Journal of Advanced Zoology

ISSN: 0253-7214
*Volume **44** Issue **S-6 Year 2023** Page **1253:1258***

Association Between Lipid Profile and Diabetic Foot Ulcer

Najlaa Mohammad Alsudairy[1], Al Abdrabalnabi, Fatimah Ahmed E[2], Shahad Abdulaziz S Alzahrani[3], Khalid Faisal Alzibali[4], Eman Mohammed Osman Mohammed Nour Mohammed[5], Rahf Mohammed Alqarni[6], Al Dhamer, Abdullah Adel A[7], Alhabeeb,Shada Habeeb S[8], Al Shuaibi, Abdulraoof Fahad A[9], Fatmh Hmedin Al Ejefi [10], Almaden,Hadi Faisal S[11], Naif Ogab Jabr Alotabi[12], Alshehri, Abdulaziz Fayez Mohammed[13]

[1]Assistant Consultant FM,National Guard Hospital, King Abdulaziz Medical City, SCOHS, Jeddah, Saudi Arabia. Email: Najlaa.Alsudairy@gmail.com
[2]SAUD AL BABTAIN CARDIAC CENTER, KSA. Email: Faaalabdrabalnabi@moh.gov.sA
[3]King Abdulaziz University, Jeddah, KSA. Email: Shahadabzhrani@gmail.com
[4]King Abdulaziz University, Rabigh, KSA. Email: Khalid432345@gmail.com
[5]Peter Lougheed Centre, Calgary-Clinical Assistant. Email: emannoor1310@gmail.com
[6] Intern, University of Tabuk, KSA. Email: Rahfmq222@hotmail.com
[7]Inter, King faisal university, work at oyun city hospital, KSA. Email: abdullah76610@gmail.com
[8]Qatif Network-Primary Healthcare Center, KSA. Email: Rosl@windowslive.com
[9] Inter, King Faisal University, KSA. Email: Raoof.fahad@hotmail.com
[10]Madrakah Health Center in Makkah Al-Mukarramah, KSA. Email: Fatmah20500@gmail.com
[11] East cluster number 1- PHC Alridha, KSA. Email: Hfalmaden@hotmail.com
[12]Nursing technician, Madrakah Health Center in Makkah Al-Mukarramah, KSA. Email: naaalotabi@moh.gov.sa
[13]Intern, King khalid university, KSA. Email: abdulazizalshehri086@gmail.com

Article History

Received: 12 June 2023
Revised: 22 Sept 2023
Accepted: 02 Dec 2023

Abstract

Diabetic foot ulcer is a serious disabling consequence of Diabetes Mellitus. They are characterized by the breakdown of skin and underlying tissues in the feet, and are a major cause of lower limb amputations. Various risk factors have been identified for the development of diabetic foot ulcers, including poor glycemic control, peripheral neuropathy, peripheral arterial disease, and impaired wound healing. it is considered that the lipid profile is one of many factors that contribute to the formation and progression of diabetic foot ulcers. To stratify the incidence of diabetic foot ulcers (DFUs), biomarkers are required. The aim of this review is to assess the relationship between the risk of DFU and lipid profile in diabetic patients.

Keywords: *Diabetic foot ulcer, Diabetes mellitus, Lipid profile, Diabetic dyslipidemia, Amputation*

Introduction

Diabetes mellitus is a chronic, life-threatening condition which is on increasing and is associated with public health problems that have a discernible impact on both human health and health care systems. The diabetic foot ulcer (DFU) is one of the most significant consequences of diabetes mellitus. Diabetes-related foot problems are increasing the long-term morbidity and mortality of the diabetic population, which results in recurrent hospital stays and expensive treatment for both the individuals and the community as a whole [1].

Each year, 1-4% of persons with type 2 diabetes develop a foot ulcer, which can lead to gangrene and lower extremity amputation. Diabetes patients are 25 times more likely to lose a limb, and those with diabetes account for up to 70% of all leg amputations [2]. Regardless of the kind of diabetes, the risk of diabetic foot ulceration (DFU) and amputation rises by two to four times as a patient's age and diabetes duration grow [3].

