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Diabetic Foot: A Few Steps towards Aetiology

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Abstract: ***This retrospective study was done on diabetic foot infections, to look into their etiological diversity and ever-changing antimicrobial susceptibility. Among the 85 micro-organisms isolated, Gram negative aerobic bacilli collectively shared the major proportion of 53%, Gram positive cocci 42.3% and anaerobic bacteria 4.7%. While anaerobic bacteria were uniformly sensitive to metronidazole, aerobic bacteria showed significant level of resistance to cotrimoxazole, penicillins, cephalosporins, fluoroquinolones and combination drugs. Vancomycin and linezolid showed predictable efficacy for all Gram positive cocci, while imipenem was the most effective drug for Gram negative isolates.***

Keywords: diabetic foot infections**,** aetiology, antibiotic resistance**.**

1. Introduction

Diabetes mellitus is a menace to us for its impacts on different organ systems of the body. Uncontrolled diabetes leads to nephropathy, neuropathy, retinopathy, and macrovascular complications, which are the leading causes of diabetes related morbidity. [1],[2]. Approximately 15% cases of all diabetes patients develop foot ulcers progressing to osteomyelitis which impose as a major health care burden seeking for hospital admission.[3],[4]. The predisposing factors are peripheral neuropathy, muscle atrophy, foot deformity and neuropathic fractures which eventually lead to development of diabetic foot infections in approximately 20% of all diabetic patients. Diabetic foot infections may present as ulceration, gangrene, Charcot joint, or fracture and are a major risk for amputation. [5] This study was done in a tertiary care hospital of West Bengal, India, on patients admitted with diabetic foot infections over a period of ten months. This retrospective study aims to determine the microbiological profile of diabetic foot infections and the antibiotic susceptibility pattern of the clinical isolates prevalent in this region to throw some lights on this burning problem.

2. Materials and Methods

This retrospective study was conducted over ten months period spanning from March 2016 to December 2016 in a tertiary care medical college and hospital of West Bengal, India. Patients with diabetic foot infections were included in this study if they had an infected ulcer, wound, osteomyelitis or previous amputation and received treatment either in the outpatient or inpatient departments of this hospital. The specimens were inoculated in Blood agar, Chocolate agar and MacConkey agar and incubated under aerobic and anaerobic conditions at 37^0C temperature. The isolates were identified by conventional identification techniques. Antibiotic susceptibility was done by Kirby–Bauer disc diffusion method. The

following antibiotic discs were employed: ampicillin (10 µg /mL), co-trimoxazole (25 µg/mL), vancomycin (30 µg/mL), linezolid (30 µg/mL), ampicillin-sulbactam (20 µg/mL), amoxicillin –clavulanic acid (30 µg/mL), gentamicin (10 µg/mL), netilmicin (30 µg/mL), amikacin (30 µg/mL), erythromycin (15 µg/mL), azithromycin (15 µg/mL), cefuroxime (30 µg/mL), cefotaxime (30 µg/mL), ceftazidime (30 µg/mL), ceftriaxone (30 µg/mL), ciprofloxacin (5 µg/mL), levofloxacin (5 µg/mL), doxycycline (30 µg/mL), imipenem (10 µg/mL), piperacillin-tazobactam (110 µg/mL), metronidazole (50 µg/mL) ; and the results were interpreted following CLSI guidelines.[6]

3. Discussion

This retrospective study revealed the nature of diabetic foot infections with their prevailing bacteriological profile and antibiotic susceptibility pattern in this region. 85 bacterial isolates identified from diabetic patients with various grades of foot infections were included in this study. The clinic-bacteriological profile varied widely. Males (65.9%) outnumbered the females (34.1%) with a ratio of 1.93. The range of age was from 20 years to 83 years with the mean age of 49.2 years. Majority of the patients (63.5%) fell under the age group of 41 to 60 years. [Table 1]

These findings were in concordance with the studies of Bansal and Garg et. al. and Nadeem S. Raja. [7], [8].

Table 1: Age and gender wise distribution of patients. (n=85)

Age (Years)	*Male*	*Female*	*No. of patients (%)*
≤40	9	4	13 (15.3)
41-50	16	13	29 (34.1)
51-60	18	7	25 (29.4)
>60	13	5	18 (21.2)
Total	56	29	85 (100)

Table 2: Bacteriological profile of diabetic foot infections, (n=85)

Organisms	*Numbers*	*Percentage*
Gram negative bacilli	45	53
Klebsiella pneumoniae	15	17.6
Pseudomonas aeruginosa	12	14.1
Escherichia coli	7	8.2
Proteus mirabilis	5	5.9
Proteus vulgaris	2	2.3
Klebsiella oxytoca	2	2.3
Citrobactor sp.	1	1.2
Acinetobactor sp.	1	1.2
Gram positive cocci	36	42.3

Staphylococcus aureus	24	28.2
CONS	10	11.7
Enterococcus sp.	2	2.3
Anaerobic bacteria	4	4.7
Total	85	100

