Anatomy Physiology & Biochemistry
International Journal
ISSN: 2476-1400

Juniper Publishers
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Research Article
Volume 2 Issue 4 – May 2017
DOI: 10.19080/APBIJ.2017.02.555593

Anatomy Physiol Biochem Int J

Diabetic Foot Infection: A Study in a Tertiary Care Hospital

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Submission: April 28, 2017; **Published:** May 31, 2017

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Abstract

Background: Diabetic foot ulcer is very serious and debilitating complication embodying microbial insult in interaction with risk factors. Management of infection in such cases is an exigent task which involves a careful detection of the causative organisms and conducting the right antimicrobial therapy. Surgical approach is often necessitated in advanced stages or upon failure of the conservative management.

Objective: A treatment-oriented evaluation of case-records of hospitalized patients at a tertiary care hospital of North India was performed.

Methods: The neurovascular risk factors, diabetes control, microbial diagnosis of infection and sensitivity profile are elaborated and analyzed by descriptive statistics. Perspectives of successful current and future management are discussed in the light of findings.

Conclusion: Poor diabetic control has been the major contributing factor to foot infections in the diabetics. The infection was found to be most common in the age-group of 51-60 years of diabetic patients. The best modality of management is early debridement followed by antimicrobial coverage. In future, to optimize the recovery and long-term outcomes in the patients, evaluation of new therapeutic regimes, those targeting revascularization is warranted.

Keywords: Diabetic foot ulcer; Diabetic complications; Diabetic infection

Introduction

As per projections half a billion people would suffer maturity onset diabetes by 2030, world over, with concentration in middle income nations [1]. Diabetes and its complication involve complex etiology including increased susceptibility to infections. Diabetic foot ulcer is common major complication [2]. Around 15% of patients with type 2 diabetes have foot problem increasing instances of hospitalization. [3]. Neuropathy, peripheral vascular insufficiency, repeated trauma is traditionally believed to contribute to the complications. Besides the neurovascular alterations, age, gender, body mass index, duration of diabetes, glycosylated hemoglobin profiles etc are found influential in various studies [4]. Evidence on predictive value of simple indicators for risk of diabetic foot is crucially required in addressing the problem. Clinical history, examination, diagnostic investigation data must undergo continuous evaluation with such intent [5]. Infection management in diabetic foot is challenging task wherein microbial diagnosis is critical. Infective organisms and their sensitivity patterns are studied regularly with changing time, demography and region. The present study has analyzed the reports of the cases of diabetic foot infections from middle and upper middle income group of North Indian patient treated at a tertiary care hospital.

Material and Methods

50 patients admitted at Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala between January 2013 and June 2015, for management with diagnosis of infected diabetic foot were studied. The precise diagnosis including severity of foot involvement, age, gender, habits were noted. Details of clinical findings, requisitioned laboratory investigation data, identified microbes with sensitivity pattern and employed chemotherapy were recorded. Presence of hypertension, retinopathy, peripheral neuropathy, peripheral vascular defect and albuminuria were particularly scrutinized and noted. The data was analyzed using descriptive statistics

Results

Among the 50 cases studied, 23 were males and 26 females. Age of the patients ranged from 36 to 83 years. 26 of total 50 cases (52%) were in the age-group of 51 to 60 years (Figure 1). Poor control of the glycaemic status was the most common risk factor found to be associated (92% of the cases) (Table 1). The clinical manifestation was mostly in the form of ulcers (42%) while gangrene developed in 10% of the patients (Table 2). Regarding the management, the most common approach was the debridement of the wound which was performed in 40% of cases while in 5% of cases; amputation was performed (Figure 2). Gram-negative aerobes like *Pseudomonas aeruginosa* and Klebsiella species and gram-positive aerobes like staphylococcus were the commonest to be found (Table 3). Majority of the cases (62%) exhibited mixed infection with more than one causative microorganism (gram-negative) involved (Figure 3). Combinations of Vancomycin and Linezolid for gram-positive and Gentamycin or Amikacin for gram-negative organisms have been found to be most effective as antimicrobial therapies in the patients (Tables 4 & 5).

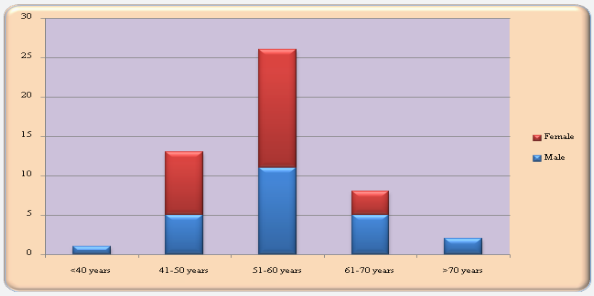

Figure 1: Demographic profile of the study-group.