The most dreaded outcome for patients with DFU is amputation, occurring in 6–43% of instances [4]. The lipid profile has been linked to the emergence of diabetic foot ulcer [5]. However, by taking specific precautions including lipid management and changing the lifestyle, this disease can be avoided [6]. Furthermore, in order to prioritize surveillance, diabetic individuals who are more likely to acquire this illness must be identified early on thanks to instruments. For these uses, biomarkers are useful instruments. Numerous biomarkers, including platelet-to-lymphocyte ratio, apolipoproteins, creatinine, lipid profile, hemoglobin A1c, and others, have been explored to date with the goal of stratifying the risk of developing DFU [7-8]. Consequently, our goal is to compile the data pertaining to the relationship between the risk of diabetic foot ulcer and the lipid profile.

Prevalence of diabetic foot ulcer

According to International Diabetes Federation (IDF) data and statistical research, 425 million persons worldwide are predicted to have diabetes mellitus (DM), and by 2045, that figure is expected to increase to 629 million [9]. Diabetic foot ulcer (DFU), one of the most serious effects of diabetes, is becoming a growing problem for public health systems in diabetic individuals. The global frequency of DFU is estimated to be 6.3%, with North America having the greatest prevalence (13.0%) [10]. Many longitudinal epidemiological studies have also shown that the prevalence of diabetic foot ulcers is around 15%, with a lifetime incidence of up to 25% [11].

The diversity that binds DFU to lipid profil:

Regional variations must be taken into consideration, even though the results indicate that low HDL and high TG and Lp(a) values might be used to predict the development of diabetic foot ulcers. Variations in the prevalence of diabetic dyslipidemia could account for some of the explanation; for example, the prevalence of diabetic dyslipidemia is higher among the South Asian population [12]. Furthermore, these disparities might be explained by geographical variances in lipid profiles. While the prevalence of total cholesterol is generally lower in Southwest Asian nations than in European, North American, or South American nations, the differences in prevalence are contingent upon the respective wealth levels of the nations. While the mean plasma cholesterol value declined in high-income nations, it grew along with TG values in low- and middle-income countries [13]. Similarly, there might be regional variations in these values in big nations like China [14]. Consequently, geographical differences in the control of cholesterol through statin use also exist. Statins do, in fact, have cholesterol-independent benefits through reducing oxidative stress linked to diabetic dyslipidemia, promoting wound and fracture healing, and modifying the immunological response. Hence, by enhancing endothelial nitric oxide synthase's capacity to produce nitric oxide in endothelial cells despite lipid-lowering effects, statins will not only prevent macrovascular illnesses but also decrease the advancement of microvascular complications of diabetes. Moreover, statins can enhance endothelial function and lessen oxidative stress in addition to reducing cholesterol levels, which enhances microvascular performance [15]. Consequently, high-income nations utilize them more frequently than low-income nations, where few people have access to statins [16].

Nevertheless, factors like the potential impact of the patients' gender have not been taken into account. For instance, research on diabetic patients in China revealed that the ApoB/ApoA1 ratio predicted men's risk of cardiovascular disease. Conversely, in women, TC, LDL, ApoB, LDL/HDL, and TC/HDL were superior predictors [17].

The impact of dietary status on the outcomes was not assessed, yet it is well recognized that it affects the lipid profile. Thus, the geographical differences in obesity and malnutrition may help to explain the differences in results between nations, together with the regional variations in the lipid profile and the usage of statins [18]. Furthermore, a comprehensive study discovered that in individuals with diabetic foot ulcers, there is a relationship between inadequate nutritional status and the development of ulcers or delayed healing [19].

Risk factors of diabetic foot ulcer

The development of DFU is typically influenced by three factors: diabetic neuropathy, trauma with secondary infection, and vascular occlusive disease. These characteristics are more likely to manifest in patients with diabetes because they frequently have altered apolipoproteins and lipid profiles [20]. These changes are complex, but one of the most significant ones has to do with the glycosylation of proteins, such low-density lipoprotein (LDL). This phenomenon

hinders lipoproteins from being recognized by cell receptors, which prolongs their duration in circulation. Later, lipoproteins would be taken up by macrophages, which would lead to an increase in the synthesis of cholesterol esters. Accumulation of lipoproteins induces macrophages to become foam cells, which produce the fatty streak and subsequently start the atherosclerotic process [21].

