J u r n a l   B e r k a l a
EPIDEMIOLOGI
PERIODIC EPIDEMIOLOGY JOURNAL

ORIGINAL RESEARCH

PROFILE OF DIABETIC FOOT ULCER PATIENTS AT TERTIARY CARE HOSPITAL IN SURABAYA, INDONESIA

Profil Pasien Ulkus Kaki Diabetik di Rumah Sakit Tersier di Surabaya, Indonesia

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ARTICLE INFO

ABSTRACT

Background: Diabetic Foot Ulcer (DFU) has been associated with a high mortality rate of Diabetes Mellitus (DM) patients. Both behavioral and biological factors cause predisposition to DFU. **Purpose:** This research describes the profile of hospitalized DFU patients at a tertiary care hospital in Surabaya. **Methods:** A retrospective descriptive study that analyzed medical records of hospitalized T2DM patients with DFU in Dr. Soetomo General Hospital. Sampled respondents were patients ≥ 21 years old who were hospitalized between 2016–2018. Demographic data, clinical characteristics, medical histories, length of hospital stay, laboratory results, precipitating factors, microorganism culture results, treatment, and outcome were analyzed. Descriptive analysis is presented in the form of narratives, tables, and diagrams. **Results:** 9.08% of hospitalized Type 2 DM (T2DM) cases were related to foot ulcers. The average patient age was 57.00 ± 9.83 years with no gender predominance. DM was poorly controlled (Mean HbA1C $9.78\pm2.83\%$; RBG 251.83 ± 158.15 mg/dL). The majority of patients had sepsis (68.26%) and renal function impairment (62.72%). Ulcers with Wagner grades of 4–5 were frequent (41.31%). The highest percentage of sepsis (80.49%) and the average leukocyte level $(22.60\pm11.95 \ x10^9/L)$ were found in gangrenous feet. Anemia was more predominant and severe in ulcers with higher Wagner grades. Trauma and *Escherichia coli* were the most common precipitating factors and microorganisms isolated, respectively. Amputation was performed for 82.36% of patients who were admitted to hospital with gangrene. The Lower Extremity Amputation (LEA) and mortality rates were 14.11% and 40.93%, respectively. **Conclusion:** DFUs were found to have a relatively high prevalence among T2DM patients, and

must never be neglected due to the high associated mortality rate.

ABSTRAK

*Latar Belakang: Diabetic Foot Ulcer (DFU) dikaitkan dengan tingkat kematian pasien Diabetes Melitus (DM) yang tinggi. Faktor perilaku dan biologis merupakan predisposisi terjadinya DFU. **Tujuan:** Penelitian ini untuk mendeskripsikan profil pasien DFU yang dirawat di Rumah Sakit Perawatan Tersier di Surabaya. **Metode:** Sebuah studi deskriptif retrospektif menggunakan rekam medis pasien DMT2 yang dirawat di rumah sakit dengan DFU di RSUD Dr. Soetomo. Sampel merupakan pasien berusia ≥ 21 tahun yang dirawat antara tahun 2016-2018. Data demografis, karakteristik klinis, riwayat medis, durasi dirawat di rumah sakit, hasil laboratorium, faktor pencetus ulkus, hasil kultur mikroorganisme, pengobatan, dan outcome dianalisis. Analisis deskriptif disajikan dalam narasi, tabel, dan diagram. **Hasil:** 9.08% kasus DMT2 yang dirawat di rumah sakit dari tahun 2016-2018 terkait dengan ulkus kaki. Usia rata-rata adalah 57.00 ± 9,83 tahun tanpa dominasi gender. Pasien memiliki pengendalian DM yang buruk (Mean HbA1C 9,78 ± 2,83%; RBG 251,83 ± 158,15 mg/dL). Mayoritas pasien mengalami sepsis (68,26%) dan gangguan fungsi ginjal (62,72%) Ulkus berderajat wagner 4-5 mendominasi pasien. Persentase sepsis tertinggi (80,49%) dan rata-rata kadar leukosit (22,60 ± 11,95 x 10^9/ L) didapatkan pada pasien kaki gangren. Anemia lebih dominan dan berat pada ulkus dengan derajat wagner lebih tinggi. Trauma dan Escherichia coli adalah faktor pencetus ulkus dan mikroorganisme terisolasi paling umum. 82,36% dari amputasi dilakukan pada pasien yang datang ke rumah sakit dengan gangren. Tingkat amputasi ekstremitas bawah dan kematian masing-masing adalah 14,11% dan 40,93%. **Kesimpulan:** DFU memiliki prevalensi yang relatif tinggi di antara pasien DMT2 dan tidak dapat diabaikan karena tingkat kematian mereka yang tinggi.*

INTRODUCTION

Diabetes Mellitus (DM) is a non-communicable disease that has been a burden on many countries, including Indonesia. Indonesia was ranked sixth worldwide in 2017 in terms of DM prevalence, with a total of 10.3 million DM patients aged 20–79 years old; this number is expected to rise to 16.70 million in 2045 (International Diabetes Federation, 2019). Six per cent of deaths at all ages in Indonesia (approximately 100,000) were caused by DM (World Health Organization, 2016). This high mortality rate is associated with DM complications, including Diabetic Foot Ulcer (DFU) (International Diabetes Federation, 2019).

