

Evaluation of Peripheral Arterial Disease in Patients Presenting with Diabetic Foot Ulcer to Endocrine Clinic

KHALID USMAN¹, SALMAN KHAN², HAMZA MUHAMMAD³, TAHIR GHAFAR⁴, HAJRA TARIQ⁵, FAIZ UR REHMAN⁶

¹Associate Professor, Department of Diabetes and Endocrinology, Hayatabad Medical Complex, Peshawar

²Associate Professor Medicine GMC/ MTI Dera Ismail Khan

³Medical Officer, DHQ Hospital, Jhelum

⁴Assistant Professor, Department of Diabetes and Endocrinology, Hayatabad Medical Complex, Peshawar

⁵PGR Medicine, DHQ hospital, Mirpur AJK

⁶House Officer Medicine, Hayatabad Medical Complex, Peshawar

Corresponding author: Salman Khan, Email: salmankhn663@yahoo.com

ABSTRACT

Background and Aim: Diabetes mellitus is an increase in blood glucose levels results in altered fat, protein metabolism, and carbohydrate which leads to cardiac, eye, nervous system dysfunction, and kidney. The major cause of hospitalizations in patients with diabetes mellitus (DM) is diabetic foot ulcers (DFU). The purpose of the present study was to evaluate the peripheral arterial disease in diabetic foot ulcer patients presented to endocrine clinic.

Patients and Methods: This descriptive cross-sectional study was carried out on 206 diabetic foot ulcers patients presented to the endocrine clinic in Peshawar from January 2021 to December 2022. Patients were enrolled after taking written informed consent from each individual. Patient's details such as gender, age, peripheral artery disease (PAD), diabetes types, heart failure, wound size, diabetes duration, end-stage renal disease, DFU history, prior history of amputation, and peripheral neuropathy were recorded. Angiography and revascularization may be required if arterial Doppler ultrasound confirmed PAD. Additionally, wound debridement and topical dressings were applied. In the treatment of wound ischemia, pentoxifylline, and calcium blockers were recommended along with diabetes control procedures and appropriate antibiotics. SPSS version 27 was used for data analysis.

Results: Of the total 206 DFU patients, there were 142 (68.9%) male and 64 (31.1%) females. The prevalence of peripheral artery disease (PAD) was 58.3% (n=120). Age-wise distribution of patients were as follows: 31 (15%) in 25-45 years, 107 (52%) in 46-65 years, 60 (29.1%) in 66-85 years, and 8 (3.9%) >85 years. Out of 206 DFU patients, the prevalence of type-I diabetes mellitus and type-II diabetes mellitus was 8 (3.9%) and 198 (96.1%) respectively. PAD prevalence was significantly associated with Type 2 diabetes. The incidence of PAD in plantar foot, non-plantar foot, and heel was 66 (55%), 42 (35%), and 12 (10%) respectively among 120 cases. Out of 206 DFU cases, the incidence of peripheral neuropathy, DFU history, amputation history, heart failure, and chronic renal failure was 142 (68.9%), 104 (50.5%), 54 (26.2%), 46 (22.3%), and 42 (20.4%) respectively.

Conclusion: The present study concluded that the prevalence of peripheral artery disease (PAD) was 58.3% among diabetic foot ulcers. Results indicate that DFU and PAD are significantly related. It has been found that male patients with DFU were more likely to suffer from PAD as compared to women with statistically insignificant association.

Keywords: Peripheral artery disease, diabetic foot ulcers, type-II diabetes mellitus

INTRODUCTION

Diabetes mellitus (DM) and Diabetic foot ulcer (DFU) are the most serious health issues and prevalent reasons for hospitalization [1]. Diabetes mellitus (DM) is defined by high blood sugar levels, and changes in carbohydrate, lipid, and protein metabolism lead to eye, renal, cardiovascular, and nervous system dysfunction. Diabetes incidence has climbed by roughly 6% per year over the last decade, and the globe has faced a diabetes pandemic [2, 3]. Diabetes is one of the leading causes of chronic renal failure and amputation, accounting for 70% of all limb amputations [4]. Because of its substantial relationship with failure to heal and amputation, peripheral artery disease (PAD) early and precise detection in patients with diabetic foot ulceration is critical [5, 6]. While PAD is frequent below the knee in diabetic individuals, it was previously considered that the foot arteries were immune to occlusive disease [7]. Recent angiographic investigations, however, have found foot artery disease in up to 48% of diabetic individuals, presenting with significant ischemia of the foot [8].

