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Cohort Study

Pattern and type of amputation and mortality rate associated with diabetic foot in Jeddah, Saudi Arabia: A retrospective Cohort Study

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ABSTRACT

Background: Diabetic foot complications constitute a major public health problem worldwide, especially in Jeddah, Saudi Arabia, where the prevalence of diabetes is high. Our study was designed to determine the pattern and type of amputations performed on patients with diabetic foot admitted to a tertiary center in Jeddah, Saudi Arabia; we also aimed to determine the 7-year mortality rate of patients with diabetic foot at the same institution.

Materials and methods: This retrospective study was conducted between January 2013 and September 2020 at a tertiary center in Jeddah, Saudi Arabia. It included all patients previously diagnosed with diabetes mellitus who presented to the hospital with either diabetic foot ulcers or foot gangrene (dry/wet/gas). The medical records of 358 patients were reviewed to acquire information regarding demographics, admission history regarding diabetes and its outcome, medical and surgical history, the level of amputation, and the presence of infection.

Results: Among the participants, 84.9% underwent amputation, 38.2% underwent minor amputations, 40.1% underwent major amputations, and 21.7% underwent both types of amputation. The most common cause of amputation was infection (50.3%). There were 75 deaths and a 7-year mortality rate of 20%. Low mean hemoglobin and high mean creatinine levels were significantly associated with mortality ($p < 0.05$).

Conclusion: Efforts to decrease the risk of amputation and mortality among patients with diabetic foot complications are required. Early detection of the risk factors and intervention in specialist centers with a multidisciplinary approach is essential.

1. Introduction

Patients with diabetes are at high risk of developing diabetic foot ulcers (DFUs), with the vast majority requiring amputation within 4 years of diagnosis [1]. DFUs are caused by a variety of factors, including neuropathy, angiopathy, physical stress, and high blood glucose levels [2]. Infection of ulcers is a major cause of morbidity and prolonged hospitalization, and it results in nearly double the rate of amputations compared with non-infected ulcers [2,3].

The global prevalence of DFUs is 6.3%, with male patients with type 2 diabetes being more likely to develop them [4]. According to one study, the 1-year incidence of diabetic foot syndrome among patients with type 2 diabetes in Saudi Arabia is 16.7% [5]. Lower-extremity amputations are common in the Saudi Arabian population of patients with type 2 diabetes, with most patients undergoing minor amputations [6].

The three cornerstones of DFU management are debridement (removal of necrotic tissue, periwound calluses, and foreign bodies), offloading, and infection control. The goal of these cornerstones is to preserve the patient's foot and as much viable tissue as possible for future reconstruction. If the initial management is adequate, an additional step—such as a revascularization procedure—may prevent some patients from losing their feet. If all the above mentioned interventions fail and the patient still has ischemic extremities, which are septic or may cause sepsis, amputation of the necrotic non-viable tissue is considered [7].

Toe (33.2%), transtibial (28.2%), transfemoral (26.1%), and foot (10.6%) amputations are the most common types of amputations [8]. According to most studies, amputees may have a higher mortality rate than non-amputees of the same population [9]. Amputation has a

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significant impact on a patient's physical, functional, and psychosocial status. Furthermore, it increases the financial burden owing to hospitalization, treatment, and lost wages [10]. No recent studies have examined the pattern of amputation and its relationship to and effects on mortality rate.

Therefore, the aim of this study was to determine the pattern and type of amputations performed on patients with diabetic foot admitted to a tertiary center in Jeddah, Saudi Arabia, as well as to determine the 7-year mortality rate of patients with diabetic foot at the same institution. This study will help to determine the type of amputation that has the greatest impact on patients, as well as which patients are at higher risk and may require increased future critical care.

2. Methods

2.1. Study design and setting

This retrospective study was conducted between January 2013 and September 2020 at a tertiary and educational center, which is one of the largest hospitals in the western region of Saudi Arabia. This project was performed in line with Srengthening the Reporting of Cohort Studies in Surgery (STROCSS) criteria [11]. Moreover, this study was registered in ClinicalTrials.gov with a unique identifying number (UIN) NCT05123157.

2.2. Study participants

The study included the data of all patients who had been previously diagnosed with diabetes and presented to the hospital with either DFUs or foot gangrene (dry/wet/gas), which was diagnosed by the surgical team based on clinical presentation and laboratory findings. A total of 358 patients' records were obtained.

2.3. Study instrument

A checklist was prepared to collect data on the patients' age, date of birth, and sex. Additionally, data on the last amputation admission date, number of admissions related to their diabetes status, duration of diabetes, diagnosis upon admission, date of admission, site of admission, comorbidities, type of ulcer, foot infection, presence of osteomyelitis, previous surgeries, amputation history, intensive care unit (ICU) admission, outcome of the admission, and cause of death were recorded. We subsequently divided patients according to the date and degree (major/minor) of amputation; below-knee and above-knee amputations were considered major, whereas toe and transmetatarsal amputations were considered minor.

