Journal of Medicine in Scientific Research

Volume 1 | Issue 3 Article 8

Subject Area:

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El-Saied Shaheen
Shebin El Kom Teaching Hospital, shahins6666@yahoo.com

Feisal Goda
Shebin El Kom Teaching Hospital

Helmy M. Elshazly
Menoufia University

Recommended Citation

Shaheen, El-Saied; Goda, Feisal; and Elshazly, Helmy M. (2018) "Renal function and diabetic foot ulcer," *Journal of Medicine in Scientific Research*: Vol. 1: Iss. 3, Article 8.
DOI: https://doi.org/10.4103/JMISR.JMISR_54_18

Original Article

Renal function and diabetic foot ulcer

El-Saied Shaheen[a], Feisal Goda[b], Helmy M. Elshazly[c]

Departments of [a]Internal Medicine and [b]General Surgery, Shebin El Kom Teaching Hospital, [c]Department of Hepatology and Gastroenterology, National Liver Institute, Menoufia University, Menoufia, Egypt

Abstract

Introduction

Diabetic nephropathy has been identified as an essential risk factor for foot ulceration and amputation. Renal failure has been reported to independently predict the risk of nonhealing ischemic and neuroischemic foot lesions and major amputation.

Objective

In this study, we aimed at assessing the renal function of diabetic foot infected patients.

Patients and methods

We included 120 patients with type 2 diabetes mellitus, patients participated from the medical and surgical unit, Shebin El Kom Teaching Hospital, Egypt. They were divided into two main group; group 1 included 80 patients with an active diabetic foot ulcer (DFU) and group 2 included 40 patients without an active or past history of DFU. Also, group 1was subdivided into two groups; 40 patients were included in group A, who had antibiotic therapy with a low profile of renal toxicity (ceftriaxone, clindamycin, and ciprofloxacin) and 40 patients were included in group B who had antibiotic therapy with a high profile of renal toxicity (imipenem, aminoglycosides, and vancomycin).

Results

Patients with DFU had significant increase in neuropathy, history of lower limb amputation, and cerebrovascular accident. Also, patients with DFU had increased fasting blood glucose, 2 h postprandial glucose, glycated hemoglobin. Moreover, patients with DFU had increased serum creatinine and decreased estimated glomerular filtration rate. Also, serum creatinine was high in patients with DFU who received antibiotics with higher nephrotoxicity.

Conclusion

There was a strong association between the degree of renal impairment and DFU. Renal function decreased after antibiotherapy. In patients receiving antibiotics with higher nephrotoxicity, its decline was steeper. Further study is required to identify factors affecting renal function in patients with a DFU.

Keywords: Amputation, diabetic foot, renal function

Introduction

Diabetes type 2 is a globally common chronic disease, with its prevalence and vascular complications taking a toll on the health system [1]. Worldwide, the commonly occurring complication of diabetes is the diabetic foot with subsequent infection and is the direct cause of morbidity and premature mortality in diabetics [2]. Owing to neuropathy and potential coexisting vascular disease, about 25% of all diabetic individuals during their lifetime are affected, following a trauma that often goes unnoticed, ulceration occurs, and diabetic foot process is initiated [3]. It is complicated by ulceration and result in lower limb amputation if it is not promptly and comprehensively assessed [4].

Diabetic nephropathy has been identified as an essential risk factor for foot ulceration and amputation [5]. Additionally, dialysis treatment has been reported as an independent risk factor in diabetic patients with chronic kidney disease [6].

Access this article online

Quick Response Code:

Website: www.jmsr.eg.net

DOI: 10.4103/JMISR.JMISR_54_18

Correspondence to: El-Saied Shaheen, MD, Department of Internal Medicine, Shebin El Kom Teaching Hospital, Menoufia, Egypt, Tel: +20 100 948 3001. E-mail: shahins6666@yahoo.com

How to cite this article: Shaheen ES, Goda F, Elshazly HM. Renal function and diabetic foot ulcer. J Med Sci Res 2018;1:180-4.