DFUs are multifactorial complications initiated by DM-related complications, specifically Peripheral Vascular Disease (PVD) and neuropathy. Predisposing factors of DFU include both intrinsic factors (e.g., foot deformity) and extrinsic factors (e.g., trauma and bad footcare behavior). Infection is a secondary phenomenon of DFU preceding sepsis, which represents the end-stage of DFU and often leads to amputation or death (Boulton, 2019; Forsyth, 2016). DM patients have a 15–25% risk of developing foot ulcers (Yazdanpanah et al., 2018). Lower Extremity Amputation (LEA) occurs every 30 seconds worldwide (International Diabetes Federation, 2019). Additionally, the mortality rate of DFU patients was found to be approximately 40%

(Jupiter, Thorud, Buckley, & Shibuya, 2016). This research describes the profile of hospitalized DFU patients at a tertiary care hospital in Surabaya, with specific focus on the characteristics and outcomes of the patients. The results demonstrate how devastating DFU is.

METHODS

This research was a retrospective descriptive study employing the medical records of hospitalized Type 2 DM (T2DM) patients with DFU in Dr. Soetomo General Hospital, Surabaya, Indonesia. A total of 397 samples were included. The samples were patients ≥ 21 years old between 2016–2018. A total sampling technique was employed in this research using available medical records. A diagnosis of T2DM patients with ulcers was defined by ICD–10 code E11.5. Finally, DFU was confirmed by the doctors' handwritten diagnosis in the medical record. Ethical clearance was obtained from the Medical Ethics Committee of Dr. Soetomo General Hospital (1379/KEPK/VIII/2019).

The data collected were as follows: demographic data (age, gender, occupation); anamnesis (duration of DM, history of insulin admission, duration of DFU, history of foot ulceration, previous amputation, precipitating factors of DFU); physical examination (systole, diastole, diagnosis of the diseases, Wagner severity grade of ulcer); therapy records (daily foot ulcer treatment, debridement, necrotomy, underwent amputation); laboratory results (serum creatinine, Random Blood Glucose (RBG), glycated hemoglobin (HbA1C), albumin serum, hemoglobin, leukocytes, C-Reactive Protein (CRP), platelets); radiology findings (previous amputation, Wagner severity grade of ulcer); microorganism culture results; summary (diagnosis of the diseases, causes of death, length of hospital stay). Some data were obtained from more than one source. Data that was obtained from demographic data, anamnesis, physical examination, and laboratory results were collected when the patients were admitted to the hospital. eGFR was calculated by employing the Modification of Diet in Renal Disease (MDRD) formula, which required age, gender, and serum creatinine level. Systole and diastole were used to diagnose hypertension using Joint National Committee (JNC) VII classification.

The characteristics of all patients with medical records were included. Descriptive analysis was presented in the form of narrative, tables, and diagrams. Mean, Standard Deviation (SD), Median, Maximum, and Minimum were statistically employed to analyze the numerical data. If the value of SD was higher than the Mean, the Median with Maximum and Minimum data was utilized for fit data. The characteristics and therapy were also illustrated in the tables based on the Wagner severity grade of ulcers.

RESULTS

This research employed 397 hospitalized T2DM patients with foot ulcers from 2016–2018 (Table 1). The average duration of the patients' hospital stay was 6.75 ± 5.60 days. The prevalence of DFU among T2DM hospitalized patients was 9.08%. In total, 10.58% of patients with apparent foot ulcers during their hospital admission were newly diagnosed with T2DM. Patients who had previous and first-time foot ulcers amounted to 13.85% and 86.15%, respectively, while amputation had previously been performed on 12.59% of the patients. The average patient age was 57.00 ± 9.83 years. There was no significant difference in the number of male patients (47.36%) and female patients (52.64%). Most patients worked as salarymen (35.26%) or were housewives (27.71%).

Sepsis was the major complication that occurred (68.26%), which developed into septic encephalopathy in 23.25% of patients. Subsequent DM-related chronic complications included impaired renal function (62.72%), hypertension (27.20%), macrovascular disease (19.40%), and retinopathy (2.27%). Furthermore, respiratory diseases (tuberculosis, pneumonia, and pleural effusion) were found in 128 patients (32.24%). Multiorgan Dysfunction Syndrome (MODS) as a further complication developed in 9.57% of patients (Table 1).

The RBG of patients was 251.83 ± 158.15 mg/dL on average, while HbA1c was $9.78 \pm 2.83\%$ on average, indicating poor glycemic control. The majority of patients had hypoalbuminemia (89.67%), with an average albumin level of 2.63 ± 0.60 mg/dL. Average hemoglobin levels were low (9.70 ± 2.25 mg/dL) and most patients had anemia (71.03%). Patients that underwent amputation (76.36%) and died (73.81%) predominantly had anemia. The high average level of leukocytes (20.68 ± 11.12 x 10^9 / L), the dominance of abnormal leukocyte levels (86.90%), and the median level of CRP (142.82 (0.70–471.73)) indicated severe infection (Table 1).

