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Distribution and prevalence of microorganisms causing diabetic foot infection in Hospital Serdang and Hospital Ampang for the year 2010 to 2014

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ABSTRACT

Background: In developing countries like Malaysia, the prevalence of diabetes mellitus is increasing at an alarming rate. Various complications develop in patients diagnosed with diabetes. Diabetic foot is one such complication that is a threat to morbidity and mortality rate owing to its risk of amputation. Understanding the microbiology of diabetic foot infection becomes an essential part of management as it can help to channel the exact treatment rather than empirical treatment.

Aim: To determine the distribution and prevalence of microorganism causing diabetic foot infection in Hospital Serdang and Hospital Ampang for the year 2010 till 2014.

Methodology: This was a cross-sectional study using retrospective data from January 2010 to December 2014 of 885 patients with diabetic foot infection in Hospital Serdang and Hospital Ampang, tertiary hospitals in Klang Valley. Data were analyzed using IBM SPSS Statistics version 22.0 for Windows.

Results: A total of 1356 pathogens were isolated from 885 patients, with a rate of 1.53 isolates per culture (IPC). The prevalence of gram-negative bacteria was predominant in DFI accounting for 71.27% whereas gram-positive was only 28.73%. Among the gram-negative isolates, the most common pathogen was *Pseudomonas aeroginosa* accounting for 24.49% followed by *Proteus mirabilis* (14.34%) and Klebsiella spp. (11.12%). Gram-positive isolates consist of *Staphylococcus aureus* with a percentage of 66.77% and Streptococcus spp. 33.23%. The Methicillin-Resistant *Staphylococcus aureus* (MRSA) accounts for 26.24% of the isolates. There were more monomicrobial cultures than polymicrobial culture (465 vs. 420). The most common antibiotic prescribed is ampicillin/sulbactam (55.57%) followed by cloxacillin (13.29%) and penicillin (10.77%)

Conclusion: The prevalence of gram-negative bacteria in DFI is higher than gram-positive bacteria. The most common gram-negative bacteria is *Pseudomonas aeroginosa* followed by *Proteus mirabilis* and Klebsiella spp. whereas the most common gram-positive bacteria is *Staphylococcus aureus*. The rate of monomicrobial infection is slightly higher than polymicrobial infection. Ampicillin/sulbactam is the most commonly prescribed antibiotic for a patient with DFI.

1. Introduction

Diabetic foot infection is a dreadful complication of the poorly controlled disease. DFI remains a significant clinical problem which contributes to almost 30% of orthopedic hospital admission and 10% of total patient admission in most developing countries. This complication often causes burdening to the already malnourished, overstrained body immunity with end-organ damage. This paper has outlined the common etiological organisms and prophylactic antibiotic used in 2 tertiary hospitals.

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Table 1
Distribution of patients by age.

	Age	Number of patients (n)	Percentage (%)
Hospital Serdang			
	20–29	8	1.3
	30–39	25	4.1
	40–49	113	18.5
	50–59	216	35.4
	60–69	168	27.5
	70–79	69	11.3
	80–89	12	2.0
Hospital Ampang			
	20–29	7	2.6
	30–39	19	6.9
	40–49	40	14.6
	50–59	101	36.9
	60–69	74	27.0
	70–79	30	10.9
	80–89	2	0.7
	90–99	1	0.4
Overall			
	20–29	15	1.70
	30–39	44	4.97
	40–49	153	17.29
	50–59	317	35.82
	60–69	242	27.34
	70–79	99	11.19
	80–89	14	1.58
	90–99	1	0.11

2. Method and materials

This was a cross-sectional study using retrospective data from January 2010 to December 2014 of 885 patients with diabetic foot infection in Hospital Serdang and Hospital Ampang, tertiary hospitals in Klang Valley. Hospital admissions with diabetic foot infection as primary diagnosis were included. Exclusion criteria included admission for other causes of foot infection including dermatology and dry gangrene of the foot. All the data was accessed from both Hospital – Hospital Information Sheet Live (e-HIS Live). Proforma was used to collect all the required data. All data were analyzed using the Social Package for social Science Version 21.0 (SPSS). For descriptive analysis, frequency and percentage were used to describe the categorical data. Various ethical committee approval was obtained including National Medical Research Registry of the Ministry of Health Malaysia.

