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Original Article

Potential risk factors and outcomes of infection with multidrug resistance among diabetic patients having ulcers: 7 years study

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ABSTRACT

Diabetes Mellitus is characterized as a hyperglycemic condition, which results due to alteration in the secretion of insulin or action of insulin. The development and spread of microorganisms is known as a key health concern, and such cases are growing drastically in hospitals and communities. Therefore, the study aims to determine the potential risk factors and infection outcomes among diabetic patients with multi drug resistance, who are suffering from foot ulcerations. A prospective cohort analysis was carried out among 192 diabetic patients admitted in the Rajiv Gandhi Centre for Diabetes and Endocrinology of Jawaharlal Nehru Medical College Hospital, Aligarh Muslim University, India. The patients having ulcer or ulcers in their foot during the period December 2008–June 2015 were included in the study. The results indicated the rate of resistance to CS and PC, which was 56.7% and 51.9%. The most common isolates included *Escherichia coli* (25.5%), *Staphylococcus aureus* (22.6%), and *Klebsiella sp* (5.4%). A total of 121 isolates from 278 were associated with the MDR. Furthermore, anaerobic isolates were also included in the study which included *Peptostreptococcus spp, Propionibacterium spp, Clostridium perfringens, Eggerthella lenta, and Bacteroides ureolyticus*. Ulcer was found among majority of patients with the duration of 1 month; whereas, the ulcer size was also the major risk factor for diabetic patients. Therefore, it is concluded that there is a major need for surveillance of resistant bacteria to reduce the risk of major complications.

What is already known about the topic?

- Diabetic patients are at higher risk of developing neuropathy, retinopathy, and nephropathy.
- Foot ulceration among diabetic patients is leading cause of morbidity and mortality among developing countries.
- Development of foot ulcers may result in significant tissue destruction, leading to subsequent amputation of foot.

What new information this manuscript provides?

- Ulcer size is a major risk factor among diabetic patients.
- Neuropathy was the major complication found among MDR-DM patients.
- Hypertension was the most prevalent complication among NMDR-DM patients.

1. Introduction

Prolonged hyperglycemic condition has negative impact on eyes, kidneys, heart, nerves, and blood vessels. It is believed that the number of individuals, suffering from diabetes, is likely to increase by 300 million in 2025 [1]. Moreover, two-third of diabetic patients belong to developing countries, where the proportion of diabetes is

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increasing within the younger age groups [1]. The diabetic patients are at higher risk of developing certain complications, like neuropathy, retinopathy, and nephropathy.

The development and spread of microorganisms associated with the multi-drug resistance is known as a key health concern among the population of developing countries. These cases have been observed to grow drastically in hospitals and communities. The resistant organisms emerge in the body of individuals taking drugs as a result of expansion of spontaneous generation of subpopulations [2]. Foot ulceration among diabetic patients is considered as a major social and economic problem. It is also a leading cause of morbidity and mortality among developing countries [3]. It has been estimated that 15% of the diabetic patients are likely to suffer from foot ulcerations at some point of their lives [4]. The development of foot ulcers is highly susceptible to rapid spread of infections, which may result in significant tissue destruction, leading to subsequent amputation of foot [5].

The peripheral neuropathy is defined as an important predisposing factor causing foot ulcerations, which lead to the development of infection. Majority of the cases of foot ulceration are confused with bacterial infections; however, there is no resemblance in both conditions [6]). The diabetic foot ulcerations need proper management through appropriate selection of antibiotics. The selection of antibiotics is based on the testing of antimicrobial susceptibility. Appropriate antibacterial therapy is required, when these infections are diagnosed early to avoid any further complications. Therefore, the study aims to determine the potential risk factors and infection outcomes among diabetic patients with multi drug resistance, who are suffering from foot ulcerations.

2. Methods

A prospective cohort analysis has been carried on among 192 diabetic patients admitted in the Rajiv Gandhi Centre for Diabetes and Endocrinology of Jawaharlal Nehru Medical College Hospital, Aligarh Muslim University, India. The patients having ulcer or ulcers in their foot during the period December 2008–June 2015 were included in the study. Foot ulcer was defined as a full-thickness skin defect that required 14 days for healing. The study was carried out in accordance with principles of the Declaration of Helsinki as revised in 2001 and all patients gave informed consent to take part in this research. The patients with inflammatory or infectious diseases, autoimmune and rheumatic diseases, cancer, hematological diseases, severe renal or liver failure, recent venous thromboembolism, and patients under treatment with anti-inflammatory drugs, were excluded from the study.