Association between lipid profile and DFU

The lipid profile is one such element that has been thoroughly researched related to diabetic foot ulcers. Lipids, including cholesterol and triglycerides, are important components of cell membranes and play a vital role in various physiological processes, including inflammation and wound healing. Substantial research in recent years has indicated that lipid problems might possibly be involved in the pathophysiology of diabetic foot ulcers. People with diabetes frequently have dyslipidemia, which is defined by increased levels of low-density lipoprotein (LDL) cholesterol, triglycerides, and total cholesterol and lower levels of high-density lipoprotein (HDL) cholesterol [22].

Several studies have shown an association between dyslipidemia and development of diabetic foot ulcers. It has been demonstrated that high levels of triglycerides, LDL cholesterol, and total cholesterol are independent risk factors for the development of foot ulcers in diabetics. These lipids have been linked to the development of atherosclerosis, which can impede blood flow to the lower limbs and raise the risk of developing foot ulcers [23].

Moreover, dyslipidemia has been demonstrated to delay wound healing, which is crucial in the treatment of diabetic foot ulcers. Increased levels of pro-inflammatory cytokines, such as interleukin-6 and tumor necrosis factor-alpha, have been linked to high levels of LDL cholesterol and triglycerides and can impede the healing of wounds. Furthermore, dyslipidemia may hinder angiogenesis, the process of new blood vessel development necessary for sufficient tissue regeneration and wound healing [24].

However, it is crucial to note that the association between lipid profile and diabetic foot ulcers is complex and multifaceted. Other factors, such as glycemic management, smoking, obesity, and comorbidities such as hypertension and renal illness, can all influence the formation and progression of foot ulcers in diabetics. As a result, it is critical to include these aspects when examining the relationship between lipid profile and diabetic foot ulcers [25].

Diabetic dyslipidemia

Patients with type 2 diabetes are more likely to have dyslipidemia, which increases their chance of developing complications like stroke, coronary artery disease, nephropathy, and neuropathy [26]. Insulin resistance is associated with diabetic dyslipidemia, which may present as an early symptom before the disease develops. The primary quantitative aberration in lipoproteins is the increase in TG. Sub-fraction of large VLDL and small and dense LDL particles has increased, however the fundamental qualitative abnormality of diabetic dyslipidemia is still the same. Because diabetes plays a major role in the development and progression of atherosclerosis, individuals with diabetic dyslipidemia are more likely to experience cardiovascular events and peripheral vascular disease than individuals without the illness [12].

Peripheral neuropathy linked to the impact of fatty acids on mitochondrial trafficking is linked to diabetic dyslipidemia and other microvascular problems. These lipid metabolism-related compounds accumulate and lead to oxidative stress, which is followed by an upregulation of pro-inflammatory cytokines and death of the neurons [27].

The initial lipid profile of the patient who was recently diagnosed with diabetes is even linked to this neuropathic impairment. The Anglo-Danish-Dutch investigation revealed an interesting correlation between peripheral neuropathy and baseline waist circumference, body mass index, HDL, and LDL. 13 years after being diagnosed with diabetes [28].

Amputation

The most prevalent endocrine condition, diabetes mellitus, is well-known for its numerous side effects, among which are diabetic foot ulcers (DFU), which frequently lead to amputation as one of the worst cases. According to the Global Lower Extremity Study Group, LEA is defined as a full loss of any part of the lower extremity, regardless of the source [29].

Approximately 82% of LEAs are performed on diabetic patients, the majority of which occur as a result of foot ulceration [30].