3. Result

3.1. Distribution of patients by age

Table 1 shows the distribution of patient with diabetic foot infection by age. In Hospital Serdang and Hospital Ampang, the age group which was most commonly affected by diabetic foot infection is 50–59 with a percentage of 35.4% and 36.9% respectively. Overall the highest occurrence of diabetic foot infection was in those aged 50–59 (35.82%) followed by 60–69 (27.34%) and 40–49 (17.29%).

3.2. Distribution of patients by gender

Table 2 shows the distribution of patient with diabetic foot infection by gender. In Hospital Serdang there was more female diabetic foot infection patient (50.90%) whereas in Hospital Ampang there were more male patients (57.3%). Cumulatively, it was found that the number of male and female patients were almost equal.

3.3. Distribution of patient by race

Table 3 shows the distribution of patient with diabetic foot infection by race. In Hospital Serdang and Hospital Ampang, Malays account for the highest percentage of admission. (61% and 70.1% respectively).

Table 2
Distribution of patients by gender.

	Gender	Number of patients (n)	Percentage (%)
Hospital Serdang			
	Male	300	49.10
	Female	311	50.90
Hospital Ampang			
	Male	157	57.3
	Female	117	42.7
Overall			
	Male	457	51.64
	Female	428	48.36

Table 3
Distribution of patient by race.

	Race	Number of patients (n)	Percentage (%)
Hospital Serdang			
	Malay	383	62.7
	Chinese	80	13.1
	Indian	142	23.2
	Others	6	1.0
Hospital Ampang			
	Malay	192	70.1
	Chinese	42	15.3
	Indian	39	14.2
	Others	1	0.4
Overall			
	Malay	575	64.97
	Chinese	122	13.79
	Indian	181	20.45
	Others	7	0.79

Table 4
Distribution of isolated microorganism based on gram stain.

	Gram stain	Number of isolates (n)	Percentage (%)
Hospital Serdang	Positive	211	30.62
	Negative	478	69.38
Hospital Ampang	Positive	122	25.96
	Negative	348	74.04
Overall	Positive	333	28.73
	Negative	826	71.27

3.4. Distribution of isolated microorganisms based on gram stain

Table 4 shows the distribution of isolated microorganism based on gram stain. In Hospital Serdang and Hospital Ampang the gram-negative bacteria was most common, 69.38% and 74.04% respectively. Hence, the overall percentage was also highest in gram-negative bacteria (71.27%).

3.4.1. Distribution of gram-positive bacteria

Table 5 shows the distribution of gram-positive bacteria. In Hospital Serdang, Staphylococcus aureus and Streptococcus spp, 41.63% and 34.45% respectively. In Hospital Ampang Staphylococcus predominates with a percentage of 62.30% whereby Streptococcus spp was only 31.14%. Overall, Staphylococcus aureus was most common (49.25%) followed by Streptococcus spp (33.23%) and MRSA (17.52%).

3.4.2. Distribution of gram-negative bacteria

Table 6 shows the distribution of gram-negative bacteria. In Hospital Serdang the most prevalent gram-negative bacteria was Pseudomonas Aeroginosa (28.80%) followed by Proteus Mirabilis (18.17%)

Table 5
Distribution of Gram-Positive Bacteria.

	Microbe	Number of isolates (n)	Percentage (%)
Hospital Serdang			
	Staphylococcus aureus	87	41.63
	MRSA	50	23.92
	Streptococcus spp	72	34.45
Hospital Ampang			
	Staphylococcus aureus	76	62.30
	MRSA	8	6.56
	Streptococcus spp	38	31.14
Overall			
	Staphylococcus aureus	163	49.25
	MRSA	58	17.52
	Streptococcus spp	110	33.23

Table 6
Distribution of gram-negative bacteria.