Most of the workers found polymicrobial nature of diabetic foot infections with Gram negative organisms as the prevalent causative agents [7], [9, 10, 11], But majority of cases included in this study were monomicrobial and less severe in nature; which were supported by the study of N.S. Raja. [8]

According to this study, Gram negative bacilli were the most common isolates (53%) with *Klebsiella pneumoniae* (17.6%) and *Pseudomonas aeruginosa* (14.1%) predominating over *Escherichia coli* (8.2%), *Proteus mirabilis* (5.9%), *Klebsiella oxytoca* (2.3%), *Proteus vulgaris* (2.3%), *Citrobactor species* (1.2%) and *Acinetobactor species* (1.2%). Overall Gram positive cocci were 42.3%, comprising of *Staphylococcus aureus*, CONS, and *Enterococcus Species*. But as far as single bacterial isolate is considered, *Staphylococcus aureus* took the lead with 28% of all isolates. Anaerobic organisms were isolated in 4.7 % of cases. [Table 2]

Antibiotic resistance remained a matter of concern with all the isolates. Anaerobic bacteria responded well to metronidazole clinically. Almost all of aerobic isolates showed very high level of resistance to all types of antibiotics. Gram positive cocci showed significant resistance to cell wall active antibiotics, quinolones and cotrimoxazole. Aminoglycosides and doxycycline were effective in most of the cases, while predictable efficacy was showed by Vancomycin and linezolid. [Table 3]

Gram negative bacteria, too, were resistant to Ampicillin, cephalosporins and even combinations like ampicillin/ sulbactam, or amoxicillin/clavulanic acid. Piperacillin/ tazobactam was able to retain its efficacy to some extent. Azithromycin, Fluoroquinolones, and injectable aminoglycosides also showed similar pattern of increased resistance. Imipenem remained the only antibiotic for Gram negative bacteria with some hope. [Table 4]

Table 3: Resistance (percentage) shown to antibiotics by Gram positive bacteria (N=36)

Antibiotics	*S. aureus (24)*	*CONS (10)*	*Entero-coccus Sp. (2)*
Penicillin	100	90	100
Ampicillin	100	70	100
Ampicillin-sulbactam	60	20	50
Amoxicillin –clavulanic acid	85	40	100
Ceftriaxone	80	60	100
Cefotaxime	55.6	60	50
Cefuroxime	55.6	60	100
Ciprofloxacin	86	50	100
Levofloxacin	29	20	50
Doxycycline	50	20	50
Amikacin	47	40	50
Gentamicin	47	50	50
Vancomycin	9	1	0
Linezolid	0	0	0
Imipenem	-	-	50
Erythromycin	53.8	30	50
Cotrimoxazole	62.5	60	100

Table 4: Resistance (percentage) shown to antibiotics by Gram negative bacteria, (N=45)

Antibiotics	*Klebsiella pneumoniae (15)*	*Pseudomonas aeruginosa (12)*	*Escherichia coli (7)*	*Proteus mirabilis (5)*	*Proteus vulgaris (2)*	*Klebsiella oxytoca (2)*	*Citrobactor species (1)*	*Acinetobactor species (1)*
Ampicillin	100	100	100	100	100	100	100	100
Ampicillin-sulbactam	80	50	40	40	100	50	100	100
Amoxyclav	91	90	75	75	100	100	100	100
Piperacillin tazobactam	20	17	28.5	25	0	0	0	100
Amikacin	58.3	25	57	25	50	50	0	100
Gentamicin	58.3	30	57	20	50	0	0	0
Netilmicin	62.5	25	43	20	50	50	0	0
Azithromycin	80	33	-	40	50	0	-	-
Co-trimoxazole	100	100	100	80	100	100	100	100
Ciprofloxacin	60	75	100	80	100	50	100	100
Levofloxacin	60	80	57	40	0	50	100	0
Imipenem	23	8	25	20	0	0	0	100
Cefuroxime	86.7	82	75	80	100	50	100	100
Cefotaximre	86.7	67	75	80	100	50	100	100
Ceftazidime	75	67	75	80	0	50	100	100
Ceftriaxone	86.7	82	75	80	100	50	100	100
Doxycycline	75	50	25	40	100	50	0	0

4. Conclusion

According to this study, diabetic foot infections in uncontrolled diabetes were more prevalent in the above forty age group and less common in the twenties or thirties of ages. Early or mild infections were mostly monomicrobial in nature, whereas multiple organisms or mixed infections were found in more severe cases. Varied and increasing level of resistance to almost all groups of antibiotics, rendered in-vitro antibiotic sensitivity testing a compulsory step towards management. Vancomycin and linezolid were of predictable efficacy in case of gram positive cocci, and metronidazole for anaerobic, while, despite some extent of resistance,

imipenem and piperacillin/ tazobactam were still suggested for gram negative isolates.

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