Original Article

OPEN ACCESS

Frequency of Myocardial Infarction in Type II Diabetic Patients with Peripheral Arterial Disease

Malik Muhammad Arif[1], Muhammad Arif Mahmood[2], Mehboob Qadir[3], Muzammil Irshad[4], Humayun Riaz Khan[5], Sheikh Abdul Khaliq[6]

[1]Senior Registrar, Nishtar Medical University Multan
[2]Associate Professor of Medicine, Quaid-e-Azam Medical College, Bahawalpur
[3,5]Senior Registrar, [4]FCPS Trainee (Medicine), Nishtar Medical University and Hospital Multan

Author`s Contribution	ABSTRACT
[1,3]*Substantial contributions to the conception or design of the work; or the acquisition, analysis and* [2]*Final approval of the version to be published* [3-6]*Active Participation in active methodology, literature review* **Address of Correspondent** *Dr Malik Muhammad Arif* *Senior Registrar* *Nishtar Medical University Multan* *drmalikarif@gmail.com*	**Objective:** To determining the frequency of MI in diabetic Pakistani patients with PAD in a Pakistani tertiary care hospital. **Methodology:** A cross-sectional study was carried out at Diabetes Research Centre, Nishtar Hospital Multan for six months from July 2018 to January 2019. As per study inclusion/exclusion criteria, the patients suffering from DM with PAD were enrolled, after signing the study informed consent. Each patient underwent electrocardiogram (ECG) recording by the first researcher himself. Patients having pathological Q waves (0.04 seconds wide and 2 mm deep) in two relevant leads were labeled as having a myocardial infarction. **Results:** Out of a total of 290 patients (men: 56.2% and women: 43.8%) with mean age of the patients was 51.29 ± 8.54 years with age range of 40-85 years. There were 71 (24%) smokers and 219 (76%) non-smoker patients. Fifty percent of the total patients were obese. The mean duration of diabetes was 7.39 ± 0.36 years whereas mean duration of peripheral arterial disease was 1.604 ± 0.005 years. The frequency of MI among diabetic patients with PAD was 14.8%. **Conclusion:** Prevalence of 14.8% MI in the present study alarms to diagnose and treat diabetes and PAD patients at an earlier stage. **Keywords:** Diabetes Mellitus, Peripheral Arterial Disease, Myocardial infarction, Ischemic heart disease.

Introduction

PAD is a serious condition that arises due to stenosis or occlusion of arteries excluding those arteries which take the blood to the heart and brain. This blockage results in changes in normal quality of life.[1,2] Patients who have PAD are found to be complaining about the fatigue, cramping, and pain that is usually common in the lower extremities. More than 200 million people had developed PAD with varying symptoms.[3,4]

Multiple reasons are there which are a common part of life but cause PAD. The most common cause of PAD is smoking.[5] Smoking causes the lower oxidation of the blood resulting in the accumulation of plaque in the arteries.[(6)] High blood pressure, atherosclerosis, high cholesterol are the other leading risk factors for PAD. These risk factors become dangerous when they are

present in concomitant with diabetes mellitus. Both men and women are affected by PAD; however, African Americans have an increased risk of PAD.[7] Hispanics may have similar to slightly higher rates of PAD compared with non-Hispanic white people. Approximately 6.5 million people age 40 and older in the United States have PAD. PAD is a symbol of closed or narrowed arteries which develop pressure on the heart. As the supply of oxygenated blood deficits, the heart suffers from myocardial infarction.[8] Diabetes mellitus is an emerging epidemic, which refers to persistent hyperglycemia or glucose intolerance due to relative or absolute deficiency of insulin. Type I diabetes mellitus (T1DM) is caused by the autoimmune destruction of pancreatic B cells while T2DM is a heterogeneous syndrome characterized by abnormalities in carbohydrate and fat metabolism.[9]

