

Management and Outcomes of Vascular Complications in Lower Limb due to Diabetes: A Prospective Observational Study

AKANKSHA YACHMANENI¹, SUHAS JAJOO², CHANDRASHEKHAR MAHAKALKAR³, SAMYUKTH KATAM⁴

ABSTRACT

Introduction: Diabetes mellitus is a metabolic disorder characterised by hyperglycaemia, leading to vascular complications, including Peripheral Artery Disease (PAD) and gangrene.

Aim: To assess the vascular complications in the lower limbs of diabetic patients by evaluating clinical and radiological findings and analysing treatment outcomes.

Materials and Methods: The present prospective observational study was conducted among 60 diabetic patients with signs of diabetes-related vascular problems in their lower limbs at the Acharya Vinoba Bhave Rural Hospital, Sawangi, Wardha, Maharashtra, India from July 2022 and concluding in March 2024. Angiography or Doppler ultrasonography combined with patient data collection and clinical evaluation were used to diagnose and assess patients. The collected data were analysed to identify patterns and trends in the patient population. Descriptive statistics were used to summarise the data, means and standard deviations, frequencies and percentages were calculated for categorical variables by employing Statistical Package for Social Sciences (SPSS)-22 (SPSS 22.00 for Windows; SPSS Inc., Chicago, USA).

Results: The majority of patients were male subjects 52 (86.7%) and only 8 (13.3%) patients were females. Mean age of male subjects included in study was 59.73 ± 11.9 years and 59.5 ± 15.7 years for females. An 81.7% of the study population received their diagnosis through doppler ultrasonography. Glycated Haemoglobin (HbA1c) >7 was present in 66.7% of subjects. Gangrenous changes were identified in 60% of subjects as doppler ultrasonography revealed the presence of ischaemia in all subjects. Interventional treatment was the primary approach, with 90% of subjects receiving procedures like Intraarterial Thrombolysis (IAT) and stenting. However, 36.7% showed progression, requiring further intervention.

Conclusion: In conclusion, the present study emphasises the significance of clinical and radiological assessment in managing vascular complications in the lower limbs of diabetic patients. The findings suggest that interventional treatment approaches, such as IAT and stenting, are effective in managing the condition. However, a considerable proportion of patients may require further intervention, highlighting the need for close monitoring and follow-up care. The study's results can inform clinical practice and guide treatment decisions for diabetic patients with vascular complications.

Keywords: Angiopathy, Diabetes mellitus, Doppler ultrasonography, Intraarterial thrombolysis, Ischaemia, Stenting

INTRODUCTION

A class of metabolic diseases known as diabetes mellitus is characterised by hyperglycaemia, which can be due to abnormalities in insulin secretion, action, or both [1,2]. Diabetic patients are prone to foot-related illnesses due to interplaying pathogenic processes, including poor wound healing, PAD, and abnormal foot biomechanics. Neuropathy disrupts normal defense systems, leading to unrecognised trauma, callus formation, and foot deformities. Autonomic neuropathy causes anhidrosis, altered blood flow, and skin drying, increasing the risk of fissures and infections. PAD and poor wound healing delay the healing of small skin wounds, allowing them to become larger and infected [3,4]. In those over 40, atherosclerosis is the primary cause of PAD [5,6]. Diabetics are more likely to develop atherosclerosis, and epidemiological research has proven a connection between the rise in the prevalence of PAD and diabetes [7,8].

The PAD incidence is linked to a two to four-fold increase in diabetics compared to non-diabetic persons. The incidence of PAD is 9.5% among adults over 40 who are diabetic individuals, which is twice as high as the 4.5% prevalence among non-diabetics [9-12]. Consequently, the Ankle-brachial Index (ABI) should be used as a measure of detection in all diabetes persons >50 years of age or those who have had the condition for more than ten years,

according to a consensus recommendation made by the American Diabetes Association (ADA) [12]. Further for diabetic patients, PAD is a significant predictor of foot pressure ulceration. Given that up to 50% of diabetic patients have PAD, physicians should assess vascular status and ischaemia in patients with diabetes and foot ulcers. However, diagnosing and assessing PAD severity in diabetic patients can be challenging due to altered clinical presentation and limitations in diagnostic techniques. Furthermore, PAD is not the only factor affecting wound healing; infection, pressure, and co-occurring conditions also play a role [13-15].

