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Original Article

A study to identify bacteriological profile and other risk factors among diabetic and non-diabetic foot ulcer patients in a Guyanese hospital setting

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ABSTRACT

Diabetic foot infection is a global epidemic and a major public health concern. Development of microbial resistance to many antimicrobial agents in foot ulcer leads to serious complications. Therefore, the study aims to identify the microbiological profile and the potential risk factors among diabetic and non-diabetic foot ulcer patients.

A prospective cross sectional study was carried out among 183 ulcer patients from diabetic foot clinic and wound dressing clinic at the public health hospital, Guyana.

A total of 254 bacteria were isolated from the study with an average of 1.4 organism per lesion. Gram negative bacteria (63.0%) were prevalent than gram positive bacteria (37.0%) in this study. Among DF patients, *Pseudomonas aeruginosa* (18.8%) was the most common isolate followed by *Escherichia coli* (13.9%) among gram negative group. Were as MRSA (12.1%) followed by MSSA (7.9%) dominated among gram positive group in diabetic foot patients. Almost 42.1% (95% CI 34.8–49.6) of the infections were caused by poly-microbial. Interestingly, a stepwise logistic regression model determined increasing age and lack of health education as independent risk factor identified for acquiring an MDR wound infection ($OR = 1.1$; $p \geq 0.05$; 95% CI 1.0–1.1). Mild, moderate and severe infection among MDR and NMDR patients were recorded as 45.3% (95% CI 32.8–58.3), 26.5% (95% CI 16.3–39.1), 28.1% (95% CI 17.6–40.8) and 51.3% (95% CI 41.9–60.5), 32.8% (95% CI 24.4–42.0), 16.0% (95% CI 9.9–23.8). Therefore, it is concluded that there's an urgent need for surveillance of resistant bacteria in diabetic foot infections to reduce the risk of major complications.

1. Introduction

Diabetic foot infection has become one of the most important public health concern and is a growing problem [1]. One of the main explanation for its increase is due to rapid socioeconomic changes and unhealthy lifestyles [2,3]. Global incidence of diabetes has almost quadrupled in the last 30 years, with 422 million adults diagnosed with the disease worldwide now, increasing the global prevalence from 4.7% to 8.5% [4]. And within the diabetic population, annually, foot ulcers develop in 9.1 million to 26.1 million people worldwide, which is one-in-four patient's having the risk during lifetime [5,6].

Studies estimate that at least 20% increase in diabetes patients occur in low and middle income countries between 2010 and 2030 [7]. And almost 15% of the diabetic patients are likely to suffer from foot ulcerations at some point during their lives [8]. Among all other complications of diabetes patients, foot ulceration is considered as a major social and economic problem. Moreover, it is also known as a leading cause of morbidity and mortality among developing countries [9]. Diabetic foot ulcers (DFU) is responsible for more than 20% of diabetes-related hospital admissions and it also causes complications in lower limbs or life threatening diabetic foot infections (DFI) among admitted patients. One of the major reason of amputation among diabetic patients is usually triggered by the development of a chronic wound, clinically defined as a wound that fails to heal within 30 days [10]. Chronic wound leads to significant tissue destruction and are highly susceptible to rapid spread of infections leading to subsequent amputation of foot [11]. Diabetes will increase the incidence of foot ulceration admission by 11-fold, accounting over 80% of all amputations and increasing

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hospital costs of more than 10-fold over the 5 years. The majority of these costs are related to the treatment of infected foot ulcers [12].

Due to improper foot-care, the development and spread of microorganisms associated with the multi-drug resistance (MDR) is known as a key health concern among the diabetic patients of developing countries. Antimicrobial resistance (AMR) is associated with both national antibiotic consumption rate and prior antimicrobial agents (AMAs) usage status of individual patients. It is well known fact that diabetics have high exposure to AMAs due to frequent infections, which can enrich the development of AMR [13]. Countries and hospitals with poor adherence to national antibiotic policy are particularly vulnerable to the problems associated with AMR especially in DFI patients. Guyana has no national policy on rational antibiotic prescribing and also faces limited antibiotic resources with higher rates of infectious diseases [14]. World Health Organization (WHO) states that in Guyana antibiotics can be purchased without prescription leading to overuse/misuse of antimicrobials in the country [15].