Cardiovascular diseases (CVDs) are an important public health issue and the leading cause of death globally.[10] This is even a bigger problem for developing countries like Pakistan, which still face the heavy burden of both communicable diseases and non-communicable diseases.[11] Myocardial infarction is sub-entity of Ischemic Heart Disease (IHD) in which there is formation of occlusive thrombus at the site of rupture or erosion of an atheromatous plaque in the coronary artery. Diabetes mellitus, peripheral arterial disease (PAD) and others like smoking and obesity are recognized risk factors of IHD.[12]

Peripheral Arterial Disease (PAD) refers to a clinical disorder where stenosis or occlusion occurs in the aorta or arteries of the lower limbs.[13] The incidence of MI in patients with PAD is 5.2%.[14]

Diabetes, smoking, hypertension, and hyperlipidemia are important risk factors for peripheral arterial disease.[15] PAD is reported to be common among diabetic patients in Pakistan that needed to be evaluated.[16]

This study was conducted to determine the frequency of MI in diabetic patients with PAD, using non-invasive testing to determine the frequency of Q-wave myocardial infarction. This study will elucidate the early screening of the patients with T2DM and PAD, adopting preventive measures to decrease the frequency of MI in these patients.

Methodology

A cross-sectional study was carried out at Diabetes Research Centre, Nishtar Hospital, Multan for six months from July 10, 2018, to January 09, 2019. Patients of age 18 years or above suffering from DM and PAD were included in the study. Patients having any other major disease like a chronic renal failure (CRF), cerebrovascular accident (CVA), and cirrhosis of liver were excluded. The study was approved by the institutional ethical board and written informed consent was attained from all participants. The sample size of the study is estimated using 95% confidence interval with a 5% margin of error as 290 cases of DM.

The patients with fasting plasma glucose concentration of > 126 mg/dl (7.0 mmol/L) were regarded as diabetics.[17] Ankle Brachial Index (ABI <1.0) was used to diagnose PAD.[18] ABI measures the ratio of blood pressure in lower legs to blood pressure in the arms. Myocardial infarction (MI) was diagnosed based on electrocardiogram (ECG) changes consistent with

pathological Q wave (0.04 seconds wide and 2 mm deep) in two relevant leads i.e. inferior wall (II, III & aVF leads), lateral wall leads (1, aVL, V5 and V6 leads) and anteroseptal wall (V1, V2, V3 and V4 leads)[19]

Patients who fulfilled the inclusion and diagnostic criteria as mentioned above were included. Each patient was subjected to ECG recording done by the researchers themselves. All data were entered in a specifically designed proforma, which were then entered into software SPSS version 20.0. Mean and standard deviation (SD) were calculated for age. Frequencies (percentages) were calculated for gender and the presence or absence of pathological Q waves on ECG. Data was analyzed using SPSS version 23inc. Descriptive statistics was estimated and presented in form of tables..

Results

Out of 290 patients, 163 (56.2%) were males and 127 (43.8%) were females with male to female ratio of 1.3:1 Mean age of the patients was 51.29 ± 8.54 years with age range of 40-85 years. There were 121 (41.72%) patients between 40–49 years, 107 (36.90%) patients between 50–59 years, 50 (17.24%) patients between 60–69 years, and 12 (4.14%) patients of the age 70 years or above. There were 71 (24%) smokers and 219 (76%) non-smoker patients (Figure 1).
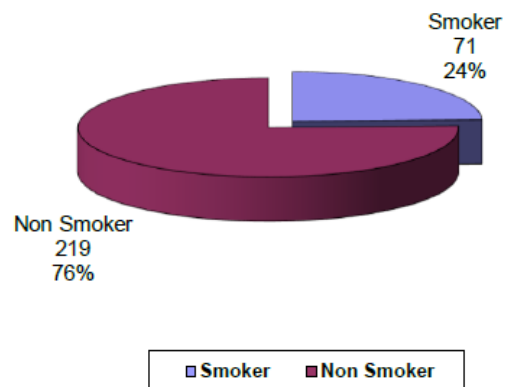