Risk factors for DFU include high blood sugar levels, blood pressure problems, foot deformities, and vision impairment [9]. Cellulite, necrotizing fasciitis, abscess, osteomyelitis, and myositis are all symptoms of DFU, which can turn to amputation of lower extremity. Almost half cases of DFU develop an infected lesion 18 months after amputation, and other organ's amputations varies from 50% to 65% 3 to 5 years later [10]. DFU assessment necessitates a thorough review of clinical histories, examination, and treatments. Diabetic patient screening has a significant role in the prevention and treatment of lesions [11]. Clinical evaluations are required for a successful treatment strategy. Even if they do not complain of foot issues, all diabetes patients should be evaluated by their physician at least once a year [12, 13].

There are numerous treatment guidelines for people with PAD and persistent limb-threatening ischemia (CLTI). Unfortunately, most studies reporting on PAD outcomes do not include a diabetic subgroup, despite the fact that majority of the included patients are likely to have diabetes. Moreover, many studies on PAD and diabetes involve only individuals with intact feet or fail to accurately document the existence of neuropathy, ulcer, infection, or other conditions that contribute to poor outcomes [14]. Certainly, DFU patients, X-rays imaging, neurological, and vascular tests are also utilized to help in the diagnosis and assessment of abnormalities [15]. Diabetic individuals benefit from prompt detection and management of foot ulcer causes. Managing blood sugar levels and quitting smoking can both help to decrease the course of neuropathy and vascular disease. PAD was found in almost half of diabetic foot patients [16]. In terms of the problem's relevance, PAD recognizing and treating is a critical for diabetic foot patients and amputation decreasing is the most essential techniques [17]. As a result, the current study aimed to evaluate the PAD in patients with DFU presented to endocrine clinic.

METHODOLOGY

This descriptive cross-sectional study was carried out on 206 diabetic foot ulcers patients presented to the endocrine clinic in Peshawar from January 2021 to December 2022. Patients were enrolled after taking written informed consent from each individual. Patient's details such as gender, age, peripheral artery disease (PAD), diabetes types, heart failure, wound size, diabetes duration, end-stage renal disease, DFU history, prior history of amputation, and peripheral neuropathy were recorded. Angiography and revascularization may be required if arterial Doppler ultrasound confirmed PAD. Additionally, wound debridement and topical

dressings were applied. In the treatment of wound ischemia, pentoxifylline, and calcium blockers were recommended along with diabetes control procedures and appropriate antibiotics. The acquired information was analyzed using the SPSS version 27. Mean and standard deviation was used for quantitative variables. Frequencies and percentages were used for qualitative variables. Chi-square test was used for comparing different parameters by taking 5% level of significance.

RESULTS

Of the total 206 DFU patients, there were 142 (68.9%) male and 64 (31.1%) females. The prevalence of peripheral artery disease (PAD) was 58.3% (n=120). Age-wise distribution of patients were as follows: 31 (15%) in 25-45 years, 107 (52%) in 46-65 years, 60 (29.1%) in 66-85 years, and 8 (3.9%) >85 years. Out of 206 DFU patients, the prevalence of type-I diabetes mellitus and type-II diabetes mellitus was 8 (3.9%) and 198 (96.1%) respectively. PAD prevalence was significantly associated with Type 2 diabetes. The incidence of PAD in plantar foot, non-plantar foot, and heel was 66 (55%), 42 (35%), and 12 (10%) respectively among 120 cases. Out of 206 DFU cases, the incidence of peripheral neuropathy, DFU history, amputation history, heart failure, and chronic renal failure was 142 (68.9%), 104 (50.5%), 54 (26.2%), 46 (22.3%), and 42 (20.4%) respectively. Gender's distribution is illustrated in Figure-1. Age-wise distribution of patients are shown in Table-I. Figure-2 depicts the incidence of type-I and type-II diabetes mellitus. Wound locations are demonstrated in Figure-3. The incidence of PAD in diabetic foot ulcer patients are illustrated in Figure-4. Association of peripheral artery disease with wound location, types of diabetes, and duration of diabetes are shown in Table-II.