Ulcers of Wagner grades 4 and 5 (representing gangrene) occurred frequently (41.31%) (Figure 1). Overall, 40.05% of patients came to the hospital with less than a month's duration of DFU, while only 3.02% had old ulcers that had been present for more than a year.

The main precipitating factors of DFU (Figure 2) were trauma (12.59%) due to falling from a height, followed by blister (10.33%), and swelling (9.82%). Microorganisms were found in 98 out of 112 patients when microorganism cultures were performed. Thirty-four patients (34.69%) had polymicrobial results. Gram-negative (70.41%) microorganisms were more prevalent than Gram-positive (61.22%) microorganisms. The culture showed various results, with *Escherichia coli* (20.41%), *Enterococcus faecalis* (13.27%), *Staphylococcus aureus* (12.24%), *Acinetobacter baumanni* (12.24%), *Proteus mirabilis* (11.22%), *Klebsiella pneumoniae* (7.14%), *Pseudomonas aeruginosa* (6.12%), and *Streptococcus agalactiae* (6.12%) as the main microorganisms that infected DFU patients.

Table 2 presents the characteristics of DFU patients based on the Wagner grade of their ulcers. The average age of patients with Wagner grade 2 ulcers was the highest (57.79 ± 8.33 years). The median of both duration of DM and DFU showed no significant difference in number between Wagner grades. The average length of hospital stay was higher in patients with severe ulcers without gangrene. On the other hand, patients with gangrene in their feet had shorter hospital stay durations than patients with Wagner grade 3 ulcers. The lower the Wagner grade of the ulcer, the higher the Mean of RBG. Furthermore, the higher the Wagner grade of the ulcer, the higher the Mean of HbA1c, except for Wagner grade 2. The highest percentage of sepsis (80.49%) and the average leukocyte levels were found in gangrenous feet (22.60 ± 11.95 x 10^9/L), confirming that the infection was severe in that grade of ulcer. Anemia was also more predominant and severe in the higher Wagner grade of ulcers (Table 2).

Table 3 shows that 72.29%, 30.73%, and 17.88% of DFU patients had daily foot ulcer treatment, debridement, and necrotomy, respectively. Those treatments were most frequent in ulcers of Wagner grade 3. A total of 57 patients (14.11%) underwent amputation while hospitalized.

Table 1
Demographic and Clinical Characteristics

Characteristics	Total	%
Age (Years)	57.00 ± 9.83	
21 – 45	48	12.09
46 – 65	285	71.79
> 65	64	16.12
Gender		
Male	188	47.36
Female	209	52.64
Occupation		
Public Officer	96	24.18
Salaryman	140	35.26
Entrepreneur	9	2.27
Housewife	110	27.71
Retired	9	2.27
Others	23	5.79
No Occupation	5	1.26
No Data	5	1.26
Hospital Stay (Days)	6.75 ± 5.60	
Duration of DM (Years)	5 (0-48)	
Newly diagnosed	42	10.33
< 10	201	50.88
≥ 10	118	29.72
No Data	36	9.07
History of Insulin Admission	50	12.59
Duration of DFU Before Hospital Admission (Week)	4 (0.10-260.00)	
< 4	159	40.05
4 - 52	150	37.78
> 52	12	3.02
No Data	76	19.14
History of Foot Ulceration	55	13.85
Previous Amputation	50	12.59
Impaired Renal Function (eGFR < 60 mL/minutes/ 1,73 m²)	249	62.72
eGFR (mL/minutes/1,73 m²)	51.41 ± 40.78	
Serum Creatinine (mg/dL)	1.50 (0.32-25.00)	
Retinopathy	9	2.27
Macro-vascular Disease	77	19.40
Hypertension	108	27.20
Systole (mmHg)	120.78 ± 25.78	
Diastole (mmHg)	72.50 ± 13.44	
Sepsis	271	68.26
Encephalopathy	73	18.39
Sepsis	63	86.30*
Hepatic	3	4.11*
Metabolic	2	2.74*
Uremic	2	2.74 *
Others	3	4.11*

(Continued)

Table 1
Continued

Characteristics	Total	%
Respiratory Disease	128	32.24
MODS	38	9.57
RBG (mg/dL)	251.83 ± 158.15	
< 70	12	3.02
70 - 200	171	43.07
≥ 200	214	53.91
HbA1C (%)	9.78 ± 2.83	
Serum Albumin (mg/dL)	2.63 ± 0.60	
Serum Albumin < 3.4 mg/dL	356	89.67
Anemia (Hemoglobin < 11 g/dL)	282	71.03
Hemoglobin (mg/dL)	9.70 ± 2.25	
Leukocytes (n x 10^9/L)	20.68 ± 11.12	
< 4	4	1.01
4 – 10.4	52	13.1
> 10.4	341	85.89
CRP (mg/L)	142.82 (0.70-471.73)	
Platelets (n x 10^9/L)	418.74 ± 192.19	
Total	397	100.00