It has been shown that people with diabetes have higher prevalence of many lipoprotein abnormalities than people without diabetes. The impact of lipid and lipoprotein abnormalities on the risk of amputation in DFU has been the subject of very few published investigations. According to a recent study by Zubair et al., the risk of amputation was linked to fasting triglyceride levels (>150 mg/dL), cholesterol levels (>150 mg/dL), LDL cholesterol levels (>100 mg/dL), and HDL cholesterol levels (<40 mg/dL) [31]. Of all the factors taken into account, only hypertriglyceridemia has been shown to predict LEA (OR 5.87, 95% CI 1.84–18.97; p=0.003) using plasma lipoproteins; the other fractions do not appear to be related to amputation. To determine the relevance of hypertriglyceridemia in these diabetes sequelae, more research is obviously required.

Specifically, research on individuals with DFU revealed that a low TG level was a risk factor in and of itself for limb amputation. Likewise, a different study found a correlation between a low HDL level and a decreased risk of lower limb amputation and diabetic foot ulcer-related mortality [23]. This aspect is significant since individuals with a higher risk of amputation due to some degree of ulceration were among the participants analyzed in the trials included in the evaluation.

Prevention of Diabetic Foot Ulcer

The lifestyle changes such as diet and exercise, are essential components of any strategy required to prevent diabetic foot complications. Exercise is one of the most prevalent diabetes lifestyle needs, and it promotes tissue perfusion, which is necessary for wound healing. It has also been reported to improve wound size reduction in DFU [32]. Foot care is one of the most effective ways to avoid DFU.

Blood glucose control must be strictly adhered to in order to avoid both macrovascular and microvascular problems. Adequate hypertension and dyslipidemia management is critical for preventing vascular problems.

A thorough foot examination is performed once a year, with an emphasis on neuropathic, vascular, and structural assessment. Patients who are at high risk require more frequent checkups.

Treatment of diabetic foot ulcer

The DFU takes a long time to heal and requires a multidisciplinary treatment plan that includes blood glucose control, antibiotics, wound care, ulcer debridement, unloading (no load or pressure), and revascularization or enhanced blood flow. Effective treatment management can lessen additional complications associated with diabetes mellitus and hasten the healing of wounds [33].

One adjuvant therapy to speed up wound healing in a chronic wound is hyperbaric oxygen therapy (HBOT). This therapy may have an impact on lipid profiles by raising triglyceride and low-density lipoprotein (LDL) cholesterol while lowering total and high-density lipoprotein (HDL) cholesterol. The metabolic aspects of the DFU patient may be impacted by this therapy [34].

Consequently, Cardiovascular disease (CVD) and increased mortality are linked to diabetic foot. When diabetic patients with foot ulcers receive lipid-lowering therapy, their risk of CVD morbidity and death decreases. Specifically, fibrates are beneficial to people with a particular lipid profile, while statins reduce CVD mortality and increase survival in patients with diabetic foot. Due mostly to their effect on peripheral artery disease, statins slow the advancement of the local illness, relieving symptoms and lowering amputation rates. Fibrates seem to improve neuropathy, which lowers the number of amputations. They also lessen the likelihood of ulcer recurrence and enhance ulcer healing [35].

Conclusion

In conclusion, it has been demonstrated that high levels of triglycerides, LDL cholesterol, and total cholesterol are independent risk factors for foot ulcers, which leads to development of dyslipidemia as it can impede the healing of wounds. Nevertheless, more investigation is required

to clarify the underlying processes and identify the best ways to manage diabetes in order to avoid and treat foot ulcers. Finally, it should be noted that there is a complex and multifaceted interaction between lipid profile and diabetic foot ulcers that needs more research.