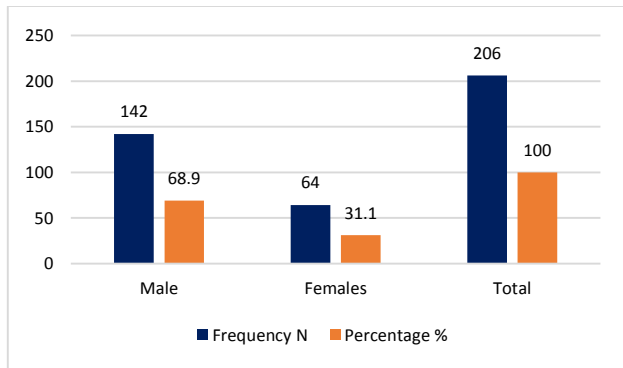


Figure-1: Gender's distribution (n=206)

Table-1: Age-wise distribution of diabetic foot ulcers (n=206)

Age group (years)	Frequency (N)	Percentage (%)
25-45	31	15
46-65	107	52
66-85	60	29.1
>85	8	3.9
Total	206	100

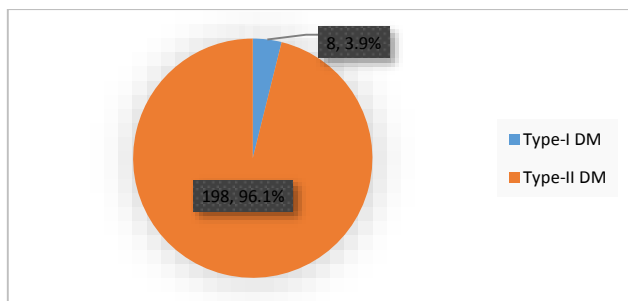


Figure-2: incidence of type-I and type-II diabetes mellitus (n=206)

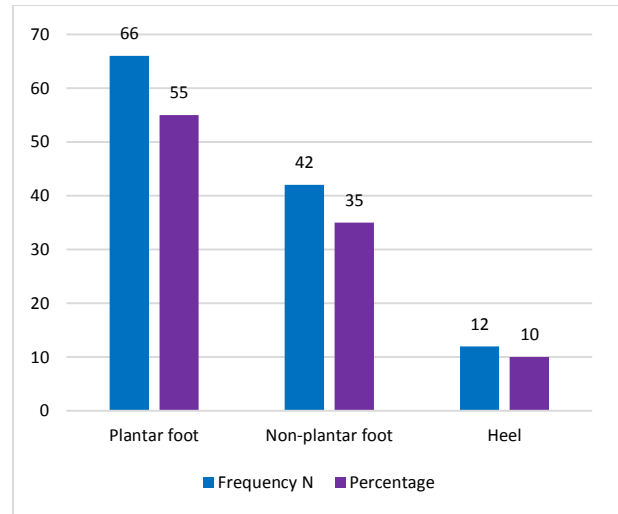


Figure-3: Wound locations (n=120)

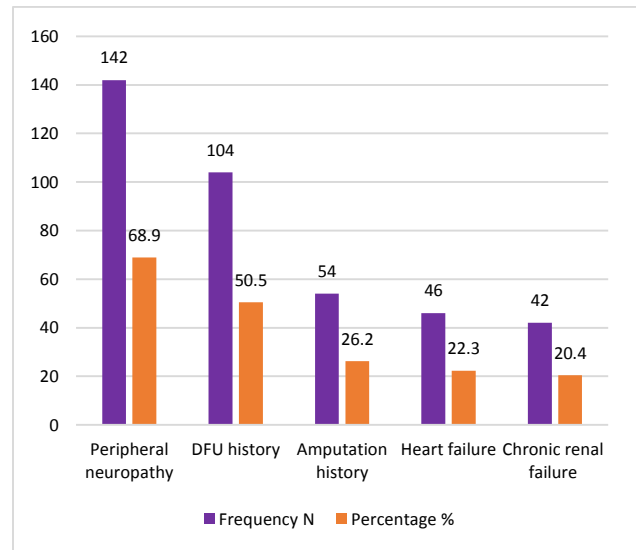


Figure-4: prevalence of PAD in diabetic foot ulcer patients (n=206)

Table-2: Association of peripheral artery disease with duration of diabetes, and wound location