Data are presented as follows: *Mean ± SD* or *Median (Min-Max)*, *eGFR* – estimated glomerular filtration rate, *MODS* – Multiple Organ Dysfunction Syndrome, *RBG* – Random Blood Glucose, *HbA1c* – glycated hemoglobin, *CRP* – C-Reaction Protein.
*Percentage of Total Encephalopathy
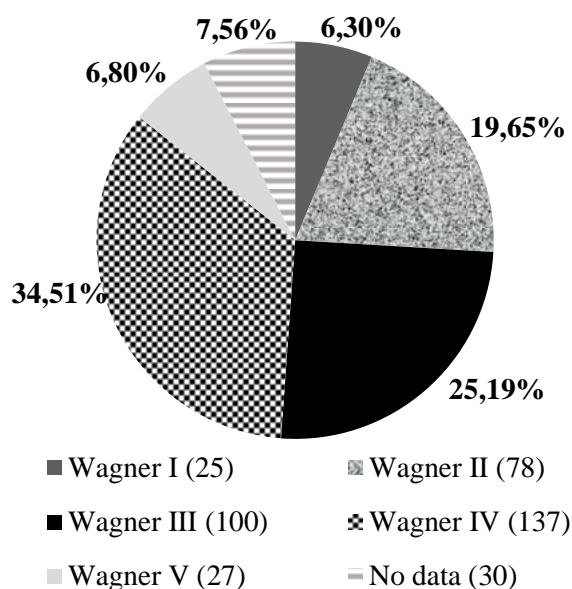
Figure 1. Wagner Severity Grade of Ulcer

There were 21 major amputations (above and below the knee), 35 minor amputations (digiti site), and one unknown site amputation. Patients with ulcers of Wagner grade 1 received no amputation. A major (above-knee) amputation was performed on a patient with a Wagner grade 2 ulcer that progressed to grade 4. Moreover, only 17.54% of amputations were performed on patients who were admitted to the hospital with a non-gangrenous foot; the remainder (82.36%) were performed on patients with gangrenous feet (Table 3).

In our hospital, 19.57% of T2DM patients with foot ulcers died between 2016–2018. Moreover, the mortality rate of DFU patients overall was 40.93%. Septic shock was the major cause of death (67.62%), followed by cardiovascular events (13.81%), respiratory failure (10.48%), cerebrovascular events (2.86%), multiorgan failure (0.95%), and hypovolemic shock (0.48%); moreover, 5.24% of patients' causes of death are unrecorded.

DISCUSSION

The prevalence of foot ulcers among T2DM hospitalized patients in the hospital under investigation was 9%; in terms of other tertiary hospitals, this figure was lower in Semarang (4%) (T. G. D. Pemayun & Naibaho, 2017) and higher in Makassar (12%) (Yusuf et al., 2016). Length of hospital stay in our study was 6.75 days on average, which is somewhat shorter than in other studies (T. G. D. Pemayun & Naibaho, 2017; Rigato et al., 2018). Our population was characterized by either early death or discharge from the hospital due to a good prognosis, resulting in relatively short durations of hospitalization. Hospital stay duration could be predicted by the Wagner severity grade of the ulcers, as was determined in a previous study (Tabur et al., 2015). The results in Table 2 indicate that more severe DFU without gangrene resulted in more extended hospital stays. Moreover, and surprisingly, gangrene patients had shorter durations of hospital stay than those with Wagner grade 3 ulcers; however, this was due to severe prognosis leading to early in-hospital mortality.

Our study reported that elderly patients dominated the population, with 71.79% aged between 45–65, while 16.12% were above 65 years old. Moreover, previous research Al-Rubeaan et al (2015) has found that older patients were at higher risk than younger ones for more complications, including DFU, which explains the older study population in our research. The percentage of females (52.64%) was slightly higher than males (47.36%). Only 16.12% of the patients were classified as being in retirement or old age (> 65 years old), with an average age of 57

