Influence of Demographic Factors on the Outcome of Diabetic Foot Infections (DFI)- A Tertiary Care Hospital Based Study

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ABSTRACT

Introduction: Diabetes Mellitus (DM) is the 7th leading cause of death and 1st leading cause of blindness, amputation and kidney failure. DFI is the main cause not only for hospitalization, but also for prolonged hospitalization among diabetics, owing to 82, 000 amputations/year worldwide. The risk factors for complicated and severe DFIs are grade of diabetic foot ulcer, overall glycaemic control, previous hospitalizations, and infection with Multidrug Resistant Organisms (MDRO). Our objective was to elaborate the influence of demographic factors on DFI and study the rates of MDRO and poly microbial infections in relation to outcome of DFI.

Material and methods: In this hospital based, longitudinal, observational study done in NRIIMS, Sangivalasa, Visakhapatnam for 2 months (June- July2015), as a part of 2015 ICMR -STS project, out of 54 DFI patients attended our OPD, 48 patients were enrolled in our study.

Results: There was significant influence of previous hospitalizations ($p<0.01$), size of the ulcer ($p<0.05$), smoking ($p<0.05$) and alcoholic intake ($p<0.05$), male gender ($p<0.001$) on DFI. Isolates/ patient ratio increased from Grade 2 (1.1: 1) to grade 5 (1.6: 1). There is highest ratio of Isolate: patient noticed in DFI Patients who were diagnosed as Diabetic for the first –time i.e. 1.7:1 when compared to others. In our study, 73% prolonged hospitalization, 92% surgical debridements and 91% amputations were due to MDR DFIs.

Conclusion: A well-documented past clinical, treatment history and a systemic uniform method of evaluating patients for diabetic complications by physical examination is required to assess the severity, risk and prognosis of DFIs.

Keywords: multidrug resistance, poly microbial, Wagner's grade, diabetic foot ulcer, diabetes mellitus, longitudinal study,

INTRODUCTION

Diabetes Mellitus (DM) is one of the most critical health state, world wide. This is not only in terms of the incidence of diabetics, disability due to DM and premature mortality due to DM, but also the health care costs winding in governing and treating its complications.[1]

The diabetic population is currently increasing world-wide, especially in developing countries. world wide, from 30 million adults suffering from DM in 1985, the figure amounted to 135 million in 1995, 191 million in 2003, 422 million in 2016. Now this is expected to reach a total of 640 million by 2040. About two-thirds of diabetics live in developing countries where the epidemic is most intense with an increasing proportion in younger age groups.[2] According to WHO's ten facts about diabetes, it is an emerging global epidemic, responsible for 1.5 million deaths in 2012 being the 7th leading cause of death and the most common cause of blindness, amputation and kidney failure.

Amidst all chronic complications associated with DM, the diabetic foot infection (DFI) is the main cause of hospital admission and also prolonged hospitalization among these patients. DFI is often a challenging clinical problem, in some cases the initial presentation of undiagnosed diabetes.[3]

Peripheral neuropathy is a common complication of diabetes mellitus[4], leading to loss of pressure and pain sensations which along with reduced joint mobility, compromised vascular supply (secondary to DM) make patients vulnerable to DFIs.[5] Increased risk of foot ulceration caused by unperceived trivial trauma[6] along with infection increases the probability of DFI leading to Charcot's joint, fracture and amputation.[7] World population data indicate that about 82, 000 people have diabetes related amputations of feet and lower extremities each year.[3] 14-20% of diabetic patients with DFI undergo an amputation, while 85% of amputations are preceded by DFIs.[5]

The Wagner classification system is widely accepted stratification of DFIs, mostly infected with polymicrobial flora consisting aerobic, gram-negative, gram-positive, and anaerobic bacteria.[8] The risk factors for severe and complicated DFIs are past history of DFI, grade of the ulcer, overall glycaemic control, previous hospitalizations, and presence of infection with more virulent microorganisms like Multi-Drug Resistant Organisms (MDRO).[9,10]

