

*Pregledni rad /  
Review article*

DIABETIC FOOT SYNDROME -  
A BRIEF REVIEW

SINDROM DIJABETESNOG STOPALA -  
KRATAK PREGLED

**Correspondence to:**

**Džemail S. Detanac**

General hospital Novi Pazar,  
Novi Pazar, Serbia  
dzemail.detanac@gmail.com

Džemail S. Detanac<sup>1</sup>, Mehmed Mujdragić<sup>1</sup>, Dženana A.  
Detanac<sup>1</sup>, Mersudin Mulić<sup>2</sup>, Biljana Lazović<sup>3</sup>

<sup>1</sup> General hospital Novi Pazar, Novi Pazar, Serbia

<sup>2</sup> State university Novi Pazar, Serbia

<sup>3</sup> Clinical center Zemun, Belgrade, Serbia

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**Abstract**

Diabetes mellitus (DM) is a chronic disease of global significance with a growing number of patients. Diabetic foot syndrome (DFS) is defined as ulceration of the foot which develops as a result of peripheral neuropathy, ischemia as a result of peripheral vascular disease, repetitive trauma, and infection. It can be classified as the neuropathic and ischemic foot and the treatment is always multidisciplinary. Patients with DM lower limb amputations and ulceration rates can be reduced by the implementation of therapeutic and preventative foot care strategies.

**INTRODUCTION**

Diabetes mellitus is a chronic disease of global significance with a growing number of patients, both in developed and developing countries, with the prevalence of 8.8% among adults aged 20–79 years old in 2015 (1,2). According to International Diabetes Federation (IDF), 415 million people have diabetes in the world, in Europe there is almost 60 million people and by 2040 this number will rise to more than 71 million. In Serbia, there were 863,800 cases of diabetes in 2015 (3). There is a great number of patients with DM in Asia, and accounts for 60% of the world's diabetic population (4). The progression of diabetes leads to numerous potentially life threatening complications such as: coronary artery disease, chronic kidney disease, cerebrovascular disease and retinopathy (5,6).

Of all diabetic complications, the most devastating one is diabetic foot and present major cause of hospitalization and amputation in diabetic patients and can cause a number of emotional, psychological, social problems and conflicts with significant health care costs and affects the quality of life of the people (7,8).

**Epidemiology of Diabetic Foot Syndrome**

Diabetic foot syndrome (DFS) is defined as ulceration of the foot which develops as a result of peripheral neuropathy, ischemia as a result of peripheral vascular disease, repetitive trauma, and infection (7,9) and become the biggest reason for lower-extremity amputations (10,11).

According to North West Diabetes Foot Care Study approximately 2% of patients with DM will develop new foot ulcers each year (12).

Diabetic foot is more common in people over 60, more common in men, and can develop in all types of diabetes (6,13). According to Bartus et al the annual incidence of foot ulcers is from 1.0% to 4.1% (14). Foot ulcers commonly become infected and lead to amputation. Ramsey et al reported that approximately 56% of ulcers become infected and 20% of these will require some level of amputation. About 85 % of the patients with diabetes who suffer an amputation have foot ulcers (15). Chammas et al. confirmed that the diabetic patients with ulcers have a lower 5-year survival than nondiabetic patients. The 5-year relative mortality after diabetic foot ulcer is 48% (16,17). Foot ulcers occur in 15-25% of people with diabetes (18,19)

**Foot**

**Etiopathogenesis of diabetic foot syndrome**

DFS is a consequence of neuro-ischemic changes that are occasionally complicated by additional infections.

Ulcerations, infections and gangrene of the foot present the most common reasons for hospitalization among diabetic patients (Figure 1,2,3). Pathogenesis of DFS is multifactorial. Several factors together lead to foot ulceration in these patients. There are a lot of risk factors for diabetic foot ulcers such as: past history of foot ulcers/amputation, chronic renal disease (especially patients on dialysis), post renal transplant, retinopathy, plantar callus and foot deformity, edema, ethnicity, lower social status, smoking etc, but the most important are diabetic neuropathy, peripheral vascular disease and trauma (7). Hyperglycemia is a trigger for oxidative stress on nerve cells and leads to neuropathy and damage to the sensory, motor and autonomic components.

Vascular changes affect both large and small blood vessels. Diabetic foot is a medical, social, economic and personal problem.