	Microbe	Number of isolates (n)	Percentage (%)
Hospital Serdang			
	Acinetobacter spp	46	6.79
	Citrobacter spp	22	3.25
	Enterobacter spp	38	5.62
	Enterococcus spp	34	5.02
	Escherichia coli	69	10.19
	Klebsiella spp	67	9.90
	Klebsiella spp (ESBL)	10	1.48
	Morganella Morgani	37	5.47
	Proteus Mirabilis	123	18.17
	Proteus spp	16	2.36
	Providencia spp	8	1.18
	Pseudomonas Aeroginosa	195	28.80
	Serratia spp	12	1.77
Hospital Ampang			
	Acinetobacter spp	21	6.03
	Citrobacter spp	14	4.02
	Enterobacter spp	42	12.07
	Enterococcus spp	24	6.90
	Escherichia coli	26	7.47
	Klebsiella spp	47	13.51
	Klebsiella spp (ESBL)	6	1.72
	Morganella Morgani	28	8.05
	Proteus Mirabilis	24	6.90
	Proteus spp	32	9.20
	Providencia spp	6	1.72
	Pseudomonas Aeroginosa	56	16.09
	Serratia spp	22	6.32
Overall			
	Acinetobacter spp	67	6.54
	Citrobacter spp	36	3.51
	Enterobacter spp	80	7.80
	Enterococcus spp	58	5.66
	Escherechia coli	95	9.27
	Klebsiella spp	114	11.12
	Klebsiella spp (ESBL)	16	1.56
	Morganella Morgani	65	6.34
	Proteus Mirabilis	147	14.34
	Proteus spp	48	4.68
	Providencia spp	14	1.37
	Pseudomonas Aeroginosa	251	24.49
	Serratia spp	34	3.32

Table 7
Distribution of nature of the infection.

	Nature	Number of patients (n)	Percentage (%)
Hospital Serdang	Monomicrobial	362	59.25
	Polymicrobial	249	40.75
Hospital Ampang	Monomicrobial	103	37.60
	Polymicrobial	171	62.40
Overall	Monomicrobial	465	52.54
	Polymicrobial	420	47.46

and Escherichia coli (10.19%). In Hospital Ampang the most prevalent was Pseudomonas Aeroginosa (16.09%) followed by Klebsiella spp (13.51%) and Enterobacter spp (12.07%). Overall the most common gram-negative bacteria was Pseudomonas Aeroginosa (24.49%) followed by Proteus Mirabilis (14.34%) and Klebsiella spp (11.12%).

3.5. Distribution of nature of the infection

Table 7 shows the distribution of the nature of infection. In Hospital Serdang the occurrence of monomicrobial infection was more common (59.25%) while in Hospital Ampang the occurrence of polymicrobial infection was more common (62.40%). Overall the occurrence of monomicrobial and polymicrobial was 52.54% and 47.46% respectively.

3.6. Antibiotic regimen

Table 8 shows the antibiotic prescribed to patients with a diabetic foot infection. In Hospital Serdang, the most common antibiotic prescribed was ampicillin/sulbactam (58.40%) followed by cloxacillin (15.45%) and penicillin (12.74%). In Hospital Ampang the most common antibiotic prescribed was ampicillin/sulbactam (50%) followed by ceftazidime (16.22%) and cloxacillin (9.04%). Overall the most common antibiotic prescribed was ampicillin/sulbactam (55.57%) followed by cloxacillin (13.29%) and penicillin (10.77%).

Table 8
Antibiotic prescribed to patients with a diabetic foot infection.

