

Diabetic Foot Ulcer and Multidrug-Resistant Organisms: Prevalence and Bacteriological Profile

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Abstract

Aim: To study the prevalence and bacteriological profile of multi-drug resistant organism (MDRO) infection in diabetic foot ulcers. **Methods:** 150 Diabetic patients with foot ulcer were prospectively studied. Detailed clinical history and clinical examination of the ulcer were done for all patients. The microbiological profile was analysed, in detail, for each patient. The multi-drug resistant organisms (MDRO) were identified, using internationally accepted criteria. **Results:** 153 MDROs were isolated, out of a total of 279 organisms (54.8%). These were isolated from 99 out of 150 patients (66%). The commonest MDRO isolated was *Escherichia coli*, followed by *Pseudomonas aeruginosa*. **Conclusion:** The prevalence of MDRO is alarmingly high in infected diabetic foot ulcers.

Keywords: Diabetic Foot Ulcer; Multi-Drug Resistant Organisms (MDRO).

Introduction

Foot ulceration is a major cause of morbidity in diabetes mellitus. It is said that a sixth of all patients with diabetes mellitus develop foot ulcers at some point in their lifetime [1]. Infections in diabetic foot ulcers have become increasingly difficult to treat, because of the emergence of multi drug resistant organisms (MDRO). In the past, the problem of MDRO was less well

understood, because of a lack of uniform definition of MDRO. This study was done, as very few studies have been done in India to analyse the prevalence of MDRO in diabetic foot ulcers.

Patients and Methods

Conducted between January 2011 and July 2012 at PSG Institute of Medical Sciences & Research, Coimbatore, India, this is a prospective observational study to find the prevalence of MDRO in diabetic foot ulcers. Prior approval from the institution review board was obtained. 150 diabetic patients with foot lesions were included in the study. Written informed consents were obtained from the patients. Detailed clinical history of the patient and other relevant data were collected using structured case report forms.

Wound swabs were obtained from the floor of the ulcer, before starting on empirical antibiotic therapy. Direct microscopic examination and aerobic cultures were done by standard methods. The bacteriological spectrum and the sensitive antibiotics were noted for each patient. MDROs were identified using the ECDC and CDC criteria [2].

Results

Seventy Eight percent (78%) of the patients were 51 years or older, with the average age being 58.21. 74.6% of the patients were males. Almost all the patients had Type II diabetes, with only 4% of them having Type I. Only 19.33% of patients had a good glycaemic control, with HbA1c 6-7%. 40% of patients with foot ulcer had diabetes for less than 5 yrs.

Sixty eight percent (68%) of patients had ulcers of less than one month duration. Most of the patients had Wagner's grade II, III, or IV ulcers. There were very few

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ulcers with Wagner’s grade V. There was almost an equal distribution of necrotic and non-necrotic ulcers. Recurrent and non-recurrent ulcers also were equal in distribution. 34% of ulcers had associated osteomyelitis. As far as the site of the ulcer was concerned, 28% were seen in the heel, followed by digits/interdigital areas (21.33%).

Microbiological Observations

A total of 279 organisms were isolated from 150 patients. On an average 1.86 species were isolated from each patient. 58.66% of patients had polymicrobial culture. Among the isolates, most were gram negative rods (69.89%) and the rest were gram positive cocci, with the exception of a solitary gram negative coccus.

Gram positive to gram negative ratio was 1: 2.3. Among the isolates, *Escherichia coli* was the most common one constituting 17.9%, followed by *Staphylococcus aureus* 17.6 % and *Pseudomonas aeruginosa* (16.5%).

MDRO, as per the criteria laid down by European centre for Disease Prevention and Control, were seen in 99 of the 150 patients. Antibiotic resistance was observed in 58.6% (115 out 196) of gram negative organisms compared to 45.78% (38 out of 83) in gram positive organisms. Multidrug resistance was noted in 78% of *Escherichia coli*, 74% of *Pseudomonas aeruginosa*, 70% of *Proteus mirabilis* and 61.53% of *Acinetobacter baumannii*. 55% of *Staphylococcus aureus* species and 47.36% of *Enterococcus faecalis* species were MDROs.