Parameters	PAD Positive prevalence N (%)	PAD negative prevalence N (%)	P-value
Diabetes types			0.082
Type-I DM	2 (25)	6 (75)	
Type-II DM	118 (59.6)	80 (40.4)	
Diabetes duration (years)			0.039
<5	19 (46.3)	22 (55.7)	
6-10	39 (62.9)	23 (37.1)	
>10	62 (60.2)	41 (39.8)	
Wound location			0.846
Plantar	66 (63.5)	38 (36.5)	
Non-plantar	42 (50)	42 (50)	
Heel	12 (66.7)	6 (33.3)	

DISCUSSION

The present study mainly focused on the assessment of peripheral artery disease in diabetic foot ulcers presented to endocrine clinic and found that PAD was seen in a significant proportion of diabetic individuals with DFU. Controlling PAD as a key risk factor for DFU in diabetics will require more stringent treatments. Diabetic patients' neurovascular assessments and early detection of PAD

may be effective therapies to avoid the DFU's development. Individuals with diabetes who have an intact foot should have a full clinical evaluation for PAD that includes a history, pulse palpation, and ankle brachial pressure index testing. Patients with clinical suspicion of illness should undertake particular cardiovascular risk modification utilizing current advice since they are at significantly elevated cardiovascular risk.

The etiology of diabetes-related macro-vascular illness involves cellular alterations in endothelial, vascular smooth muscle cell, and platelet function [18]. Diabetes-related metabolic dysfunction, such as insulin resistance, dyslipidemia, hyperglycemia, and high amounts of free fatty acids, underlies the cellular processes that contribute to vascular dysfunction. According to population research, there is a graded and independent relationship between glucose control and incident/prevalent PAD in diabetic individuals [19, 20].

Peripheral artery disease is an autonomous risk factor for acquiring ulceration and limb loss, and it is present in up to 50% of diabetic foot ulcer patients. It is more prone to arise in elderly people and is existing in > 70% of diabetic patients over the age of 70 who have a foot ulcer [21]. Diabetes patients often have widespread peripheral vascular involvement that is particularly severe in the crural arteries, with a high frequency of lengthy occlusions [22-24]. Medial sclerosis (calcification of the tunica media) is also common and can impair peripheral vascular compliance and hence tissue perfusion. Diabetes impairs the development of collateral arteries in response to major artery occlusions, which may exacerbate the problem of tissue ischemia compared to people without diabetes [25].

Barshes et al., [26] discovered a greater frequency of neuropathy in males as neuropathy between men and women varies. Our findings revealed that 68.9% of patients were male, which may represent the gender ratio for foot ulcers developing in the population. The present study findings were also similar to Barshes et al., who found that male DFU patients were 73%. Neuropathy prevalence rose with age, as reported in previous research [27].

Our study discovered that diabetes duration had a significant influence on DFU outcomes. Of 206 patients, 60.2% had diabetes for more than 10 years, indicating that the diabetes duration significantly improved peripheral artery and DFU risk involvement. Our findings were comparable with a prior study conducted by Wang et al., who discovered that diabetic patients for >10 years were 68.75% [28]. Prior research has shown that diabetes has inhibitory effects, and that the diabetes duration may be as essential as total blood glucose management [29].

Neuropathy was found in 68.9% of the patients in this study, and PAD was significantly associated with neuropathy. According to Lehrman et al., found that neuropathy was found in 23.9% patients, but Azzopardi et al. reported 14.9%. [31, 32] Our findings were consistent with the findings of other research, and so in diabetic individuals, vasculopathy may be an essential risk factor in determining the amputation need.

CONCLUSION

The present study concluded that the prevalence of peripheral artery disease (PAD) was 58.3% among diabetic foot ulcers. Results indicate that DFU and PAD are significantly related. It has been found that male patients with DFU were more likely to suffer from PAD as compared to women with statistically insignificant association.

REFERENCES

1. Janbakhsh A, Abedinfam M, Sobhiyeh MR, Rezaie M, Aslani PS, Vaziri S, et al. Prevalence of peripheral artery disease in patients with infectious diabetic foot ulcer in Imam Reza Hospital in Kermanshah during 2019–2020. *J Edu Health Promot* 2021; 10:170.
2. Hinchliffe RJ, Forsythe RO, Apelqvist J, Boyko EJ, Fritridge R, Hong JP, Katsanos K, Mills JL, Nikol S, Reekers J, Venermo M. Guidelines on diagnosis, prognosis, and management of peripheral artery

