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Medicine

SURVEILLANCE OF INFECTION IN DIABETIC FOOT FROM AN INDIAN TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT

Background: Foot infection is a frequent complication of patients with diabetes mellitus, accounting for up to 20% of diabetes-related hospital admissions. Some infectious agents are associated with the worst outcomes, which may ultimately lead to amputation of the infected foot
unless prompt treatment strategies are ensured. The present study sought to reveal the bacterial profile of diabetic foot ulcers in Eastern India where socio-economic status of the population is low.

Methods: A 10-month-long descriptive study was carried out to analyse the aerobic and anaerobic bacterial isolates of all patients admitted with diabetic foot infections presenting with Wagner grade 2–5 ulcers. Bacteriological diagnosis and antibiotic sensitivity profiles were carried out and analysed using standard procedures.

Results: Diabetic poly-neuropathy was found to be common (56.8%). Gram-negative bacteria (57.6%) were isolated more often than gram-positive ones (42.4%) in the patients screened. The most frequent bacterial isolates were Staphylococcus aureus, coagulase-negative staphylococci (CONS), Pseudomonas aeruginosa, and Enterobacteriaceae. Forty-nine cultures (68%) showed polymicrobial involvement. About 44% of P. aeruginosa were multi-drug-resistant, and MRSA was recovered on eight occasions (10.3%). Bacteroides spp. and Peptostreptococcus spp. were the major anaerobic isolates.

Conclusions: Our study supports the viewpoint put forth by previous Eastern Indian authors that the distribution of gram-negative bacteria (57.6%) is more common than gram-positive ones (42.3%). Also it is contrary to the viewpoint that diabetic foot infections are frequently monomicrobial. Furthermore, recovery of multi-drug-resistant P. aeruginosa isolates is of serious concern, as almost no one has reported the same from the Eastern Indian milieu.

KEYWORDS : Diabetes; Foot ulcer; antibiotics, Bacteria, co-morbidity

Introduction:

Diabetes is a chronic disorder that affects a large number of people globally and is a major public health problem (1). Approximately one-fourth of people with diabetes develop a foot ulcer during their lifetime, and as many as half of these ulcers will become infected(2) (3). In people with diabetes and foot ulcers, several factors, such as inappropriate antibiotic treatment, the chronic nature of the wound, and frequent hospital admission, can influence the presence of multidrug-resistant microorganisms in the ulcer(4). Moreover, the specific organisms identified in diabetic foot infections can differ not only from patient to patient and hospital to hospital but also from one part of the country to another(5). Infections are associated with amputation of the infected foot if not treated promptly and correctly. Inappropriate treatment may result increase in duration of hospital stay and the cost of management as well as morbidity and mortality(6). Most diabetic foot infections are true emergencies; therefore, antibiotic therapy should be started immediately to improve the chances of salvaging the limb. Initial empirical therapy should be based on clinical presentation, gram-staining results, and knowledge of the organisms that are most frequently isolated from a particular area (7). The appropriate selection of antibiotics based on the antibiograms of isolates from diabetic foot infections is extremely critical for the proper management of these infections. The aim of the present study was to evaluate the bacteriology of diabetic foot ulcers in IMS & SUM Hospital, Bhubaneswar, Odisha, India in order to determine the relative frequencies of bacterial isolates cultured from foot infections and to assess the in vitro antibiotic resistance and susceptibility of the isolated bacteria to a variety of commonly used antibiotics.

