features.

Additionally, nicotine has immediate actions on the cellular factors in plaque development. These results of nicotine predispose to PAD (Gregg et al., 2004), plus throughout the release of development components that creates vascular muscle cell expansion. Furthermore, nicotine has immediate methods on the cellular factors taking part in plaque development to improve plaque development individually of plasma lipid valuations (Yancy et al., 2016).

Within this research, gender, current hypertension, period of diabetes, kind of anti-diabetic drug used, and Body mass index wasn't considerably related to peripheral artery disease. It is demonstrated that female gender, current hypertension, being on sulfonylurea glibenclamide, period of diabetes, and Body mass index are substantially linked to peripheral artery disease. This difference may be because of an alteration in features of the research population, sample size, medication compliance, and research design (Edward et al., 2001).

Limitation of the Research: This research had constraints that need to be considered. As the research participants had been taken from just one diabetes center, the results might not signify that of the common diabetic people. Although the usage of antiplatelet agent medicines might impact vascular function, we could not find data regarding it. Despite all these constraints, we identified peripheral artery disease using color Doppler sonography, the best imaging method to identify peripheral artery disease with no negative effects.

CONCLUSION

The frequency of peripheral artery disease among diabetics was high. Age group, glycated hemoglobin, and smoking were considerably connected with peripheral artery disease. Physicians should protect against peripheral artery disease; test all diabetic sufferers, particularly those older, with higher glycated hemoglobin, and smokers; and cure them on time. Large-scale research, including lipid profiles along with other essential lab tests, must be done in several diabetes centers.

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