Culture specific antimicrobial therapy along with aggressive surgical debridement of the necrotic tissue remains gold standard in the management of DFIs.[11] The major problem in the management and study of DFI is that there is no unifying standard in diagnosing the infection, scoring the DFIs and no global accepted guidelines for DFI therapy. There is a shortage of evidence in development of guidelines for DFI therapy. Though culture supported standard specific targeted therapy is the gold standard, there must be a role for initial Emperical therapy.[13] This involves crucial decisions about severity of diabetic foot infection, route of drug administration, co-morbidities and spectrum of organisms to be covered.[12]

Since the studies from rural India (where most of the people are bare footed and agricultural field workers) on DFIs are scarce, we in this study (from rural Visakhapatnam, Andhra Pradesh, India) tried to study and elaborate the role of various

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demographic factors like Habitat, Habits, Size and Site of DFI and duration of Diabetes on the occurrence of DFIs with MDROS' and polymicrobial infections. We aimed to elaborate the factors predisposing this DFIs with MDROs and studied effect of MDRO and polymicrobial aetiology on the outcome of the DFI patients.

MATERIAL AND METHODS

This was a hospital based, longitudinal, descriptive (observational) study done (as a part of ICMR- STS 2015) in NRI Institute of Medical Sciences (NRIIMS), Sangivalasa village, Visakhapatnam district, A.P, India. Present study was done on 48 DFI Patients attending our Outpatient Department (OPD) for 2 months i.e. June 2015 to July 2015. The Study is conducted after obtaining Institutional ethical committee clearance. Written informed consents (local language-telugu) were obtained from DFI patients, after explaining them about their role in detail in the study.DFI Patients with Wagner's grade 2 to 5 DFIs are included while grade 1 diabetic foot ulcer patients are excluded from this study.

Methodology

Entire clinical information including detailed history and examination findings were collected and entered into Questionnaires and case report forms. Demographic factors of patients; like Gender, Age, Habitat, Occupation, Habit of Alcohol consumption or Smoking, Diabetes Mellitus duration, present DFI duration, Grade of ulcer, Size of ulcer and Site of the ulcer, Previous h/o Hospitalization, h/o Antibiotic Usage, Overall Glycaemic control and any complications of Diabetes with which the patient suffering from; were entered into questionnaire forms. Samples were followed from the time of collection (done by the surgeons prior to the antibiotic administration under strict aseptic techniques)until microbiology culture laboratory.

Specimen collection: Chronic wounds can be colonized on the surface by a varied group of organisms, including aerobic Gram- positive cocci, Enterobacteriaceae, Non-Fermentative GNB and Anaerobic bacteria.

Isolates from superficial swab cultures may not represent the underlying infecting pathogen.[14] Therefore, culture samples in our study are obtained after surgical debridement, which is the best guide for targeted antibiotic therapy.[15]

Microbiological workup: The tissue was placed in 2 ml of sterile physiologic saline and the tissue was then homogenized in a tissue processor and divided into 3 portions.[16]

1st portion was sent for direct smear examination, 2nd portion for plating on Blood agar plates (with 5% sheep blood) and Macconkey medium and 3rd portion for inoculation into Brain Heart Infusion (BHI) biphasic medium. All media were incubated at 37^0c for 18-24 hours and isolates are identified by specific Biochemical Reactions like Catalase, Coagulase, Indole, Methyl Red, Citrate, Urease, Triple Sugar Iron agar, Oxidase etc. AST was performed by standard Kirby- Bauer disc diffusion method and MDROs were identified according to CLSI guidelines.[17]

STATISTICAL ANALYSIS

All the tables were made with the help of Microsoft office 2007. Descriptive statistics and chi square test were used to interpret the data.