Diabetes is a metabolic syndrome characterized by hyperglycemia, which has become a heavy burden to India [8]. Deregulated metabolism in diabetics is linked to many complications including neuropathy, retinopathy, nephropathy, atherosclerosis, and foot ulcers [9]. Diabetic foot ulcer (DFU) is an outcome of complicated amalgam of several risk factors such as peripheral vascular disease, peripheral neuropathy, trauma, and impaired resistance to infection [10]. DFU continues to be a major reason for lower extremity amputation worldwide [11]. Diabetic foot infection (DFI) was considered as one of the most frequent and disastrous complications of diabetes. As reported, 60% of DFU are infected at presentation [11], which can increase the risk of a lower extremity amputation by 50% compared to the DFUs without infection [12, 13]. Because infection can worsen quickly in diabetics, clinician must pursue the diagnosis aggressively [14] to select an initial antibiotic regimen for the likely pathogens, which need more microbiological information about the DFUs before the wound swab culture and antibiotic sensitivity test report arrives. Thus, there is an urgent need for the bacterial profile and antibiotic resistance suggestion in more details to give their empirical antibiotic selection “a best guess.” Several researches reported that acute DFI is usually caused by aerobic Gram-positive cocci, but deep or chronic wounds often harbor aerobic Gram-negative and obligate anaerobic bacteria, often polymicrobial flora [15–18]. According to the patient's clinical features noted at the “first sight” of clinician, including the patient as a whole (e.g., cognitive, metabolic, and fluid status), the affected foot or limb (e.g., the presence of neuropathy and vascular insufficiency) and the infected wound [19], different classification systems are used to assess the severity of DF. The most often used is the Wagner-Meggit classification system that takes into consideration the depth of ulcer, presence of gangrene, and level of tissue necrosis [20] and IDSA/IWGDF classification system for defining the presence and severity of an infection of DF [14]. Besides, DF can be classified into three types according to whether with or without peripheral arterial or nerve diseases [16], named ischemic foot ulcer (IFU), neuropathic foot ulcer (NFU), and neuro-ischemic foot ulcer (N-IFU), respectively. More detailed information about pathogens and antibiotic resistance according to different DFU grades and types presents further practical significance for suggesting a more specific antibiotic choice. On the other hand, to provide optimal antimicrobial therapy, clinician should be familiar with the common microbial isolates and antibiotic resistance/sensitivity patterns in their own region of practice. Many studies from different regions showed different bacterial profiles in DFIs, especially in warm climate in Asia and Africa [3].

2. Materials and Methods

In this prospective study 2000 diabetic patients were screened for foot ulcers and the bacteria isolated were subjected to antibiotic sensitivity pattern. This study is approved by the Institutional Ethics Committee of our institute. The swab samples from wound were collected from the patients of diabetes. All the samples were cultured in suitable culture media and incubated at 37°C for 18 hrs. For pure culture, individual colonies were streaked in an agar plate and then processed according to previous method (21-23). The bacterial colony morphology was noted (Table 1) for further identifications with Gram stain and biochemical tests.

All Gram-negative bacteria were identified basing on the biochemical results with previous methods (24,25); whereas all Gram-positive bacteria were identified basing upon the test, catalase, and coagulase results. The results are compared with the colony morphology of the culture result also. In Staphylococcus aureus golden yellow (Fig 1), opaque, circular colonies white butyrous consistency were observed on nutrient agar whereas, yellow colonies were observed on mannitol salt agar, and beta-hemolysis was seen on blood agar. After identification, individual bacterial were tested for antibiotic sensitivity pattern with Kirby-Bauer method. Then, the sensitive or resistances of the used antibiotics were detected by measuring the diameter of inhibitor zone created by the antibiotics (Fig. 2). All the organisms were identified basing on the previous methods [26].

3. Results:

A total of 2000 diabetic patients were screened for foot ulcers. Among them 323 patients were found to have foot ulcer. The incidence of diabetic foot ulcer in this study is 16.15%. On accessing for how many years the person is suffering from diabetes, it was revealed that those having diabetes for 11 to 20 years had maximum incidence of foot ulcer while those having diabetes for more than 30 years had less incidence of foot ulcer (Table 1).

From clinical examination, investigation reports and questionnaires it was revealed that most of the patients of diabetic foot ulcer had other diabetic complications/co-morbidities. These were polyneuropathy (81.11%), chronic renal failure (31.89%), CAD (56.97%), cerebro vascular disease (34.67%), DKA (1.86%), hyperosmolar coma (1.24%), hypoglycemia (3.7%), and other unrelated co-morbidities (13.00%) (Table 2).

With the swab stick of diabetic foot ulcer several organisms were grown. These were single colony in 138 (42.72), double colony in 68 (21.05%), multiple colonies in 38 (11.76%) and rest 79 (24.46%) had no growth (Table 3,4). Among the bacteria, S. aureus was found in highest number i.e. 154 (35%) and Acenetobacter baumanii was the least 9 (2.05%) (Table 5).