Similar to the Infectious Disease Society of America (IDSA) guidelines, Lipsky et al. suggests that empirical antibiotic choice needs to be guided by the history, clinical examination, severity of infection, as well as etiological agent and previous antimicrobial sensitivity pattern for the diagnosis and treatment of DFI [14,16]. It is not unusual that in most clinical settings, DFIs are treated wrongly due to lack of dedicated and specialized diabetic foot care units. It is a fact that lack of dedication and specialized diabetic foot care units could lead to wrong DFI treatment. This would include treatment of DFI without culture and anti-microbial sensitivities done or antibiotics prescribed for wrong duration [17]. Diabetes mellitus and diabetic foot complication is one of the major public health challenges for the Caribbean in the twenty-first century [18,19]. Diabetic foot has also led to cause heavy economic burden on health care resources in the Caribbean. Diabetic foot complications were once the most common admitting diagnosis at the surgery department of public hospital in Guyana with 42% lower extremity amputations [20,21].

Moreover, the microbial etiology of these infections are usually complex. Many of these infections are either mono-microbial or poly-microbial in nature. Poly-microbial leads to rapid spreading of DFIs and along with MDR organisms are increasing dramatically [22–24]. Hence this is the first attempt to identify the microbiological profile of bacterial pathogens and associated risk factors among diabetic and non-diabetic foot ulcers.

2. Methodology

2.1. Study subjects

The study was conducted from November 2016 to February 2017 at the only tertiary facility in Georgetown, Guyana. The study was a cross-sectional and multicenter analytical based study. All foot ulcer patients attending both diabetic foot outpatient clinic and the wound dressing clinic during the study period were selected for the study. Two community health centers under the tertiary hospital were also included in the study.

2.2. Study location

Guyana is an English-speaking developing country on the Northern coast of South America. Guyana shares its borders with Suriname, Venezuela and North Atlantic Ocean. The country is situated near the equator and has a tropical climate. World's largest tropical rainforest, Amazon rainforest stretches in southern Guyana with immense biodiversity. Guyana is culturally and economically tied to the Caribbean nations and is classified as a Caribbean country by the International Diabetes Federation (IDF) [25]. Guyana is also the third poorest country in South America when compared to the surrounding Caribbean and South American countries and as such suffer frequent migration of expertise and thus face scarcity of health care expertise [26,27].

2.3. Sampling technique

A non-probability technique of purposive sampling method was used in the study. All subjects attending the health care facilities fulfilling the inclusion criteria were included in this study.

2.3.1. Inclusion criteria

Patients with known foot ulcer, presence of bacteria, older than 18 years, new patients, willing to participate and were available during the sample/data collection period.

2.3.2. Exclusion criteria

Patients with gestational diabetes mellitus, patients younger than 18 years, inpatients, physical and mental illness, revisit patients, missed questions.

DF or DFU- A diabetic foot ulcer is an open wound or sore on the skin of diabetes patients that is slow to heal.

NDF or NDU- A non-diabetic foot ulcer is an open wound or sore on the skin of non-diabetes patients.

2.4. Ethical consideration

This study was approved by the Institutional Review Board of Ministry of Public Health, Guyana and University of Guyana. Participants were informed about the study and their right to withdraw from the study at any stage of the study. A written informed consent was obtained from all patients before participation in the study. All patient information were kept confidential.

Patients information included information on age, sex, marital status, educational level, ethnicity, employment status, income, body mass index (BMI), smoking status, type of diabetes, diabetes duration, type of diabetes treatment (oral anti-diabetes agents, herbal or insulin usage), HbA1c, diabetic retinopathy, diabetic nephropathy, hypertension, dyslipidemia, CAD, PAD, history of DFU or amputation etc. The study used criteria from the Infectious Diseases Society of America and the International Working Group on the diabetic foot to classify diabetic wounds as uninfected or infected, with mild, moderate, and severe grades of infection [28].

2.5. Microbiological methods

Culture specimens were obtained at the time of admission; after the surface of the wound had been washed vigorously by saline during admission and followed by debridement of superficial exudates. Specimens were either obtained by scrapping the base of ulcer or the deep portion of the wound edge with sterile curette or ulcer with a sterile swab stick. Either soft tissue specimens or pus aspiration syringe were promptly sent to the Microbiology department and processed for aerobic bacteria. Identification of aerobic bacteria was employed by using standard methods.

2.6. Susceptibility testing

Antimicrobial susceptibility testing of aerobic isolates was performed by standard disc diffusion method as recommended by CLSI guidelines. A microorganism was classified MDR if it was found resistant to two or more classes of antimicrobial agents.