Table 1: Burden of risk factors for complications at admission.

Risk Factors	Number of Cases
Poor diabetes control	46
Peripheral neuropathy	38
Hypertension	37
Albuminuria	29
Retinopathy	28
Hyperlipidaemia	25
Past history of Angina/MI	17
Smoking	9
Alcohol	5
Past history of TIA (transient ischaemic attacks)	4

Most common risk factor seems to be the lack of proper control of diabetes.

Table 2: Clinical severity profile of diabetic foot disease.

Clinical Category	Number of Cases
Cellulitis	10
Ulcer	21
Ulcer with Deep tissue/Bone involvement	14
Gangrene	5

Table 3: Profile for Isolated Pathogens in Ulcer Swab Culture

Organism types	Number of cases
Gram positive aerobes-	16
i) Staphylococcus aureus	7
ii)Streptococcus pyogenes	4
iii) Methicillin-Resistant Staph aureus (MRSA)	5
Gram negative aerobes-	34
i) Pseudomonas aeruginosa	10
ii) Klebsiella pneumoniae	8
iii)Acinetobacter Species	6
iv)Proteus-mirabilis v) Escherichia coli	4
vi) Enterobacter cloacae	3
	3

50 microbial species were detected in all. All patients have aerobic infections in which gram- negative organisms were twice as prevalent as the gram positive organisms.

Table 4: Percentage of sensitivity among isolated common gram-positive aerobes to various antibiotics/chemotherapeutic agents.

Antibiotics/ Chemotherapeutic Agents	Staph. Aureus (n=7)	Strep. Pyogenes (n=4)	MRSA (n=5)
Penicillin	14	100	0
Oxacillin	100	100	0
Erythromycin	71	50	0
Chloramphenicol	71	100	40
Sulfamethoxazole+ Trimethoprin	86	75	80
Gentamycin	100	100	0
Ciprofloxacin	86	75	80
Cefuroxime	100	100	0
Ampicillin/sulbactam	86	100	0
Amoxycillin/ clavulanic acid	100	100	0
Imipenem	100	100	20
Vancomycin	100	100	100
Linezolid	100	-	100
Fusidic acid	71	75	0

n- number of infected cases, MRSA-Methicillin-resistant *Staphylococcus aureus*

Besides Vancomycin and Linezolid, the Fluroquinolones and Cotrimaxazole also appeared reasonably effective against the Methicillin-resistant staphylococci in the study sample.

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Table 5: Percentage sensitivity among isolated common gram-negative aerobes to various antibiotic/chemotherapeutic agents.

Antibiotics/ Chemotherapeutic Agents	*Pseudo-monas aeruginosa* (n=10)	*Kleibsiella species* (n=8)	*Acinetobacter species* (n=6)	*Proteus species* (n=4)	E.Coli (n=3)	*Entero-bacter clocae* (n=3)
Chloramphenicol	30	88	50	100	100	100
Ampicillin	10	100	-	50	66	-
Sulfamethoxazole + Trimethoprin	0	88	33	75	66	66
Gentamycin	100	100	66	100	100	100
Amikacin	100	100	83	100	100	100
Ciprofloxacin	100	100	50	75	100	100
Cefuroxime	20	100	33	100	100	66
Ceftazidine	90	100	50	100	100	100
Ampicillin/Sulbactam	30	88	50	100	66	66
Amoxycillin/Clavulanate	20	100	17	100	100	66
Imipenem	100	100	66	100	100	100
Polymyxin	100	00	100	-	-	-

n- number of infected cases

Aminoglycosides (Gentamycin and Amikacin) exhibited impressive efficacy against most gram-negative organisms causing diabetic foot.

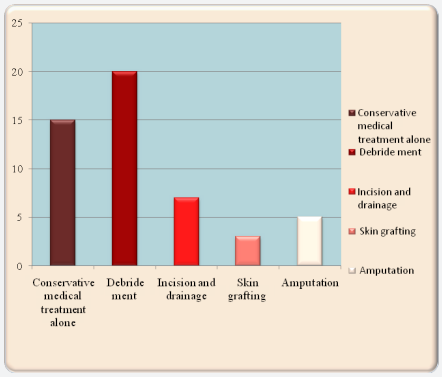

Figure 2: Management of cases of diabetic foot.