About 20% of diabetic patients develop foot ulcers during early initiation of dialysis [7], and the amputation rate is 4% every year in dialysis therapy [8]. Moreover, renal failure has been reported to independently predict the risk of nonhealing ischemic and neuroischemic foot lesions and major amputations [9]. Uremia has an adverse effect on ulcer healing. With nonuremic patients having a 2.45 increasing probability of primary healing of the ulcer [10]. Additionally, end-stage renal disease (ESRD) has a stronger adverse effect in diabetic patients with peripheral arterial disease (PAD) than in those without this complication [11]. The antibiotic treatment (antibiotherapy) plays a strong role in treatment strategy for infections. Wounds without infection of soft tissue or bone tissue do not require antibiotic treatment. Empiric treatment, is covering gram-positive cocci, is used for the treatment of mild and moderate infection. When antibiotics are needed for severe infections, it must be covering gram-negative aerobes and obligate anaerobes [12].

Antibiotics used mainly against gram-positive organisms are amoxicillin, co-amoxiclav, flucloxacillin, erythromycin, clarithromycin, fucidin, doxycycline, rifampicin, clindamycin, vancomycin, linezolid, trimethoprim, tigecycline. Antibiotics used mainly against gram-negative organisms are ciprofloxacin, septrim, ceftriaxone, ceftazidime, piperacillin/tazobactam, ticarcillin/clavulanic acid, imipenem with cilastin, meropenem, ertapenem, tigecycline, and aminoglycosides. Antibiotics used against anaerobic organism are metronidazole, clindamycin, meropenem, piperacillin/tazobactam, and entrapenem [13].

Patients and methods

This study included 120 patients with type 2 diabetes mellitus (DM). Patients participated from the medical and surgical unit, Shebin El Kom Teaching Hospital, Egypt.

They were divided into two main group; group 1 included 80 patients with an active diabetic foot ulcer (DFU) and group 2 involved 40 patients without a history of an active or past DFU. Also, group 1 was subdivided into two groups; which included 40 patients in group A who received antibiotics with a low profile of renal toxicity (ciprofloxacin, ceftriaxone, and clindamycin) and included 40 patients in group B who received antibiotics with a high profile of renal toxicity (aminoglycosides, vancomycin, and imipenem).

Exclusion criteria; included pati ents who were with the ESRD; patients with hemodialysis, and patients with lower knee amputation.

Inclusion criteria; included type 2 DM patients, age more than 35 years, diabetic foot diagnosis was established on the basis of clinical criteria; current foot ulcer, history of nontraumatic ulcer, and all ulcer and limb threatening lesions that occur on or below the malleoli [14].

Stages of foot ulceration were recorded according to the Wagner criteria:

(1) Grade 0: ulcers are preulcerative or postulcerative lesions.
(2) Grade 1: ulcers are superficial, involving partial or full skin thickness.
(3) Grade 2: ulcer are deeper penetrating down to ligaments and joint capsule.
(4) Grade 3: are deep lesions with abscesses or osteomyelitis.
(5) Grade 4: forefoot gangrene.
(6) Grade 5: whole foot gangrene [15].

Full clinical history of hypertension, ischemic heart disease, and cerebrovascular accident was analyzed. Comprehensive clinical examination was carried out for BMI, blood pressure, examination of peripheral pulse, and presence of neuropathy. Evidence of PAD defined as a history of surgical revascularization of a peripheral artery or angiography confirming PAD [16]. The absence of two or more foot pulse on palpation or an ankle-brachial index less than 0.9 [17].

Albuminuria was determined by nephelometry in the first morning through urine samples, and urine albumin–creatinine ratio was done. Serum creatinine, lipid profile, glycated hemoglobin (HbA1c) was measured. Estimated glomerular filtration rate (eGFR) was calculated according to the Modification of Diet in Renal Disease equation.

Statistical analysis

Statistical analysis was performed using SPSS, version 13.0 (Corporate headquarters 1 New Orchard Road Armonk, New York 10504-1722 United States US: 914-499-1900). Data were analyzed using χ^2 test and Student's *t* test, *P* value less than 0.05 was accepted as significant.

Results

Table 1 shows demographic and anthropometric characteristics of the study groups. Group 1 included 80 patients with an active foot ulcer, mean age 57.5 ± 7.2 years that was significantly higher than the mean age of group 2, which was 43.2 ± 7.5 years. No significant difference was found between both the groups with respect to BMI and treatment of oral hypoglycemics.