Figure 1. Frequency of smokers in the study

Fifty percent (145) of the total patients were obese (Figure 2). Out of 290 cases, duration of diabetes was 0-9 years in 207 (71.4%) patients, 10-19 years in 67 (23.1%) patients, 20-29 years in 13 (4.5%) patients, and ≥30 years in 3 (1%) patients with mean duration of diabetes of 7.39 ± 0.36 years.
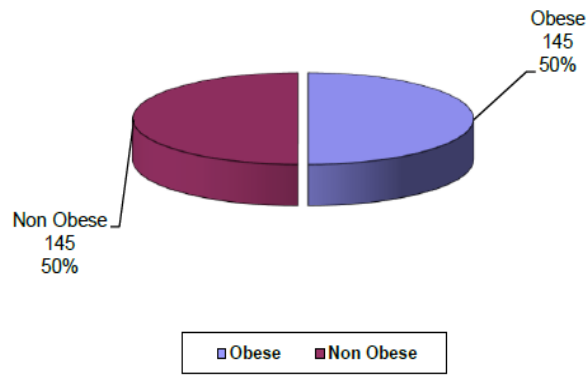
Figure 2. Frequency of the obese cases in the study

Duration of PAD was 1–3 years in 259 (89.3%) patients, with mean duration of peripheral arterial disease of 1.604 ± 0.005 years. The frequency of myocardial infarction among diabetic patients with PAD was 14.8%. Myocardial infarction on Q-wave was detected on inferior wall leads (II, III, & aVF) in 18 (41.9%) patients, on lateral wall leads (I, aVL, V5 & V6) in 15 (34.9%) patients and on anteroseptal wall leads (V1,V2,V3 & V4) in 10 (23.2%) patients (Table I). There was no significant difference for the duration of disease, gender and obesity But a significant difference was noted for myocardial infarction in the smokers as compared to non smokers (Table II)

Table I: Baseline Clinico-Social Parameters in the Study Participants

Variable		Mean+SD/N(%)
Duration of DM (years)		7.39±0.36
Duration of PAD (years)		1.604±0.005
Duration of DM(years)	0-9	207(71.4%)
	10-19	67(23.1%)
	20-29	13(4.5%)
MI in DM with PAD	Yes	43(14.8%)
	No	247(85.2%)
Q-wave Findings in Diabetic Patients	Lead II, III, aVF	18(41.9%)
	Lead I, aVL, V5, V6	15(34.9%)
	Lead V1, V2, V3, V4	10(23.2%)

Discussion

Diabetes mellitus is a global public health problem associated with disturbing complications. In the general population, Diabetes Mellitus (type II) is associated with high risk of mortality especially in the patients with cardiovascular disease.[20, 21] Major cardiovascular events are responsible for more than half of total mortality in diabetic patients.[21] These patients increase the 2-3 folds of risk for developing coronary artery disease, CVD and

PAD.[22] These patient's disease severity associated with the chronic level of hyperglycemia with an increasing frequency of cardiovascular events. The coronary heart disease and ischemic stroke are the major cardiovascular events contributing the morbidity and mortality in diabetic patients. Basit et al[23] have reported frequency of coronary artery disease (CAD) as 15.1% in T2DM. PAD is frequently encountered in diabetic patients. [24]A number of studies have been carried out to elucidate relation between T2DM and CVD resulting in MI. Similarly, an immense body of literature is available that describes the association between PAD and subsequent cardiac events such as MI. However, only a few studies have been conducted on the frequency of MI in T2DM patients having PAD.

Table II: Impact of the Clinico-social variables on the presence of Myocardial Infarction.