RESULTS

Out of 54 DFI Patients admitted in our Rural Hospital in 2 months period, 6 patients were excluded (Wagner's Grade 1 ulcer) and 48 DFI Patients were included in our study. From these 48 DFI Patient samples a total of 68 bacteria were isolated. The demographic and host factors for all DFI patients were collected (Questionnaire form) and studied for significant influence (P value) on MDRO and Poly microbial association of DFIs and showed in Table-1. The different factors included in our study were

- Gender of the Patient.
- Age of the Patient
- Habitat of the Patient.
- Occupation of the patient
- Habits like Alcohol consumption; Smoking
- Duration of Diabetes Mellitus
- Duration of the present DFI
- Grade of the Ulcer
- Size of the Ulcer
- Site of the ulcer
- Previous Hospitalization
- Previous Antibiotic Usage
- Overall Glycaemic control of Diabetics
- Complications of Diabetes in the patient.

For Poly/Mono microbial DFIs there was a significant association with male gender ($p<0.001$) previous Hospitalizations ($p<0.01$) and a less significant association with size of the ulcer ($p<0.05$) and H/O alcohol intake ($p<0.036$). For MDR/Non-MDR DFIs there was a significant association with H/O smoking ($p<0.049$). Of the 48 DFI patients -33 were male, 15 were female. There was 80% and 68% of MDRO among male and female respectively. There was 25% and 80%polymicrobial aetiology among male and female patients. There was 75% MDRO among patients aged more than 75 years, 76% MDRO among patients in 50-75 years' category, 70% MDRO among patients in 25-50 years' age category, 2 MDR isolates among 1 out of 1 patient aged less than 25 years. Among 48 DFI patients, 41 from rural (with 74.5% MDRO) and 7 from urban areas (with 77.7% MDRO). Among them 21 were agricultural labourers with 76% MDRO among 29 isolates.

Though there was a declining trend in the isolate patient ratio from newly diagnosed diabetic patients to diabetic patients of 20-30 years' duration; there was an increasing trend observed in MDRO from 60% in newly diagnosed diabetic patients to 77% in diabetic patients with 10 years' duration and 78% in diabetic patients with 20 years' duration, 1 out of 1 among patient diabetic for 30 years' duration. There was 78% and 70% association of MDROs among the patients with and without H/O multiple antibiotic usage. MDRO association was studied in relation to factors like size, site, duration and grade of the ulcers. There was 81.4% MDR observed in ulcers of more than $5cm^2$ size and 64% MDR in ulcers of size less than 5 cm^2. 88.2% and 70.6%MDRO observed in ulcers of more than 1 month duration and less than 1 month duration respectively. There was an increasing trend observed in MDRO from grade 2- 4 ulcers i.e. 73% in Grade-2, 80% in Grade-3, 87.5% in grade-4. But there was 70.6% of MDRO in grade-5 ulcers.

Different Grades of DFI and Duration of Diabetes in relation to MDR status and bacteriological profile were studied and

