Turkish Journal of Geriatrics
2013; 16 (4) 359-364

Ömer COŞKUN[1]
Ümit SAVAŞÇI[4]
Ahmet KARAKAŞ[1]
Kemal ŞİMŞEK[2]
İsmail Yaşar AVCI[1]
Sabahattin SARI[3]
Can Polat EYİGÜN[1]

RESEARCH

EVALUATION OF DIABETIC FOOT INFECTIONS IN ELDERLY PATIENTS

ABSTRACT

Introduction: Foot infections are among the most common complications encountered in patients with diabetes mellitus in clinical practice. This disease and its sequelae are one of the main causes of hospitalization among patients with diabetes mellitus. The primary objective in the treatment of diabetic foot infection is to prevent amputation and to help recover the functions. In this study, various clinical parameters of diabetic foot infection patients have been evaluated and these parameters have been correlated with variables such as risk factors and level of infection.

Materials and Method: The study was conducted retrospectively on the records of 32 diabetic foot infection patients (24 males, 8 females) who stayed and were treated in Gulhane medical hospital department of infectious diseases and Clinic between 2005 and 2012.

Results: Mean score of the participants' age was 63.53±9.9. Results revealed that uncontrolled diabetes significantly increased diabetic foot infection risk. As to body temperature, peripheral leukocyte, acute phase reactants and biochemical parameters, the results demonstrated that they could not be correlated to the degree of the disease; however, they might change in an unspecific way in acute or advanced stages. Single growth in blood culture proved to be more common. Combined antibiotic treatment was highly preferred. Patients, even those under the risk of amputation, responded positively to hyperbaric oxygen therapy.

Conclusion: Diabetic foot infections are serious cases that require a multidisciplinary treatment approach. Accordingly, a proper anamnesis taken from the patient, clinical evaluation, early diagnosis via appropriate radiological and microbiological methods, and accurate treatment will prevent loss of limb

Key Words: Diabetic Foot; Infection; Aged.

ARAŞTIRMA

YAŞLI HASTALARDA DİYABETİK AYAK ENFEKSİYONLARININ DEĞERLENDİRİLMESİ

ÖZ

Giriş: Ayak enfeksiyonları diyabetik hastalarda klinik pratikte en sık rastlanılan komplikasyonlardan biridir. Bu hastalık ve onun sekelleri diyabetik hastalar arasında hastaneye yatışın en önemli nedenlerinden biridir. Diyabetik ayak enfeksiyonu tedavisinde esas hedef uzuv kaybının önüne geçmek ve fonksiyonlarını yerine getirmesini sağlamaktır. Bu çalışmada diyabetik ayak enfeksiyonu hastalarına ait çeşitli klinik parametreler değerlendirildi ve risk faktörleri enfeksiyonun derecesi gibi durumlarla kıyaslamaları yapıldı.

Gereç ve Yöntem: Gülhane Tıp Fakültesi hastanesi enfeksiyon hastalıkları kliniğinde 2005-2012 yılları arasında yatırılarak tedavi gören diyabetik ayak enfeksiyonu tanısı konulmuş 32 (24 erkek ve 8 kadın) hastanın dosyaları geriye dönük olarak incelenerek yapıldı.

Bulgular: Hastaların yaş ortalaması 63.53±9.9 idi. Kontrolsüz diyabete sahip olmanın diyabetik ayak enfeksiyonu riskini arttırdığı tespit edildi. Ateş, periferik lökosit, akut faz reaktanları ve biyokimyasal parametreler açısından bakıldığında hastalığın derecesi ile ilişkilendirilemeyeceği ancak akut veya ileri safhada spesifik olmayan bir şekilde değişebileceği tespit edildi. Kültürde tek çeşit üreme daha fazla tespit edildi. Kombine antibiyotik tedavisi yüksek oranda tercih edilmişti. Hiperbarik oksijen tedavisine bazı amputasyon düşünülen hastalar dâhil iyi yanıt verdiği tespit edildi.