Diabetic Foot Ulcers (DFUs) are a common complication in patients with diabetes mellitus that result in higher healthcare costs and substantial negative consequences on their quality of life. However, a proper assessment of the limb's vascular condition is not carried out while examining a patient with DFU [16]. Previous studies have highlighted the significant impact of diabetes on vascular complications, particularly in the lower limbs. A strong association between diabetes and Lower Extremity Amputation (LEA) has been reported highlighting the importance of primary prevention and post-disease care in reducing diabetic vascular complications [17,18]. Furthermore, systematic foot health services in primary care play a crucial role in preventing diabetic foot amputations [19]. However, despite the growing burden of diabetes-related vascular

complications, there remains a knowledge gap in the comprehensive assessment of vascular difficulties in the lower limbs caused by diabetes.

Therefore, the current study aimed to fill this knowledge gap by investigating the vascular complications in the lower limbs of diabetic patients, assessing the results of radiological evaluation by angiography or by doppler study and clinical examinations that comprises gangrenous changes, choosing medical or other intervention, and monitoring the effects of that course of action. By doing so, the present study sought to provide valuable insights into the management of diabetic vascular complications and inform clinical practice.

MATERIALS AND METHODS

The present prospective observational study was conducted among 60 diabetic patients with signs of diabetes-related vascular problems in their lower limbs at the Acharya Vinoba Bhave Rural Hospital (AVBRH) in Sawangi, Wardha, Maharashtra, India. The study spanned over one and half years, commencing in July 2022 and concluding in March 2024. The study was commenced after obtaining ethical approval from the Datta Meghe Institute of Higher Education and Research's Institutional Ethics Committee (Reference Number: DMIHER (DU)/IEC/2022/1080). The study participants comprised of patients who arrived to AVBRH with a history of diabetes and symptoms suggestive of ischemic gangrene. All patients provided informed consent for study participation as part of which they received notification about leaving the study anytime they desired along with assurance of complete confidentiality in data management.

Sample size calculation: Sample size was calculated based on prevalence of cases reporting at the present tertiary institute. Prevalence reported in other studies ranged from 3.9% to 8.3% (age-standardised 6.5%) [20,21].

Sample size was calculated using:

$$n = \frac{Z_{\alpha/2}^2 p(\%)q(\%)}{d(\%)^2}$$

Where, p is the observed prevalence of peripheral vascular disease in lower limb in DM.

$q=100-p$ d is the margin of error= $5\%=0.05$

$2 Z_{\alpha}$ is the ordinate of standard normal distribution at $\alpha\%$ level of significance Calculations: $n=1.962 \times 0.05 \times (1-0.06)/0.052=58.32$. Hence, the minimum sample size required in the present study was 58. It was increased to 60.

Inclusion and Exclusion criteria: Patients who showed signs of diabetes-related vascular problems in their lower limbs irrespective of age were included in the present study. Patients with traumatic gangrene were excluded from participating in this study. People primarily diagnosed with infective gangrene were also excluded. All participants in this study had to present symptoms of diabetes.

Study Procedure

A comprehensive data collection process was undertaken to gather information on various health variables from patients presenting with clinical gangrene. A standardised data collection form was utilised to record detailed information on the patient's medical history, including the duration of diabetes.

Data on patients age, gender, previous treatment history, including surgical and medical interventions, were collected. Co-morbidities, such as hypertension, cardiovascular injury, and coagulation disorders, were also documented. Glycaemic control was assessed using HbA1c levels, which were categorised as <7 or >7 . This information provided valuable insights into the patient's overall health status and potential risk factors for gangrene development.

Gangrenous changes: A thorough clinical assessment was conducted to investigate various factors that may have contributed to the development of gangrene. This included an examination of Intermittent Claudication (IC), a symptom indicative of peripheral arterial disease. The progression of pregangrenous and gangrenous changes over time was also evaluated to better understand the disease's progression.

Mode of diagnosis: The diagnosis of vascular complications was primarily made using two modes of diagnostic imaging: Doppler and angiography. Doppler ultrasonography was used to diagnose patients using Philips CX 50 devices [22].