Factors		MDR n=51	NMDR n=17	p-value	POLY n =20	MONO n=28	p-value
1. Gender	M	32	8	0.255 (NS)	8	25	p<0.001
	F	19	9		12	3	
2. Age	0-25	2	-	0.773 (NS)	1	-	0.428 (NS)
	26-50	17	7		6	13	
	51-75	29	9		11	15	
	>75	3	1		2	-	
3. Duration of DM	Newly Diagnosed	6	4	0.236 (NS)	4	3	0.513 (NS)
	0-10	37	11		14	19	
	10-20	7	2		2	5	
	20-30	1	-		-	1	
4. Duration of ulcer	<1M	36	15	0.258 (NS)	16	19	0.546 (NS)
	>1M	15	2		4	9	
5. Grade of the ulcer	2	8	3	0.741 (NS)	2	8	0.166 (NS)
	3	12	3		4	6	
	4	7	1		2	4	
	5	24	10		12	10	
6. Habitat	Rural	44	15	0.836 (NS)	18	23	0.73 (NS)
	Urban	7	2		2	5	
7. Occupation	AGR	22	7	0.887 (NS)	8	13	0.658 (NS)
	Non-AGR	29	10		12	15	
8. Habits	smoking +	29	5	0.049	9	16	0.406 (NS)
	alcohol+	23	6	0.479 (NS)	6	17	0.036
9. Previous hospitalisation	Rare	22	8	0.778 (NS)	12	6	p<0.01
	Multiple	29	9		8	22	
10. Multiple antibiotic usage	Yes	32	9	0.474 (NS)	10	21	0.074 (NS)
	No	19	8		10	7	
11. Size of ulcer	<5CM²	16	9	0.11 (NS)	5	15	p<0.05
	>5CM²	35	8		15	13	
12. Glycemic control	G-	13	3	0.219 (NS)	5	6	0.236 (NS)
	M-	25	7		11	10	
	P-	13	7		4	12	
13. Complications of DM	Gastric-12	17	1	0.056 (NS)	6	6	0.499 (NS)
	Retinopathy-24	22	9	0.482 (NS)	7	17	0.079 (NS)
	Nephropathy-29	33	7	0.088 (NS)	10	19	0.212 (NS)
	PVD-22	27	6	0.207 (NS)	10	12	0.624 (NS)
	Neuropathy-38	42	12	0.489 (NS)	16	22	0.81 (NS)
14. Site of the ulcer	Leg-13	19	2	0.096 (NS)	7	6	0.297 (NS)
	Ankle-12	15	3	0.526 (NS)	5	7	0.999 (NS)
	Dorsum-34	38	12	0.999 (NS)	15	19	0.591 (NS)
	Plantar-5	7	1	0.664 (NS)	3	2	0.69 (NS)
	Toes-17	16	9	0.11 (NS)	9	8	0.241 (NS)

Table-1: Association of different factors with/ without mdro and poly/mono microbial dfis.

tabulated (Table-2). Highest numbers of isolates (34 out of 68 i.e.50%) were reported from Grade-5 ulcers. There is increasing trend noticed in Isolate: Patient ratio in relation to Wagner's grade of Diabetic foot ulcer from grade 2 to grade 5 from 1.1: 1 to 1.6: 1.Though Highest numbers of Bacterial isolates (48 out of 68 i.e. 71%) were isolated from patients with < 10yrs of Diabetic History, there is highest ratio of Isolate: patient noticed in DFI Patients who were diagnosed as Diabetic for the first –time i.e. 1.7:1 when compared to others (1.5:1 in <10 years, 1.1:1 in 10-20 years, 1:1 in 20-30 years' duration of DM).

The Different outcomes of DFIs like Prolonged Hospitalization, Surgical amputations and death of the Patient were studied for MDRO and Poly microbial association for significance by P value and showed in Table-3.

DISCUSSION

In our study smoking habit of the Diabetic patient had a significant influence ($p<0.05$) on MDRO association. No significant association was found with Patient characteristics, Ulcer type, Duration of ulcer or hospital stay. Same findings were reported by Gadepalli et al.[19] In his study significance was found with Neuropathy, Osteomyelitis, Size of the ulcer (>4cm²) and frequent surgical interventions.

In our study, male gender, previous hospitalizations, size of the ulcer and H/O alcohol intake had a significant influence on the poly/mono microbial infection of DFIs, where as in the study by Andrew et al[13] (2010) Polymicrobial aetiology and MDROs were significantly associated with Chronic, deep DFIs and with previous multiple antibiotic usage.