± 9.83 years. This might explain the roughly equal gender distribution, as both females and males were still in their productive years (T. G. D. Pemayun & Naibaho, 2017). High levels of RBG and HbA1C on average confirmed uncontrolled DM. Moreover, T2DM patients with intensive control of blood glucose had better sensory nerve function and reduced risk of amputation (Hasan et al., 2016).
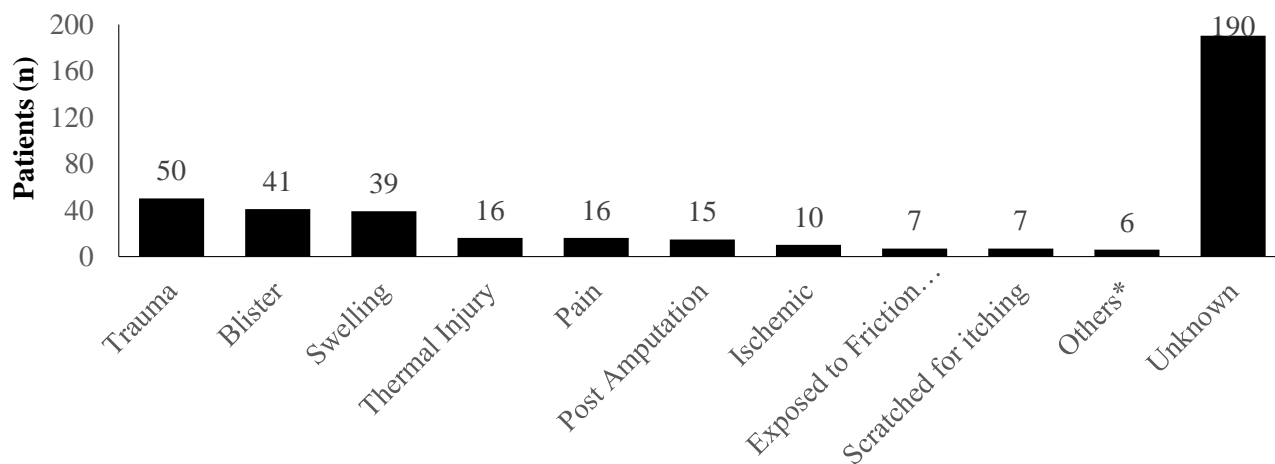
The Precipiting Factors

*1 Deformity, 2 Corpus Alineum, 1 Immobilisation, 2 Rat-bite

Figure 2. Precipitating Factors of DFU.

Table 2
Characteristics of DFU Patients based on Wagner Grade

Characteristics	Wagner Grade							
	1		2		3		4 – 5	
	n	%	n	%	n	%	n	%
Mean Age (Years)	55.64 ± 10.94		57.79 ± 8.33		55.68 ± 9.33		57.36 ± 10.66	
Duration of DM (Years)								
Newly diagnosed	7	28.00	7	8.97	6	6.00	17	10.36
< 10 Years	11	44.00	39	50.00	58	58.00	83	50.61
≥ 10 Years	5	20.00	24	30.77	24	24.00	54	32.93
No data	2	8.00	8	10.26	12	12.00	10	6.10
Median	2 (0-30)		5 (0-30)		5 (0-25)		5 (0-48)	
Duration of DFU (Weeks)								
< 4 Weeks	12	48.00	28	35.90	50	50.00	61	37.20
4 – 52 Weeks	7	28.00	28	35.90	33	33.00	70	42.68
> 52 Weeks	1	4.00	5	6.41	1	1.00	5	3.05
No data	5	20.00	17	21.79	16	16.00	28	17.07
Median	2 (0.1-104.0)		4 (0.1-260.0)		3 (0.1 – 78.0)		4 (0.2 – 208.0)	
Mean Hospital Length of Stay (Days)	6.44 ± 5.39		6.72 ± 4.44		7.63 ± 5.38		6.75 ± 6.33	
Mean RBG (mg/dL)	269.12 ± 173.15		259.95 ± 162.10		251.35 ± 165.14		250,24 ± 149.81	
Mean HbA1C (%)	9.25 ± 2.97		10.72 ± 3.20		8.99 ± 2.39		9.96 ± 2.88	
Mean Leukocytes (n × 10^9/L)	15.99 ± 7.45		18.88 ± 10.59		21.11 ± 10.88		22.60 ± 11.95	
Sepsis	10	40.00	40	51.28	68	68.00	132	80.49
Anemia	14	56.00	53	67.95	65	65.00	129	78.66
Mean Hemoglobin (g/dL)	10.87 ± 2.06		10.12 ± 2.33		9.76 ± 2.35		9.26 ± 2.10	
Total	25	6.30	78	19.65	100	25.19	164	41.31

Table 3
Treatment of DFU Patients based on Wagner Grade

Treatment	Wagner Grade												Total Treatment	
	1		2		3		4		5		No data			
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Daily DFU Treatment	15	60.00	64	82.05	85	85.00	96	70.07	15	55.55	12	40.00	287	72.29
Debridement	6	24.00	26	33.33	35	35.00	46	33.58	7	25.93	2	6.67	122	30.73
Necrotomy	1	4.00	11	14.10	25	25.00	28	20.44	5	18.52	1	3.33	71	17.88
Amputation														
Above Knee	0	0.00	1	1.28	0	0.00	8	5.84	4	14.82	0	0.00	13	22.81*
Below Knee	0	0.00	0	0.00	1	1.00	4	2.92	3	11.11	0	0.00	8	14.03*
Digiti (Single)	0	0.00	3	3.85	1	1.00	14	10.22	2	7.41	0	0.00	20	35.09*
Digiti (Multiple)	0	0.00	0	0.00	4	4.00	7	5.11	3	11.11	1	3.33	15	26.32*
Unknown site	0	0.00	0	0.00	0	0.00	1	0.73	0	0.00	0	0.00	1	1.75*
Total Amputation	0	0.00	4	5.13	6	6.00	34	24.82	12	44.44	1	3.33	57	14.11

*Percentage of Total Amputation (n=57)

Anemia and hypoalbuminemia were signs of chronic diseases and malnutrition that could be initiated by DFU (Jeyaraman, Berhane, Hamilton, Chandra, & Falhammar, 2019). The majority of patients had hypoalbuminemia (89.97%), with an average level of 2.63 ± 0.60 mg/dL. Secondly, there is a compensatory response impairment to decreased hemoglobin levels in DM patients; this leads to reduced oxygen delivery to tissues, causing poor healing and infection control (Khanbhai, Loukogeorgakis, Wright, Hurel, & Richards, 2012). Most of the patients in the current study had anemia. Moreover, an increased Wagner grade of ulcers was associated with increased anemia rate and decreased Hb on average. Furthermore, amputees (76.36%) and patients who died (73.81%) were predominantly anemic.