- disease in patients with foot ulcers and diabetes (IWGDF 2019 update). *Diabetes/Metabolism Research and Reviews*. 2020; 36:e3276.
3. Kaboudi M, Dehghan F, Ziapour A. The effect of acceptance and commitment therapy on the mental health of women patients with type II diabetes. *Ann Trop Med Public Health* 2017; 10:1709-13.
4. Muthiah A, Kandasamy R, Nagulan S, Madasamy A. A study on diabetic foot and its association with peripheral artery disease. *Int Surgery J* 2017; 4:1217-21.
5. Elgzryi T, Larsson J, Thörne J, Eriksson KF, Apelqvist J. Outcome of ischemic foot ulcer in diabetic patients who had no invasive vascular intervention. *Eur J Vasc Endovasc Surg* 2013; 46:110-7.
6. Azar FE, Solhi M, Darabi F, Rohban A, Abolfathi M, Nejhadadgar NJD. Effect of educational intervention based on PRECEDE-PROCEED model combined with self-management theory on self-care behaviors in type 2 diabetic patients. *Diabet Metabo Syndrome: Clin Res* 2018;12(6):1075-8.
7. Zhang P, Lu J, Jing Y, Tang S, Zhu D, Bi Y. Global epidemiology of diabetic foot ulceration: a systematic review and meta-analysis. *Ann Med*. 2017;49(2):106-116. <https://doi.org/10.1080/07853890.2016.1231932>.
8. Narres M, Kvitkina T, Claessen H, Droste S, Schuster B, Morbach S, Rügenapf G, van Acker K, Icks A. Incidence of lower extremity amputations in the diabetic compared with the non-diabetic population: a systematic review. Grabowski A, ed. *PLoS One*. 2017;12(8):e0182081. [doi:https://doi.org/10.1371/journal.pone.0182081](https://doi.org/10.1371/journal.pone.0182081).
9. Rigato M, Pizzol D, Tiago A, Putoto G, Avogaro A, Fadini GP. Characteristics, prevalence, and outcomes of diabetic foot ulcers in Africa. A systemic review and meta-analysis. *Diabetes Res Clin Pract*. 2018;142:63-73. <https://doi.org/10.1016/j.diabres.2018.05.016>.
10. Younis BB, Shahid A, Arshad R, Khurshid S, Ahmad M, Yousaf H. Frequency of foot ulcers in people with type 2 diabetes, presenting to specialist diabetes clinic at a Tertiary Care Hospital, Lahore, Pakistan. *BMC Endocr Disord*. 2018;18(1):53. <https://doi.org/10.1186/s12902-018-0282-y>.
11. Mariam TG, Alemayehu A, Tesfaye E, Mequannt W, Temesgen K, Yetwale F, Limenih MA. Prevalence of Diabetic Foot Ulcer and Associated Factors among Adult Diabetic Patients Who Attend the Diabetic Follow-Up Clinic at the University of Gondar Referral Hospital, North West Ethiopia, 2016: Institutional-Based Cross-Sectional Study. *J Diabetes Res*. 2017; 2017:2879249.
12. Nongmaithem M, Bawa AP, Pithwa AK, Bhatia SK, Singh G, Gooptu S. A study of risk factors and foot care behavior among diabetics. *J Family Med Prim Care*. 2016;5(2):399-403.
13. Forsythe RO, Apelqvist J, Boyko EJ, et al. Effectiveness of revascularisation of the ulcerated foot in patients with diabetes and peripheral artery disease: A systematic review. *Diabetes Metab Res Rev*. 2020;36(S1):e3279.
14. Waaijman R, de Haart M, Arts ML, Wever D, Verlouw AJ, Nollet F, Bus SA. Risk factors for plantar foot ulcer recurrence in neuropathic diabetic patients. *Diabetes Care*. 2014;37(6):1697-705.
15. Mathur R, Sahu K, Saraf S, Patheja P, Khan F, Gupta P. Low-level laser therapy as an adjunct to conventional therapy in the treatment of diabetic foot ulcers. *Lasers Med Sci*. 2017;32(2):275-82.
16. Thiruvoipati T, Kielhorn CE, Armstrong EJ. Peripheral artery disease in patients with diabetes: epidemiology, mechanisms, and outcomes. *World J Diabetes*. 2015;6(7):961-9.
17. Schmidt BM, Wrobel JS, Holmes CM. Physician knowledge of a rare foot condition –influence of diabetic patient population on self-described knowledge and treatment. *Clin Diab Endocrinol*. 2017;3(1):2.
18. Forsythe RO, Apelqvist J, Boyko EJ, et al. Performance of prognostic markers in the prediction of wound healing or amputation among patients with foot ulcers in diabetes: A systematic review. *Diabetes Metab Res Rev*. 2020;36(S1):e3278.
19. Anderson SG, Shoo H, Saluja S, Anderson CD, Khan A, Livingston M, Jude EB, Lunt M, Dunn G, Heald AH. Social deprivation modifies the association between incident foot ulceration and mortality in type 1 and type 2 diabetes: a longitudinal study of a primary-care cohort. *Diabetologia*. 2018; 61(4):959-67.
20. Richter L, Freisinger E, Lueders F, Gebauer K, Meyborg M, Malyar NM. Impact of diabetes type on treatment and outcome of patients with peripheral artery disease. *Diab Vasc Dis Res*. 2018;15(6):504-510. <https://doi.org/10.1177/1479164118793986>.
21. Blinc A, Kozak M, Šabovic M, et al. Survival and event-free survival of patients with peripheral artery disease undergoing prevention of cardiovascular disease. *Int Angiol*. 2017;36(3):216-227. <https://doi.org/10.23736/S0392-9590.16.03731-7>.