		Myocardial Infection		P-Value
		Yes	No	
Gender	Male	25(15.3%)	138(64.7%)	0.45
	Female	18(14.2%)	109(85.8%)	
Duration of Diabetes Mellitus	1-9 year	33(15%)	174(84.1%)	0.76
	10-19 year	8(11.9%)	59(68.1%)	
	20-29 year	2(15.4%)	11(84.6%)	
	>30 year	0(0%)	3(100%)	
Smoking	Yes	23(32.4%)	48(67.6%)	0.001*
	No	20(9.1%)	199(90.9%)	
Obesity	Yes	24(15.5%)	131(84.5%)	0.43
	No	19(14.1%)	116(85.9%)	

*p-value<0.05 as significant

It has been studied that prevalence of DM in the patient with PAD is 25%.[25] Diabetes in combination with PAD manifests broad clinical characteristics, resulting in major cardiovascular complications such as MI.[26] In fact, PAD confers poor prognosis in patients with T2DM. Saely et al.[27] prospectively studied 1049 patients to determine the single and combined effect of T2DM and PAD on the risk of cardiovascular events. They reported a significant risk of cardiovascular events (71.2%) in the patient's PAD and DM as compared to those with T2DM only (22.2%) or PAD only (52.6%). They demonstrated that DM in PAD escalates atherothrombotic disease, increasing the risk of CVD. Their study also reflected that PAD itself is a significant risk for cardiovascular events. They reported 40 non-fatal MI among cardiovascular events. In the present study, MI was reported in 23.2% patients with T2DM and PAD.

Although PAD and T2DM increase the risk of cardiovascular events when they do not coexist; however,

the risk of these events accumulates in the coexistence of PAD and T2DM.[26] Circulating fibrinogen plays an important role in the occurrence of cardiovascular events as it increases plasma viscosity, enhances platelet activation and accelerates plaque formation.[26] In this regard, Chen et al[28] conducted a cross sectional study including 1096 diabetic patients to investigate the fibrinogen levels in T2DM and its relation with PAD. Their study population had 80.9% patients with PAD, reporting higher serum levels of fibrinogen in the patients with PAD as compared to those without PAD. Therefore, it is clear that coexisting PAD and T2DM intensifies the risk of cardiovascular events such as MI.

In Pakistan, no study has been conducted to determine the frequency of MI among patients with DM and PAD. However, one of the studies carried out at Nishtar Hospital Multan has reported PAD in 25.1% with DM [29] It demonstrated that PAD is a frequent co-morbidity in diabetic patients, increasing the risk of CVD. Therefore, all the patients with T2DM should be looked for PAD for early prevention and detection of CVD. [30, 31] MI occurred in 683 patients (4.9%). Risk factors associated with the risk of MI were age, diabetes.[32]

Moreover, further studies at a large scale are required to shed light on MI and all other cardiovascular events in the patients with coexisting T2DM and PAD. Limitations of the study include a single hospital study, small sample size and half of the patients were obese increasing the risk of adverse events. Prevalence of 14.8% myocardial infarction in the present study alarms to diagnose and treat T2DM and PAD patients at an earlier stage. Every diabetic patient with PAD should be screened for MI.

Conclusion

Conclusively, it is observed that diabetes cause various type of heart disease but when it leads to PAD, the situation becomes more alarming. 14% of cases who have diabetes along with PAD had developed myocardial infarction. Keeping in view, the cases of diabetes should be screened for the PAD so that priority could be established and management plan be opted accordingly.

References

1. Hardman RL, Jazaeri O, Yi J, Smith M, Gupta R, editors. Overview of classification systems in peripheral artery disease. Seminars in interventional radiology; 2014: Thieme Medical Publishers. https://doi.org/10.1055/s-0034-1393976

2. Criqui MH, Aboyans V. Epidemiology of peripheral artery disease. Circulation research. 2015;116(9):1509-26. https://doi.org/10.1161/CIRCRESAHA.116.303849

3. Olinic D-M, Spinu M, Olinic M, Homorodean C, Tataru D-A, Liew A, et al. Epidemiology of peripheral artery disease in Europe: VAS Educational Paper. International angiology: a Int Angiol. 2018;37(4):327-34.