Patients with renal disease who were undergoing dialysis had a higher risk of developing ulcers and of amputation (Al-Rubeaan et al., 2015; Dòria et al., 2016). Furthermore, a correlation was found between serum creatinine and the number of microbiological agents growing in diabetic foot infections (Zubair, Malik, & Ahmad, 2019). Moreover, the majority (62.72%) of our DFU patients' renal function was impaired. Hypertension and macro-vascular disease (i.e., coronary artery disease, cerebrovascular disease, PVD) were risk factors for DFU, reported in 27.20% and 19.40% of our study patients, respectively. Therefore patients with DM-related chronic complications were at risk of foot ulcers because the same mechanism preceded chronic DM complications among most of the patients (Singh, Bali, Singh, & Jaggi, 2014).

Gangrene in the foot and respiratory complications preceded sepsis at rates of 41.31% and 32.24%, respectively, in our research (Chen et al., 2018; Forsyth, 2016). Sepsis developed among patients with both DFU and respiratory disease tended to be worse; thus, 2.24% of patients had a poor prognosis. Diabetic foot sepsis diminished both the blood supply and the delivery of antibiotics to the infected site, thus decreasing the natural healing (Forsyth, 2016).

The median duration of ulcers of Wagner grades 2, 3, and 4–5 among DFU patients with DM was five years; this is the same as the median of DM duration in general, indicating that the severity of the ulcers was not affected. Nevertheless, pre-diabetes patients suffer neuropathy, which is one of the main etiologies of DFU (Dimova et al., 2017). More than half of gangrene patients had DFU for more than four weeks; meanwhile, only 10.36% of gangrene patients had been newly diagnosed with DM. Furthermore, 3.02% of the patients had had ulcers for more than a year. These findings show that foot ulcers that remain untreated in DM patients (who tend to have angiopathy and neuropathy complications) lead to DFU (Boulton, 2019).

Minor trauma was found to be the most common precipitating factor of DFU (12.59%), supporting the findings of T. G. D. Pemayun & Naibaho (2017). It is crucial to immediately seek medical care for DFU, since it can proceed to sepsis and end in amputation or death; this is true

even if the appearance of the patient's ulcer is initially mild. A total of 47.86% of patients found the ulcers in their feet spontaneously at home or in hospital (Forsyth, 2016). Some of these patients had risk factors for DFU, such as previous foot ulcers, previous amputation, impairment of sight, and poor social circumstances (Boulton, 2019; Lim, Ng, & Thomas, 2017). Among the 397 DFU patients in this study, nine patients had retinopathy that impaired their sight, 55 had previous ulcers, 50 had previous amputations, 64 were above 65 years of age and nine were retired, which suggested the possibility of being in poor social circumstances. Impaired renal function tends to lead to End-Stage Renal Disease (ESRD) if not treated immediately, while ESRD patients also have a higher risk of developing DFU. Foot deformity in one patient was also a risk factor for ulceration (Boulton, 2019).

Recurrence of ulcers was reported in 13.85% of patients, similar to the study conducted by Bondor et al (2016). Our study determined post-amputation to be one of the predisposing factors of ulcer recurrence in 15 patients. Unsolved etiologies of previous healed DFUs were among the reasons for ulcer recurrence, as well as bad patient behavior (Armstrong, Boulton, & Bus, 2017).

This research found *Escherichia coli* to be the most common microorganism infecting DFU (20.41%). On the other hand, previous studies in Indonesia reported *Staphylococcus aureus* (T. Pemayun & Naibaho, 2016; Radji, Putri, & Fauziyah, 2014). Despite this, there was no significant difference in number between the microorganisms resulting from the culture, and *Staphylococcus aureus* was still one of the main microorganisms infecting DFU patients. Similar to our study, Jeyaraman, Berhane, Hamilton, Chandra, & Falhammar (2019) and T. Pemayun & Naibaho (2016) reported that Gram-negative microorganisms were more prevalent than Gram-positive microorganisms. Gram-positive cocci (*Staphylococcus spp.* and *Streptococcus spp.*) are mainly colonized short-duration Diabetic Foot Infections (DFIs), whereas chronic DFIs are characterized by poly-microbial infections, including both aerobic (*Staphylococcus, Streptococcus, Enterococcus, Pseudomonas spp*) and anaerobic pathogens. Furthermore, pathogenic microorganisms were not found in DFIs with poly-microbial infection reported in 34.69% of the isolates of this research (Heravi, Zakrzewski,

Vickery, Armstrong, & Hu, 2019; Jneid, Lavigne, La Scola, & Cassir, 2017).