Discussion:

To our knowledge, this is the first prospective study from this part of India on microbiological profile and antibiotic resistance pattern of the diabetic foot infection based on the deferent classification systems. DFI continues to be a major reason for lower extremity amputation worldwide [11], about half of which are infected at presentation[18]. In our study, 84.53% DF patients suffered from DFI. 30.2% of which were infected, mostly with chronic ulcer[12, 27]. As the other studies, Staphylococcus is the predominant Gram positive bacteria, including Staphylococcus aureus and CN-S (Coagulase-negative staphylococcus). Compared with the Gram positive bacteria, there were more species of Gram negative bacteria found in DFIs. Proteus and Pseudomonas aeruginosa were the predominant pathogens in Gram negative bacteria, followed by Klebsiella pneumoniae. It was different from some reports from Guangzhou in which the dominating Gram-negative flora was Escherichia coli [28], which may bedue to the warm climate. However, the predominant flora was Enterobacteriaceae Coinciding with some studies which showed that Gram negative organisms were the most frequent isolates in DFIs in warm climates, especially in South- east Asia and Africa [29].

For the DFIs, selection of an initial antibiotic regimen is usually empirical, so the likely pathogens and their antibiotic sensitivity often are “guessed” by the clinician before the microorganism culture and sensitivity tests. Therefore, a detailed bacterial profile and antibiotic resistance pattern associated with the different severity and types of DFIs is needed for the clinicians. Actually, the severity of the infection is first determined by the clinical classification scheme. Various classification systems have been proposed to assess the severity of diabetic foot lesion that attempt to encompass different characteristics of ulcer including ulcer size, depth, ischemia, infection, and neuropathy [10]. Wagner-Meggit classification system is the most widely used classification system [30] but cannot help to take into consideration about ischemia and infection. Another classification system given by the Infectious Disease Society of America (IDSA) and International Working Group on the Diabetic Foot (IWGDF) can define the presence and severity of an infection of the diabetic foot, named IWGDF/ IDSA classification [14]. With the aggravation of the wound, more of Gram-negative bacterial species were harbored, especially the proportion of Pseudomonas, a common nosocomial infection, resistant to many kinds of antibiotics; this coincided with earlier study[31]. The polymicrobial infection was distributed mainly in moderate wound (Wagner's grade 2 DFIs) and which was beyond our expectation. We expected that more severe the wound, more chances of the wound being polymicrobial. The patients with moderate wound in our study had more newly diagnosed DFI rate compared with the other groups probably since this group had not received systemic antibiotic treatments. When the patients were evaluated by Wagner-Meggit classification system and IWGDF/IDSA classification system, and the ulcers were typed as IFU, NFU or N-IFU, clinicians could choose the overlapping of different systems according to Table 3. For example, if the wound of a DFI patient was graded as Wagner-Meggit grade 2 and IWGDF/IDSA grade 3 and was diagnosed as an ischemic foot ulcer (IFU), combined with the bacterial profile and antibiotic resistance, the clinician can try β-Lactamase, carbapenem, fluoroquinolone, or aminoglycosides as the empirical antibiotics to cover the main possible pathogens and avoid penicillin, ampicillin, the first to third generation cephalosporin and tetracycline in order to prevent the infective treatment and MDR bacteria due to antibiotic abuse. If the DFI patient was classified in more severe IWGDF grades, less potential empirical regimens could be chosen and more should be avoided. However, this paper only provided the empirical regimens selected suggestion about the predominant gram negative bacteria (GNB) and gram positive bacteria(GPB), while did not cover all the pathogens. Actually, some other pathogens showed higher resistance rates to more antibiotics due to their natural resistance, for example, the Pseudomonas aeruginosa, and Enterococcus faecium. Therefore, more attention should be paid to the DFIs with high risk of the natural resistance pathogens above, like the Wagner's grade 4 and IWGDF/IDSA grade 4 wound.