#### *Diabetic neuropathy (DN)*

The definition for diabetes neuropathy is “the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after the exclusion of other causes” (20).

DN may be presented as: a) sensory neuropathy in acute (rarely) or chronic form (about half of the patients with diabetes have this form which is manifested with unpleasant sensations like burning pain, prickling, electric shocks, paresthesia, hyperesthesia, deep aching pain, abnormal cold or hot feelings etc, most commonly experienced in the feet and lower extremities); b) focal and multifocal neuropathies and c) autonomic neuropathies (with clinical manifestations like orthostatic hypotension, erectile dysfunction, tachycardia, gastroparesis, constipation etc) (20).

One of the outcomes of neuropathy is the development of insensitive foot, which increases the risk of ulceration (21)

The important role in development of the diabetic neuropathy have metabolic disorders induced by hyperglycemia and angiopathy. Hyperglycemia leads to metabolic disturbances at the molecular level, which results in axon edema and damage of the Schwann cells and is correlated with vascular damage too, which together leads to the loss of sensation to pain caused by ulcers, wounds, or infections which are the major causes of some kind of amputation (21).

A great number of patients are unaware of the existence of peripheral neuropathy and are usually asymptomatic. So, these patients can have diabetic foot ulcer even without any neuropathic symptoms (6). Damage to the motor nerves leads to damage to the muscles of the foot which increases instability in gait, deformities of the feet and the appearance of ulceration on the skin.

#### *Peripheral vascular disease*

Micro and macrovascular complications such as: cerebrovascular disease, retinopathy, nephropathy, peripheral vascular disease etc, result in organ and tissue damage in up to 50% of people with diabetes.

Many structural and metabolic changes initiate diabetic vascular complications because of the high level of hyperglycemia and inadequate treatment of hyperglycemia.

Peripheral artery disease is characterized by the occlusion of the lower-extremity arteries causing claudication and pain, ischemia and inability to heal, which leads to the fact that small wounds often progress to larger because of inability or reduced possibilities of healing and makes it one of the major reasons for lower limb amputations(22).

According to Dohmen A et al in Germany each year about 40 000 amputations of the lower limbs are done and 70% of the patients are diabetics. The prevalence of diabetes mellitus in the German population is 7%, and around 90 000 people have Diabetic foot syndrome (DFS) with angiopathic component (23).

According to the results from the National Health and Nutrition Examination Survey, 1999–2000 in the general US population, the prevalence of peripheral vascular disease among individuals with diabetes was 10.8% compared with 3.6% of individuals without diabetes (24).

Early diagnosis of PVB allows for the timely implementation of therapeutic measures that will prevent the onset of gangrene. Therefore, part of the standard treatment and monitoring of diabetics must be to check for pulses on all available arteries. The presence of popliteal pulses in the absence of pedals is a classic clinical finding.

#### *Skin disorders in patients with DM*

Skin disorders, associated with hyperglycemia, are common complications in patients with diabetes mellitus, and can lead to a major complications with prevalence from 51-90% worldwide (25). The most frequent disorder, in around 20% of patients with DM is infection, with more prevalent fungal than bacterial infection (25) (Figure 4). In the study of Galdeano et al, about 90% had some kind of skin disorder (26). According to a study conducted in Brazil, 97 % of all patients had at least one skin lesion, and the most common were tinea pedis (35 %) and candidiasis of the skin/nail with 26 % (25,27). Studies show that the pathogens causing DF usually are Gram-positive cocci (especially *S aureus* and streptococci), and the less common pathogens are *Enterobacteriaceae*, *Pseudomonas aeruginosa*, obligate anaerobes) (28).

All of the above factors, less often alone, can more often jointly lead to the onset of diabetes foot and ulceration. Most often ulcers occur on the soles of the foot, usually in the projection of the heads of the metatarsal bones. The most common sites of ulceration are the first, second and third head of the metatarsal bone and the thumb(29).

#### *Diabetic foot treatment*

The diabetic foot is classified as a neuropathic and ischemic foot, and treatment is determined on the basis of this division as well as the existence of other complications and comorbidities. It should be emphasized that treating such changes is always multidisciplinary. Neuropathic ulcer and neuropathic oedema with a good circulation are characteristic for neuropathic foot. In the ischaemic foot the dominant factor is atherosclerosis which leads to a reduction in blood flow and is characterized by rest pain, ulceration, and gangrene (7).