Sonuç: Diyabetik ayak enfeksiyonları multidisipliner tedavi yaklaşımı gerektiren önemli bir durumdur. Bu amaçla hastadan alınan iyi bir anamnez, klinik değerlendirme, uygun radyolojik ve mikrobiyolojik yöntemlerle erken tanı ve uygun tedavi muhtemel bir fonksiyon bozulmasını ve uzuv kaybını önleyecektir.

Anahtar Sözcükler: Diyabetik Ayak; Enfeksiyon; Yaşlı.

İletişim *(Correspondance)*

Ömer COŞKUN
GATA Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji
ANKARA

Tlf: 0312 304 43 03
e-posta: ocoskun@gata.edu.tr

Geliş Tarihi: 13/08/2012
(Received)

Kabul Tarihi: 05/01/2013
(Accepted)

[1] GATA, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji, ANKARA
[2] GATA, Sualtı Hekimliği ve Hiperbarik Tıp ANKARA
[3] GATA, Radyoloji ANKARA
[4] Sarıkamış Asker Hastanesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji, KARS

Introduction

Diabetes mellitus is a disease causing chronic complications. Diabetic foot infection is one of the most problematic ones and a significant cause of morbidity (1). Important factors for development of diabetic foot infection (DFI) include neuropathy, peripheral vascular disease, and hyperglycemia. In patients with one or more of these risk factors, trauma precipitates development of wounds that can be poorly healing and susceptible to secondary infections. In addition to causing severe morbidities, they account for the longest diabetes-related hospital bed–days and they are likely the most common, non-traumatic cause of amputations (2). Preventing the diabetic foot using the multidisciplinary team approach is an appropriate step in the right direction. Early recognition of lesions, prompt initiation of appropriate antimicrobial therapy, and surgical debridement of necrotic tissue and bone are essential not only to control the infection, but also to prevent additional morbidity. In this study, DFI patients' demographic and clinical information, laboratory data, and treatment approaches have been evaluated. These parameters have been correlated with variables such as the treatment method, risk factors and the level of infection.

Materials and Method

This study was conducted retrospectively on the records of 32 DFI patients (24 males and 8 females) who stayed and were treated in the department of infectious diseases clinic between 2005 and 2012. Ethics committee approval was taken from the local ethics committee (Ethics committee 01.08.2012 Report no: 06). Risk factors for DFI; race, age, long duration of diabetes, poor glycemic control, peripheral neuropathy, retinopathy, nephropathy, biomechanical factors (stiffening of connective tissue, increased plantar pressure), fungal infections of the foot, smoking, obesity, history of previous foot ulceration and amputation, socio-cultural factors, bare foot walking, religion, improper foot care and customs respectively (3, 4). Patients were monitored for risk factors known to be associated with lower extremity complications. The data collected from the participants were recorded on patient follow-up forms. Resistant bacteria, osteomyelitis, duration of hospitalization, amputation, and the factors related to the treatment in diabetic foot infections were analyzed. Infection was diagnosed clinically by a trained physician according to Wagner's classification (5). Patients with newly diagnosed diabetic foot pathology, recurrent infection after being totally cured, and a history of amputation below the metatarsus were included in the study. After cleansing and debridement of the wound, the specimens for culture were obtained by swabbing the ulcer base, curettage, or needle aspiration or biopsy, depending on the wound depth. The samples were implanted in blood agar, eosin methylene blue (EMB) agar, and sabouraud agar and incubated in aerobic or anaerobic conditions at 37°C for 48 hours. Gram staining was performed in view of the reproductive characteristics and colony morphology of the bacteria. Identification of bacteria was performed with automatic BD Phoenix 100 (Becton-Dickinson, Maryland, USA) instrument; antibiotic susceptibility was tested with disc diffusion and MIC methods as described in NCCLS M100-S16. The diagnosis of osteomyelitis was based on the positive findings in any of the following tests: bone biopsy, X-ray, magnetic resonance imaging (MRI), scintigraphy. Positive monofilament test result or neuropathy was diagnosed by a neurologist. Glycemic control was evaluated with HbA1c. Poor glycemic control was defined as HbA1c >7.5%. Diagnosis of hypertension was based on patients taking antihypertensive therapy or a measured blood pressure above 90/140 mm Hg. Body mass index was calculated by dividing the weight in kilograms by the square of the height.

