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Emerging Antibiotic Resistance in Diabetics-A Myth or Reality

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Abstract

Emerging antibiotic resistance and super bugs have been a potential threat to the mankind since the beginning of usage of antibiotics and now it is posing severe hinderance in the treatment of many diseases and is increasing the morbidity and mortality. Diabetes is the most common disease in India and India is named as diabetic capital of the world. One of the complications of diabetes mellitus is peripheral neuropathy which might lead to non-healing diabetic ulcers. Emerging antibiotic resistance has become an important problem in the treatment of these diabetic ulcers. The current study is undertaken to understand the bacteriological profile and the antibiogram in diabetic patients with foot ulcers.

The present study design: Cross sectional study, study population: Diabetic patients with foot ulcers, sample size: 106 (sample size calculated based on previous related articles), method of collection: Two swabs were collected from the ulcer for Gram's staining and culture.

The antibiotic sensitivity testing was done using Muller Hinton agar plates by Kirby Bauer disc diffusion method using commercially available discs.

The present study concludes that most common bacterial isolate is Escherichia coli [26.4%] followed by Pseudomonas aeruginosa [23.6%] and most of the bacterial isolates are resistant to commonly used antibiotics like Tobramycin [100%], Tetracycline [100%], Penicillin [96.8%].

If the antibiotic resistance is to be continued at this rate then within near future existing antibiotics will become extinct in respect of their use. It is highly necessary to spread awareness among the present day physicians and patients about judicious usage of antibiotics to prevent a superbug pandemic.

Keywords: Emerging Antibiotic Resistance, Diabetic Foot Ulcers, Antibiotic Susceptibility, Diabetes Complications, Bacterial Infections

Introduction

Diabetes is the most common disease in India with a prevalence rate of 12-17% in the urban and 2.5% in the rural population [1]. One of the complications of diabetes mellitus is peripheral neuropathy which might lead to non-healing diabetic ulcers [2]. Foot ulceration and infection in diabetic patients is one of the significant causes of amputation which accounts for about 20% of all hospital admissions in diabetic patients [3]. Wound healing is a stepwise repair of the lost extracellular matrix which forms the most significant component of the dermal skin layer and this is disturbed by diabetes [4]. Impaired circulation in diabetics limits the access of phagocytes to the injured area, and this result in decreased antibiotic concentration. Blood supply is further compromised to lower limbs by improper foot care. Further,

diabetic neuropathy leads to the insensitivity of feet which makes them more prone to get injured and infections leading to diabetic foot ulcers [2]. Mostly, the diabetic foot ulcers or infections are of mixed bacterial flora and proper management of these diseases requires an appropriate antibiotic selection which is done through culture and sensitivity tests [2]. Multidrug resistance has now become a significant issue in treating these infections. The efficient way of combating these infections is through empirical therapy that is using appropriate antibiotics [5].

With this background, this study was undertaken to find out the most common bacterial isolate that is associated with the diabetic foot ulcers and to know the drug sensitivity -resistant pattern of these bacteria in diabetics attending a tertiary care health facility.

Aims & Objective

1. To identify and describe the bacteriological profile in diabetic foot ulcers.
2. To determine the susceptibility and resistance pattern of the organisms isolated.

Materials & Methods

Study design: Hospital-based cross sectional study

Study setting: Diabetic OPD clinic and surgery inpatient department of a tertiary care centre

Study population: Diabetic patients with foot ulcers

Duration of study: 2 months (June-July, 2018).

Sampling method: Convenience sampling method

Sample size: 90 (based on Puducherry study¹, where the prevalence of bacterial culture positives was 77%; with 12% allowable error of this prevalence)

Inclusion Criteria: Diabetic patients with foot ulcers

Exclusion Criteria:

1. Patients with foot ulcers without diabetes
2. Patients having other systemic illnesses other than diabetes
3. Those not willing to participate in the study

Study tools: For each person, a proforma was used for data collection.

Method of Collection of Data

A detailed history was taken followed by general physical and systemic examination to rule out any other illnesses. The

samples were collected using two sterile swabs from the edges, margins, base, deeper portions of the ulcers/ wounds. The samples were transferred immediately to the microbiology laboratory of the tertiary care centre for further processing. The sample from one swab was subjected for Gram's staining and the second sample for culture to identify the organism through conventional methods. The antibiotic sensitivity testing was done using Muller Hinton agar plates by Kirby Bauer disc diffusion method using commercially available discs (Hi Media).

