

## **Prevalence of Multidrug Resistant Organisms in Diabetic Foot Ulcer in a Tertiary Care Hospital**

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Date of Submission: 16-07-2018

Date Of Acceptance: 30-07-2018

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### **I. Introduction**

A serious public health problem which remain the major cause of morbidity and mortality worldwide is found to be Diabetes Mellitus (DM) <sup>1</sup>. The most common complication associated with uncontrolled DM is Foot ulcer, Retinopathy, Neuropathy, Macro Vascular Complications (MVC) <sup>2, 3</sup>. Of all the complications of DM, foot ulcers impose a heavy burden on health service <sup>4</sup>. Peripheral Neuropathy (PN), muscle atrophy and foot deformity remains the reason for developing diabetic foot ulcer in 20% of patients with uncontrolled DM. This ulcer may lead to diabetic foot infection which leads to gangrene formation. Charcot joint fracture is the major risk factor for Amputation <sup>5</sup>.

These infections are poly-microbial in nature, which include Aerobic organisms such as Staphylococcus, Streptococcus, and Enterobacter, Anaerobic bacteria such as Clostridium, Peptostreptococcus and fungus<sup>6, 7</sup>. Infection with multiple drug organisms may increase hospital stay duration and cost of management which cost additional morbidity and mortality <sup>8</sup>. One of the most feared complications of diabetes is diabetic foot <sup>9, 10</sup>. When compared to foot ulcers due to other cases of diabetic foot has 15 to 46 time higher risk of limb amputation<sup>11</sup>. More than one million diabetic patients undergo limb amputation every year<sup>9</sup>. Diabetic foot causes impaired micro vascular circulation which limits the access of phagocytosis leading to the development of infections<sup>12, 10</sup>.

There are various reported studies about the microbes and their antibiotic susceptibility pattern for diabetic foot infection which was published in various developed countries. The aim of this study is to find out, the Prevalence of Multidrug Resistant Organisms in Diabetic Foot and antibacterial sensitivity pattern in diabetic foot infections.

### **II. Materials & Methodology**

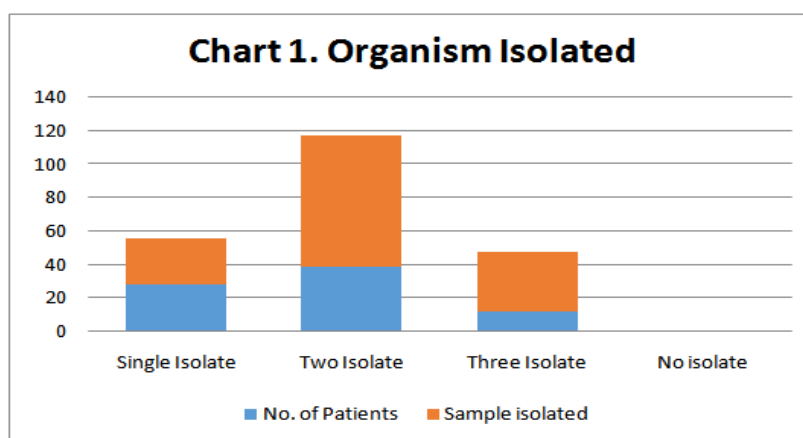
The prospective study was performed over the period of 9 months from September 2016 to may 2017. The study was conducted at Tertiary Care Centre, Chennai, India. The study includes 80 diabetic patients that include 46male and 34 female patients diabetic patients. All diabetic foot infection with Wagner's classification 3 to 5 was included. Pus or discharges from base of the ulcer and debraded necrotic tissue were obtained at the time of admission. The specimen were immediately taken to Microbiology department and processed. Gram staining was done simultaneously, sample were incubated in blood agar and Mac conkey agar for isolation of aerobic bacteria. After 24 hours of incubation at 37<sup>0</sup> C, bacterial isolates were identified based on standard bacteriological methods<sup>13</sup>.

Test was performed by Kirby boyar disk diffusion method according to CLSI<sup>14</sup>. Vancomycin resistant Enterococcus, gram negative bacilli producing ESBL, MDR organisms, Pseudomonas aeruginosa resistant to > 3 anti-Pseudomonas class of Anti-biotic. Acetobacter spp. Resistant to > 3 classes of anti microbial agents are defined as MDR pathogens. The results were tabulated and statistical analysis done<sup>15-17</sup>.

### **III. Result**

The study included 80 diabetic patients that included 46 male patients and 34 female patients. all the patients had Diabetic foot ulcer with Wagner's classification 3 to 5. All the subjects were type 2 DM, mean age of the subjects were 52.9 ±13.3 and mean duration of diabetes were 12.6±4.2 in that 84.5% had diabetic neuropathy and 74% had PVD. In these diabetic patients 46.3% had lesion above 3 months. Ulcer were necrotic in 21.5% of patients and 63% had received surgical treatment.

Totally 142 isolates obtained from the sample averaging 1.8. In 28 patients only one pathogen were isolated and in 51 patients more than one pathogen were isolated, in that 39 were infected with 2 pathogen and 12 were infected with 3 pathogen and one patient had no growth [Chart 1].



The most common organism isolated were Klebsiella pneumoniae 32 isolates 23% , followed by Pseudomonas aeruginosa 24 isolates 17% shown in detail in [Table 1].