The amputation rate among patients in the present study (14%) was comparatively lower than that in other research in Indonesia, which reported 36% (T. G. D. Pemayun & Naibaho, 2017). In addition, the amputation rate was higher in cases of severe DFU (24.82% and 44.44%). Tabur et al (2015) and Ugwu et al (2019) demonstrated that the severity of ulcers based on Wagner classification was useful in predicting amputation. Daily foot ulcer treatment while hospitalized was performed for 72% of patients. The remainder (28%) were either discharged from the hospital due to good prognosis or died before the ulcer could be treated. Good prognosis patients would receive daily foot ulcer treatment after being discharged from the hospital. Finally, the mortality rate of DFU in this population was 40.93%, similar to the findings of the systematic review conducted by Jupiter, Thorud, Buckley, & Shibuya (2016).

CONCLUSION

The prevalence of DFU among T2DM patients in the tertiary care hospital under investigation was relatively high. Most of the patients had poor glycemic control, a high Wagner's grade of ulcer, anemia, sepsis, and renal complications when admitted to the hospital. DFU must never be neglected due to its high mortality rate; early and aggressive treatment is a necessity.

CONFLICT OF INTEREST

The authors declare that no conflict of interest in this study.

AUTHOR CONTRIBUTIONS

ASH: Conceptualization, Methodology, Collecting data, Analyzing data, Writing—Original draft, Editing; HN: Conceptualization, Methodology, Writing—Reviewing, Supervision; ME: Methodology, Writing—Reviewing, Supervision

ACKNOWLEDGMENTS

REFERENCES

Al-Rubeaan, K., Al Derwish, M., Ouizi, S., Youssef, A. M., Subhani, S. N., Ibrahim, H. M., & Alamri, B. N. (2015). Diabetic foot complications and their risk factors from a large retrospective cohort study. *PLoS ONE, 10*(5), 1–17. https://doi.org/10.1371/journal.pone.0124446

Armstrong, D. G., Boulton, A. J. M., & Bus, S. A. (2017). Diabetic foot ulcers and their recurrence. *New England Journal of Medicine, 376*(24), 2367–2375. https://doi.org/10.1056/NEJMra1615439

Bondor, C. I., Veresiu, I. A., Florea, B., Vinik, E. J., Vinik, A. I., & Gavan, N. A. (2016). Epidemiology of diabetic foot ulcers and amputations in Romania: results of a cross-sectional quality of life questionnaire based survey. *Journal of Diabetes Research, 2016*, 2–8. https://doi.org/10.1155/2016/5439521

Boulton, A. J. M. (2019). The diabetic foot. *Medicine (United Kingdom), 47*(2), 100–105. https://doi.org/10.1016/j.mpmed.2018.11.001

Chen, C.-H., Lai, C.-C., Wang, Y.-H., Wang, C.-Y., Wang, H.-C., Yu, C.-J., … Taiwan Clinical Trial Consortium for Respiratory Diseases (TCORE). (2018). The impact of sepsis on the outcomes of COPD patients: a population-based cohort study. *Journal of Clinical Medicine, 7*(11), 1–13. https://doi.org/10.3390/jcm7110393

Dimova, R., Tankova, T., Guergueltcheva, V., Tournev, I., Chakarova, N., Grozeva, G., & Dakovska, L. (2017). Risk factors for autonomic and somatic nerve dysfunction in different stages of glucose tolerance. *Journal of Diabetes and Its Complications, 31*(3), 537–543. https://doi.org/10.1016/j.jdiacomp.2016.11.002

Dòria, M., Rosado, V., Pacheco, L. R., Hernández, M., Betriu, À., Valls, J., … Mauricio, D. (2016). Prevalence of diabetic foot disease in patients with diabetes mellitus under renal replacement therapy in Lleida, Spain. *BioMed Research International, 2016*, 1–8. https://doi.org/10.1155/2016/7217586

Forsyth, J. M. (2016). Diabetic foot sepsis. *InnovAiT, 9*(11), 687–693. https://doi.org/10.1177/1755738016665133

Hasan, R., Firwana, B., Elraiyah, T., Domecq, J. P., Prutsky, G., Nabhan, M., … Murad, M. H. (2016). A systematic review and meta-analysis of glycemic control for the prevention of diabetic foot syndrome. *Journal of Vascular Surgery, 63*(2S), 22S-28S. https://doi.org/10.1016/j.jvs.2015.10.005

Heravi, F. S., Zakrzewski, M., Vickery, K., Armstrong, D. G., & Hu, H. (2019). Bacterial diversity of diabetic foot ulcers: current status and future prospectives. *Journal of Clinical Medicine, 8*(11), 1–18. https://doi.org/10.3390/jcm8111935

International Diabetes Federation. (2019). *IDF diabetes atlas* (9th ed.). USA: International Diabetes Federation. Retrieved January 24, 2020, from https://diabetesatlas.org/upload/resources/material/20200302_133351_IDFATLAS9e-final-web.pdf