4. Criqui MH, Denenberg JO, Langer RD, Fronek A. The epidemiology of peripheral arterial disease: importance of identifying the population at risk. Vasc Med. 1997;2(3):221-6. https://doi.org/10.1177/1358863X9700200310

5. Ruiz-Canela M, Martínez-González MA. Lifestyle and dietary risk factors for peripheral artery disease. Circulation Journal. 2014:CJ-14-0062.

6. Cho SW, Kim BG, Kim DH, Kim BO, Byun YS, Rhee KJ, et al. Prediction of coronary artery disease in patients with lower extremity peripheral artery disease. Int. Heart J. 2015;56(2):209-12. https://doi.org/10.1536/ihj.14-284

7. Hiramoto JS, Katz R, Weisman S, Conte M. Gender-specific risk factors for peripheral artery disease in a voluntary screening population. . Am. Heart Assoc. 2014;3(2):e000651. https://doi.org/10.1161/JAHA.113.000651

8. Attar R, Wester A, Koul S, Eggert S, Andell P. Peripheral artery disease and outcomes in patients with acute myocardial infarction. Open heart. 2019;6(1):e001004. https://doi.org/10.1136/openhrt-2018-001004

9. Ndisang JF, Vannacci A, Rastogi S. Insulin resistance, type 1 and type 2 diabetes, and related complications 2017. Hindawi; 2017. https://doi.org/10.1155/2017/1478294

10. Ruan Y, Guo Y, Zheng Y, Huang Z, Sun S, Kowal P, et al. Cardiovascular disease (CVD) and associated risk factors among older adults in six low-and middle-income countries: results from SAGE Wave 1. BMC public health. 2018;18(1):1-13. https://doi.org/10.1186/s12889-018-5653-9

11. Williams J, Allen L, Wickramasinghe K, Mikkelsen B, Roberts N, Townsend N. A systematic review of associations between non-communicable diseases and socioeconomic status within low-and lower-middle-income countries. Journal of global health. 2018;8(2) https://doi.org/10.7189/jogh.08.020409

12. Otsuka F, Yasuda S, Noguchi T, Ishibashi-Ueda H. Pathology of coronary atherosclerosis and

thrombosis. Cardiovasc Diagn Ther. 2016;6(4):396. https://doi.org/10.21037/cdt.2016.06.01

13. Morcos R, Louka B, Tseng A, Misra S, McBane R, Esser H, et al. The evolving treatment of peripheral arterial disease through guideline-directed recommendations. Journal of clinical medicine. 2018;7(1):9. https://doi.org/10.3390/jcm7010009

14. Makdisse M, Pereira AdC, Brasil DdP, Borges JL, Machado-Coelho GLL, Krieger JE, et al. Prevalence and risk factors associated with peripheral arterial disease in the Hearts of Brazil Project. Arquivos brasileiros de cardiologia. 2008;91(6):402-14. https://doi.org/10.1590/S0066-782X2008001800008

15. Urbano L, Portilla E, Muñoz W, Hofman A, Sierra-Torres CH. Prevalence and risk factors associated with peripheral arterial disease in an adult population from Colombia. Archivos de cardiología de México. 2018;88(2):107-15. https://doi.org/10.1016/j.acmx.2017.02.002

16. Akram J, Aamir AuH, Basit A, Qureshi MS, Mehmood T, Shahid SK, et al. Prevalence of peripheral arterial disease in type 2 diabetics in Pakistan.J Pak Med Assoc. 2011;61(7):644.