S.No.	Bacteria	No. of isolates	Percentage
1	Klebsiella pneumoniae	32	23
2	Pseudomonas aeruginosa	24	17
3	Staphylococcus aureus	24	17
4	Escherichia coli	21	15
5	Coagulase-negative staphylococci	11	8
6	Proteus mirabilis	8	6
7	Enterococcus spp.	7	5
8	Citrobacter spp.	5	4
9	Proteus vulgaris	4	3
10	Acinetobacter spp.	4	3
11	Pseudomonas spp.	2	1
		142	100%

In the above isolate 56% were ESBL and 48% were MRSA. sensitivity pattern of organism were given in detail in [Table 2 and 3]

Table 2. Sensitivity Pattern of Gram Negative Bacteria

	A/C	P/T	TE	CI	TS	GM	AK	NC	CFX	CTR	CAZ	IP
Escherichia coli	62	86	30	28	25	37	70	-	14	14	-	100
Klebsiella pneumoniae	52	70	52	43	13	36	79	-	22	18	-	98
Proteus mirabilis	28	100	100	86	53	82	98	-	38	100	-	98
Proteus vulgaris	16	96	66	64	64	14	34	-	16	82	-	100
Citrobacter spp.	43	100	13	26	13	42	86	-	28	70	-	100
Pseudomonas aeruginosa	-	78	-	54	-	50	63	43	-	-	28	92
Pseudomonas spp.	-	100	-	0	-	0	100	50	-	-	0	50
Acinetobacter spp.	-	84	52	32	66	18	52	-	-	32	34	65

A/C – amoxicillin-clavulanic acid, P/T – piperacillin-tazobactam, TE – tetracycline, CI – ciprofloxacin, TS – trimethoprim-sulfamethoxazole, GM – gentamicin, AK – amikacin, NC – netilmicin, CFX – cefuroxime, CTR – ceftriaxone, CAZ – ceftazidime, IP - imipenem

**Table 3:** Sensitivity Pattern of Gram Positive Bacteria

	P	A/C	E	TS	TE	CI	GM	CTR	OX	VA
<b>Staphylococcus aureus</b>	0	23	68	36	65	30	40	44	65	100
<b>Coagulase-negative staphylococci</b>	24	35	94	24	94	40	53	56	40	100
<b>Enterococcus spp.</b>	66	-	42	-	76	64	65	-	-	88

P – penicillin, A/C – amoxicillin-clavulanic acid, E – erythromycin, TS – trimethoprim-sulfamethoxazole, TE – tetracycline, CI – ciprofloxacin, GM – gentamicin, CTR – ceftriaxone, OX – oxacillin, VA – vancomycin.

#### IV. Discussion

Diabetic patients are more prone for chronic non healing foot ulcers due to several factors such as neuropathy, high plantar pressure and PAD<sup>18</sup>. These long standing ulcers are prone for delayed wound healing with wide range of bacteria causing infections. In this study, Gram Negative Bacteria(GNB) were more predominant pathogens- Klebsiella pneumoniae being the commonest (32 isolates), followed by Pseudomonas aeruginosa (24 isolates) and Staphylococcus aureus (24 isolates), Similar to this study, there were two recent studies showing GNB being the commonest isolates<sup>12,19</sup>. But in earlier studies, statistical analysis shows Gram positive organism were more common<sup>20, 21</sup>. This shows that there is a change in trend of organism causing diabetic foot infections from gram positive to gram negative.

Poly microbial infections were observed in 35.9% of patients which is almost similar to the studies<sup>10, 11, 19</sup>. In case of severe diabetic foot infections 3 to 5 microbes are cultured<sup>22</sup>. Few studies have shown prevalence rate of 80 to 87.2% Poly-microbial infections in diabetic foot<sup>23, 24</sup>. Choosing of appropriate antibiotics plays a major role in treating the diabetic foot infections. In earlier studies enterobacteriaceae were found to be uniformly sensitive to Gentamicin and ciprofloxacin<sup>10</sup>. In this study except Proteus spp. many were resistant to these antibiotics, this correlate to study Gadepalli R et al<sup>12</sup>. However enterobacteriaceae were found to be sensitive to Amikacin, Piperacillin- Tazobactam and Imipenem .This shows combinations of these antibiotics plays important role in appropriate treatment.

Increase resistance to cefuroxime and ceftriaxone were noted in Klebsiella pneumoniae and Escherichia coli. In our study there was 56 % production of ESBL. There were even non ESBL producing organism showing resistance to cefuroxime, cefotaxim, ceftriaxone and ceftazidime, which can be due to Ampc beta lactamases<sup>25</sup>. It was observed that 56% were ESBL producing which were similar to the study<sup>12</sup>. S. aureus isolates were mostly Sustainable to Vancomycin in which 48% were MRSA which correlate with study<sup>12,16,19,27</sup>. In the present study 48% of the isolates were MRD pathogens which correlates with earlier studies reporting 20 to 40% of isolated to be MDR<sup>19</sup>. Most of the patients who attended our hospital were already treated by various other diabetic centre and clinics.

To avoid selective antibiotic pressure that lead to the development of resistance, most of the authorities treat only for clinically infected wounds and use narrow spectrum therapy<sup>28</sup>. Inappropriate use of antibiotics can be the reason for high prevalence of MDR pathogens<sup>29</sup>.

The limitation in our study is failure to detect anaerobic bacteria which also plays a major role in diabetic foot infection.

#### V. Conclusion

Diabetic foot infection was often caused by Gram Negative organism with high prevalence of MDR pathogens. Combination regimen consisting of Amikacin, Piperacillin - Tazobactam, Imipenem and Vancomycin was found to be an effective combination for the treatment of diabetic foot infections.

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Parthasarathy K "Prevalence of Multidrug Resistant Organisms in Diabetic Foot Ulcer in a Tertiary Care Hospital." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, vol. 17, no. 7, 2018, pp 45-48.