22. Lipsky BA, Senneville É, Abbas ZG, et al. Guidelines on the diagnosis and treatment of foot infection in persons with diabetes (IWGDF 2019 update). *Diabetes Metab Res Rev.* 2020;36(S1):e3280.
23. Jeffcoate WJ, Bus SA, Game FL, et al. Reporting standards of studies and papers on the prevention and management of foot ulcers in diabetes: required details and markers of good quality. *Lancet Diabetes Endocrinol.* 2016;4(9):781-788. [https://doi.org/10.1016/S2213-8587\(16\)30012-2](https://doi.org/10.1016/S2213-8587(16)30012-2).
24. Bunte MC, Jacob J, Nudelman B, Shishehbor MH. Validation of the relationship between ankle-brachial and toe-brachial indices and infragenicular arterial patency in critical limb ischemia. *Vasc Med.* 2015;20(1):23-29. <https://doi.org/10.1177/1358863X14565372>.
25. Vriens B, D'Abate F, Ozdemir BA, et al. Clinical examination and noninvasive screening tests in the diagnosis of peripheral artery disease in people with diabetes-related foot ulceration. *Diabet Med.* 2018;35(7):895-902. <https://doi.org/10.1111/dme.13634>.
26. Barshes NR, Flores E, Belkin M, Kougias P, Armstrong DG, Mills JLS. The accuracy and cost-effectiveness of strategies used to identify peripheral artery disease among patients with diabetic foot ulcers. *YMVA.* 2016;64(6):1682. <https://doi.org/10.1016/j.jvs.2016.04.056>.
27. Tehan PE, Barwick AL, Sebastian M, Chuter VH. Diagnostic accuracy of resting systolic toe pressure for diagnosis of peripheral artery disease in people with and without diabetes: a cross-sectional retrospective case-control study. *J Foot Ankle Res.* 2017;10(1). <https://doi.org/10.1186/s13047-017-0236-z>.
28. Wang Z, Hasan R, Firwana B, et al. A systematic review and metaanalysis of tests to predict wound healing in diabetic foot. *YMVA.* 2016;63(2):29S-U99. <https://doi.org/10.1016/j.jvs.2015.10.004>
29. Forsythe RO, Apelqvist J, Boyko EJ, et al. Effectiveness of bedside investigations to diagnose peripheral artery disease among people with diabetes mellitus: A systematic review. *Diabetes Metab Res Rev.* 2020;36(S1):e3277.
30. Hart T, Milner R, Cifu A. Management of a diabetic foot. *JAMA.* 2017;318(14):1387-1388. <https://doi.org/10.1001/jama.2017.11700>.
31. Lehrman ED, Plotnik AN, Hope T, Saloner D. Ferumoxytol-enhanced MRI in the peripheral vasculature. *Clin Radiol.* 2019;74(1):37-50. <https://doi.org/10.1016/j.crad.2018.02.021>.
32. Azzopardi YM, Gatt A, Chockalingam N, Formosa C. Agreement of clinical tests for the diagnosis of peripheral arterial disease. *Prim Care Diabetes.* 2019;13:82-86.