Table 1:

Organisms	Total	MDRO N (%)	Ulcers with MDRO (%)
Gram- Positive COCCI			
<i>Enterococcus avium</i>	1	1 (100%)	0.66%
<i>Enterococcus faecalis</i>	19	9 (47.36%)	6%
<i>Enterococcus faecium</i>	4	1 (25%)	0.66%
<i>Granulicatellaadiacens</i>	2		
<i>Staphylococcus aureus</i>	49	27 (55%)	18%
Group C Streptococci	1		
Group G Streptococci	1		
<i>Streptococcus pyogenes</i>	4		
<i>Streptococcus viridans</i>	2		
Gram-Negative Rods			
<i>Acinetobacter baumannii</i>	13	8 (61.53%)	5.3%
<i>Citrobacterdiversus</i>	9	3 (33.33%)	2%
<i>Citrobacter species</i>	2		
<i>Enterobacteraerogenes</i>	8	3 (37.5%)	2%
<i>Enterobacter cloacae</i>	1		
<i>Enterobacter species</i>	3		
<i>Escherichia coli</i>	50	39 (78%)	26%
<i>Klebsiella pneumoniae</i>	24	10 (41.66%)	6.6%
<i>Morganella morganii</i>	4	2 (50%)	1.3%
<i>Proteus mirabilis</i>	20	14 (70%)	9.3%
<i>Proteus vulgaris</i>	3		
<i>Pseudomonas aeruginosa</i>	46	34 (74%)	22.6%
<i>Pseudomonas fluorescens</i>	1		
<i>Providencia species</i>	2	2 (100%)	1.3%
Others	9 (3.2%)		
Gram-Negative COCCI	1 (0.4%)		
Total	279	153 (54.8 %)	

Table 2: List of Multidrug Resistant Organisms

MDROs	N	Percent
GRAM- POSITIVE COCCI		
<i>Staphylococcus aureus</i> (MRSA)	17	6.1 %
<i>Staphylococcus aureus</i> (MRCONS)	10	3.6 %
MDR <i>Enterococcus avium</i>	1	0.4 %
MDR <i>Enterococcus faecalis</i>	9	3.2 %
MDR <i>Enterococcus faecium</i>	1	0.4 %
GRAM-NEGATIVE RODS		
<i>Enterobacter aerogenes</i> (AMPC)	3	1.1 %
<i>Escherichia coli</i> (ESBL)	33	11.8 %
<i>Escherichia coli</i> (ESBL + AMPC)	6	2.2 %
<i>Klebsiella pneumonia</i> (ESBL)	10	3.6 %

<i>Proteus mirabilis</i> (ESBL)	13	4.7 %
<i>Proteus mirabilis</i> (AMPC)	1	0.4 %
MDR <i>Acinetobacter baumannii</i>	8	2.8 %
MDR <i>Citrobacter diversus</i>	3	1.07 %
MDR <i>Morganella morganii</i>	2	0.7 %
MDR <i>Pseudomonas aeruginosa</i>	34	12.18 %
MDR <i>Providencia species</i>	2	0.7 %
Total	153	54.9 %

Discussion

There are reports of nearly 20% of hospital admissions being infected diabetic foot ulcers [3] and with the growing problem of MDRO [4]. This study presents a microbiological profile of infected diabetic foot ulcers, in relation to MDRO.

In our study the foot ulcers were more prevalent in the fifth and sixth decade of life. They were commoner in males. Most of our patients with ulcer, had diabetes of less than 5 years duration, in contrast with other studies conducted in the country [5,6]. A majority (68%) had ulcers of less than 1 month duration which is similar to the observations from another study [6]. Ulcers with acute onset often have systemic symptoms which bring the patients to the hospital, while in chronic ulcers the symptoms are mild and localised. Most of the patients in the present study had poor glycaemic control. This was comparable with the literature [5,6]. Majority of the patients in our study had higher grade of ulcers (Wagners grade III or worse) similar to the other studies [5,6].

The bacteriological evaluation showed that the gram negative organisms were found have a higher occurrence than gram positive organisms, as seen in some of the other Indian studies [3,5,6]. However, most of the western literature showed a predominance of gram positive organisms as opposed to gram negative organisms [7-10]. This could be partly due to differences in the causative organisms occurring over time, geographical variations, or the types and severity of infection included in the studies [11].