Study variables: The variables studied included palpation of peripheral pulses (specifically popliteal artery and femoral artery) and treatment approach comprised interventional and medical, further these variables are analysed in relation to the presence or absence of palpable pulses in the popliteal and femoral arteries. Level of block was analysed radiologically (level of femoral artery, level of popliteal artery and level of iliac artery).

Identification of venous and peripheral artery disorders: Patients underwent palpation of peripheral pulses, specifically popliteal and femoral arteries, to assess blood flow and potential blockages. Patients received radiological examinations to determine the level of blockage in their arteries, which informed treatment decisions.

Treatment approaches and outcome: Patients received either interventional procedures or medical management based on blockage severity and location [23,24]. Interventions included balloon angioplasty with or without stenting, IAT alone or with angioplasty, and stenting in various arteries. Patients were followed-up after 15 days to assess disease progression and need for further intervention, tracking outcomes like success, complications, and additional procedures.

STATISTICAL ANALYSIS

The collected data were analysed to identify patterns and trends in the patient population. Descriptive statistics were used to summarise the data, means and standard deviations, frequencies and percentages were calculated for categorical variables by employing SPSS-22 (SPSS 22.00 for Windows; SPSS Inc., Chicago, USA).

RESULTS

In present study, subjects were divided according to age. Maximum study subjects fell in age group 50-70 years 40 (66.67%) followed by 10 (16.67%) subjects each in <50 and >70 years age group [Table/Fig-1]. The majority of which were male subjects 52 (86.7%) and only 8 (13.3%) patients were females. Mean age of male subjects included in study was 59.73 ± 11.9 years and of female subjects were 59.5 ± 15.7 years [Table/Fig-2].

Variables		N=60	%
Age (in years)	<50	10	16.67
	50-70	40	66.67
	>70	10	16.67
Gender	Male	52	86.7
	Female	8	13.3

[Table/Fig-1]: Age and gender wise distribution among the study groups.

Gender	Mean age (in years)	SD
Male	59.73	11.9
Female	59.5	15.7

[Table/Fig-2]: Mean age among males and females (n=60).

Doppler was the most commonly used method for diagnosis, accounting for 49 (81.7%) of cases, while angiography was used in 11 (18.3%) of cases [Table/Fig-3]. Eighteen (30%) subjects gave history of medical treatment and 12 (20%) gave history of surgical treatment [Table/Fig-3].

Variables		N	%
Mode of diagnosis	Angiography	11	18.3
	Doppler	49	81.7
Previous treatment history	Medical	18	30
	Surgical	12	20

[Table/Fig-3]: Distribution according to mode of radiological diagnosis and previous treatment history - surgical and medical.

In the present study, HbA1c >7 was present in 40 (66.7%) subjects and <7 was found in remaining 20 (33.3%) patients. Co-morbidities present among subjects was also recorded and only 17 (28.3%) subjects gave history of associated hypertension with diabetes and 6.67% revealed cardiovascular injury [Table/Fig-4]. In the present study, gangrenous changes were found among 36 (60%) subjects and signs of ischaemia were present in 60 (100%) patients. Among the 36 gangrenous patients; progression was reported in 41.67% of the subjects [Table/Fig-4].

Variables		N	%
Co-morbidities	Any coagulation disorder	0	0
	Cardiovascular injury	4	6.67
	Hypertension	17	28.3
	HbA1c (%)		
	<7	20	33.3
	>7	40	66.7
Gangrenous changes	Signs of ischaemia	60	100
	Gangrenous changes (n=36) (60%)		
	Progressive	15	41.67
	Non progressive	21	58.33

[Table/Fig-4]: Co-morbidities among the study subjects.

Palpation of popliteal artery was found in nine subjects clinically [Table/Fig-5] and 13 subjects radiologically [Table/Fig-6]. Out of nine cases of popliteal artery; interventional and medical treatment was done in seven and two subjects, respectively [Table/Fig-5].

Signs	Interventional	Medical
Palpation of popliteal artery		
No	47	4
Yes	7	2
Palpation of femoral artery		
No	44	2
Yes	10	4

[Table/Fig-5]: Treatment based on palpation of peripheral pulses (n=60).