Ethical clearance:

The study was given approval by the Institutional Human Ethics Committee (IHEC).

Statistical Analysis of data:

The data were entered into MS Excel 2010 version and further analyzed using SPSS 20 version. For descriptive analysis; the categorical variables were analyzed by using percentages and the continuous variables by calculating mean \pm Standard Deviation.

Observation & Results

Though the sample size for the study was 90, a total of 92 participants were considered for the final analysis. Table 1 shows that the age group varies from 36 to more than 65 years of age and most of the patients with diabetic foot ulcers are male 53(57.6%) when compared to females 39(42.4%).

Table 1: Distribution of study participants (n=92)

Age (years)	Gender		Total
	Male	Female	
36-45	8 (50.0%)	8 (50.0%)	16 (100.0%)
46-55	18 (52.9%)	16 (47.1%)	34 (100.0%)
56-65	16 (59.3%)	11 (40.7%)	27 (100.0%)
>65	11 (73.3%)	4 (26.7%)	15 (100.0%)
Total	53 (57.6%)	39 (42.4%)	92 (100.0%)

In this study, a total of 98 samples were subjected to culture, which included 6 extra samples from the participants with polymicrobial infection. Growth was seen among 80 cultures (81.6%), i.e., "culture positives" and no growth was seen among 18 cultures (18.4%), i.e., "culture negatives". Among the 80 culture positives, gram positive isolates were only 16(20.0%), while the majority were gram negative isolates 56(70.0%). A total of 62 cultures obtained in our study were monomicrobial (77.5%), while 10 cultures were polymicrobial (12.5%). Coagulate negative staphylococci (CONS) were seen in 8 cultures, accounting to around (10%). (Table 2 & Figure 1)

Table 2: Pattern of microbial isolation among the study participants

Variable	Frequency	%
Culture (n=98)		
Positive	80	81.6
Negative	18	18.4
Gram's stain (n=80)[#]		
Gram Positive	16	20.0
Gram Negative	56	70.0
CONS	8	10.0
Type (n=80)[#]		
Monomicrobial	62	77.5
Polymicrobial	10	12.5
CONS	8	10.0

(#excluding 18 'no growths')

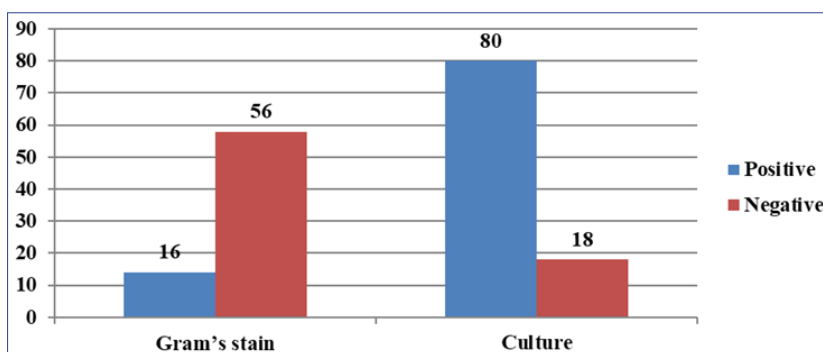


Figure 1: Pattern of microbial isolation among the study participants

Table 3 shows that among the culture 80 culture positives after excluding the normal flora we have isolated 72 organisms from among which the commonest isolate in the present study being *Escherichia coli* 19(26.4%), followed by *Pseudomonas aeruginosa* 17(23.6%) & *Staphylococcus aureus* 12(16.7%). Methicillin resistant *Staphylococcus aureus* (MRSA) were found to be 2(2.8%), and Non-Fermenting Gram Negative Bacilli (NFGNB) was only 1(1.4%). (Table 3 & Fig 2).

Table 3: Type of Bacteria in the isolates of the study participants

Type of Bacteria	Frequency (n=72)#	%
<i>Escherichia coli</i>	19	26.4
<i>Pseudomonas aeruginosa</i>	17	23.6
<i>Staphylococcus aureus</i>	12	16.7
<i>Proteus</i>	9	12.5
<i>Klebsiella</i>	8	11.1
<i>Enterococcus</i>	2	2.8
<i>Enterobacter</i>	2	2.8
MRSA	2	2.8
Other NFGNB	1	1.4

(*excluding 18 'no growths' & 8 'CONS')