2.1. Clinical evaluations

A detailed history and physical examination was carried out for every subject. Age, Sex, anthropometric measurements (body mass index), duration of diabetes, glycemic control prior to and during the hospital stay, lipid profile, presence of retinopathy, nephropathy (creatinine >1.5 mg% or presence of micro or macro-albuminuria), neuropathy (absence of perception of the Semmes-Weinstein monofilament at 2 of 10 standard planter sites on either foot) were noted in every patient. Furthermore, peripheral vascular disease (ischemic symptoms and intermittent claudication of rest pain, with or without absence of pedal pulses or posterior tibial pulses), hypertension, duration, site, and size of ulcer, history of smoking, history of previous amputation and clinical outcome were also noted in every patient. Clinical assessment for signs of infection (swelling, exudates, surrounding cellulitis, odor, tissue necrosis, crepitation and pyrexia) was made by one researcher classifying the ulcers and determining the presence of clinical signs of infection.

Ulcer size was determined by multiplying the longest and the widest diameters and expressed in centimeters square. The wound was graded and staged at the time of hospitalization according to the University of Texas Wound classification system as grade 1 (superficial wound, not involving, tendon, capsule or bone), grade 2 (wound penetrating to tendon or capsule) and grade 3 (wound penetrating bone or joint). Grade 0 patients (pre- or post-ulcerative site that has healed and have no infection) were excluded from the study. Diagnosis of extension to the bone was made in majority of patients by probing with a sterile steel probe. In the absence of sinus tract or an exposed bone, a standard radiograph showing signs of osteomyelitis in the bone was considered definitive and later on MRI was done to confirm the osteomyelitis in suspected patients. Amputation was defined as the complete loss in the transverse anatomical plane of any part of the lower limb [3].

2.2. Microbiological methods

Culture specimens were obtained at the time of admission; after the surface of the wound had been washed vigorously by saline and followed by debridement of superficial exudates. Specimens were then obtained by scrapping the base of ulcer or the deep portion of the wound edge with a sterile curette after cleaning the base of ulcer with a sterile swab stick [7]. The soft tissue specimens and pus aspirated from syringe were promptly sent to the Microbiology department and processed for aerobic and anaerobic bacteria. Standard methods for isolation and identification of aerobic [8] and anaerobic bacteria were used [9,10].

2.3. Susceptibility testing

Antimicrobial susceptibility testing of aerobic isolates was performed using the disk diffusion method as described by the CLSI [11]. Antimicrobial disk used were Imepenem (10 μg), Aztreonam (30 μg), Amoxyclav (30 μg), Cefpodoxime (10 μg), Metronidazole (5 μg), Cefepime (30 μg), Cefoperazone (75 μg), Cefoperazone/sulbactum (75/10 μg), Cefixime (5 μg), Piperacillin (100 μg), Piperacillin/tazobactum (100/10 μg), Ceftazidime (30 μg), Ceftazidime/clavulanic acid (30/10 μg), Amikacin (30 μg), Amoxycillin (20 μg), Cephotaxime (30 μg), Ofloxacin (5 μg), Cephotaxime/clavulanic acid (30/10 μg), Ceftriaxone (30 μg), Cefoxitin (30 μg), Oxacillin (1 μg), Chloramphenicol (30 μg), Gentamicin (10 μg), Gatifloxacin (5 μg), Levofloxacin (5 μg), Sparfloxacin (5 μg), Streptomycin (10 μg), Vancomycin (30 μg), Clindamycin (2 μg), Tobramycin (10 μg), Azithromycin (15 μg), Erythromycin (15 μg), and Bacitracin (μg). All discs were obtained from Hi-Media labs, Mumbai, India. Inter-pretative criteria for each antimicrobial tested were those recommended by manufacturer's guideline (Hi-Media labs, Mumbai, India). The obtained data was analyzed using SPSS version 13.0 for descriptive statistics.