Diabetic foot infections are usually polymicrobial in nature [3,5,6,11,12,13]. In our study, 58.66 % of ulcers had polymicrobial culture. Polymicrobial infection, to a certain extent, may be due to prior treatment [14,15,16].

In our study, the rate of isolation of organism per ulcer was 1.86 while the other two Indian studies showed a rate of 2.3 and 1.25 organisms per ulcer [5,6]. The commonest organism isolated in our study was *Escherichia coli* followed by *Staphylococcus aureus*, *Pseudomonas* and *Klebsiella pneumoniae*. This is similar to the observations from a south Indian study [12]. But most of the other studies from India [5,6] and other countries [9,11,17] showed *Staphylococcus aureus* as the commonest isolate from diabetic foot ulcers. There was a high recovery of *Pseudomonas* (16.5 %), like in 2 other studies [3,9].

Sixty six percent (66%) of our patients grew MDRO and 54.8% of isolated organisms were multi drug resistant. In view of there being no uniform definition for MDRO until recently, the overall prevalence of MDRO, as seen in the literature, could not be studied. MRSA, ESBL, VRE which have been extensively studied in literature, and other MDRO like MDR *Pseudomonas*, *Acinetobacter*, *Enterococcus*, and *Enterobacteriaceae* were identified in our study. The high prevalence of MDRO was also observed in another north Indian study [5]. Western studies have shown lower figures of 22% and 40% in 2 studies respectively [9,18]. The higher degree of antibiotic resistance in tertiary care hospitals is because of abuse of antibiotics in the community. The increasing occurrence of MDROs is disconcerting because the choice of antibiotic treatment is limited.

Our study showed that 75% of all MDROs isolated were gram negative organisms. Gram negative organisms have a unique outer membrane which does not allow certain antibiotics to penetrate. With regard to the gram negative organisms in our study, *E.coli* showed greater antibiotic resistance, followed by *Pseudomonas aeruginosa*. 78% of isolated *E.coli* and 74% of isolated *Pseudomonas* were multi-drug resistant.

In the last two decades, we have seen the emergence of extended spectrum beta lactamase (ESBL) producing gram negative organisms, which have often posed therapeutic challenges. All multi drug resistant *E.coli*, in our study, were ESBL producers and 12% produced both ESBL and Amp C. 65% of *Proteus mirabilis* and 41.66% of isolated *Klebsiella pneumoniae* were ESBL producers. 62 out of the 196 gram negative isolates (31.63%) were ESBL producers, which were isolated from 26.59% of the ulcers in our study. Other Indian studies have shown higher figures [5,6]. However, a paper from Brazil reported that only 6% of isolated *E.coli* were ESBL producers [19]. A french study has showed that 26.9% of *Pseudomonas* and 25% of *Acinetobacter baumannii* were MDROs [9]. In our study 61.5% of *Acinetobacter baumannii* were multidrug resistant.

Fifty five percent (55%) (27 out of 49 isolates) of *Staphylococcus aureus* isolated from our study were methicillin resistant, similar to another Indian study [6]. But studies from other countries in Europe showed a lower percentage ranging from 30 to 40% [7,8,9]. A much lower percentage of 16% was observed in a Malaysian study [17]. MRSA was seen in 18% of the patients in our study.

0.4 % of isolated *Staphylococcus aureus* were methicillin resistant and coagulase negative (MRCONS). We also identified other multi drug resistant gram positive organisms such as MDR *Enterococcus avium*, *Enterococcus faecalis*, and *Enterococcus faecium*. These, in relation to diabetic ulcers have not been looked at in the previous studies.

Thus MDROs appear to be firmly entrenched in our patients, and posing questions to clinicians and microbiologists alike, with regard to patient management and the development of antibiotic policies.

Conclusion

The prevalence of multi-drug resistant organisms is alarmingly high in infected diabetic foot ulcers. *ESBL Escherichia coli* is the commonest multi-drug resistant organism derived from infected diabetic foot ulcer.

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