Statistical Analyses

Statistical analyses were performed using SPSS for Windows 15.0 pro evolution (Chicago, IL, USA) software. Descriptive statistics were presented as frequency counts and percentage. Chi square test was used to evaluate the significance of difference for categorical variables. A p value of <0.05 was accepted as statistically significant.

Results

The records of 32 DFI patients [24 (75%) males, 8 (25%) females] treated in the department of infectious diseases were studied retrospectively. All of the patients were Caucasian. Mean age of the participants was 63.53±9.9. Four patients (12.5%) were found to be smokers, 8 (25%) were non-smokers and smoking status of 20 patients (62.5%) were unknown. Obesity was found in 4 (12.5%) of the patients. And inter-digital fungal infection was detected in only one patient. The subjects had been diagnosed with diabetes for 16±9.3 years. When the relationship between the time the patients spent after the diagnosis and their attack rate was analyzed (Table 1), the results indicated that the DFI rate of

Table 1— The Correlation Between the Duration of Diabetes and Having DFI Attacks.

		Duration of Diabetes (years)			
		<10	**10-20**	**>20**	**Total**
DFI	1 attack-number (%)	7 (53.3%)	3 (27.3%)	5 (55.6%)	15 (46.9%)
	2 attacks-numbers (%)	5 (41.7%)	7 (63.6%)	1 (11.1%)	13 (40.6%)
	3 attacks-numbers (%)	-(-)	1 (9.1%)	3 (33.3%)	4 (12.5%)
Total (n)		12	11	9	32

patients who had the disease for over 20 years was significantly higher than that of other participants (p=0.05). It was found out that those with diabetes for over 20 years had at least three DFI attacks. There was no significant statistical correlation between the number of attacks and the gender of the patients.

The results showed that the 84.4% of the patients with DFI used insulin. With regards to the DFI attacks, no significant difference could be found between the patients who used insulin and those who were on oral antidiabetic medication. There was no significant correlation between HbA1c level and the frequency of DFI attacks. The percentage of patients with HbA1c level >7.5% was 79%, whereas those with HbA1c level <7.5% was 21% (p<0.05).

The duration of hospital stay was 22.7±10.3 days. The number of patients with a diagnosis of osteomyelitis was 14 (44%). Of these 14 patients, 11 (78.5%) developed neuropathy. All 11 patients, who developed neuropathy, were found to have diabetic foot osteomyelitis (DFO) as well. 93.8% of the patients with DFI had ulcer in their wounds. Ulcer was most commonly seen on plantar surface of the foot and toes. It was noted that duration of hospitalization was increased for the patients with hypoalbuminemia (p=0.019) (Table 2). Results demonstrated that specialist consultations were requested for 27 patients (84.4%) and that requested consultations were from at least four different specialties for each patient. The hemoglobin value for anemia was set at 11 mg/dl for female patients and 12 mg/dl for males, and 12 (38%) patients were diagnosed with anemia. Body temperature was measured normal (36-37.2^{0}C) in 87.5% of the patients. According to the preliminary leukocyte levels, 59.4% of the patients had leukocytosis (>10.000/mm^3). Erythrocyte sedimentation rate (ESR) was >100 mm/h in 45% of the patients, 50-100 mm/h in 42% of the patients, and 20-49 mm/h in 13% of them. C-reactive protein (CRP) values were found >100 mg/dl in 16% of the patients, 50-100 mg/dl in 24% of the patients, 6-50 mg/dl in 44% of the patients, and <6 mg/dl in 16% of them. No significant statistical association

Table 2— The Correlation Between Duration of Hospitalization and Albumin Rates.