2.4. Ethical clearance

This study was approved Bio-Ethical Committee (BEC) of Faculty of Medicine, Aligarh Muslim University, Aligarh registered under Drug Controller General of India (DCGI), Government of India under registration Number: ECR/419/Inst/UP issued under Rule 122DD.

3. Results

Table 1 has shown the baseline characteristics of diabetic foot ulcer patients with respect to multiple drug resistance and non-multiple drug resistance. The data has shown that out of 192, 126 (69%) were males and 58 (31%) were females. The findings have

Table 1
Baseline characteristics of diabetic foot ulcer patients.

N	Total	MDR	NMDR-
	N1 = 192	N2 = 151	N3 = 41
Sex (Female)	67 (34.9%)	52 (34.4%)	15 (36.6%)
Age > 40 years	143 (74.5%)	106 (70.2%)	37 (90.2%)
Type 2 diabetes	159 (82.8%)		
Ulcer duration >1 month	72 (37.5%)	62 (41.1%)	10 (24.4%)
Ulcer size >4 cm^2	156 (81.3%)	132 (87.4%)	24 (58.5%)
Discharge Status	192 (100%)		
Hospital stay (>1month)	47 (24.5%)	36 (23.8%)	11 (26.8%)
HbA1c (>6.9%)	183 (95.3%)	145 (96%)	38 (92.7%)
WBC count (10^3/μl)	143 (74.4%)	104 (68.8%)	39 (95.1%)
Hb (g/dl)	100 (52.1%)	76 (50.3%)	24 (58.5%)
Serum creatinine (>1.5 mg/dl)	52 (27.0%)	47 (31.1%)	5 (12.2%)
SGOT/AST (>34IU/L)	71 (36.9%)	62 (41.0%)	9 (21.9%)
SGPT/AST (>35 IU/L)	101 (52.6%)	86(56.9%)	15 (36.5%)
LDL-C (>100 mg/dl)	97 (50.5%)	72 (47.6%)	25 (60.9%)
Total cholesterol(>150 mg/dl)	116 (60.4%)	101 (66.8%)	15 (36.5%)
HDL-C (<40 mg/dl)	49 (25.5%)	42 (27.8%)	7 (17.0%)
Triglycerides (>200 mg/dl)	57(29.6%)	39(25.8%)	18(43.9%)

WBC, white blood cells, Hb, haemoglobulin; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; SGOT/AST, serum glutamic oxaloacetic transaminase/aspartate transaminase; SGPT/AST, serum glutamate-pyruvate transaminase/aspartate transaminase.

shown that neuropathy was the major complication found among MDR-DM patients (62.85%) whereas hypertension was the most prevalent complication among NMDR-DM patients (28.5%). Moreover, the findings have indicated that all female patients were alive after discharging from hospital. Fig. 1 has presented the Kaplan Meier curve for HbA1c in DFU patients with size of ulcer and grade of ulcer in DFU patients with size of ulcer, respectively.

A total of 278 bacteria (255 aerobic + 21 anaerobic) were isolated, averaging of 1.32 species per patient. 78.6% patients had MDR infection and NMDR etiology was observed in 21.3%. Among the bacterial isolates, aerobic gram positive cocci comprised of 34.5% and aerobic gram negative bacilli for 65.7%. Gram positive to gram negative ratio was 1:1.7. The frequency of bacterial isolates from the DFU is shown in Table 2. *Escherichia coli* was the most common isolate, followed by *Staphylococcus aureus*, *Pseudomonas aeruginosa* 23.7%, *Klebsiella spp.* Anaerobic culture was done in 67 DFU patients in whom the pus sample was aspirated by the sterile syringe. Air from the syringe was removed immediately. Anaerobes alone not observed in in a single case. Among the anaerobic bacteria isolated, *Peptostreptococcus spp* was the most common isolate, *Propionibacterium spp*, *Clostridium perfringens*, *Bacteroides ureolyticus* and *Eggerthella lenta*. The findings have indicated that *E coli* was the most prevalent organism among MDR patients followed by

Table 2
Frequency of distribution of isolates from 192 DFU patients in relation to treatment and Risk factor analysis of MDR to the basic factors of DFU.