2.6.1. ESBL confirmatory test

While performing antibiotic testing, Cephalosporin disc (Ceftazidime (30 μg) and Cefotaxime (30 μg)) and Cephalosporin with clavunate disc (Ceftazidime/Clavulanic acid (30/10 μg) discs were placed on Muller Hinton Agar (MHA) plate on which 0.5 McFarland of test organism was swabbed. If there was a zone size of ≥5 mm diameter with Ceftazidime/Clavulanate disc or of Ceftazidime disc alone, was considered as ESBL.

2.6.2. MRSA confirmatory test

Staphylococcus species isolated in this study was tested for methicillin resistance by using Cefoxitin (30 μg) disc.

2.7. Statistical analysis

Data were entered in MS Excel and statistical analysis was performed using SPSS version 21.0. Data were expressed as percentages for categorical variables and as mean ± SD for quantitative variables. A value of $p \leq 0.05$ was taken as statistically significant.

3. Results

A total of 200 patients from various clinics were enrolled in the study at the initial stage. Only 183 patients information were collected due to the inclusion and exclusion criteria with a response rate of 91.5%. Of the total participants 59.6% (95% CI 52.1–66.7) were DF and 40.4% (95% CI 33.3–47.9) were NDF patients. The study recorded 35.0% (95% CI 28.1–42.4) MDR and 65.0% (95% CI 57.6–71.9) NMDR strains.

Table 1 compares the demographic and background characteristics of patients with respect to MDR and NMDR. Female's recorded higher percentage of MDR (51.6%) compared to males. MDR patients were older (mean age, 60.0 ± 17.0 years) than NMDRs patients (mean age, 53.6 ± 14.5 years). The duration of diabetes was higher in NMDR patients (53.6%) than MDR patients (40.0%). Out of 183 patients, East Indian ethnic group dominated both in MDR (54.7%) and NMDR (49.6%) groups. The findings showed that except for "family history, no health education and CAD", MDR patients showed higher prevalence with other risk factors. The mean (±SD) of BMI was 28.3 ± 3.8, and the mean HbA1c was 7.7 ± 2.0% among MDR patients.

Fig. 1 shows the severity status of ulcer among MDR and NMDR patients. Mild, moderate and severe infection among MDR and NMDR patients were recorded as 45.3% (95% CI 32.8–58.3), 26.5% (95% CI 16.3–39.1), 28.1% (95% CI 17.6–40.8) and 51.3% (95% CI 41.9–60.5), 32.8% (95% CI 24.4–42.0), 16.0% (95% CI 9.9–23.8).

A total of 254 bacteria were isolated from the study with an average of 1.4 organism per lesion. Gram negative bacteria (63.0%) were predominated than gram positive bacteria (37.0%). Among DF patients, *Pseudomonas aeruginosa* (18.8%) was the most common isolate followed by *Escherichia coli* (13.9%) among gram negatives. Were as MRSA (12.1%) followed by MSSA (7.9%) dominated among gram positive group as shown in Table 2. On the other hand, NDF patients also showed *Pseudomonas* sp (18.0%) as dominating pathogen. *Staphylococcus aureus* (47.2%) was the most prevalent MDRO, followed by *E. coli* (14.6%) and *Pseudomonas* sp (10.1%). Almost 42.1% (95% CI 34.8–49.6) of the infections were caused by poly-microbials.

In this study, Ciprofloxacin, Chloramphenicol and Erythromycin showed higher percentage of resistance among Gram positive bacteria were as Piperacillin, Septrin and Ciprofloxacin were the most effective antimicrobial agents for the Gram negative organisms. The resistant pattern of gram positive and gram negative bacteria are summarized in Tables 3 and 4. Fig. 2 presented the Kaplan Meier curve for onset of foot ulcer among DF and NDF patients.

Table 1
Socio demographic status and associated risk factors among participants.

