FREQUENCY OF LMS AND TVD IN TYPE 2 DIABETIC ADULTS VS NON-DIABETICS IN CAD POPULATION OF PAKISTAN

Dr Ayesha Fayyaz[1], Dr Khayyam Haider[2], Dr Ikram Ullah[3*], Dr Arshad Mehmood[4], Dr Syed Hassan Iftikhar[5], Dr Asaf Syed[6]

[1]Cardiology, Lady Reading Hospital and Medical Teaching Institute, Peshawar, Pakistan
[2]House Officer, General Surgery, Lady Reading Hospital, Peshawar, Pakistan
[3*]Associate Professor, Lady Reading Hospital and Medical Teaching Institute, Peshawar, Pakistan
[4]Postgraduate Resident General Medicine, Hayatabad Medical Complex, Peshawar, Pakistan
[5]Internal Medicine, Lady Reading Hospital and Medical Teaching Institute, Peshawar, Pakistan
[6]House Officer, Internal Medicine, Ayub Teaching Hospital, Abbottabad, Pakistan

*Corresponding Author: Dr Ikram Ullah
*E-mail: Ikramcardio@yahoo.com

ABSTRACT
Objective: The current study aimed to compare the prevalence of left central stem disease and triple vessel disease in coronary artery (CAD) patients with and without type 2 diabetes.
Study Design: Cross-sectional study
Research Setting and Duration: The study was conducted at the cardiology department, Lady Reading Hospital, Peshawar, from 6th June 2022 to 26th December 2022.
Methods: In this study, 155 patients diagnosed of having CAD were identified. In all the patients, coronary angiography was performed to evaluate the status of the coronaries. Patients with occlusion of LAD, RCA, and LCX on angiography were considered to have triple vessel disease and LMS occlusion was consider as a separate entity.
Results of the study: The patients' ages ranged from 40 to 70 years. The mean age was 59.3±12.3 years. Male to female ratio was 3:1. Out of the 155 participants, 65 (41.9%) were diabetic, and 92 (59.4%) were hypertensive. As per the number of vessels obstructed, 37(23.87%) patients had single-vessel CAD, 47(30.32%) had double-vessel CAD, and 71(45.81%) had triple-vessel CAD. There were a total of 15 (9.68%) LMS cases, out of which 8(5.33%) were diabetic patients, and 7(4.52%) were nondiabetic patients. There was a significant association found between diabetes and TVD.
Conclusion: In CAD patients, there is a high prevalence of triple vessel coronary artery disease, and diabetic patients are more prone to have TVD than non-diabetic patients.

Keywords: CAD, Triple vessel CAD, Double vessel CAD, Single vessel CAD, Coronary artery

Introduction
Background:
Around the world, the rates of cardiovascular diseases (CVD) have considerably risen and coronary artery disease (CAD) is the primary cause of it. This in terms of clinical care of advanced stages of CAD namely left main stem disease (LMS) and triple vessel disease (TVD) poses serious challenges.

University of Liverpool. Here in Pakistan, according to the current prevalence rates, 20% of middle-aged people are suffering from CAD, and amongst those, a good percentage have LMS disease; that is, whenever there is 50% or more stenosis in the left main coronary artery. As for drug therapy this disorder has a 50 percent three year mortality rate and this must be dealt with as urgent. In addition, He further stated that multivessel CAD; which they defined as double or triple stenosis of the respective 70% or more of the LCA, RCA, or left circumflex artery, is present in 70% instances of LMS disease (1).

Cardiovascular disease has a complex genetic and environmental determinants in conjunction with the lifestyles. The CAD risk factors include Homocystinuria, Diabetes Mellitus, Hypertension, Smoking, Obesity and Hyperlipidemia (2). Among these, diabetes mellitus (DM) is the leading chronic disease in the globe and has a firm association with CAD (3). DM patients have been additionally recognized to have a faster progression of atherosclerosis, endothelial injury as well as coronary plaque formation and due to this, they have higher chances of developing multivessel coronary disease (4).

Pakistan is ranked eighth in the world for the prevalence of diabetes, with 16.98% of the population estimated to have type 2 diabetes in 2017. Predictions suggest that the number of diabetes cases in Pakistan will continue to rise, making it the fourth most affected nation by 2030 (5). Having trouble with glucose increases the risk of CAD. The advancement of atherosclerosis is made worse by elevated glucose levels, insulin resistance in diabetes mellitus, and oxidative stress brought on by inflammation. People with CAD who are diabetics have a greater risk of major adverse cardiac events (MACE) compared to those without diabetes (6).