In patients with DM lower limb amputations and ulceration rates can be reduced by the implementation of therapeutic and preventative foot care strategies from 45-85% (1). This includes self-examinations of the feet and regular medical check-ups, imaging, identification of at-risk feet, appropriate footwear, patient/staff education (1). At the same time, it is necessary to treat preventable conditions such as foot deformities, but also fungal nail infections, onychomycosis, etc., correction of hyperglycemia ( HbA1c reduction for 1% can decrease the risk of microvascular complications up to 37% (20) etc. Adequate and timely diagnosis reduces complications and improves quality of life. Conservative treatment of PVD is effective only in the early stages of the disease, whereas in the late stages of the disease only surgical reconstruction can have effects.

Primary in the treatment of diabetic foot is to allow wound healing, which in turn depends on the size of the change, vascular status and presence of infection. The next thing to do is to provide the places of highest pressure, especially for foot deformities, by using special inserts.

Locally, at the site of skin change the following is indicated: surgical, enzymatic, mechanical and biological debridement, infection therapy. Surgical debridement of the wound involving removal of necrotic and fibrotic tissue as well as callus on the foot is mandatory.

New topical diabetic ulcer treatment modalities have been developed: wound dressings, honey-impregnated dressings, alginate dressing, polyurethane foam, tulle dressing, hydrocolloids, and calcium alginate swabs (6).

Medicinal treatment of diabetic foot, depending on changes and how invasive the process involves: aldose reductase inhibitors (ARI), vasodilatory drugs, advanced glycation end products (AGEs), mesenchymal stem cells-MSCs, secret neurotrophic and angiogenic factors, platelet-derived growth factors, antibiotics...(30).

In patients who have no progress in wound healing with conservative therapy and with the appearance of an ischemic lesion, a vascular surgeon is required.

Pelvic, upper and proximal lower leg arteries are the main target vessels for bypass surgery, but nowadays arteries right down to the foot can be successfully revascularized. Surgical interventions—including prophylactic and revascularisation surgeries, play a role in preventing foot ulceration, improving wound healing and reducing the incidence and site of lower limb amputations (1). Diagnostic imaging implies angiological examination: the anklebrachial index (ABI), the toe-brachial index, doppler blood pressure measurement, oscillography, angiography.

Surgical treatment methods entail: bypass surgery (femoro-popliteal, crural-pedal bypass surgery) and interventional surgery (stents, long balloons for diffuse long segment stenoses, laser angioplasty, atherectomy) (23).

The 5-year rates for bypass patency and limb preservation are approximately 60% and 80%.

Conservative treatment also includes: adequate oxygenation of the blood (hyperbaric oxygenation therapy), any infection requires systemic antibiotic treatment, pain treatment, lumbar sympathectomy(23).

In patients with diabetic foot no amputation should be performed unless all possibilities of crural and pedal revascularization are exhausted before that. Crural and pedal revascularization, whether achieved by interventional means, open surgery, or a combination of both, achieves limb preservation rates of 90% to 95% after 1 year and 80% to 90% after 3 to 5 years (23).

**CONCLUSION**

Diabetic foot is essentially preventable. Adequate prevention at all levels of health care, patient education and timely initiation of therapy for manifest changes are necessary.

*Abbreviations*

- DM- Diabetes mellitus
- DFS- Diabetic foot syndrome
- IDF- International Diabetes Federation
- DN-Diabetic neuropathy
- PVD-Peripheral vascular disease



**Figure 1.** Diabetic foot gangren.



**Figure 2.** Digital amputation



**Figure 3.** Diabetic foot infection.



**Figure 4.** Skin disorders of the foot.

### Sažetak

Dijabetes melitus (DM) je hronična bolest od globalnog značaja, s rastućim brojem bolesnika. Sindrom dijabetesnog stopala (DFS) definiše se kao ulceracija stopala koja se razvija kao rezultat periferne neuropatije, ishemije kao rezultat periferne vaskularne bolesti, ponavljajuće trauma i infekcije. Može se klasifikovati kao neuropatsko i ishemijsko stopalo, a lečenje je uvek multidisciplinarno. Procenat amputacija donjih ekstremiteta i ulceracija kod pacijenata sa dijabetes melitusom, može se smanjiti primenom terapijskih i preventivnih mera nege stopala.

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