	Antibiotic	Number of patients (n)	Percentage (%)
Hospital Serdang			
	Ampicillin/ sulbactam	431	58.40
	Cloxacilin	114	15.45
	Cefuroxime	69	9.35
	Gentamicin	1	0.14
	Ciprofloxacin	6	0.81
	Metronidazole	21	2.85
	Ceftazidine	2	0.27
	Penicillin	94	12.74
Hospital Ampang			
	Ampicillin/ sulbactam	188	50.00
	Cloxacillin	34	9.04
	Cefuroxime	18	4.79
	Gentamicin	8	2.13
	Ciprofloxacin	8	2.13
	Metronidazole	33	8.78
	Ceftazidine	61	16.22
	Penicillin	26	6.92
Overall	Ampicillin/sulbatam	619	55.57
	Cloxacillin	148	13.29
	Cefuroxime	87	7.81
	Gentamicin	9	0.81
	Ciprofloxacin	14	1.26
	Metronidazole	54	4.85
	Ceftazidine	63	5.66
	Penicillin	120	10.77

Table 9
Association between gender and age.

Gender	Diabetic foot infection				x^2 value	P value
	Young		Old		0.152	0.753
	N	%	n	%		
Male	107	23.4	350	73.6		
Female	105	24.5	323	75.5		

Table 10
Association between gender and site of infection.

Gender	Diabetic foot infection						x^2value	P value
	Right		Left		Bilateral			0.123
	N	%	n	%	n	%		
Male	219	47.9	218	47.7	20	4.4	4.193	
Female	233	54.4	175	40.9	20	4.7		

3.7. Association between gender of patients with diabetic foot infection and age

Diabetic foot infection was highest in those who are of female gender and old (75.5%) and the lowest is in a young male (23.4%). The P-value is more than 0.05, thus fail to reject the null hypothesis. Therefore there is no significant association between gender and age group of diabetic patient with a foot infection. Table 9

3.8. Association between gender and site of infection

According to Table 10, diabetic foot infection was highest in the right leg of females (54.1%). The P-value is more than 0.05, thus fail to reject the null hypothesis. Therefore there is no significant association between gender and site of infection in a diabetic patient with a foot infection.

4. Discussion

Diabetic foot infection (DFI) remain a common problem across all ages and ethnic groups in Malaysia. DFI management encompasses many aspects including the recognization of the pathogenesis, risk factors, microbiological profile, treatment, and prevention nature of this often-devastating infection. Most studies focused on the more immediate course of DFI such as the treatment (antibiotic susceptibility testing) which leave the main culprit of the infection, the microbes to be less defined. The identification of the microbiological profile of DFI which is the main purpose of this study can be described in terms of the type of bacteria according to culture and sensitivity test and also the nature of infection. Identifying these factors will help in selecting the correct antibiotics which in turn play a role in curbing the increasing antibiotic resistance (Devaraj, 2017).

In our study, a total of 1356 pathogen were isolated from 885 patients, with a rate of 1.53 isolates per culture (IPC). This concurs with results of recent literature; with an IPC of 1.16 (Turhan et al., 2013) and 1.24 (Hayat et al., 2011), indicating that DFI usually involves more than one microbe due to underlying immunosuppression caused by diabetes mellitus alone.

The prevalence of gram-negative bacteria in this study is far more predominant in DFI, affecting 71.3% of DFIs whereas gram-positive bacteria only found in 28.7% of DFIs. This result is supported by previous studies in Malaysia, India and Turkey that recorded similar observations where gram-negative bacteria predominate in DFI (Gadepalli et al., 2006; Raja, 2007). In contrast to that, studies from the western countries showed more DFIs caused by gram-positive bacteria (Lipsky, 2007; Dang et al., 2003; Lipsky et al., 1997). The difference in the nature of microbes infecting the DFIs could result from the difference in environmental factors such as sanitary habits, e.g. use of water for perianal wash (ablution) after defecation that can often lead to contamination of hands with fecal flora that is rich in gram-negative bacteria. This opinion is supported by an article by Ramakant et al. (2011).