A thorough assessment of the literature reveals that nothing is known regarding the incidence of severe LMS and triple vessel disease in diabetes patients in Pakistan. There are no conclusions that can be drawn from literature and applied generally. So, the researchers intended to count how many CAD patients had triple vessel disease and how it is linked with diabetes in Pakistani individuals. This research aims to compare the prevalence of left main disease and triple vessel disease in coronary artery disease (CAD) patients with and without diabetes.

MATERIALS & METHODS
Study Design and Participants
Consequently, the design used in the study was cross-sectional to determine the prevalence rate of TVD and LMS in CAD patients. This research work was conducted on patients attending the Cardiology department in Lady Reading Hospital, Peshawar for a period extending from 6th June 2022 to 26th December 2022. The ethical consent was obtained from the Research Review Board of Lady Reading Hospital (356/LRH/MTI) and try to include the patients of the Cardiology indoor department with inclusion criteria.

Inclusion and Exclusion Criteria
In this study, the required number of participants with CAD comprised 155 patients. 65 diabetic and 90 non-diabetic patients who underwent coronary angiography were chosen. These patient populations include; patients above 40 years of age, type 2 diabetes patients, Acute coronary syndrome, Chronic coronary syndrome. Those with familial hypercholesterolemia, a history of prior revascularization (PCI or CABG), chronic kidney disease, connective tissue disorders, and hypercoagulable states were excluded. Coronary angiography was done to look for luminal stenosis(CAD) with the intention of possible revascularisation. LAD, RCA and LCX occlusion on angiography were categorised as triple vessel disease, and LMS occlusion was studied separately. Patients' informed consent was sought to avoid disclosure of their identity and no possible harm would be inflicted on them in the process of the study. An interview schedule used to gather information from the participants was developed. Previous; patients' demographic information was

gathered which included age (years), gender, a history of hypertension, smoking, and diabetes, and weight and height to determine the BMI (kg/m2). The individual attained a BMI of 18. 5-24. The normal body weight for a man is about 9 kg/m2 while the recommended normal body weight range for a woman is within 20 – 25. 0-29. overweight as having a body mass index of between 25 and 29. 9 kg/m2, and obese as having a body mass index of 30 kg/m2 and above. In the second step, basic investigation were commanded such as HbA1c. HbA1c test result requirements must be below 5. 7% was normal or non-diabetic according to the status. Patients were defined based on prediabetes with values ranging from 5. 7% and 6. 4%. As well as what if HbA1c was 6. Diabetic was defined if the person had a self-reported diagnosis of diabetes, or if the participant's fasting blood sugar level was equal to or greater than 5% or if the person used insulin or oral hypoglycemic agents. Next, ECG and echocardiography of the patients were done to the presence of old ischemic changes and wall motion abnormalities. Elective and urgent coronary angiography was done following guidelines for high-risk patients.

The coronary angiographies were done by consultant cardiologist with a minimum of 05 years post fellowship experience and the researcher assisted them. Coronary artery disease was described in relation to how often the patients had triple vessel coronary artery disease. Severe and moderate stenosis of LAD, LCX, and RCA equal or more than 70% by visual estimation and by using quantitative analysis on coronary angiogram was defined as TVD and severe stenosis or more than 50% on left main coronary angiogram as LMS; LAD = left anterior descending artery; LCX = left circumflex artery; RCA = right coronary artery. Statistical analysis was done by the IBM SPSS version 23 statistical analysis program. For qualitative variables which are gender, as well as the triple vessel and left main-stem disease, frequencies and percentages were recorded. For quantitative variables; age, and HbA1c values the mean ± standard deviation was calculated. On the association of LMS with other variables, test used was chi-square test. To find the odds of Diabetes as a predictor of triple vessel CAD, multiple logistic regression test was carried out. P-value ≤ 0. 05 was regarded as significant on the statistical level.

RESULTS
In this study therefore, the ages of the patients ranged from 40 to 70 years. The mean age was 59.3±12.3 years. As per the gender distribution, 75.5% were males and 24.5% were females. Based on the BMI categorization, 83.8% of the patients were average weight, and 16.2% were overweight. Related to the habit of smoking, only 19.4% were smokers, and 80.6% were non-smokers. Data is summarised in Table 1.