	Name of isolates	Total	MDR	NMDR
		n	n	N
AEROBIC = 257(93.7)				
	Gram positive cocci	**88(34.5)**	**24**	**64**
1	*Staphylococcus aureus*	60	16	44
2	*Enterococcus faecalis*	9	3	6
3	*Beta hemolytic streptococcus*	6	2	4
4	*CONS*[a]	5	1	4
5	*Corynebacterium spp*	7	2	5
	Gram negative bacilli	**169(65.7)**	**97**	**72**
6	*Escherichia coli*	70	43	27
7	*Pseudomonas aeruginosa*	40	22	18
8	*Klebsiella sp*	33	20	13
9	*Proteus vulgaris*	13	5	8
10	*Acinetobacter spp*	10	6	4
11	*Morganella morganii*	2	1	1
ANAEROBIC		**21**		**21**
12	*Peptostreptococcus spp*	10	–	**10**
13	*Propionibacterium spp*	5	–	5
14	*Clostridium perfringens*	3	–	3
15	*Eggerthella lenta*	1	–	1
16	*Bacteroides ureolyticus*	2	–	2
	Total aerobic	**255**	**121**	**136**
	Total anaerobic	**21**	**0**	21
	Total	**278**	**121**	**157**

[a] Coagulate negative *Staphylococcus* spp.

Pseudomonas and *Klebsiella*. Table 3 shown risk factor analysis of MDR to the basic factors of DFU. The findings have indicated that MDR patients were significantly associated with type 2 diabetes, ulcer size, discharge status, Hospital stay, HbA1c, WBC count, Hb, and Total cholesterol.

The result of resistance studies are summarized in Table 4. High degree of antibiotic resistance was exhibited by *Pseudomonas aeruginosa (62.0%), Enterococcus faecalis (55%), CONS (52.8%), beta hemolytic sp (45%), Staphylococcus aureus (43%), Escherichia coli* (42.0%), *Proteus sp* (40%), *Klebsiella sp* (28%). Higher percentage of resistance (73.5%) was shown among the Penicillin group (74.5%) followed by Macrolids (69.8%), Monobactams (67.3%), Quinolones & Fluroquinolones (59.5%), Cephalosporin group (58.8%), Lincosamides (53.7%), chloramphenicals (52.4%), Aminoglycosides group (40.2%), beta lactam inhibitors (21.2%) and Carbapenems (16.2%).

4. Discussion

The baseline characteristics of diabetic foot ulcer patients were

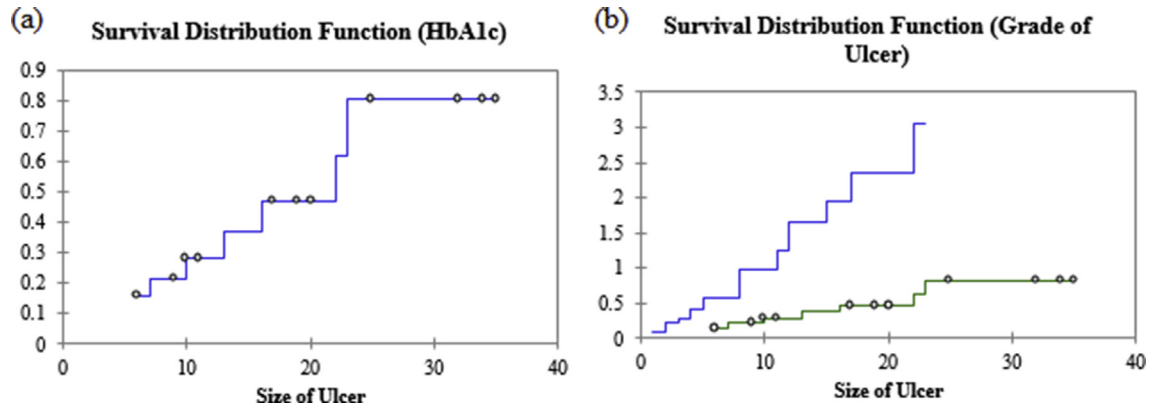

Fig. 1.