Bacterial isolates	Total no	Grade of DFI				Duration of DM			
		2	3	4	5	Newly Diagnosed	0-10	10-20	20-30
1. S. Aureus	8	3 (38%)	1 (13%)	1 (13%)	3 (38%)	1 (13%)	6 (75%)	1 (13%)	-
2. Cons	8	1 (13%)	2 (25%)	1 (13%)	4 (50%)	1 (13%)	6 (75%)	1 (13%)	-
3. Enterococcus	6	-	2 (33%)	2 (33%)	2 (33%)	1 (17%)	3 (50%)	2 (33%)	-
4. Moraxella	1	-	1 (100%)	-	-	-	1 (100%)	-	-
5. E. Coli	14	-	5 (36%)	2 (14%)	7 (50%)	3 (21%)	9 (64%)	1 (7%)	1 (7%)
6. Klebsiella	6	2 (33%)	1 (17%)	-	3 (50%)	1 (17%)	4 (67%)	1 (17%)	-
7. Enterobacter	2	-	-	-	2 (100%)	-	2 (100%)	-	-
8. Proteus	15	1 (7%)	2 (13%)	2 (13%)	10 (67%)	2 (13%)	11 (73%)	2 (13%)	-
9. Pseudomonas	5	3 (60%)	-	-	2 (40%)	1 (20%)	3 (60%)	1 (20%)	-
10. Acinetobacter	3	1 (33%)	1 (33%)	-	1 (33%)	-	3 (100%)	-	-
Total	68	11	15	8	34	10	48	9	1

Table-2: Frequency of isolates within wagner's grades and duration of diabetes

Different outcome	MDR N=51	NON-MDR N=17	p-value	Polymicrobial	Mono microbial	p-value
1. Prolonged Hospitalization (>15days)	16	4	0.759 (NS)	7	8	0.636 (NS)
2. Multiple Surgical Debridements	19	2	0.096 (NS)	8	5	0.089 (NS)
3. Surgical Amputations	13	1	0.162 (NS)	3	8	0.451 (NS)
4. Death of patient	2	-		1	-	

Table-3: Different outcomes of DFI patients in relation with/without MDRO and poly/MONO microbial infection.

Among Grade-2 ulcers S. aureus and Pseudomonas were in equal predominance. In Grade-3 E. Coli was predominant. In Grade-4 Enterococci, E. Coli and Proteus were in equal predominance. In Grade-5 Proteus species were predominant. Highest numbers of isolates (34 out of 68 i.e.50%) were reported from Grade-5 ulcers with increasing trend noticed in Isolate/ Patient ratio in relation to Wagner's grade of Diabetic foot ulcer from grade 2 to grade 5 from 1.1: 1 to 1.6: 1.Though Highest numbers of Bacterial isolates (48 out of 68 i.e. 71%) were from patients with < 10yrs of Diabetic History, there is highest ratio of Isolate: patient noticed in DFI Patients who were diagnosed as Diabetic for the first –time i.e. 1.7:1 when compared to others (1.5:1 in <10 years, 1.1:1 in 10-20 years, 1:1 in 20-30 years' duration of DM.

In our study the presence of MDROs and Polymicrobial infections in DFIs had no influence on the outcome. Similar results were observed in various other studies by J.L. Richard[20]; Game et al.[21] In a study by J.L. Richard[20] (2008) by multivariate analysis, presence of MDRO had no significant influence on Healing time.

In our present study 25% (10 out of 40 MDRO DFIs) association of surgical amputations with MDRO was found while in Mhd. Zubair 18 study, amputations among MDR DFI Patients were 71.4%. Death rate was about 2.5% among MDR DFI Patients in our study (1 death reported among 40 MDR DFI Patients) while in Mhd.Zubair[18] study, it was 15.3% (2 deaths among 14 MDR DFI Patients).

A well-documented past clinical and treatment and medication history of a DM is to be strictly observed, as diabetes is a chronic and life time disease. A systematic and uniform method of evaluation of patients for complications of DM, physical examination is very much required to assess the severity and risk of DFIs. A universally accepted reporting of drug resistance method has to be developed and practiced to prevent unnecessary confusion in the reporting of prevalence rates of MDROs so that comparisons can be made more meaningful from all the geographical areas of the world. The National and International working organisations on DM, have to make HbA1C test or any other test mandatory for all DM patients for a better and easy follow –up of the patient's overall glycaemic control.