Table 1. Distribution of samples as per demographic details

Variables	
Age (mean±std)	59.3±12.3
Gender n (%)	
Male	117(75.5%)
Female	38(24.5%)
BMI n(%)	
Normal	130(83.8%)
Overweight	25(16.2%)
Smoking n(%)	
Smokers	26 (19.4%)
Non-smokers	129 (80.6%)

In the second section of the study, participants were asked about their comorbidities, and their HbA1c test was performed. Results concluded that the mean HbA1c value was 6.7±2.3. Out of the 155 participants, 65 (41.9%) were diabetic and 92 (59.4%) were hypertensive. Data is summarised in Table 2.

Table 2. Distribution of samples as per the prevalence of co-morbidities

Variables	
HbA1C (mean±std)	6.7±2.3
Diabetes n (%)	
Yes	65(41.9%)
No	90 (58.1%)
Hypertension n (%)	
Yes	92 (59.4%)
No	63 (40.6%)

As the population under study was the CAD patients, their type of CAD was evaluated, and it was found that 37(23.87%) patients had single-vessel CAD, 47(30.32%) had double vessel CAD, and 71(45.81%) had triple vessel CAD. Patients were further categorized based on the prevalence of the type of CAD with the comorbidities, and it was seen that 43(27.7%) diabetic patients had TVD and 50 (32.26%) hypertensive patients had TVD. Data is summarised in Table 3.

Table 3. The distribution of number of vessels involved in CAD with the prevalence of co-morbidities

	svcad	dvcad	tvcad	Total
Diabetes Mellitus				
yes	12 (7.75%)	10 (6.45%)	43 (27.74%)	65 (41.94%)
no	25 (16.13%)	37 (23.87%)	28 (18.06%)	90 (58.06%)
Hypertension				
yes	20 (12.9%)	22 (14.19%)	50 (32.26%)	92 (59.35%)
no	17 (10.97%)	25 (16.13%)	21 (13.55%)	63 (40.65%)

Under Angiogram, 15 (9.68%) participants were found to have LMS occlusion, there were 9(5.8%) males, 6(3.87%) were females, 10(6.45%) were hypertensive, 8(5.35%) were diabetic and 3(1.94%) were smokers. Based on the Chi-square test there was no significant association found between LMS and other variables, presented in Table 4.

Table 4. Distribution of samples based on frequency of LMS

Variables	Frequency (%)	p-value
Gender		
Male	9 (5.8%)	**0.127**
Female	6 (3.87%)	
Hypertension		
Yes	10 (6.45%)	**0.376**
No	5 (3.23%)	
Diabetes		
Yes	8 (5.33%)	**0.251**
No	7 (4.52%)	
Smoking		
Yes	3 (1.94%)	**0.94**
No	12 (7.74%)	

To determine whether there is an association of the independent variables with types of CAD, multiple logistic regression tests were conducted. It was seen that there was a significant association between diabetes and TVD ($p<0.05$) as well as BMI was found to be significantly associated with TVD, too. Data is summarized in Table 5.

Table 5: Multivariate analysis of the association of number of vessels involved in CAD with other variables

Type of CAD		B	Std. Error	Wald	Sig.	Exp(B)	95% Confidence Interval for Exp(B)	
							Lower Bound	Upper Bound
dvcad	Intercept	1.137	1.965	.335	.563			
	Gender	-.755	.567	1.773	.183	.470	.154	1.429
	Smoking	.446	.525	.721	.396	1.562	.558	4.375
	BMI	-1.038	.632	2.694	.101	.354	.103	1.223
	HTN	.092	.472	.038	.845	1.096	.435	2.765
	DM	.188	.545	.118	.731	1.206	.415	3.511
tvcad	Intercept	6.259	1.883	11.053	.001			
	Gender	-.897	.539	2.771	.096	.408	.142	1.173
	Smoking	-.018	.529	.001	.973	.982	.348	2.770
	BMI	-1.138	.577	3.888	.049	.320	.103	.993
	HTN	-.551	.463	1.415	.234	.576	.232	1.429
	DM	-1.473	.484	9.281	.002	.229	.089	.591
a. The reference category is: svcad.								