The most common gram-negative pathogen isolates were *P. aeruginosa,* accounting for 24.5% followed by *P. mirabilis* (14.3%) and Klebsiella spp. (11.1%). The apparent predominance of *P. aeruginosa* is not surprising as it tallies with many previous studies by Abdulrazak et al. (2005) that reported a 17.5% of *P. aeruginosa* among all isolates while studies in India (Ramakant et al., 2011) and Pakistan (Hayat et al., 2011) also reported high rates of 27.05% and 20.1%, respectively. This observation may be attributed in part to the opportunistic nature of *P. aeruginosa* infesting chronic and non-healing ulcers as proposed by Turhan et al. (2013).

Gram-positive isolates mainly consist of *S. aureus* at 66.7% (including methicillin-resistant isolates) and Streptococcus spp. at 33.2%. The Methicillin Resistant *S.aureus* (MRSA) microbe alone accounts for 26.2% of the isolates. *S. aureus* has long been recognized as the predominant pathogen in DFIs. In this study, it comes second after *P. aeruginosa*. This is similar to a study on causative bacterial agents in diabetic foot infection by Turhan et al. (2013). The high prevalence of MRSA infecting DFIs is also supported by previous literature since the 1990's as reported by Şerefhanoğlu et al. (2006). In this article, MRSA accounts for 12–40% of all Staphylococcus species isolated from DFI.

As mentioned earlier, the nature of DFI can be either monomicrobial or polymicrobial. Several studies have repeatedly shown the high prevalence rate (80% – 87.2%) of polymicrobial infection in DFI (Wright, 2001; Loan et al., 2005). It was also found that the more severe the diabetic foot infection, the more likely it yields polymicrobial isolates (Frykberg, 2003). In our study, however, the rate of monomicrobial infections (52.5%) was slightly higher than the rate of polymicrobial infection (47.5%). The 5% difference in the prevalence may be caused by the availability of an earlier access to care that was sought by patients and targeted antibiotic therapy that prevented the growth of opportunistic pathogens. This concurs with a local study conducted in University Malaya (Raja, 2007).

A recent review reported an increase in antibiotic resistance among diabetic patients with foot infections and recommended the avoidance of unnecessary use of a wide empirical antibiotic (Lima et al., 2011; Devaraj, 2017). In our study, the most common antibiotic prescribed was ampicillin/sulbactam combination (Unasyn©) (55.5%) followed by cloxacillin (13.3%) and penicillin (10.8%). All three of these antibiotics belong to the group of beta-lactamase inhibitors, which are very potent and broad spectrum in nature.

Ampicillin/sulbactam combination is usually reserved as a second-line therapy in cases where bacteria have become resistant to other antibiotics, including cloxacillin and penicillin, which cover a narrower spectrum of microbes. However, in this study, it was found that ampicillin/sulbactam combination is prescribed mainly as first-line antimicrobial therapy irrespective of the causative pathogen. This may be due to the delay in obtaining culture results and concern about the worsening of the DFIs if treatment with antibiotics were delayed. The use of Unasyn© aims to maximize the eradication of the pathogen and also to prevent the development of resistance, much in contrast to what is recommended by Lima et al. (2011).

5. Conclusion

In conclusion, the prevalence of gram-negative bacteria in DFI was higher than gram-positive bacteria. The most common gram-negative bacteria is *P. aeruginosa* followed by *P. mirabilis* and Klebsiella spp. whereas the most common gram-positive bacteria is *S. aureus*. The rate of monomicrobial infection was slightly higher than polymicrobial infection. Ampicillin/sulbactam combination is the most commonly prescribed antibiotic for a patient with DFI.

The strength of this study was that it examined all DFI patients over

a period of five years in two major hospitals in Klang Valley, Malaysia with findings largely agree with many studies in the literature. Limitations include the inability to generalize the study to whole Malaysia as it was mainly concentrated to the states of Selangor and Kuala Lumpur. Future studies should include more hospital and health clinics nationwide to determine the exact nature of DFIs plaquing the vulnerable diabetic population in Malaysia.

Conflicts of interest

The authors declare no competing interests.

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