The major limitation of this study is the lack of anaerobic culturing. Further study is required to evaluate the anaerobic distribution and drug sensitivity in the different grades of DFIs. Another limitation is the small number of included patients, especially those with Wagner-Meggit grade 1 or IWGDF/IDSA grade 1 wound, and rarely neuropathic ulcerations. Tissue biopsy is known as the most standard method, and swab cultures are considered as not reliable since it generally includes the colonizers and not the causative pathogen [15]. But in this study, the swabs were obtained after a complete debridement in order to avoid the colonizers, and the CNS, as the main colonized organisms in the skin, were detected lower than 10% in this study, which showed that the swabs were reliable.

5. Conclusions

Different bacterial profiles and antibiotic sensitivity were found in different Wagner's grades, IWGDF grades, and DFI types. Clinician should try to stay updated in antibiotic resistance pattern of common pathogens in their area, especially for practice on the empirical antibiotic use. This paper provided the detailed practical information (potential empirical regimens and alarming empirical regimens) to the clinician based on the assessments to the DFIs from the different aspects in this region.

Fig 1. Pure culture of S. aureus with streaking method on Nutrient agar.
Fig 2. Antibiotic sensitivity pattern with disc diffusion method.

Table 1

Known to have DM (in years)	Total Number of patients	Foot ulcer	%
≤10	556	61	3.05
11 to 20	912	175	8.75
21 to 30	406	79	3.95
>30	126	8	0.4
Total	**2000**	**323**	**16.15**

Table 2

Co-morbidities in DFU	Frequency	%
Poly neuropathy	262	81.11
Chronic renal failure	103	31.89
CAD	184	56.97
Cerebro-vascular disease	112	34.67
DKA	6	1.86
Hyperosmolar coma	4	1.24
Hypoglycemia	12	3.72
Others	42	13.00

Table 3

Bacterial collony	Frequency	%
No growth	79	24.46
Growth of bacteria		
Single colony	138	42.72
Double colony	68	21.05
Multiple colony	38	11.76
Total with bacterial colongy	244	75.5

Table 4.

Organisms	Frequency	%
Staphylococcus aureus	154	35.00
Klebsiella pneumoneae	94	21.36
Klebsiella Oxytoca	78	17.73
Proteus vulgaris	38	8.64
Proteus mirabilis	26	5.91
Eserichia coli	19	4.32
Citrobacter Sp.	12	2.73
Pseudomonas aeruginosa	10	2.27
Acenetobacter baumanii	9	2.05
Total	440	100.00

Table 5 Antibiotic sensitivity pattern of S. aureus isolated from diabetic foot ulcer.

SL NO	ANTIBIOTIC	RESISTANT (%)	SENSITIVE (%)
1.	AK	22.2	77.8
2.	CTR	100	0
3.	LE	0	100
4.	OF	78	22
5.	AMC	66.7	33.3
6.	NET	0	100
7.	PIT	11.11	88.89
8.	LZ	11.1	88.9
9.	CFS	11.1	88.9
10.	IPM	33	67
11.	CFM	100	0
12.	L	88	12
13.	VA	11.1	88.9
14.	CLR	44.4	55.6
15.	MET	88.9	11.1
16.	MO	55.6	44.4
17.	CAT	33	67
18.	CIT	44.4	55.6

Note: Antibiotics (µg/disc): AK: Amikacin 30, GEN: Gentamicin 30, NET: Netillin 30, TOB: Tobramycin 10, AT: Aztreonam 30, PI: Piperacillin 100, PIT: Piperacillin/tazobactam 100/10, CPM: Cefepime 30, CPZ: Cefoperazone 75, CFS: Cefoperazone/sulbactam, Antibiotics (µg/disc): Ak: Amikacin 30, Ac: Amoxyclav 30, Am: Ampicillin 10, Cf: Cefpodoxime 10, Ctr: Ceftriaxone 30, Ge: Gentamicin 30, Of: Ofloxacin 5, Ox: Oxacillin

Fig.1

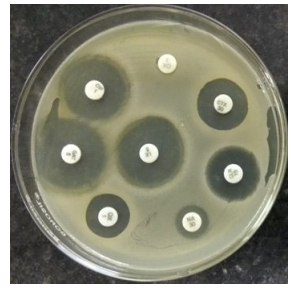

Fig.2

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