Palpation of femoral artery was found in 14 subjects clinically [Table/Fig-5] and 29 subjects radiologically [Table/Fig-6]. Out of 14 cases of popliteal artery; interventional and medical treatment was done in 10 and four subjects, respectively [Table/Fig-5]. As depicted in [Table/Fig-6], majority of subjects went under surgical treatment i.e., 28 at the level of femoral artery, eight at the level of popliteal artery and 18 at the level of iliac artery. Only six patients i.e., one subject at the level of femoral artery and five at the level of popliteal artery went for medical treatment. As depicted in [Table/Fig-7], partial block was found in 52 (86.7%) subjects and complete block was present in 8 (13.3%) patients. All patients with complete blockage (n=8) and 46 with partial blockage underwent surgical treatment and six patients with partial blockage were lined up for medicinal treatment. Only six patients were given only medical treatment.

Level of block	Interventional	Medical
Level of femoral artery	28	1
Level of popliteal artery	8	5
Level of iliac artery	18	0

[Table/Fig-6]: Treatment based on level of block radiologically (n=60).

Block	N	%	Interventional	Medical
Partial	52	86.7	46	6
Complete	8	13.3	8	0

[Table/Fig-7]: Level of block.

Of the 54 (90%) subjects who underwent surgical treatment, maximum 27 (45%) went for IAT, 17 (28.3%) were lined up for IAT plus balloonplasty, 3 (5%) went under iliac artery stenting, two each went under balloonplasty or IAT plus iliac stent, one subject each either went under balloonplasty with left common iliac artery stent or balloon dilatation plus femoral stent or superficial femoral artery stenting [Table/Fig-8].

Type	Number	Percentage (%)
Medical	6	10
Interventional	54	90
Balloonplasty with left common iliac artery stent	1	1.7
Balloon dilatation plus femoral stent	1	1.7
Balloonplasty	2	3.3
*IAT	27	45.0
IAT plus balloonplasty	17	28.3
IAT plus iliac stent	2	3.4
Iliac artery stenting	3	5.0
Superficial femoral artery stenting	1	1.7

[Table/Fig-8]: Type of treatment.

*IAT: Intraarterial thrombolysis

In 38 (63.3%) subjects; no progression of disease was found 15 days after treatment and in 22 (36.7%) progression of disease was present [Table/Fig-9]. A total of 39 (65%) subjects had no progression of disease after 15 days of treatment and hence did not require any second intervention. In remaining 21 patients, seven underwent above knee amputation, 10 were subjected to below knee amputation, two for IAT and 1 each for IAT plus balloonplasty or iliac artery stenting [Table/Fig-9].

Variables		N	%
Progression	No	38	63.3
	Yes	22	36.7
Second intervention	No	39	65
	Yes	21	35
	Above knee amputation	7	11.7
	Below knee amputation	10	16.7
	IAT	2	3.3
	IAT plus		
	Balloonplasty	1	1.7
	Iliac artery stenting	1	1.7

[Table/Fig-9]: Progression after 15 days and second intervention.

DISCUSSION

The present study enrolled 60 patients with signs of diabetes-related vascular problems in their lower limbs. Clinical assessment, Doppler ultrasonography, and angiography were used for assessment. Treatment approaches included interventional procedures, such as balloon angioplasty, IAT, and stenting, as well as medical management. Patients were followed-up after 15 days to assess disease progression and if they need for further intervention. Interventional treatment was effective in managing the condition, with 90% of patients receiving procedures like IAT and stenting 36.7% of patients showed progression of disease after 15 days, and 35% required a second intervention, including amputations and additional endovascular procedures. The study's findings suggest that a comprehensive approach to managing diabetic vascular

complications can improve patient outcomes, but close monitoring and follow-up care are essential to prevent disease progression.

The present study's demographic analysis showed a predominantly male population, with 52 (86.7%) males and 8 (13.3%) females. Similar masculine dominance was observed in studies by Ntuli S et al., and Mutharaju KR., which reported 86% and 86.7% male populations, respectively [19,25]. In contrast, a study by Piotrkowska R et al., study found a more balanced distribution, with 36.7% women in the endovascular group and 28.8% in the surgical group [26].