	MDR n = 64	NMDR n = 119
Gender		
Female	33 (51.6)	57 (47.9)
Male	31 (48.4)	62 (52.1)
Ethnicity		
East Indian	35 (54.7)	59 (49.6)
Afro-Guyanese	25 (39.1)	56 (47.1)
Amerindians	2 (3.1)	4 (3.4)
Mixed	2 (3.1)	0
Education		
Primary	23 (35.9)	48 (40.3)
Secondary	23 (35.9)	53 (44.5)
Tertiary	9 (14.1)	10 (8.4)
Illiterate	9 (14.1)	8 (6.7)
Marital status		
Married	24 (37.5)	61 (51.3)
Window	6 (9.4)	4 (3.4)
Single	11 (17.2)	22 (18.5)
Separated	4 (6.3)	6 (5.0)
Divorced	19 (29.7)	26 (21.8)
Occupation		
Employed	24 (37.5)	40 (33.6)
Unemployed	40 (62.5)	79 (66.4)
Income (GYD)		
<50, 000	39 (60.9)	67 (56.3)
50, 000–100,000	25 (39.1)	50 (42.0)
>100, 000	0	2 (1.7)
Diabetes Types		
T2DM	32 (80.0)	48 (69.6)
T1DM	7 (17.5)	15 (21.7)
Age during diabetes		
> 45	16 (40.0)	29 (42.0)
Treatment type		
OHA	28 (70.0)	44 (63.8)
Herbal	1 (2.5)	8 (11.6)
OHA & Insulin	3 (7.5)	8 (11.6)
Insulin	2 (5.0)	8 (11.6)
Diet	6 (15.0)	1 (1.4)
Run out of medicines		
Few times	21 (52.5)	21 (30.4)
Most times	3 (7.5)	10 (14.5)
Never	16 (40.0)	36 (52.2)
Every time	0	2 (2.9)
Diabetic foot		
DF	40 (62.5)	69 (58.0)
NDF	24 (37.5)	50 (42.0)
Diabetes duration		
≤ 10 years	24 (60.0)	32 (46.4)
> 10 years	16 (40.0)	37 (53.6)
Previous ulcer		
Present	48 (75.0)	75 (63.0)
Absent	16 (25.0)	44 (37.0)
Amputation		
Present	23 (35.9)	40 (33.6)
Absent	41 (64.1)	79 (66.4)
Smoking habit	26 (40.6)	37 (31.1)
Alcohol intake	35 (54.7)	63 (52.9)
No Exercise	38 (59.4)	66 (55.5)
Family History	39 (60.9)	79 (66.4)
No Health Education	19 (29.7)	53 (44.5)
Hypertension	27 (42.2)	44 (37.0)
Dyslipidemia	27 (42.2)	39 (32.8)
CAD	15 (23.4)	34 (28.6)
PAD	30 (46.9)	46 (38.7)
Nephropathy	19 (29.7)	27 (22.7)
Retinopathy	5 (7.8)	9 (7.6)
Recurrent Ulcer	18 (28.1)	16 (13.4)
Foot deformity	7 (10.9)	10 (8.4)
HbA1c	7.7 ± 2.0	7.6 ± 1.6
BMI	28.3 ± 3.8	28.7 ± 4.3
Age	60.0 ± 17.0	53.6 ± 14.5

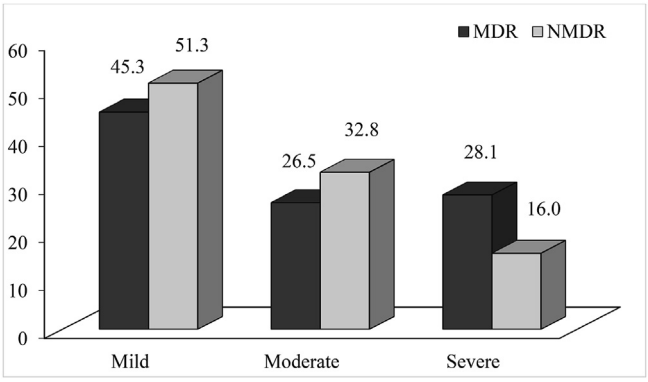

Fig. 1. Severity of ulcer among MDR and NMDR foot ulcer.

Table 2
Prevalence of bacteria isolated among DF and NDF patients.

Organism	DF	NDF	Total
Gram negative bacteria			
Acinetobacter sp.	10 (6.1)	6 (6.7)	16 (6.3)
Citrobacter sp.	2 (1.2)	1 (1.1)	3 (1.2)
Enterobacter sp.	5 (3.0)	6 (6.7)	11 (4.3)
E. coli	23 (13.9)	3 (3.4)	26 (10.2)
P. aeruginosa	31 (18.8)	16 (18.0)	47 (18.5)
K. pneumoniae	11 (6.7)	5 (5.6)	16 (6.3)
M. morganni	4 (2.4)	1 (1.1)	5 (2.0)
Proteus sp.	22 (13.3)	5 (5.6)	27 (10.6)
Providencia sp.	10 (6.1)	1 (1.1)	11 (4.3)
Others	1 (0.6)	1 (1.1)	2 (0.8)
Gram positive bacteria			
Enterococcus sp.	6 (3.6)	3 (3.4)	9 (3.5)
MRSA	20 (12.1)	22 (24.7)	42 (16.5)
Streptococcus sp.	7 (4.2)	2 (2.2)	9 (3.5)
MSSA	13 (7.9)	17 (19.1)	30 (11.8)

Table 3
Antibiotic resistance pattern of gram positive organism from wound infection.