Jeyaraman, K., Berhane, T., Hamilton, M., Chandra, A. P., & Falhammar, H. (2019). Amputations in patients with diabetic foot ulcer: a retrospective study from a single centre in the Northern Territory of Australia. *BMC Endocrine Disorders, 19*(1), 1–7. https://doi.org/10.1186/s12902-018-0327-2

Jneid, J., Lavigne, J. P., La Scola, B., & Cassir, N. (2017). The diabetic foot microbiota: a review. *Human Microbiome Journal, 5*(6), 1–6. https://doi.org/10.1016/j.humic.2017.09.002

Jupiter, D. C., Thorud, J. C., Buckley, C. J., & Shibuya, N. (2016). The impact of foot ulceration and amputation on mortality in diabetic patients. I: From ulceration to death, a systematic review. *International Wound Journal, 13*(5), 892–903. https://doi.org/10.1111/iwj.12404

Khanbhai, M., Loukogeorgakis, S., Wright, J., Hurel, S., & Richards, T. (2012). Anemia, inflammation, renal function, and the diabetic foot: what are the relationships? *The Diabetic Foot Journal, 15*(4), 15–158.

Lim, J. Z. M., Ng, N. S. L., & Thomas, C. (2017). Prevention and treatment of diabetic foot ulcers. *Journal of the Royal Society of Medicine, 110*(3), 104–109. https://doi.org/10.1177/0141076816688346

Pemayun, T. G. D., & Naibaho, R. M. (2017). Clinical profile and outcome of diabetic foot ulcer, a view from tertiary care hospital in Semarang, Indonesia. *Diabetic Foot & Ankle, 8*(1), 1–8. https://doi.org/10.1080/2000625X.2017.1312974

Pemayun, T., & Naibaho, R. M. (2016). Diabetic foot ulcer registry at a tertiary care hospital in Semarang, Indonesia: an overview of its

clinical profile and management outcome. *Diabetes Management, 6*(4), 82–89.

Radji, M., Putri, C. S., & Fauziyah, S. (2014). Antibiotic therapy for diabetic foot infections in a tertiary care hospital in Jakarta, Indonesia. Diabetes and Metabolic Syndrome: *Clinical Research and Reviews, 8*(4), 221–224. https://doi.org/10.1016/j.dsx.2014.09.006

Rigato, M., Pizzol, D., Tiago, A., Putoto, G., Avogaro, A., & Fadini, G. P. (2018). Characteristics, prevalence, and outcomes of diabetic foot ulcers in Africa. a systemic review and meta-analysis. *Diabetes Research and Clinical Practice, 142*, 63–73. https://doi.org/10.1016/j.diabres.2018.05.016

Singh, V. P., Bali, A., Singh, N., & Jaggi, A. S. (2014). Advanced glycation end products and diabetic complications. *Korean Journal of Physiology and Pharmacology, 18*(1), 1–14. https://doi.org/10.4196/kjpp.2014.18.1.1

Tabur, S., Eren, M. A., Çelik, Y., Dağ, O. F., Sabuncu, T., Sayiner, Z. A., & Savas, E. (2015). The major predictors of amputation and length of stay in diabetic patients with acute foot ulceration. *Wiener Klinische Wochenschrift (The Central European Journal of Medicine), 127*, 45–50. https://doi.org/10.1007/s00508-014-0630-5

Ugwu, E., Adeleye, O., Gezawa, I., Okpe, I., Enamino, M., & Ezeani, I. (2019). Predictors of lower extremity amputation in patients with diabetic foot ulcer: findings from MEDFUN, a multi-center observational study. *Journal of Foot and Ankle Research, 12*(1), 1–8. https://doi.org/10.1186/s13047-019-0345-y

World Health Organization. (2016). Indonesia: diabetes country profiles. World Health Organization. Geneva. Retrieved September 26, 2020, from https://www.who.int/diabetes/country-profiles/idn_en.pdf

Yazdanpanah, L., Shahbazian, H., Nazari, I., Arti, H. R., Ahmadi, F., Mohammadianinejad, S. E., … Hesam, S. (2018). Incidence and risk factors of diabetic foot ulcer: a population-based diabetic foot cohort (ADFC study)-two-year follow-up study. *International Journal of Endocrinology, 2018*, 1–9. https://doi.org/10.1155/2018/7631659

Yusuf, S., Okuwa, M., Irwan, M., Rassa, S., Laitung, B., Thalib, A., … Sugama, J. (2016). Prevalence and risk factor of diabetic foot ulcers in a regional hospital, Eastern Indonesia. *Open Journal of Nursing, 6*(1), 1–10. https://doi.org/10.4236/ojn.2016.61001

Zubair, M., Malik, A., & Ahmad, J. (2019). Correlation of HbA1c and S. creatinine along with microbiological profiling of infected ulcers; cases of diabetic patients. *Diabetes and Metabolic Syndrome: Clinical Research and Reviews, 13*(1), 30–34. https://doi.org/10.1016/j.dsx.2018.08.011