Table 3
Risk factor analysis of MDR to the factors of DFU.

N = 192	OR	(95%CI)	p-value
n			–
Sex (Female)	0.50	0.13–1.8	0.69
Age > 40 years	0.49	0.17–1.82	0.75
Type 2 diabetes	0.72	0.19–2.68	0.000
Diabetes duration > 10 yrs	3.94	0.97–16.4	
Ulcer duration >1 month	0.74	0.09–2.03	
Ulcer size >4 cm^2	0.86	0.72–1.05	0.06
Grade of ulcer (Texas)			
Grade 1	0.43	0.16–1.13	0.55
Grade 2	0.62	0.13–2.63	
Grade 3	2.34	0.74–7.39	
Amputation	5.13	1.77–13.3	0.43
Discharge Status			
Alive	3.2	1.2–8.2	0.032
Died			
Hospital stay (>1month)	10.76	7.3–23.8	0.001
HbA1c (>6.9%)	12.6	3.9–33.5	0.004
WBC count (10^3/μl)	5.13	1.77–13.3	0.000
Hb (g/dl)	3.48	1.26–9.67	0.000
Serum creatinine (>1.5 mg/dl)	0.84	0.34–2.34	0.01
SGOT/AST (>34IU/L)	1.32	0.46–3.91	0.56
SGPT/AST (>35 IU/L)	4.37	1.06–14.6	0.001
LDL-C (>100 mg/dl)	0.25	0.09–3.25	0.005
Total cholesterol(>150 mg/dl)	3.2	1.2–8.2	0.002
HDL-C (<40 mg/dl)	0.43	0.16–1.13	0.06
Triglycerides (>200 mg/dl)	0.62	0.13–2.63	0.56

OR: Odds ratio, WBC, white blood cells, Hb, haemoglobulin; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; SGOT/AST, serum glutamic oxaloacetic transaminase/aspartate transaminase; SGPT/AST, serum glutamate-pyruvate transaminase/aspartate transaminase.

calculated in the current study. The study has considered only female patients with age greater than 40 years. The total patients were 192 out of which 151 belonged to MDR and 41 belonged to NMDR. Out of 192 patients, 67 (34.9%) were females, whereas, 143 (74.5%) were more than 40 years old. Type 2 diabetes patients were found to be 159 out of 192 patients. The obtained data was divided into MDR and NMDR corresponding to 151 and 41 patients, respectively. Ulcer was found among 72 patients with the duration of 1 month; whereas, the ulcer size was found out to be greater than 4 cm 2 among 156 (81.3%) patients. Amputation was carried out on 170 patients.

The discharge status showed that all the patients were released after their hospital stay; however, 47 patients stayed in the hospital for more than 1 month. These findings have been supported by past studies. For instance, Zubair, Malik & Ahmad [4] have found HbA1c to be greater than 6.9% in 183 patients out of which 145 belonged to MDR and 38 belonged to NMDR. WBC count was found to be in the range of 10 3/μ among 22 patients and Hb was found out among 100 patients. According to Perim [12], Serum creatinine was found to be greater than 1.5 mg/dl among 38 patients. SGOT/AST and SGPT/AST were found to be greater than 34 IU/L and 35 IU/L, respectively. LDL-C, Cholesterol, and triglycerides were found to be greater than 100 mg/dl, 150 mg/dl and 200 mg/dl; whereas, HDL-C was found to be less than 40 mg/dl. Aerobic was further divided into Gram positive cocci and Gram-negative bacilli. Aerobic were found to be 257 out of which 88 belonged to the gram-positive cocci and 169 were associated with gram negative cocci. The results suggested that out of 88 g-positive cocci 24 were MDR; whereas, 64 were NMDR. Gram positive cocci included *Staphylococcus aureus*, *Enterococcus faecalis*, beta hemolytic *streptococcus*, CONS, and *Coryneform* spp as isolates. Moreover, gram-negative bacilli included *Escherichia coli, Pseudomonas aeruginosa, Klebsiella sp, Proteus vulgaris, Acinetobacter spp*, and *Morganella morganii*. The results showed that out of 169 g-negative bacilli, 97 were associated with the MDR and 72 were NMDR. Furthermore, anaerobic isolates including *Peptostreptococcus spp, Propionibacterium spp, Clostridium perfringens, Eggerthella lenta, and Bacteroides ureolyticus* have also been included in the study.