Antimicrobial agents	Gram positive organisms (% resistant)			
	MSSA	MRSA	*Streptococcus* sp.	*Enterococcus* sp.
Piperacillin	0	0	100	33.3
Septrin	3.6	12.8	100	100
Erythromycin	48.1	90.5	28.6	100
Clindamycin	10.3	12.2	28.6	0
Chloramphenicol	75.0	0	60.0	40.0
Ciprofloxacin	100	100	100	50.0
Linezolid	50.0	0.0	20.0	33.3
Amikacin	0	0	0	0
Ampicillin	0	0	100	100
Cefazolin	0	33.3	100	100
Vancomycin	0	0	25.0	100
Imipenem	0	0	0	0

A stepwise logistic regression model was used to determine the most significant independent risk factors of DFUs. And interestingly, increasing age and lack of health education were the only independent risk factor identified for acquiring an MDR wound infection (OR = 1.1; $p \geq 0.05$; 95% CI 1.0–1.1).

4. Discussion

This study highlights a broad clinical and microbiological study of diabetic foot and non-diabetic foot ulcers among patients at the public hospital, Guyana. It also highlights some risk factors identified among the patients.

The study had majority of male participants older than female participants [29–31]. DFU being a chronic complication of diabetes could be a reason why elders present mostly with symptoms. Reveles et al. also identified the diabetic foot infection significantly higher among males than in females [32]. Patients in the age group of 51–60 years were significantly infected with diabetic foot infections. This is in contrast to a previous study done in Guyana which found women with higher prevalence with Type 2 Diabetes (T2D) although men had higher amputation rate [20].

It is not surprising that diabetic foot infections are polymicrobial in nature but this study reported high prevalence of mono-microbials. Similar reports were seen by Wu et al. [33]. Gram-negative organisms were recurrently encountered pathogens in this study, even though *S. aureus,* a Gram-positive, was the most common individual isolate. Reports of *S. aureus* being the most common pathogen has been reported in many studies including many Western countries [29,32–35]. Among Gram negative bacteria, *P. aeruginosa* was the most dominant one which is evident in other studies [30,31,37]. In our study, anaerobic culture was not performed due to limitations in handling anaerobic samples. Hence, results were analyzed for aerobic flora only. Although most literature have shown priority to aerobes and the fact that anaerobes constitutes minority (<15%) of DFU infections [37]. Emergence of microbial resistance against commonly used antimicrobials has been outlined in various reports as being largely associated with the indiscriminate use of AMAs. Recently, increased prevalence of MRSA and ESBL producing bacteria, is upsetting infection in both community and hospitals. MRSA and ESBL were reported in this study with 23.0% and 5.5%. Prevalence of both are rapidly increasing in community and hospitals settings [32,34,36].

AMR in aerobic bacteria is a global concern. However, resistance patterns in aerobes have been often overlooked. Emergence of microbial resistance against commonly used antimicrobials has been outlined in various study reports as being largely associated with the indiscriminate use of AMAs [32]. Most of the Gram positive cocci were found to be highly sensitive to Amikacin, Imipenem, and Piperacillin. Imipenem, Gentamycin, Tobramycin. Amikacin were the most effective antimicrobial agents for the Gram negative bacterial species.

No study has been done to analyze the cost of DFU in Guyana, even though it is a fact that developing countries bear the most burden. Healthcare expenditure on diabetic foot ulcer patients are five times higher when compared to patients without foot ulcers [38]. In Trinidad and Tobago, a Caribbean nation, government spends US $85 million/year, or 0.4% of their gross domestic product, exclusively to treat patients hospitalized for diabetic foot infections [19]. A study in neighboring Brazil also estimated a total annual economic burden of Int$ 361 million in 2014 [39]. Healthcare professionals face limitation in resources in developing or low-income countries and as such could not follow guidelines in treating DFIs. But in reality it is important to follow strict guidelines involving multidisciplinary foot teams to improve outcomes of DFI. In addition to that it is also very important to implement a national rational prescribing strategy in Guyana and improve surveillance of antimicrobial resistance.