CONCLUSION

It is important to study the demographic factors which play a major role in the Risk Stratification of any infected patient. This directly helps in selecting "Right Antibiotic" for Empirical therapy.

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REFERENCES

1. Renato Motta Neto et al. A case report of a multi –drug

resistant bacterial infection in a diabetic patient treated in Northeast Brazil. Diabetic Foot and Ankle. 2012:3;18656.
2. Wild S et al. Global prevalence of diabetes; estimates for the year 2000 and projections for 2030. Diabetes care. 2004;27:1047-1053.
3. Gamba MA. Lower extremity amputations in patients with Diabetes: should be preventable? Acta Paul Enferm. 1998; 11:92-100.
4. Fernando DJ Fernando DJ, Masson EA, Veves A, Boulton AJM. Relationship of limited joint mobility to abnormal foot pressures and diabetic Foot ulceration. Diabetes Care. 1991;14:8–11.
5. Boulton AJM Boulton AJM: The pathogenesis of diabetic foot problems: An Overview. Diabetes Med. 1996;13:S12–S16.
6. Flynn MD, Tooke JE. Aetiology of Diabetic foot ulceration: a role for the microcirculation? Diabetes Med. 1992,9:320-329.
7. Logerfo FW, Coffman JD. Vascular and Microvascular disease of the foot in Diabetes. N Eng. J Med. 1984; 311:1615-1619.
8. Wagner FW. Treatment of the Diabetic foot. Compr Therapy. 1984;10:29-38.
9. Green Green, Melissa F, Aliabad, Zarintaj, Bryan T. Diabetic foot: evaluation and management. South Med J. 2002;95:95–101.
10. Zafar A. Management of Diabetic foot – Two-year experience. J Ayub Med Coll Abbottabad. 2011;13:1416.
11. Boulton AJM; Foot problems in patients with DM Boulton AJM: Foot problems in patients with diabetes mellitus. In Textbook of Diabetes. Vol. 2. Pickup JC, Williams G, Eds. Oxford.U.K. K, Blackwell Science, 1997, p. 58.
12. Nicolau DP, Stein GE. Therapeutic options for Diabetic Foot Infections: a review with an emphasis on tissue penetration characteristics. J Am Podiatric Medical Association. 2010;100:52-63.
13. Andrew S. Powlson and Anthony P. Coll. The treatment of diabetic foot infections" J. Antimicrob. Chemotherapy. 2010;65(suppl 3):iii3-iii9.
14. Senneville E, et al. Culture of percutaneous bone biopsy specimens for diagnosis of diabetic foot osteomyelitis: concordance with ulcer swab cultures. Clin Infect Dis. 2006;42:57–62.
15. Bowler PG, et al. Wound microbiology and associated approaches to wound management. Clin Microbiol Rev. 2001;14:244–269.
16. Henry D. Isenberg Clinical microbiology procedures handbook; ASM press, 2007, 2nd Edition update.
17. CLSI M100 –S 23. Performance standards for antimicrobial Susceptibility testing. 23rd informational supplement; Jan 2013.
18. Mohammad Zubair et al. Clinico- bacteriology and risk factors for the diabetic foot infection with multidrug resistant microorganisms in North India. Biology and Medicine. 2010;2:22-34.
19. Gadepalli R et al. Clinico Microbiological study of Diabetic foot ulcers in an Indian Tertiary Care Hospital. Diabetes care. 2006;29:1727-1732.
20. J-L Richard et al. Risk factors and healing impact of multi-drug resistant bacteria in Diabetic foot ulcers. Diabetes and Metabolism. 2008;34:363-369.
21. Game F et al. Outcome of Diabetic foot ulcers with and without Staphylococcus aureus (MRSA). Diabetic Med. 2003;20:30.

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