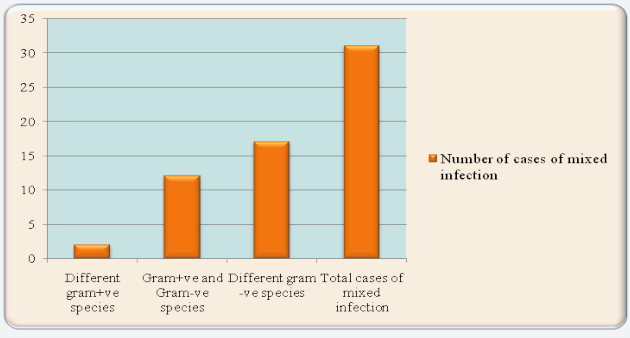

Figure 3: Pattern of mixed infections.

Discussion

Good glycaemic control is crucial to stop and even regress the complications of diabetes mellitus. Uncontrolled hyperglycemia co-exists in vast majority of studied diabetic foot infection patients. It can be the cause or effect of the complication but stands as most important target for prevention or management. The neuropathic diagnosis was derived from lost vibration sense tested with tuning fork and peripheral vascular deficiency from absent posterior tibial and/or dorsalis pedis pulsations. The two complications were present in large majority of cases. Additionally retinopathy, albuminuria and hyperlipidaemia also occurred in the subjects. Atherosclerotic basis has been suggested as dominant since diabetics have three times accelerated atherosclerosis development compared to non-diabetic individuals [6]. Observations of study underline the need of identifying and aggressively managing associated vascular risk factors eg. obesity, cigarette-smoking, dyslipidaemia, hypertension and sedentary behavior [7].

Staphylococcus aureus and beta haemolytic streptococci were the first organisms to colonize through breach of pedal skin. Chronic wound however acquires mixed infections. Inadequate episodes of infection treatment markedly increase gram-negative microbial load. *Pseudomonas aeruginosa* is specifically associated to instances of wet dressings [8]. Mixed infections provide mutual synergy among one another and add to global severity of state of infection [9]. The fact that majority of cases had mixed infections plus uncontrolled diabetes indicates diabetic foot ulcer in studied sample as vary severe disease state needing kind of intense management. The deeper involvement, especially bone was diagnosed by radiology and hence under-estimated. The antimicrobial therapy was based on wider consideration than usual sensitivity report [10].

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The patients continued to receive antimicrobial therapy often combined throughout hospitalization that lasted 1 week to 6 weeks. Reports of continued antibiotic therapy for deeper spread of infection in diabetic foot for 3 to 6 month periods indicate that as prudent for clinical success [11]. Diabetic foot infection as such is facilitated by intrinsic immunologic deficits, specially neutrophil dysfunction [12].

Among the studied 50 cases only 13 had staphylococcal infection evident in cultures. This is too low compared to expectations. Invasive staphylococcal infections are prevalent carrying poor prognosis in diabetics [13]. Diabetes also increases invasive infections due to group *B streptococci* [14]. Risk of serious infection due to *Klebsiella pneumoniae* increases in poorly controlled diabetics [15]. Urinary tract infections due to Gram-negative organisms are much increased in diabetics as well and are recurrent [16]. Over 60% instances of *Burkholderia pseudomellei* (Melioidosis) gram-negative infections occur in association with diabetes [17].

While debridement was done in majority of foot ulcers, no surgical efforts for revascularization were made in conjunction. The fact that most patients had neurovascular deficits, net impact of such deficiency on the clinical outcome is most warranted through study at centers that do surgical revascularization. Anti-angiogenic factors are believed to be raised in patients with diabetic foot ulcers that inhibit Wnt/β-Catenin signaling poor wound healing [18]. Agents becoming available, which activate β-Catenin signaling, deserve trials to improve healing of diabetic foot ulcer disease. Hyperglycemia-induced formation and build-up of advanced glycation end products (AGEs) are prime contributors to infection susceptibility in diabetes via multiple mechanisms [19-22]. Newly available agents causing breakdown of AGE products and agents inhibiting their formations must be part of therapeutic regimes in diabetic foot infection and be evaluated to build clinical evidence base.

Conclusion

Poor diabetic control has been the major contributing factor to foot infections in the diabetics in addition to peripheral neuropathy, retinopathy and nephropathy. Most commonly affected age-group was found to be 51-60 years. While few patients of diabetic foot infections respond to conservative line of management but the best modality of management is early debridement followed by antimicrobial coverage. Gram-positive aerobes like *staphylococcus* and gram-negative aerobes like *Pseudomonas aeruginosa* and *Klebsiella species* are the commonest to be found. Combination of Vancomycin and Linezolid for gram-positive and Gentamycin or Amikacin for gram-negative organisms have been found to be most effective. Evaluation of new therapeutic regimes is necessitated in the future to optimize the management and long-term outcomes in the patients.

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DOI:10.19080/APBIJ.2017.02.555593

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