Table 2 shows diabetic complications of the study population, there was the statistically significant difference between both the groups with respect to the presence of peripheral neuropathy, cerebrovascular accidents, and history of lower limb amputation. In contrast, there were no

Table 1: Demographic and anthropometric characteristics of the study population

Variables	Group 1	Group 2	*P*
Number	80	40	
Male	42 (0.52.5)	19 (47.5)	>0.05
Age (years)	57.5±7.2	43.2±7.5	<0.001
BMI	26.2±3.5	25.9±3.4	>0.05
Smoking time since diagnosis of diabetes (years)	19±10.5	4.5±2.5	<0.001
Diabetic treatment oral hypoglycemic intake	30 (37.5)	17 (42.5)	>0.05

Data are presented as mean±SD and *n* (%).

statistically significant differences between both the groups with respect to the presence of retinopathy, the presence of ischemic heart disease, mean ankle-brachial index, the presence of dorsalis pedis and posterior tibial pulsation, and performance of revascularization or performance of angiography.

Table 3 shows laboratory investigation of the study groups. There were high significant differences between both the groups with respect to fasting blood glucose, 2 h postprandial glucose, HbA1c. In contrast, there was no significant difference between both the groups with respect to lipid profile (serum cholesterol, serum low-density lipoprotein, serum high-density lipoprotein, serum triglycerides).

Table 4 shows comparison of renal function and urine albumin/creatinine ratio of the study groups. There was a high significant increase in serum creatinine (2.3 ± 0.93 vs. 1.5 ± 0.73) and no significant difference in albumin/creatinine ratio in urine (235.5 ± 274.5 vs. 219.3 ± 112.3) in group 1 versus group 2, and a considerable decrease was seen in eGFR in group 1 versus group 2 (40.3 ± 24.5 vs. 62.4 ± 23.4) ($P < 0.001$).

Table 5 shows renal function before and after antibiotics in group A (low-risk regimen), there was no statistically significant difference in renal function after treatment (40.6 ± 23.1 vs. 39.5 ± 15.1) ($P > 0.05$). In contrast, group B (high-risk regimen) there was a significant decrease in renal function after the treatment (40.0 ± 25.7 vs. 34.6 ± 17.4) ($P < 0.05$).

Table 2: Associated diabetic complications of the study population

Variables	Group 1 (*n*=80) [*n* (%)]	Group 2 (*n*=40) [*n* (%)]	*P*
Retinopathy	27 (33.8)	9 (22.5)	>0.05
Peripheral neuropathy	50 (62.5)	11 (27.5)	<0.05
IHD	28 (35)	12 (30)	>0.05
CVA	8 (10)	2 (5)	<0.05
ABI	1.023±0.25	1.071±0.23	>0,05
History of LL amputation	19 (23.8)	0.0 (0)	<0.001
Dorsalis pedis pulsation	38 (47.5)	21 (52.5)	>0.05
Posttibial pulsation	60 (75)	31 (77.5)	>0.05
Revascularization performance	12 (15)	4 (10)	>0.05
Angiography performance	16 (20)	7 (17.5)	>0.05

ABI, ankle-brachial index; CVA, cerebrovascular accident; IHD, ischemic heart disease; LL, lower limb.

Table 3: Laboratory investigation of the study groups

Variables	Group 1 (*n*=80)	Group 2 (*n*=40)	*P*
Fasting blood glucose (mg/dl)	230.2±60.4	185.4±50.3	<0.001
2 h postprandial glucose (mg/dl)	305±84.3	230±60.8	<0.001
HbA1c (%)	8.8±1.2	7.4±0.7	<0.001
Serum cholesterol (mg/dl)	240.7±55.3	230.5±60	>0.05
Serum LDL (mg/dl)	150.2±28.4	143.3±31.2	>0.05
Serum HDL (mg/dl)	40.7±11.6	42.3±13.3	>0.05
Serum triglycerides (mg/dl)	215.4±50.7	209.3±60.5	>0.05

Data are presented as mean±SD. HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Discussion

Disability in patients with DM is mainly caused by foot ulcers and infections [18]. Foot ulcers develop in about 15% of people with diabetes [19]. Infection are frequently in form of DFUs and take a long time to heal.

Our study showed that patients with DFU had high significant difference with respect to the history of lower limb amputations, cerebrovascular accidents, and peripheral neuropathy compared with type 2 DM without DFU. In agreement with our results, Abd El basset *et al.* [20] reported an association between history of DFU and peripheral neuropathy, history of lower limb amputation, and cerebrovascular accident.