The total sample of anaerobic was 21, and all of them belonged to NMDR. In a prospective study, bacteria were isolated from 41 patients with diabetic foot lesions. The antibiotic susceptibility pattern was ascertained through Kirby-Bauer disk diffusion technique and broth method. Eighty-nine bacterial isolates were attained from 30 patients (Perim et al., 2015). The infections were polymicrobial bacteremia and gram-positive bacteria. The most commonly gram-negative isolated bacteria were *Citrobacter spp, Pseudomonas spp, Enterobacter spp, Proteus spp* and *Escherichia coli.* The most commonly gram-positive bacteria were *Staphylococcus epidermidis, Staphylococcus saprophyticus, Staphylococcus aureus, Streptococcus pneumoniae and Streptococcus agalactiae*. Nine cases of methicillin-resistant *Staphylococcus aureus* (MRSA) had cefoxitin resistance [6]. Furthermore, amongst MRSA isolates, vancomycin resistance was found in three isolates, with MIC technique.

Another study [4] was conducted to ascertain the antibiotic risk of isolates and to establish the bacterial profile of the infected foot ulcer. *Staphylococcus aureus* was scrutinized to check for any methicillin resistance. 11 patients had T1DM and the rest had T2DM. 86.6% had bacterial infection, out of which 48.5% were suffering from monomicrobial infections and 40% patients had mixed bacterial infection. Additionally, 45.3% gram-negative isolates contained extended spectrum beta-lactamases. The risk

Table 4
Antimicrobial resistance pattern of bacteria isolated from Diabetic Foot ulcers in Diabetic patients.

N	Ps	Ec	Pr	Mm	Ksp	Ac	Sa	Bhs	CONS	Cr	En	Average resistance per antibiotic group
	40	70	13	2	33	10	60	6	5	7	9	
Penicillins	£	83.1	77.7	100	79.4	91.6	54.1	66.6	91.6	49.9	50.9	**74.5**
Cephalosporins	75.6	60.2	69.7	43.7	69.1	60.9	62.5	54.1	54.1	75.0	22.2	**58.8**
Monobactams	77.5	39.4	66.6	100	57.7	62.5	£	£	£	£	£	**67.3**
Carbapenems	55	42.3	0.0	0.0	0.0	0.0	£	£	£	£	£	**16.2**
Aminoglycosides	55.0	42.3	0.0	0.0	0.0	0.0	55.8	50.0	83.3	66.6	88.9	**40.2**
Chloramphenicols	62.5	38	45.8	100	12.8	50	11.7	83.3	83.3	0	88.9	**52.4**
Quinolones & fluoroquinolones	75.8	65.7	77.7	66.6	60.5	41.6	60.8	66.7	58.3	28.6	52.7	**59.5**
β lactam inhibitors	36.8	11.9	21.1	0.0	0.0	65.6	42	0.0	33.3	0.0	22.2	**21.2**
Macrolides	£	£	£	£	£	£	67.5	58.3	100	28.6	94.4	**69.8**
Lincosamides	£	£	£	£	£	£	45.0	50.0	10	85.7	77.8	**53.7**
Glycopeptide	£	£	£	£	£	£	0	0	0	0	0	**0.0**
Average resistance per organism	**62.6**	**42.8**	**40.1**	**44.3**	**28.6**	**40.1**	**43.2**	**45.3**	**52.8**	**35.6**	**55.9**	

Data give in %, £ Not tested; ¤ All Staphylococcus resistant to oxacillin have been considered resistant to all β-lactum; Ps: *Pseudomonas aeruginosa*, Ec: *Escherichia coli*, Pr: *Proteus sp*, Mm: *Morganella morganii*, Ksp: *Klebsiella sp*, Ac: *Acinetobacter sp*, Sa: *Staphylococcus aureus*, Bhs: Beta hemolytic *streptococcus*, CONS: Coagulase negative *staphylococcus* sp, Cr: *Coryneform* sp, En: *Enterococcus faecalis.*

factors that were linked to multidrug resistance were the ulcer size, which was more than 4cm2 in almost 78% patients. Moreover, other factors like the duration of the infection was taken into account, that lasted more than a month in 43.3% of participants and 66.3% patients had poor glycemic control [4].