DISCUSSION

This study found that 45.81% of people had TVD. Out of the 155 CAD patients, 41.9% were diabetic, and 27.7% of diabetic patients had TVD. The results of the study are similar to those of other recent studies. Significant LMS was found to be in 9.6% of the patients. Male patients with advanced age are more likely to have TVD. Diabetic patients are more prone to TVD than non-diabetic patients. LMS was not found to be significantly associated with diabetes. A similar study was conducted in Hyderabad, Pakistan, including 114 patients aged more than 20 years; as per their results, the majority (52%) had Left main (LM) / 3 vessels illness, 22% had single vessel illness, and 25% of people had two vessels (P value <0.0001) (7). Another similar study was conducted in Karachi; out of 250 patients taken as samples, TVD was found in 107 (42.8%) patients. A comparative analysis of triple vessel disease between diabetics and non-diabetics revealed a significant difference (p-value =0.030)(8). In Punjab, a similar study was conducted in Lahore; TVCAD was seen in 23.29% of acute coronary syndrome individuals under the age of 40 (9). There was no major study conducted in KPK, so the current study revealed that the prevalence of TVCAD in Peshawar KPK was 45.81%.

A survey by Hussein et al. revealed that 44. 7% of the patients, severe LM/3 vessel disease was identified. Meanwhile, one study by Masami et al identifying the proportion of patients with an inferior wall MI with LM/3VD noted an additional 31 percent (10). In the current study, FCG technique was used in LM/3 indication. A trial stated that an ST segment change >1mm in lead aVR and positive troponin T level on initial assessment are predictors of severe LM/ 3 valve disease (11). This research also showed that ST-segment elevation in leads aVR > 0. Scholars affiliated 4. 5mm with left severe central artery disease of (P value < 0. 0001). Regarding the quantity or dispersion of ST-segment depression in these studies, it can be stated that there is enough data to say that the ECG should be able to predict the clinical outcome in patients with NSTEMI better (12).

Hedge et al; showed that in coronary angiography, the prevalence of triple-vessel CAD was higher in diabetic patient 47% as compared to 31% in non-diabetic, and the prevalence of single-vessel disease was lower in diabetic patients, 18% compared to 32% in non-diabetic patient (17, 18).

This study aimed to compare the level of TVD occurrence to the ratio of diabetes cases, and it was identified that the rate of diabetes in the workplaces with selected essential sectors was 27. About 7% of the patients had both TVD and diabetes. Furthermore, the analysis by regression showed that TVD was significantly related with diabetes. A study was carried out further to examine the specifics of the relationship between coronary artery disease and Hba1. Overall HbA1c levels and endpoint events regarding patients with TVD and diabetes of various age groups. The subjects who self-reported to be younger indeed presented higher HbA1c level associated with increase hazards of both death and MACCE. In contrast, in the elderly patients, low HbA1c values (HbA1c < 6 %) predicated the

increased mortality and MACCE (13, 14). The current study finds a lot of support in similar research undertaken by other scholars. Afsar et al. also observed that diabetic patients had a significant prevalence in triple vessel CAD (32. 78% as against 27. 15% of non –diabetic patients (15, 16). A study by Hedge et al. showed that in coronary angiography, the prevalence of triple-vessel CAD was higher in diabetic patient 47% as compared to 31% in non-diabetic, and the prevalence of single-vessel disease was lower in diabetic patients, 18% compared to 32% in non-diabetic patient (17, 18). The current study provides an overview of the prevalence of TVCAD in KPK CAD patients and its association with diabetes.

Limitation of the study
The main limitation of this study was in terms of sample size; thus, future studies on sample size, and follow-up should be accomplished. The findings depict that as the sample has been taken from a particular hospital, it may not be generic enough to represent the population of Peshawar KPK, therefore, results cannot be generalized. Moreover, the diagnostic criteria concerning diabetes, CAD, and several types of coronary artery disease might also bring the inconsistency issue.

CONCLUSIONS
Triple vessel disease is quite prevalent in CAD patients. Significant LMS was found to be in 9.6% of the patients. Male patients with advanced age are more likely to have TVD. Diabetic patients are more prone to TVD than non-diabetic patients. LMS was not found to be significantly associated with diabetes. Studies should be done to evaluate potential treatment options for advanced vessel disease to lower the mortality related to CAD.

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