		Albumin		Total
Duration of Hospitalization (days)		**3-3.5**	**>3.5**	**<3**
0-15	n%	-(-)	4(44.4%)	10(32.3%)
15-30	n%	10(76.9%)	4(44.4%)	16(51.6%)
>30	n%	3(23.1%)	1(11.1%)	5(16.1%)
Total	n%	13(100.0%)	9(100.0%)	31(100.0%)

was found between sedimentation, CRP values and DFO development.

In the whole group, 62.5% of the patients had grade-1 peripheral vascular disease, while the rest had grade-2 and 3 diseases. It was noted that 15 patients (47%) had an additional chronic disease (chronic renal failure, hypertension). According to the Wagner classification, 14 patients (44%) had grade-2 wounds, 13 of them (40%) had grade-3, 4 patients (13%) had grade-4, and only 1 (3%) patient had grade 5 wounds. When the subjects were categorized into two groups as those with light wounds/scotch (Wagner 0., 1., 2.) and those with severe wounds (Wagner 3., 4., 5.), no significant difference could be found between the groups in terms of hospitalization period, additional chronic diseases, increased urea and creatinine levels, decreased protein and albumin levels, hyperthermia, and high ESR and CRP levels.

The total number of patients with DFO diagnosis was 14 (44%). The number of patients who were diagnosed with DFO using MRI was 8 (25%). The results revealed that out of the 9 (28%) patients, who were diagnosed using OM scintigraphically, 3 (33%) patients were diagnosed as DFO in MRI, as well. When MRI and scintigraphy were compared, the results demonstrated no significant difference regarding the efficiency of osteomyelitis diagnosis.

According to the evaluation of the wound culture results, the number of patients with polymicrobial growth was 6 (%18.8), those with single bacterial growth were 14 (%43.8),

the number of patients with no growth were 3 (%9.4), and there were 9 (%28.1) patients who did not undergo a culture test. The factors isolated in the cultures were sequentially as follows: *Staphylococcus aureus* 5 (%15.6), *methicillin resistant staphylococcus (MRSA)* 3 (%9.4), *Streptococcus spp.* 2 (%6.3), *extended spectrum betalactamase (ESBL) (+) Escherichia coli* 3 (%9.4), *Pseudomonas aeruginosa* 3 (%9.4), *Proteus mirabilis* 2 (%6.3), *Morganella morgani* 2 (%6.3), fungus 1 (%3), *Cedecea lapagei* 1 (%3), *Klebsiella pneumoniae* 1 (%3), and *Enterococcus faecalis* 3 (%9.4).

The mean duration of antibiotic treatment was 22.1±10.3 days. There was no statistically significant correlation between patients' duration of antibiotic use and the depth of the wound, the presence of osteomyelitis, and the stage of infection. It was noted that 78% of the patients received multiple antibiotic treatment. Quinolones was the preferred choice of antibiotic with 68% rate, and the rate of quinolone resistance was found to be 25%.

The number of patients who were given hyperbaric oxygen (HBO) therapy was 27 (84.4%), and the average number of sessions was 17.1±10.2. There was no significant correlation between the number of HBO session and the depth of wound or the incidence of osteomyelitis. Three patients (9.4%) had received vacuum-assisted closure (VAC). It was decided that 12 patients required surgical operation and 5 of them (%16) had amputations.

Discussion

The majority of the patients in the study were elderly patients. Elderly diabetics are prone to DFI because these people also have poor vision, they live alone and they have other concomitant medical problems. Incidence of foot infection is directly proportional to the duration of diabetes due to the contribution of other risk factors. A six fold increase of foot ulceration is seen in patients who had diabetes for 20 years or more (6). Compared to the other participants, patients with a diagnosis of diabetes for over 20 years had significantly higher DFI attack rate (p=0.05) (Table 2). Increased attention is required for these patients in terms of DFI risk.