The majority of study participants (66.67%) were between 50-70-year-old, with a mean age of 59.73 ± 11.9 years for males and 59.5 ± 15.7 years for females. Similar age ranges were reported in other studies, with mean ages ranging from 52 to 68.8 years. Ntuli S et al., (mean age: 60 years, range: 37-97 years), Yadav V et al., (23 patients <50 years, 13 patients 50-60 years, 19 patients 60-70 years), Bendermacher BL et al., (mean age: 68.8 ± 8.5 years), Akalu Y et al., (mean age: 61.2 ± 7.3 years, range: 50-91 years), and Mutharaju KR (age range: 20-80 years, mean age: 52 years). The prevalence of PAD increases with age due to thickening and hardening of arteries, compromising endothelial integrity and restricting nitric oxide availability [19,25,27-29]. Age-related changes disrupt regular blood flow, leading to fatty deposits and calcium buildup, ultimately contributing to PAD.

The pathophysiology of PAD in diabetes is characterised by atherosclerosis in the peripheral arteries, especially those supplying the lower extremities. Atherosclerotic plaques cause narrowing and stiffening of these arteries, resulting in reduced blood flow and oxygen delivery to the legs and feet. Diabetes-related factors, including hyperglycaemia and inflammation, accelerate atherosclerosis progression, leading to symptoms such as IC, non-healing ulcers, and an increased risk of limb amputation [30]. In the present study, 12 (20%) and 18 (30%) of the participants provided a history of surgical therapy and medical treatment, respectively. HbA1c >7 was detected in 40 (66.7%) of the participants in the current investigation, whereas <7 was observed in the remaining 20 (33.3%) patients. Co-morbidities were also noted for the participants; of these, only 17 (28.3%) had a history of diabetes and hypertension, and 6.67% had cardiovascular damage. Similar findings were reported by Thiruvoipati T et al., in their study, which concluded that a high prevalence of PAD was caused by insulin resistance, dyslipidemia, and hyperglycaemia, all of which were secondary to diabetes mellitus [31]. These conditions disrupted the vessel wall, causing endothelial cell dysfunction and vascular inflammation, as well as derangements of various cell types, including platelets, within the vascular wall. Similarly, studies by Piotrkowska R et al., and Krishnan MN et al., reported high prevalence of comorbidities, including arterial hypertension (69.5% and 62.94%, respectively), diabetes (39% and 55.5%), and ischemic heart disease (32.2% and 61.61%) [26,32]. Akalu Y et al., also found hypertension in 52.1% of participants [29]. Another study by Ying AF et al., found a significant interaction between diabetes and hypertension ($p=0.0006$), as well as between diabetes and increased BMI ($p=0.0002$) [17]. Diabetes status significantly modified the associations between these vascular risk factors and the risk of Chronic Limb-threatening Ischaemia (CLTI)-related LEA. These findings highlight the common co-occurrence of cardiovascular risk factors in these populations.

Angiography and doppler ultrasonography was used to diagnose patients and the cutting-edge imaging technique is essential for identifying diseases and helping to make precise diagnoses [22]. The current study found that 60% had gangrenous alterations, with 41.67% of those patients experiencing progression [Table/Fig-4]. Similar findings were reported by Mutharaju KR, who found that 2/3 of patients with PAD had toe/forefoot gangrene [25].

Many PAD patients may not experience any symptoms because they do not reach this threshold for activity. Revascularisation, either through percutaneous or surgical methods, is a treatment option for certain patients with IC who experience significant disability, difficulty with daily activities or work, and have not responded to conservative therapies. Successful revascularisation can improve functional performance and quality of life in these patients. The decision to proceed with revascularisation should be individualised, considering potential risks, anticipated benefits, and the durability of the procedure. Patients with a major impairment from IC, optimal medical care, including an exercise trial, and revascularisation alternative with a favourable risk: benefit ratio are considered ideal. Anatomic durability, non-limb-threatening nature of the issue, invasiveness of the treatment, and lack of need for recurrent interventions are all crucial factors to take into account [33,34].

Merely six patients- one at the femoral artery level and five at the popliteal artery level- received medical attention. The majority of the participants had surgery: 18 at the level of the iliac artery, 8 at the level of the popliteal artery, and 28 at the level of the femoral artery. Out of the 54 (90%) patients who underwent surgery, the most (27, 45%) had IAT; 17 (28.3%) had IAT Plus balloonplasty scheduled; 3 (5%) had iliac artery stenting; two each had Balloonplasty or IAT plus iliac stent; one subject each had Balloonplasty with left common iliac artery stent or balloon dilatation plus femoral stent or superficial femoral artery stenting on the left-side. These results were in line with research by Mutharaju KR, Bendermacher BL et al., Akalu Y et al., and Krishnan MN et al., [19,28,29,32]. Mutharaju KR discovered that out of the 58 patients, six had angioplasty and stenting and 39 CLI patients had bypass surgery [21]. Treatment for thirteen Acute Limb Ischaemia (ALI) patients involved thrombo-embolectomy.