Our study showed that patients with DFU had a high significant difference with respect to fasting blood glucose, 2 h postprandial blood glucose, HbA1c. Similarly, Wolf *et al*. [21], concluded that type 2 DM with diabetics foot syndrome were significantly higher HbA1c and had a longer duration of diabetes compared with type 2 DM without diabetics foot syndrome.

Our study is finding that significant association between renal function and DFUs, patients with foot ulcers showed significantly higher serum creatinine and substantially lower mean eGFR compared without ulcer, similar to Abd El Basset and colleagues.

Also, our study showed that nonsignificant increase in the prevalence of foot ulcer with increasing degree of microalbuminuria. Wolf and colleague reported that DFU occurs significantly more often in patients with

Table 4: Comparison of renal function and urine albumin/creatinine ratio of the study groups

Variables	Group 1 (*n*=80)	Group 2 (*n*=40)	*P*
Serum creatinine (mg/dl)	2.3±0.93	1.5±0.73	<0.001
eGFR (ml/min/1.73 m^2)	40.3±24.5	62.4±23.4	<0.001
Urine albumin/creatinine ratio	235.5±274.5	219.3±112.3	>0.05

Data are presented as mean±SD. eGFR, estimated glomerular filtration rate.

Table 5: Renal function before and after antibiotics

Variables	Before treatment eGFR	After treatment eGFR	*P*
Group A (low-risk regimen)	40.6±23.1	39.5±15.1	>0.05
Group B (high-risk regimen)	40.0±25.7	34.6±17.4	<0.05

Data are presented as mean±SD. eGFR, estimated glomerular filtration rate.

nephropathy, macroalbuminuria, ESRD, but not in those with microalbuminuria. People with diabetes and those with ESRD share three risk factors whose interaction undoubtedly increase their risk of developing foot ulceration and amputation and neuropathy. PAD increase susceptibility to infection with impaired wound healing.

In our study, GFR decreased after antibiotherapy in diabetic patients mainly because of abnormal renal function [22]. Lepantalo *et al.* believed that the essential factor for DFU is a loss of renal function [23]. Disturbance of glucose metabolism and production of glycogen is caused by damaging insulin binding to receptors that cause tissue-insulin resistance, particularly in skeletal muscles. It is also caused by the level of elevation of parathyroid hormone and uremic toxins accumulation in patients with chronic renal failure [24].

In our study, in patients with antibiotics treatment, we found a decrease in renal function. In higher renal toxicity, treatment with antibiotics significantly decreased renal function. Although, regardless of nature and mechanism, the toxicity of antibiotics, depends on the dose, concentration, duration, and another underlying disease. In diabetic patients, as renal dysfunction is more liable, antibiotherapy should be carefully monitored in these patients because antibiotics can accelerate renal dysfunction [25].