Severe hyperglycemia is associated with a higher incidence of DFI and ulceration. The majority of the patients (84%) who had DFI attacks were those on insulin. Considering the age and social status of these patients, it can be inferred that they might have experienced difficulties in application and occasionally their diabetes may not have been under control. In a 2-year study by Mantey et al., HbA1c was significantly higher in those with a DFI recurrence compared to those without a recurrence (7). Connor et al. also reported a relationship between HbA1c and a higher rate of ulceration per 10 years in patients with neuropathic foot ulcers (8). It is possible that poor long-term glycemic control may impair wound healing, but it may also reflect poorer patient compliance with various preventive measures, such as self-monitoring of glycemic control and adherence to treatment recommendations for DFI (8, 9). A higher rate of ulcer recurrence may also be associated with insufficient patient education and lack of psychological support (10). In our study, out of the 15 (79%) patients whose HbA1c level was >7.5%, 10 (66%) had higher grade wounds according to Wagner classification. It can be concluded that patients with >7.5% HbA1c level had increased DFI risks due to uncontrolled glycemia.

Neuropathy is an important risk factor for DFO. Trauma exposure is increased in patients with neuropathy, thus leading to infections. Frequency of neuropathy was high (78%) especially among the patients who had advanced infection, including osteomyelitis. Peripheral neuropathy is a significant risk factor in terms of DFI development. It was reported in 82% of the patients with foot infection and 58% of the patients with long standing disease (11). Neuropathy can be perceived as an increased risk for DFO. Neurological examination becomes crucial for these patients.

Non-vascular diabetic foot infection is mostly seen with diabetic nephropathy because as many as 40% of diabetic population have chronic renal failure (12). Nephropathy is also present in diabetic patients having co-morbidities like hypertension. Hypertension influences the prognosis of nephropathy in patients with diabetes. Although there was no significant correlation between patients' having a higher grade wound according to Wagner classification and their having a chronic disease, nearly half of the subjects were found to have one. This may be interpreted not only as a result of diabetic complications, but also as a process that contributes to such complications.

Clinicians should be aware of factors that increase the risk for DFI, and especially consider infection when the risk factors are present (12). In our group of patients, it was concluded that peripheral vascular disease constituted a risk for DFI even if the disease was grade-1 (62.5%). This may suggest that peripheral vascular disease increases the risk of amputation in DFIs.

Alteration in foot dynamics due to foot ulceration, joint deformity or amputation, causes abnormal distribution of plantar pressure and results in formation of new ulcer (13). 93.8% of our patients had ulcer, most frequently on plantar

foot. This may stem from patients' insufficient knowledge on orthopedic shoe usage, as well as lack of proper foot care on their side.

Diabetic foot infection is a condition that necessitates a multidisciplinary treatment approach. The multidisciplinary team approach to diabetic foot care has proven to result in a major reduction in amputation incidences (14). This cooperation does not mean the presence of all the specialists at the patient's bedside at the same time, but rather it involves a shared experience in diabetic foot management and the availability of immediate communication and consultation when needed.

Laboratory markers suggesting systemic infection include leukocytosis, a left-shifted leukocyte differential, and elevated inflammatory markers (ESR,CRP). Unfortunately, elevations of temperature, white blood cell count, or ESR are absent in up to one-half of the patients, even with severe DFI. When present, however, elevated inflammatory markers have been shown to predict worse clinical outcomes of treatment (15). Importantly, inflammatory markers may also have value in helping to determine when a DFI has resolved, therefore allowing discontinuation of antibiotic therapy. When the data was analyzed to see whether initial leukocyte levels and hyperthermia were significant indications of DFI, no significant difference could be found. Since diabetic patients suffer from neutrophil dysfunction and systemic response deficiency, these parameters cannot be predictive of DFI, if not misleading. Longer hospitalization periods in patients with low albumin levels may result from the effect of albumin levels on the processes of plerosis and cicatrization.