A microbiological study was conducted to discover the antibiotic vulnerability outlines of organisms, isolated from the foot ulcers and to determine their microbiological profile. Staphylococcal isolates were verified for vulnerability to oxacillin. They were tested by mec A-based PCR, disc diffusion, and screen agar methods. The production of extended spectrum beta-lactamase was checked in the gram-negative bacilli too. 72% patients were confirmed positive for multidrug resistant organisms. Methicillin resistance and ESBL production were 56 and 44.7% of bacterial isolates, respectively. MDRO-infected patients would frequently have to undergo surgery and had poor glycemic control. Additionally, MDRO-infected diabetic patients had accompanying osteomyelitis and neuropathy. It was concluded that foot ulcer infections with multidrug resistant organisms is linked with poor glycemic control and an increased possibility of undergoing surgery frequently [7].

A study has focused on infection-control evaluations, epidemiologic research, and microbiological findings of seven cases of vancomycin-resistant *Staphylococcus aureus* infection in United States. The VRSA isolates went through pulse-field gel electrophoresis, antimicrobial susceptibility testing, typing of resistance genes, and confirmatory identification. Moreover, all participants were suffering from chronic skin ulcers and had undergone vancomycin therapy before the infection. They also had a history of enterococcal infection and methicillin-resistant *S. aureus*. Transmission of the VRSA infection was prevented by its quick discovery. Subsequently, following the guidelines and precautions mentioned in the infection control measures for MDROs also helped to prevent the spread of VRSA infection [13]. A cohort study was performed on 754 diabetic patients with gram-negative bacteremia, which was complicated by severe septic shock or sepsis. It was conducted to ascertain whether patients with exposure to antibiotics in the previous 90 days were resistant to them. The most common isolates that were obtained from blood cultures were *Escherichia coli*, that was 30.8%, followed by *Klebsiella pneumoniae* which was found to be 23.2%. The last isolate that was obtained from blood cultures was *Pseudomonas aeruginosa*, which was 17.6%. Out of the 754 patients, 310 had recently been medicated by antibiotics. The common antibiotics that patients had recent exposure to were, cefepime (50%), ciprofloxacin (32.6%) and imipenem (28.7%). Higher rates of resistance were found in patients with previous exposure to antibiotics. For instance, the rate of resistance to cefepime was 29% versus 7%, piperacillin was 32% versus 11%.

Additionally, ciprofloxacin resistance was 39% as compared to 17% patients, who did not have prior exposure to this antibiotic. Subsequently, it was concluded that patients with recent exposure to antibiotics had much greater resistance to it, versus patients without prior exposure (45.4% versus 21.2%). Furthermore, Hospital mortality rates were higher in patients with prior exposure (51.3% versus 34%). Doctors need to be very cautious when framing antimicrobial management care for gram-negative bacterial infection patients with sepsis [14]. ESBLS or Extended Spectrum Beta-Lactamases are b-extended spectrum beta-lactamases bacteria that are gram-negative, and they produce an enzyme called beta-lactamase that breaks down antibiotics and make them ineffective and useless for treatment.

5. Conclusion

The study has aimed to examine potential risk factors and outcomes of infection with multidrug resistance among diabetic patients having ulcers. The findings have shown a better understanding towards the risk factors and outcoems of infection associated with multidrug resistance among diabetic patients. The study has concluded that out of 169 g-negative bacilli, 97 were associated with the MDR and 72 were NMDR. Furthermore, anaerobic isolates were also included in the study which included *Peptostreptococcus spp, Propionibacterium spp, Clostridium perfringens, Eggerthella lenta, and Bacteroides ureolyticus*. Ulcer was found among majority of patients with the duration of 1 month; whereas, the ulcer size was also the major risk factor for diabetic patients.

Conflicts of interest statement

The authors of this research declare no Conflict of Interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2018.10.014.

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