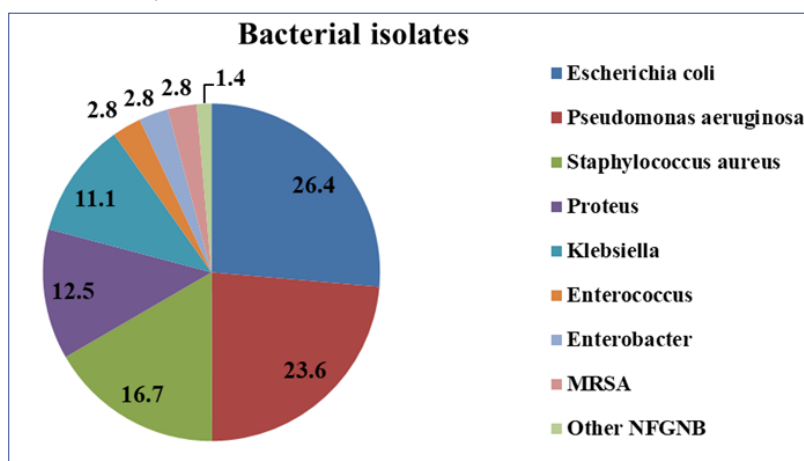


Figure 2: Type of Bacteria in the isolates of the study participants (n=72)* represented in a pie chart (*excluding 18 'no growths' & 8 'CONS')

Table 4 shows the antibiotic sensitivity patterns of various microbial isolates from the current study. It shows that maximum sensitivity is found for Imipenem, Meropenem 37(51.4%) and piperacillin + tazobactam 37(51.4%) followed by Amikacin 35(48.6%) ceftriaxone/ ceftazidime 28(38.9%) and the least sensitivity (highest resistance) is seen for tobramycin 0(0%), tetracycline 0(0%) followed by penicillin 3(4.2%). Various sensitivity patterns for various drugs are also depicted here.

Table 4: Drug sensitivity among the microbial isolation among the study participants in percentages

Variable	I (n=19)	II (n=12)	III (n=17)	IV (n=2)	V (n=8)	VI (n=9)	VII (n=1)	VIII (n=2)	IX (n=2)	Total (n=72)
Penicillin	0 (0.0)	0 (0.0)	0 (0.0)	2 (100)	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)	0 (0.0)	3 (4.2)
Erythromycin	0 (0.0)	3 (25.0)	0 (0.0)	2 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100)	7 (9.7)
Cotrimoxazole	4 (21.1)	6 (50.0)	0 (0.0)	2 (100)	2 (25.0)	0 (0.0)	1 (100)	0 (0.0)	1 (50.0)	16 (22.2)
Gentamicin	7 (36.8)	3 (25.0)	9 (52.9)	2 (100)	2 (25.0)	1 (11.1)	0 (0.0)	1 (50.0)	1 (50.0)	26 (36.1)
Ciprofloxacin	2 (10.5)	1 (8.3)	6 (35.3)	0 (0.0)	2 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	11 (15.3)
Tetracyclin	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cefoxitin	8 (42.1)	4 (33.3)	0 (0.0)	1 (50)	1 (12.5)	3 (33.3)	0 (0.0)	1 (50.0)	0 (0.0)	18 (25.0)
Ampicillin	6 (31.6)	3 (25.0)	0 (0.0)	1 (50)	0 (0.0)	1 (11.1)	0 (0.0)	0 (0.0)	0 (0.0)	11 (15.3)
Amikacin	12 (63.2)	6 (50.0)	12 (70.6)	0 (0.0)	1 (12.5)	2 (22.2)	0 (0.0)	1 (50.0)	1 (50.0)	35 (48.6)
Tobramycin	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ceftriaxone/ Ceftazidime	10 (52.6)	0 (0.0)	13 (76.5)	0 (0.0)	2 (25.0)	2 (22.2)	0 (0.0)	0 (0.0)	1 (50.0)	28 (38.9)
Imipenem/ Meropenem	17 (89.5)	2 (16.6)	10 (58.8)	0 (0.0)	3 (37.5)	5 (55.5)	0 (0.0)	0 (0.0)	0 (0.0)	37 (51.4)
Piperacillin Tazobactam	13 (68.4)	0 (0.0)	14 (82.4)	0 (0.0)	3 (37.5)	7 (77.7)	0 (0.0)	0 (0.0)	0 (0.0)	37 (51.4)

I= Escherichia coli; II= Staphylococcus aureus; III= Pseudomonas aeruginosa; IV= Enterococcus; V= Klebsiella; VI= Proteus; VII= Other NFGNB; VIII= Enterobacter; IX= MRSA

Discussion

Diabetes is a multi-systemic disease that affects various organ systems in our body including the blood vessels, the microvascular and macrovascular changes that occur in diabetes are responsible for many complications in diabetes, one of the many complications of diabetes is peripheral neuropathy and diabetic foot ulcers which if not treated judiciously may lead to amputation. So there was a need for the present study to help us understand the changing pattern of microbials and their sensitivity and resistance pattern.