5. Conclusion

Diabetic foot infections are one of the major causes of social and economic problem. *S. aureus* and *P. aeruginosa* were found to be the most predominant bacterial pathogens from diabetic foot infections in this study. Knowledge on the antibiotic susceptibility pattern of these isolates is very crucial in planning DFI management and also to create a national antimicrobial treatment guideline. This would not only limit the emergence of AMR but also reduce the burden of health care cost.

Table 4
Antibiotic resistance pattern of gram negative organism from wound infection.

	Gram negative organism (% resistant)								
Antimicrobial agents	*Acinetobacter* sp.	*Citrobacter* sp.	*Enterobacter* sp.	*E. coli*	*Pseudomonas* sp.	*Morganella* sp.	*Proteus* sp.	*Providencia* sp.	*Klebsiella* sp.
Piperacillin	33.3	100.0	66.7	92.9	38.7	66.7	50.0	75.0	87.5
Amikacin	50.0	0	0	0	4.8	0	0	0	9.1
Ampicillin	0	66.7	66.7	76.0	0	80.0	44.4	54.5	81.3
Cefazolin	0	100	66.7	94.7	75.0	100	65.0	77.8	81.8
Cefotaxime	100	0	100	57.1	0	50.0	55.6	33.3	100
Ceftazidime	40.0	33.3	50.0	43.5	14.9	33.3	41.2	55.6	92.3
Ceftriaxone	100	50.0	0	46.2	0	0	55.6	75.0	75.0
Cefuroxime	0	50.0	0	66.7	100	100	100	0	100
Ciprofloxacin	50.0	66.7	25.0	81.8	45.0	50.0	50.0	70.0	70.0
Ertapenem	100	0	0	30.0	0	0	29.4	50.0	9.1
Erythromycin	0	0	100	0	0	0	0	0	100
Gentamycin	15.4	100	14.3	8.3	21.1	0	10.0	0	33.3
Imipenem	0	0	0	23.1	0	0	9.1	25.0	0
Tobramycin	14.3	0	33.3	13.6	19.6	0	7.4	45.5	7.7

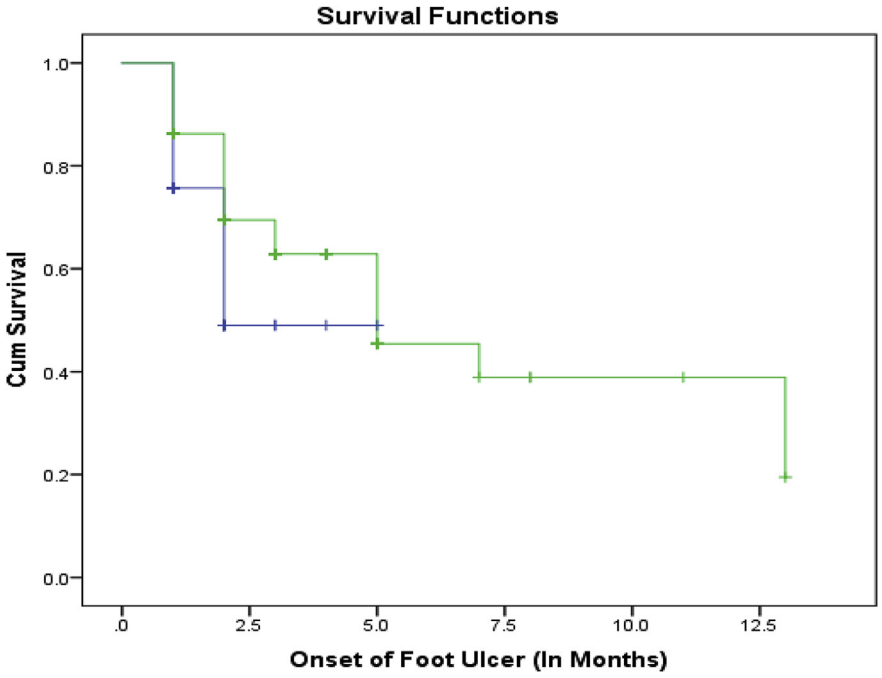

Fig. 2. Survival function for foot ulcer.

Conflicts of interest

None.

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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.2019.04.024.

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