Aggressive glycaemic control combined with early comprehensive vascular intervention is the key to prevention and treatment [35]. Patients with stable IC were recommended to receive medical therapy; the aim of the treatment is to reduce pain and increase exercise tolerance, both of which will enhance quality of life and lower the risk of cardiovascular events. It is advantageous to include cilostazol since it has vasodilatory qualities, prevents platelet aggregation, and lowers cholesterol levels [36,37].

In the event that the patient's condition worsens or does not improve with medical care one alternative is to use endovascular interventions. Conservative therapy is the first line of treatment for IC; however, pain management, wound healing, and limb loss prevention should also be considered when treating individuals who have critical limb ischaemia, rest discomfort, tissue loss, or gangrene [38]. Usually, intervention is necessary to achieve limb salvage results.

Fifteen days following treatment, there was no evidence of illness progression in 38 (63.3%) of the participants, while progression was detected in 22 (36.7%). After receiving treatment for 15 days, 39 (65%) of the participants showed no signs of illness development and therefore did not require further intervention. Of the remaining 21 patients, seven had above-knee amputations, ten had below-knee amputations, two had IATs, and one had both IAT plus balloonplasty and iliac artery stenting.

Regular check-ups and early diagnosis can help prevent vascular complications. Doppler ultrasonography should be used as a diagnostic tool. Surgical treatment should be undertaken promptly to prevent amputation. Further studies are needed to explore the role of doppler ultrasonography in diagnosis and management of vascular complications. The impact of surgical treatment on outcomes should be investigated.

Limitation(s)

Limitations of this study include a small sample size ($n=60$) and single-center design which may impact the generalisability and long-term applicability of the findings.

CONCLUSION(S)

In conclusion, this study highlights the importance of integrating clinical and radiological assessments in managing diabetic lower limb vascular complications, demonstrating the efficacy of interventional treatments and emphasising the need for rigorous monitoring and follow-up care to optimise patient outcomes and inform clinical practice.