References

1. Nyamu PN, Otieno CF, Amayo EO, McLigeyo SO. Risk factors and prevalence of diabetic foot ulcers at Kenyatta National Hospital, Nairobi. East African medical journal. 2003;80(1):36-43.
2. Alexiadou K, Doupis J. Management of diabetic foot ulcers. Diabetes Therapy. 2012 Dec;3:1-5.
3. Katsilambros N, Tentolouris N, Tsapogas P. Who is the patient at risk for foot ulceration. Katsilambros N, Dounis E, Tsapogas P and Tentolouris N Atlas of the diabetic foot, editors. Chichester. 2003:1-21.
4. Moulik PK, Mtonga R, Gill GV. Amputation and mortality in new-onset diabetic foot ulcers stratified by etiology. Diabetes care. 2003 Feb 1;26(2):491-4.
5. McNeill JH. Role of elevated lipids in diabetic cardiomyopathy. Diabetes research and clinical practice. 1996 Jul 1;31:S67-71.
6. Iraj B, Khorvash F, Ebneshahidi A, Askari G. Prevention of diabetic foot ulcer. International journal of preventive medicine. 2013 Mar;4(3):373.
7. Zhang K, Ding S, Lyu X, Tan Q, Wang Z. Correlation between the platelet-to-lymphocyte ratio and diabetic foot ulcer in patients with type 2 diabetes mellitus. Journal of Clinical Laboratory Analysis. 2021 Apr;35(4):e23719.
8. Aziz KM. Risk Factors for Developing Diabetic Foot Ulcer with Nephropathy, Diabetic Kidney Disease and Renal Failure Statistical Analysis of 10,680 Patients' Cohort. medRxiv. 2020 Jun 12:2020-06.
9. Mushtaq S, Khan S, Rashid MR. Study of Glycated Haemoglobin and lipid profile in patients with diabetic foot ulcer. International Journal of Contemporary Medical Research [IJCMR]. 2020;7(6):F1-4.
10. Zhang P, Lu J, Jing Y, Tang S, Zhu D, Bi Y. Global epidemiology of diabetic foot ulceration: a systematic review and meta-analysis. Annals of medicine. 2017 Feb 17;49(2):106-16.
11. Yazdanpanah L, Shahbazian H, Nazari I, Arti HR, Ahmadi F, Mohammadianinejad SE, Cheraghian B, Hesam S. Incidence and risk factors of diabetic foot ulcer: a population-based diabetic foot cohort (ADFC study)—two-year follow-up study. International journal of endocrinology. 2018 Mar 15;2018.
12. Athyros VG, Doumas M, Imprialos KP, Stavropoulos K, Georgianou E, Katsimardou A, Karagiannis A. Diabetes and lipid metabolism. Hormones. 2018 Mar;17:61-7.
13. Irazola V, Rubinstein AL, Taddei C, Zhou B, Bixby H, Carrillo Larco RM, Danaei G, Jackson RT, Farzadfar F, Sophiea MK, Di Cesare M. Repositioning of the global epicentre of non-optimal cholesterol.
14. Pirillo A, Casula M, Olmastroni E, Norata GD, Catapano AL. Global epidemiology of dyslipidaemias. Nature Reviews Cardiology. 2021 Oct;18(10):689-700.
15. Fox JD, Baquerizo-Nole KL, Macquhae F, Herskovitz I, Freedman JB, Vileikyte L, Margolis DJ, Kirsner RS. Statins may be associated with six-week diabetic foot ulcer healing. Wound Repair and Regeneration. 2016 Mar;24(2):454-57.
16. Chow CK, Nguyen TN, Marschner S, Diaz R, Rahman O, Avezum A, Lear SA, Teo K, Yeates KE, Lanas F, Li W. Availability and affordability of medicines and cardiovascular outcomes in 21 high-income, middle-income and low-income countries. BMJ Global Health. 2020 Nov 1;5(11):e002640.
17. Yin S, Zhao P, Ai Z, Deng B, Jia W, Wang H, Zheng J. Sex-specific differences in blood lipids and lipid ratios in type 2 diabetic foot patients. Journal of Diabetes Investigation. 2021 Dec;12(12):2203-11.
18. McLachlan S, NCD Risk Factor Collaboration. Trends in adult body mass index in 200 countries since 1975: pooled analysis of 1,698 population-based measurement studies with 19.2 million participants. The Lancet. 2016 Apr 2;387(10026).
19. Bechara N, Gunton JE, Flood V, Hng TM, McGloin C. Associations between nutrients and foot ulceration in diabetes: A systematic review. Nutrients. 2021 Jul 27;13(8):2576.
20. Wang W, Zhang Y, Liao Y, Wu J, Zhou L, Tang Y, Cao Y, Metzmann E, Wang R. Diabetic foot disease: grading inflammation by apolipoprotein AI, C-reactive protein and serum amyloid A. Clin. Lab. 2014 Dec;60:1951-9.
21. Nativel M, Potier L, Alexandre L, Baillet-Blanco L, Ducasse E, Velho G, Marre M, Roussel R, Rigalleau V, Mohammedi K. Lower extremity arterial disease in patients with diabetes: a contemporary narrative review. Cardiovascular diabetology. 2018 Dec;17:1-4.
22. Chehade JM, Gladysz M, Mooradian AD. Dyslipidemia in type 2 diabetes: prevalence, pathophysiology, and management. Drugs. 2013 Mar;73:327-39.
23. Ikura K, Hanai K, Shinjyo T, Uchigata Y. HDL cholesterol as a predictor for the incidence of lower extremity amputation and wound-related death in patients with diabetic foot ulcers. Atherosclerosis. 2015 Apr 1;239(2):465-9.