Guidelines recommend using MRI as the study of choice for patients who require further imaging, particularly when soft tissue abscess is suspected or the diagnosis of osteomyelitis remains uncertain (12). As for the DFO recognition in the current study, although no statistically significant differences were found, an advantage may be mentioned in favor of scintigraphy since it could recognize cases which MRI could not during the process. Previous DFO history of some DFI patients were unknown in view of the fact that either sufficient information was not gathered or no history was available. This may be interpreted as a problem of the healthcare system.

Diabetic foot infections are known for polymicrobial infections (16), but we observed predominantly mono-microbial infections (%43.8) and our finding was in accordance with those of another similar study by Tiwari (17). Several studies have found that 30–50% of *S.aureus* isolated from diabetic foot ulcers has been methicillin-resistant (18). In contrast to the studies in the literature, the etiological role of Gram (+) bacteria, particularly *S.aureus* (15.6%), in this study was relatively small. As a result, the rate of MRSA was also low (9.4%). In the present study, the majority of the patients fell under higher grade Wagner classification. The participants were almost evenly distributed in terms of the Gram (+) and Gram (-) bacteria. Being less than expected, MRSA and resistant Gram (-) bacteria recurrence frequency supports the assumption that the patients did not have much contact with the hospital environment previously. All infected wounds require antibiotic therapy, either topical or systemic (12). Generally, treatments that are not combined prove unsuccessful. Empirical treatment regime should be chosen according to the severity of the disease and it should be continued up to 1-3 weeks. Local resistance towards the preferred antibiotic should be taken into consideration and treatment should be modified according to the antibiogram results.

Osteomyelitis occurs in many diabetic patients with a foot wound and can be difficult to diagnose and complicated to treat. To treat DFO specifically, guidelines do not currently encourage using adjunctive treatments such as HBO, growth factors, maggots, or VAC therapy. A limited number of randomized controlled trials are available to support its use for wound healing (19, 20). However, it can be argued that such adjuvant treatment methods may still be used in DFI cases which tend to heal in a relatively slow pace and do not respond well to conventional treatment (12). The availability of HBO and VAC therapy facilities in our hospital were considered to be helpful for such patients. 27 patients had HBO therapy (84.3%). Five patients had amputations. Three patients, for whom the orthopedist had previously suggested amputation at the initial consultation amputation was not applied, once they responded positively to the HBO + antibiotherapy therapy. Therefore, it may be concluded that HBO therapy should be considered for DFI patients.

Most DFIs require some surgical intervention, ranging from minor (debridement) to major ones (resection, amputation). Diabetic foot complications continue to be the main reason for diabetes-related hospitalizations and lower extremity amputations. The median duration of hospitalization was 3 weeks and 35% of patients underwent some type of lower extremity amputation. Overall, 48% of patients had an unfavorable outcome of hospitalization. In line with this rate (38%), some form of surgical intervention was applied in the DFI treatment of our patients, such as debridement, grafting or amputation.

Some information about the risk factors were insufficient (obesity, smoking history, fungal infections, etc.) therefore we could not evaluate these.