REFERENCES

- [1] Alberti KGMM, Zimmet PZ. World Health Organization Definition, diagnosis and classification of diabetes mellitus and its complications: Report of a WHO consultation. Part Diagnosis and classification of diabetes mellitus. *Diabet Med*. 2015;15:539-53.
- [2] Keating FK, Sobel BE, Schneider DJ. Effects of increased concentrations of glucose on platelet reactivity in healthy subjects and in patients with and without diabetes. *Am J Cardiol*. 2003;92:1362-65.
- [3] Chan JC, Malik V, Jia W, Kadowaki T, Yajnik CS, Yoon KH, et al. Diabetes in Asia: Epidemiology, risk factors, and pathophysiology. *JAMA*. 2009;301:2129-40.
- [4] Asociación Latinoamericana de Diabetes. Guías ALAD de Pie Diabético. *Revista de la Asociación Latinoamericana de Diabetes*. 2010;18.
- [5] Creager MA, White CJ, Hiatt WR, Criqui MH, Josephs SC, Alberts MJ, et al. Atherosclerotic peripheral vascular disease symposium II: Executive summary. *Circulation*. 2008;118:2811-25.
- [6] Ankle Brachial Index Collaboration; Fowkes FG, Murray GD, Butcher I, Heald CL, Lee RJ, Chambless LE, et al. Ankle brachial index combined with Framingham Risk Score to predict cardiovascular events and mortality: A meta-analysis. *JAMA*. 2008;300:197-208.
- [7] Marso SP, Hiatt WR. Peripheral arterial disease in patients with diabetes. *J Am Coll Cardiol*. 2006;47:921-29.
- [8] Roca MM, Carral F, Baena G, Sánchez C, Valencia I, Aguilar Diosdado Manuel. Evaluación del a enfermedad vascular periférica en pacientes con diabetes tipo 2 mediante medición del índice tobillo-brazo. *Avances en diabetología*. 2007;23(5):370-74.
- [9] Poitier L, Halbron M, Bouilloud F, Dadon M, Le Doeuff J, Ha Van G, et al. Ankle-to-brachial ratio index underestimates the prevalence of peripheral occlusive disease in diabetic patients at high risk for arterial disease. *Diabetes Care*. 2009;32:e44.
- [10] Romero JM, Gómez FP, Cerezuela IM, Osorio AB, Vera SR, Santos PG, et al. Enfermedad arterial periférica oculta en población diabética seguida en atención primaria. *Clin Invest Arterioscl*. 2010;22:154-61.
- [11] Mukherjee D. Peripheral and cerebrovascular atherosclerotic disease in diabetes mellitus. *Best Pract Res Clin Endocrinol Metab*. 2009;23:335-45.
- [12] Hee YJ, Hwang JY, Mi-Seon S, Jung CH, Kim EH, Lee SA, et al. The prevalence of peripheral arterial disease in Korean patients with type 2 diabetes mellitus attending a university hospital. *Diabetes Metab J*. 2011;35:543-50.
- [13] Schaper NC, Andros G, Apelqvist J, Bakker K, Lammer J, Lepantalo M, et al. Specific guidelines for the diagnosis and treatment of peripheral arterial disease in a patient with diabetes and ulceration of the foot 2011. *Diabetes Metab Res Rev*. 2012;28 Suppl 1:236-37.
- [14] Beckert S, Witte M, Wicke C, Königsrainer A, Coerper S. A new wound-based severity score for diabetic foot ulcers: A prospective analysis of 1000 patients. *Diabetes Care*. 2006;29:988-92.
- [15] Schaper NC, Andros G, Apelqvist J, Bakker K, Lammer J, Lepantalo M, et al. Diagnosis and treatment of peripheral arterial disease in diabetic patients with a foot ulcer. *Diabetes Metab Res Rev*. 2012;28 Suppl 1:218-24.
- [16] Tresierra-Ayala MÁ, Rojas AG. Association between peripheral arterial disease and diabetic foot ulcers in patients with diabetes mellitus type 2. *Medicina Universitaria*. 2017;19(76):123-26.
- [17] Ying AF, Tang TY, Jin A, Chong TT, Hausenloy DJ, Koh WP. Diabetes and other vascular risk factors in association with the risk of lower extremity amputation in chronic limb-threatening ischemia: A prospective cohort study. *Cardiovasc Diabetol*. 2022;21(1):7.
- [18] Liu R, Li L, Shao C, Cai H, Wang Z. The impact of diabetes on vascular disease: Progress from the perspective of epidemics and treatments. *J Diabetes Res*. 2022;2022(1):1531289.
- [19] Ntuli S, Letswalo DM. Diabetic foot and lower limb amputations at central, provincial and tertiary hospitals-underscores the need for organised foot health services at primary healthcare level. *The Foot*. 2023;56:102039.
- [20] Mohan V, Premalatha G, Shastry NG. Peripheral vascular disease in non-insulin-dependent diabetes mellitus in South India. *Diabetes Res Clin Pract*. 1995;27(3):235-40.
- [21] Pradeepa R, Chella S, Surendar J, Indulekha K, Anjana RM, Mohan V. Prevalence of peripheral vascular disease and its association with carotid intima-media thickness and arterial stiffness in type 2 diabetes: The Chennai urban rural epidemiology study (CURES 111). *Diab Vasc Dis Res*. 2014;11(3):190-200.