In concordance with Khan DM et al study the present study also showed that the maximum number of patients are in between 45-65 age group and male preponderance compared to females in all age groups this shows that there is poor glycemic control among elderly male.

In concordance with Shanmugam P, et al. study the present study also showed that gram negative organisms 58(72.5%) are more prevalent than gram positive organisms 14(17.5%) [5].

In contrast to various other studies the present study reported more of monomicrobial isolates 62(77.5%) when compared to polymicrobial isolates 10(12.5%) only Konar J, et al. study reported similar findings [1,4,5,7].

In contrast to Jain SK, et al., Bansal E, et al., Chopdekar KA, et al. studies the present study showed that the commonest bacterial isolate among gram negative organisms being Escherichia coli

19(26.4%) followed by Pseudomonas aeruginosa 17(23.6%) [2,7,8].

In par with Hena JV, et al. study the most effective antibiotic was found to be Imipenem 37(51.4%) and in par with Sundaram CM, et al. study the present study also showed that Amikacin 35(48.6%) was effective antibiotic. The commonest isolate in this study was Escherichia coli 19(26.4%) which had been most sensitive to Imipenem 17(89.5%) followed by Piperacillin + Tazobactam 13(68.4%) and it was least sensitive to Penicillin 0(0%), Erythromycin 0(0%), Tetracycline 0(0%), Tobramycin 0(0%) group of antibiotics. The second commonest isolate in this study was Pseudomonas aeruginosa 17(23.6%) which had been most sensitive to Piperacillin + Tazobactam 14(82.4%) followed by Ceftriaxone 13(76.5%), Amikacin 12(70.6%) and it was least sensitive to Penicillin 0(0%), Erythromycin 0(0%), Cotrimoxazole 0(0%), Tetracycline 0(0%), Cefoxitin 0(0%), Ampicillin 0(0%), Tobramycin 0(0%).

The commonest isolate among gram positive in this study was Staphylococcus aureus 12(16.7%) and had been most sensitive to Amikacin 6(50.0%) and cotrimoxazole 6(50.0%) and it was least sensitive to penicillin 0(0%), tetracycline 0(0%), tobramycin 0(0%), ceftriaxone 0(0%), piperacillin tazobactam 0(0%).

According to present study the most effective antibiotics in this clinical setting were Imipenem (51.4%), Meropenem (51.4%) and Piperacillin + Tazobactam (51.4%) and most of the organisms were resistant to Tobramycin, Tetracycline and Penicillin.

There were also two MRSA organisms isolated in the present study and surprisingly both of them were sensitive to Erythromycin and one organism was sensitive to Cotrimoxazole, Gentamicin, Amikacin, Cefazidime.

Conclusion

The present study concludes that the most common organism that is isolated from diabetic foot ulcers in this clinical setting is *Escherichia coli*, followed by *Pseudomonas aeruginosa*. Analysis of the antibiotic susceptibility and resistance patterns showed that most of the organisms isolated were resistant to commonly used antibiotics such as penicillin, tetracycline, tobramycin etc. and most organisms were found sensitive to higher antibiotics like Imipenem, Meropenem, and Piperacillin + Tazobactam. This demonstrates the rapid evolving of drug resistance among microorganisms. This shows the increasing trend of multi drug resistance in general, and appropriate antibiotics usage through empirical therapy for managing diabetic foot ulcers helps in early cure and reduces the need for amputation.

Injudicious use of antibiotics is the major cause of emerging antibiotic resistance which has become a global problem today. Diabetic foot ulcers coupled with antibiotic resistance leads to increase in morbidity and mortality among diabetics. This study emphasizes on the multi drug resistant nature among the bacterial isolates. If emergence of resistance continues at this rate, then antibiotics are at the verge of extinction. Spread of knowledge among the present day physicians and public for judicious use of antibiotics is the need of the hour.

Conflicts of Interest: None

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