17. Makridakis S, Kirkham R, Wakefield A, Papadaki M, Kirkham J, Long L. Forecasting, uncertainty and risk; perspectives on clinical decision-making in preventive and curative medicine. International Journal of Forecasting. 2019;35(2):659-66. https://doi.org/10.1016/j.ijforecast.2017.11.003

18. Allison MA, Hiatt WR, Hirsch AT, Coll JR, Criqui MH. A high ankle-brachial index is associated with increased cardiovascular disease morbidity and lower quality of life. J Am Coll Cardiol. 2008;51(13):1292-8. https://doi.org/10.1016/j.jacc.2007.11.064

19. Mirvis DM, Goldberger AL. Electrocardiography. Heart disease. 2001;1:82-128.

20. Rungby J, Schou M, Warrer P, Ytte L, Andersen GS. Prevalence of cardiovascular disease and evaluation of standard of care in type 2 diabetes: a nationwide study in primary care. Cardiovasc. Endocrinol. 2017;6(4):145. https://doi.org/10.1097/XCE.0000000000000135

21. Einarson TR, Acs A, Ludwig C, Panton UH. Prevalence of cardiovascular disease in type 2 diabetes: a systematic literature review of scientific evidence from across the world in 2007–2017. Cardiovasc. Diabetol. 2018;17(1):1-19. https://doi.org/10.1186/s12933-018-0728-6

22. Adela R, Reddy PNC, Ghosh TS, Aggarwal S, Yadav AK, Das B, et al. Serum protein signature of coronary artery disease in type 2 diabetes mellitus. Journal of translational medicine. 2019;17(1):1-17. https://doi.org/10.1186/s12967-018-1755-5

23. Basit A, Hydrie MZI, Hakeem R, Ahmedani MY, Masood Q. Frequency of chronic complications of type 2 diabetes. J Coll Physicians Surg Pak. 2004;14(2):79-83.

24. Shu J, Santulli G. Update on peripheral artery disease: Epidemiology and evidence-based facts. Atherosclerosis. 2018;275:379-81. https://doi.org/10.1016/j.atherosclerosis.2018.05.033

25. Sigvant B, Hasvold P, Kragsterman B, Falkenberg M, Johansson S, Thuresson M, et al. Cardiovascular outcomes in patients with peripheral arterial disease as an initial or subsequent manifestation of atherosclerotic disease: results from a Swedish nationwide study. Journal of vascular surgery. 2017;66(2):507-14. e1. https://doi.org/10.1016/j.jvs.2017.01.067

26. Rhee SY, Kim YS. Peripheral arterial disease in patients with type 2 diabetes mellitus. Diabetes & metabolism journal. 2015;39(4):283. https://doi.org/10.4093/dmj.2015.39.4.283

27. Saely CH, Schindewolf M, Zanolin D, Heinzle CF, Vonbank A, Silbernagel G, et al. Data on the impact of peripheral artery disease and of type 2 diabetes mellitus on the risk of cardiovascular events. Data in brief. 2018;21:1716-20. https://doi.org/10.1016/j.dib.2018.10.153

28. Chen QF, Cao D, Ye TT, Deng HH, Zhu H. Peripheral arterial disease in type 2 diabetes is associated with an increase in fibrinogen levels. Int. J. Endocrinol. 2018; Article ID 3709534

29. Mahmood Q, Siddique N, Qaiser A. PERIPHERAL ARTERIAL DISEASE (PAD). The Professional Medical Journal. 2013;20(04):513-8.

30. Anselmino M, Öhrvik J, Malmberg K, Standl E, Rydén L. Glucose lowering treatment in patients with coronary artery disease is prognostically important not only in established but also in newly detected diabetes mellitus: a report from the Euro Heart Survey on Diabetes and the Heart. Eur Heart J. 2008;29(2):177-84. https://doi.org/10.1093/eurheartj/ehm519

31. Naito R, Kasai T. Coronary artery disease in type 2 diabetes mellitus: Recent treatment strategies and future perspectives. World J. Cardiol. 2015;7(3):119. https://doi.org/10.4330/wjc.v7.i3.119

32. Olivier CB, Mulder H, Hiatt WR, Jones WS, Fowkes FGR, Rockhold FW, et al. Incidence, characteristics, and outcomes of myocardial infarction in patients with peripheral artery disease: insights from the EUCLID trial. JAMA cardiology. 2019;4(1):7-15.