- [22] Freeman K, Tao W, Sun H, Soonpaa MH, Rubart M. In situ three-dimensional reconstruction of mouse heart sympathetic innervation by two-photon excitation fluorescence imaging. *J Neurosci Methods*. 2014;221:48-61.
- [23] Gul F, Janzer SF. Peripheral vascular disease. *InStatPearls [Internet]* 2023 Jun 6. StatPearls publishing.
- [24] Gornik HL, Aronow HD, Goodney PP, Arya S, Brewster LP, Byrd L, et al. 2024 ACC/AHA/AACVPR/APMA/ABC/SCAI/SVM/SVN/SVS/SIR/VES guideline for the management of lower extremity peripheral artery disease: A report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Journal of the American College of Cardiology*. 2024;83(24):2497-604.
- [25] Mutharaju KR. An outcome analysis of interventions in peripheral vascular disease. *Int J Contemp Med Res*. 2017;4(3):595-602.
- [26] Piotrkowska R, Dobosz M, Książek J, Halena G. Social, demographic and clinical characteristics of patients suffering from peripheral vascular disease treated surgically compared to patients treated with endovascular angioplasty. *Arch Med Sci Atheroscler Dis*. 2017;2(1):e9-e15.
- [27] Yadav V, Khanduri S, Yadav P, Pandey S, Tyagi E, Yadav H, et al. Diagnostic accuracy of color doppler and calcium scoring versus dual-energy computed tomography angiography in the assessment of peripheral arterial diseases of lower limb. *J Clin Imaging Sci*. 2020;10:45.
- [28] Bendermacher BL, Teijink JA, Willigendael EM, Bartelink ML, Büller HR, Ron Peters JG, et al. Symptomatic peripheral arterial disease: The value of a validated questionnaire and a clinical decision rule. *Br J Gen Pract*. 2006;56(533):932-37.
- [29] Akalu Y, Birhan A. Peripheral arterial disease and its associated factors among type 2 diabetes mellitus patients at Debre Tabor General Hospital, Northwest Ethiopia. *J Diabetes Res*. 2020;2020:9419413.
- [30] Yachmaneni A, Jajoo S, Mahakalkar C, Kshirsagar S, Dhole S. A comprehensive review of the vascular consequences of diabetes in the lower extremities: Current approaches to management and evaluation of clinical outcomes. *Cureus*. 2023;15(10):e47525.
- [31] Thiruvipati T, Kielhorn CE, Armstrong EJ. Peripheral artery disease in patients with diabetes: Epidemiology, mechanisms, and outcomes. *World J Diabetes*. 2015;6(7):961-69.
- [32] Krishnan MN, Geevar Z, Mohanan PP, Venugopal K, Devika S. Prevalence of peripheral artery disease and risk factors in the elderly: A community based cross-sectional study from northern Kerala, India. *Indian Heart J*. 2018;70(6):808-15.
- [33] Fowkes FGR, Rudan D, Rudan I, Aboyans V, Denenberg JO, McDermott MM, et al. Comparison of global estimates of prevalence and risk factors for peripheral artery disease in 2000 and 2010: A systematic review and analysis. *Lancet*. 2013;382:1329-40.
- [34] Kral CA, Han DC, Edwards WD, Spittell PC, Tazelaar HD, Cherry KJ. Obstructive external iliac arteriopathy in avid bicyclists: New and variable histopathologic features in four women. *J Vasc Surg*. 2002;36:565-70.
- [35] Schep G, Bender MH, van de Tempel G, Wijn PF, de Vries WR, Eikelboom BC. Detection and treatment of claudication due to functional iliac obstruction in top endurance athletes: A prospective study. *Lancet*. 2002;359:466-73.
- [36] Li Y, Liu Y, Liu S, Gao M, Wang W, Chen K, et al. Diabetic vascular diseases: Molecular mechanisms and therapeutic strategies. *Signal Transduction and Targeted Therapy*. 2023;8(1):152.
- [37] Hallak AO, Hallak FZ, Hallak YO, Hallak OO, Hayson AW, Tanami SA, et al. Exercise therapy in the management of peripheral arterial disease. *Mayo Clin Proc Innov Qual Outcomes*. 2023;7(5):476-89.
- [38] Stonko DP, Hicks CW. Current management of intermittent claudication. *Adv Surg*. 2023;57(1):103-13.

PARTICULARS OF CONTRIBUTORS:

1. Junior Resident, Department of General Surgery, Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra, India.
2. Professor, Department of General Surgery, Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra, India.
3. Professor, Department of General Surgery, Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra, India.
4. Junior Resident, Department of General Surgery, Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Akanksha Yachmaneni,
Junior Resident, Department of General Surgery, Jawaharlal Nehru Medical College,
Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra, India.
E-mail: 1997akanksha@gmail.com

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Jan 30, 2025
- Manual Googling: Aug 18, 2025
- iThenticate Software: Aug 20, 2025 (8%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

Date of Submission: Jan 29, 2025

Date of Peer Review: Apr 13, 2025

Date of Acceptance: Aug 22, 2025

Date of Publishing: Jun 01, 2026