24. Baltzis D, Eleftheriadou I, Veves A. Pathogenesis and treatment of impaired wound healing in diabetes mellitus: new insights. Advances in therapy. 2014 Aug;31:817-36.
25. Khan MI, Azhar U, Zubair F, Khan ZA. Can we link foot ulcer with risk factors in diabetics? A study in a tertiary care hospital. Pakistan journal of medical sciences. 2018 Nov;34(6):1375.
26. Kranenburg G, van der Graaf Y, van der Leeuw J, Nathoe HM, de Borst GJ, Kappelle LJ, Visseren FL, Westerink J. The relation between HbA1c and cardiovascular events in patients with type 2 diabetes with and without vascular disease. Diabetes care. 2015 Oct 1;38(10):1930-6.
27. Ahmadi SA, Shirzadegan R, Mousavi N, Farokhi E, Soleimaninejad M, Jafarzadeh M. Designing a Logistic Regression model for a Dataset to predict diabetic foot ulcer in diabetic patients: high-Density lipoprotein (HDL) cholesterol was the Negative predictor. Journal of Diabetes Research. 2021 Mar 18;2021.
28. Savelieff MG, Callaghan BC, Feldman EL. The emerging role of dyslipidemia in diabetic microvascular complications. Current Opinion in Endocrinology, Diabetes and Obesity. 2020 Apr 1;27(2):115-23.
29. Unwin N. Epidemiology of lower extremity amputation in centres in Europe, North America and East Asia. British Journal of Surgery. 2000 Mar;87(3):328-37.
30. Dillingham TR, Pezzin LE, MacKenzie EJ. Limb amputation and limb deficiency: epidemiology and recent trends in the United States. Southern medical journal. 2002 Aug 1;95(8):875-84.
31. Zubair M, Malik A, Ahmad J. Incidence, risk factors for amputation among patients with diabetic foot ulcer in a North Indian tertiary care hospital. The Foot. 2012 Mar 1;22(1):24-30.
32. Dufour É, Duhoux A. Re: The Effect of Foot Exercises on Wound Healing in Type 2 Diabetic Patients With a Foot Ulcer: A Randomized Control Study. J Wound Ostomy Continence Nursing. 2018; 45 (2): 123-130. Journal of Wound Ostomy & Continence Nursing. 2018 Nov 1;45(6):492-3.
33. Irawan H, Kartika K. Terapi oksigen hiperbarik sebagai terapi ajuvan kaki diabetik. Cermin Dunia Kedokteran. 2016 Oct 1;43(10):400989.
34. Bhutani S, Vishwanath G. Hyperbaric oxygen and wound healing. Indian Journal of Plastic Surgery. 2012 May;45(02):316-24.
35. Antonoglou C, Papanas N, Maltezos E. Lipid-lowering therapy in the diabetic foot: seeing the whole iceberg and not just the tip. Current Vascular Pharmacology. 2014 Sep 1;12(5):745-50.