Conclusion

There was a strong association between the degree of renal impairment and DFU. Following antibiotherapy, we observed that the renal function decreased. Antibiotics with higher nephrotoxicity in diabetic patients showed steep decline in renal function. Further study is required to identify factors affecting renal function in patients with a DFU.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Lotti MH, Saadati H, Afzali M. Prevalence of diabetes in people aged ≥30 years: the results of screening program of Yazd province. Iran. In 2012. J Res Health Sci 2013; 14:88–92.
2. Guell C, Unwin N. Barriers to diabetic foot care in a developing country with high incidence of diabetes-related amputations: an exploratory qualitative interview study. BMC Health Serv Res 2015; 15:377.
3. Ben MM, Khalfallah M, Boutiba IB, Nouira R, Slim A, Jerraya H, *et al*. Bacteriological and therapeutic profile of diabetic foot infection: a prospective study of 100 patients. La Tunisie medicale 2016;94:95-101.
4. Shitazi AA, Nasiri M, Yazdanpanah I. Dermatological and musculoskeletal assessment of diabetic foot: a narrative review. Diabetes Metab Syndr 2016; 10:S158– S164.
5. Fernando DJ, Hutchison A, Veves A, Gokal R, Boulton AJ. Risk factors for non-ischaemic foot ulceration in diabetic nephropathy. Diabetic Medicine 1991;8:223-5.
6. Ndip A, Rutter MK, Vileikyte L, Vardhan A, Asari A, Jameel M, *et al*. Dialysis treatment is an independent risk factor for foot ulceration in patients with diabetes and stage 4 or 5 chronic kidney disease. Diabetes Care 2010.
7. Game FL, Chipchase SY, Hubbard R, Burden RP, Jeffcoate WJ. Temporal association between the incidence of foot ulceration and the start of dialysis in diabetes mellitus. Nephrology Dialysis Transplantation 2006;21:3207-10.
8. Wolf G, Müller N, Busch M, Eidner G, Kloos C, Hunger-Battefeld W, *et al*. Diabetic foot syndrome and renal function in type 1 and 2 diabetes mellitus show close association. Nephrology Dialysis Transplantation 2009;24:1896-901.
9. Prompers L, Schaper N, Apelqvist J, Edmonds M, Jude E, Mauricio D, *et al*. Prediction of outcome in individuals with diabetic foot ulcers: focus on the differences between individuals with and without peripheral arterial disease. The EURODIALE Study. Diabetologia 2008;51:747-55.
10. Gershater MA, Löndahl M, Nyberg P, Larsson J, Thörne J, Eneroth M, *et al*. Complexity of factors related to outcome of neuropathic and neuroischaemic /ischaemic diabetic foot ulcers: a cohort study. Diabetologia 2009;52:398-407.
11. Bakker K, Apelqvist J, Lipsky BA, Van Netten JJ, Schaper NC. International Working Group on the Diabetic Foot (IWGDF). The 2015 IWGDF guidance documents on prevention and management of foot problems in diabetes: development of an evidence-based global consensus. Diabetes/metabolism Research and Reviews 2016;32:2-6.
12. Akbari R, Javaniyan M, Fahimi A, Sadeghi M. Renal function in patients with diabetic foot infection; does antibiotherapy affect it?. Journal of Renal Injury Prevention 2017;6:117.
13. Edmon M. The treatment of diabetic foot infection: focus on ertapenem. Vasc Health Risk Manag 2009; 5:949–963.
14. Game FL, Chipchase SY, Hubbard R, Burden RP, Jeffcoate WJ. Temporal association between the incidence of foot ulceration and the start of dialysis in diabetes mellitus. Nephrology Dialysis Transplantation 2006;21:3207-10.
15. Wagner FW. The dysvascular foot: a system for diagnosis and treatment. Foot Ankle 1981; 2:64–122.
16. Treece KA, Macfarlane RM, Pound N, Game FL, Jeffcoate WJ. Validation of a system of foot ulcer classification in diabetes mellitus. Diabetic Medicine 2004;21:987-91.
17. O'hare AM, Glidden DV, Fox CS, Hsu CY. High prevalence of peripheral arterial disease in persons with renal insufficiency: results from the National Health and Nutrition Examination Survey 1999–2000. Circulation 2004;109:320-3.
18. Mehrsay R, Pourmand GH, Shoari M, Taheri M, Mansouri D. Evaluation of frequency or aggravation of diabetes mellitus after renal transpalntation in Sina Hospital. Iranian Journal of Endocrinology and Metabolism 2001;3:133-7.
19. Jiang G, Hu C, Tam CH, Lau ES, Wang Y, Luk AO, *et al*. Genetic and clinical variables identify predictors for chronic kidney disease in type 2 diabetes. Kidney International 2016;89:411-20.
20. El Sharaawy AE, Ezzat H, Mohab A, Elwasly D. Association between Renal Function and Diabetic Foot Ulcer in Type 2 Diabetic Patients. Int J Adv Res Biol Sci 2017;4:7-15.
21. Wolf G, Müller N, Busch M, Eidner G, Kloos C, Hunger-Battefeld W, *et al*. Diabetic foot syndrome and renal function in type 1 and 2 diabetes mellitus show close association. Nephrology Dialysis Transplantation 2009;24:1896-901.
22. Wolf G, Ritz E. Diabetic nephropathy in type 2 diabetes prevention and patient management. J Am Soc Nephrol 2003; 14:1369–1405.
23. Lepantalo M, Fiengo L, Biancari F. Peripheral arterial disease in

diabetic patients with renal insufficiency: a review. Diabetes Metab Res Rev 2012; 28:40–45.
24. Layegh P, Zeraati A. Treatment of hyperglycemia in patients with diabetes. Medical Journal of Mashhad University of Medical Sciences 2014;57:866-73.
25. Eyler RF, Mueller BA. Antibiotic pharmacokinetic and pharmacodynamic considerations in patients with kidney disease. Adv Chronic Kidney Dis 2010; 17:392–403.