REFERENCES

1. Caputo GM, Cavanagh PR, Ulbrecht JS, Gibbons GW, Karchmer AW. Assessment and management of foot disease in patients with diabetes. The New England Journal of Medicine 1994;331(13):854-60. (PMID:7848417).
2. Shea KW. Antimicrobial therapy for diabetic foot infections. A practical approach. Postgraduate Medicine 1999 Jul;106(1):85-6, 89-94. (PMID:10418577).
3. Bengalorkar GM, Nagendra KT. Diabetic foot infections-A review. Int J Biol Med Res 2011;1(2):453-60.
4. Naharci MI, Bozoglu E, Karadurmus N, Turker T, Serdar MA, Doruk H. Analysis of insulin sensitivity according to vitamin D levels in prediabetic elderly subjects. Gulhane Med J 2011;53(4):277-80.
5. Wagner FW, Jr. The dysvascular foot: A system for diagnosis and treatment. Foot & Ankle 1981;2(2):64-122. (PMID:7319435).
6. Merza Z, Tesfaye S. The risk factors for diabetic foot ulceration. The Foot 2003;13:125-9.
7. Mantey I, Foster AV, Spencer S, Edmonds ME. Why do foot ulcers recur in diabetic patients? Diabetic medicine: A journal of the British Diabetic Association 1999;16(3):245-9. (PMID:10227571).
8. Connor H, Mahdi OZ. Repetitive ulceration in neuropathic patients. Diabetes/metabolism research and reviews 2004;20 Suppl 1:S23-8. (PMID:15150809).
9. Poolsup N, Suksomboon N, Rattanasookchit S. Meta-analysis of the benefits of self-monitoring of blood glucose on glycemic control in type 2 diabetes patients: an update. Diabetes technology & therapeutics 2009;11(12):775-84. (PMID:20001678).
10. Jude EB, Eleftheriadou I, Tentolouris N. Peripheral arterial disease in diabetes-a review. Diabetic medicine: A journal of the British Diabetic Association 2010;27(1):4-14. (PMID:20121883).
11. Boulton AJ. Lawrence lecture. The diabetic foot: neuropathic in etiology? Diabetic medicine: A journal of the British Diabetic Association. 1990;7(10):852-8. (PMID:2149681).
12. Lipsky BA, Berendt AR, Cornia PB, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis 2012;54(12):e132-73. (PMID:22619242).
13. Armstrong DG, Lavery LA. Diabetic foot ulcers: Prevention, diagnosis and classification. American Family Physician 1998;57(6):1325-32, 37-8. (PMID:9531915).
14. Holstein PE, Sorensen S. Limb salvage experience in a multidisciplinary diabetic foot unit. Diabetes Care 1999;22 Suppl 2:B97-103. (PMID:10097908).
15. Lipsky BA, Sheehan P, Armstrong DG, Tice AD, Polis AB, Abramson MA. Clinical predictors of treatment failure for diabetic foot infections: Data from a prospective trial. International Wound Journal 2007;4(1):30-8. (PMID:17425547).
16. Singh SK, Gupta K, Tiwari S, Shahi SK, Kumar S, Kumar A, Gupta SK. Detecting aerobic bacterial diversity in patients with diabetic foot wounds using ERIC-PCR: A preliminary communication. The International Journal of Lower Extremity Wounds 2009;8(4):203-8. (PMID:19934183).
17. Tiwari S, Pratyush DD, Dwivedi A, Gupta SK, Rai M, Singh SK. Microbiological and clinical characteristics of diabetic foot infections in northern India. Journal of Infection in Developing Countries 2012;6(4):329-32. (PMID:22505442).
18. Tentolouris N, Petrikkos G, Vallianou N, et al. Prevalence of methicillin-resistant Staphylococcus aureus in infected and uninfected diabetic foot ulcers. Clinical Microbiology and Infection 2006;12(2):186-9. (PMID:16441460).
19. Chuck AW, Hailey D, Jacobs P, Perry DC. Cost-effectiveness and budget impact of adjunctive hyperbaric oxygen therapy for diabetic foot ulcers. International Journal of Technology Assessment in Health Care 2008;24(2):178-83. (PMID:18400121).
20. Lipsky BA, Berendt AR. Hyperbaric oxygen therapy for diabetic foot wounds: has hope hurdled hype? Diabetes Care 2010;33(5):1143-5. (PMID:20427686).