2.4. Ethical considerations

Ethical approval was obtained from the Institutional Review Board of our institution (Reference No. 465–20). The requirement for informed consent was waived owing to the retrospective nature of the study.

2.5. Statistical analyses

Data were analyzed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). Qualitative data are presented as numbers and percentages, and the chi-square test (χ^2) was performed to assess the relationship between variables. Quantitative data are presented as mean ± standard deviation, and independent sample t-tests and Mann–Whitney U tests were performed according to data normality. Statistical significance was set at $p < 0.05$.

3. Results

The mean age of the participants was 63.94 ± 13.97 years, 66.5% were male, and 33.5% were female; further, 38.5% of the participants had Saudi nationality. Among all the participants, 73.2% had type 2 diabetes, nearly half (48.3%) were regularly prescribed oral hypoglycemic agents, and 57.3% were receiving insulin. The most common chronic diseases were hypertension (76%), cardiovascular disease (34.1%), and chronic kidney disease (19%). In total, 31%, 25.1%, and 8.7% of the participants had dry, wet, and gas gangrene, respectively (Table 1).

A total of 84.9% of the participants underwent amputation (mean number of amputations per participant: 1.34 ± 0.88). Among all the participants, 38.2% underwent minor amputations—16.4% at the transmetatarsal level—with a mean number of amputations per participant of 0.68 ± 0.78. A total of 40.1% underwent major amputations—34.7% above the knee—with a mean number of amputations per participant of 0.69 ± 0.75. Of all the participants who underwent amputations, 21.7% underwent both minor and major amputations. The most common cause of amputation was infection (50.3%) and peripheral vascular disease was present in 46.1% of the participants (Table 2). The mean duration of hospital stay was 20.7 ± 29.62 days, and 36% were admitted to the ICU.

We found that the participants who presented with dry or wet gangrene, as well as those who had foot infection or ischemia, constituted a significantly higher percentage of those who underwent amputation ($p < 0.05$). Moreover, participants who were admitted through the emergency room (ER) had a significantly higher amputation rate (Table 3).

The association between the duration of diabetes and the rate of amputation was not significant. Additionally, participants who had undergone both minor and major amputations constituted a significantly lower percentage of those who used oral hypoglycemic agents or

Table 1
Distribution of the participants according to their characteristics, clinical data, chronic diseases, and types of gangrene.

Variable	No. (%)
Sex	
Women	120 (33.5)
Men	238 (66.5)
Nationality	
Non-Saudi	220 (61.5)
Saudi	138 (38.5)
Type of diabetes	
Type 1	65 (18.2)
Type 2	262 (73.2)
Unknown	31 (8.7)
Oral hypoglycemic agents	
Yes	173 (48.3)
No	90 (25.1)
Not applicable	95 (26.5)
Insulin treatment	
Yes	205 (57.3)
No	104 (29.1)
Not applicable	49 (13.7)
Chronic diseases	
Cardiovascular disease	122 (34.1)
Hypertension	272 (76)
Chronic kidney disease	68 (19)
Diabetic nephropathy	14 (3.9)
Diabetic neuropathy	10 (2.8)
Malignancy	5 (1.4)
More than one chronic disease	130 (36.3)
None	45 (12.6)
Dry gangrene	
No	247 (69)
Yes	111 (31)
Wet gangrene	
No	268 (74.9)
Yes	90 (25.1)
Gas gangrene	
No	327 (91.3)
Yes	31 (8.7)

Table 2
Distribution of the participants according to amputation data.

Variable	No. (%)
Amputation	
No	54 (15.1)
Yes	304 (84.9)
Minor amputation	
No	177 (49.4)
Yes	181 (50.6)
Level of minor amputation	
Great toe or first ray	49 (13.7)
Other toes	55 (15.4)
Transmetatarsal	59 (16.4)
Not applicable	195 (54.5)
Major amputation	
No	170 (47.5)
Yes	188 (52.5)
Level of major amputation	
Above knee	124 (34.7)
Below knee	76 (21.2)
Not applicable	158 (44.1)
All amputations	
Minor	116 (38.2)
Major	122 (40.1)
Both	66 (21.7)
Cause of amputation	
Critical ischemia	24 (6.7)
Infection	180 (50.3)
Trauma	14 (3.9)
Not applicable	140 (39.1)
Peripheral vascular disease	
Yes	165 (46.1)
No	80 (22.3)
Not applicable	113 (31.6)
ICU admission	
Yes	129 (36)
No	224 (62.6)
Not applicable	5 (1.4)
Outcome	
Death	75 (20.9)
Discharged alive	261 (72.9)
Transferred to another facility	3 (0.8)
Not applicable	19 (5.3)
Death among all patients	
Yes	75 (20.9)
No	283 (79.1)
Death among patients who underwent amputation	
No amputation	15 (1)
Yes	66 (18.4)
No	238 (66.5)

ICU: intensive care unit.

Table 3
Relationship between amputation and gangrene, ischemia, foot infection, and site of admission.

Variable	Amputation		χ^2	p-value
	No No. (%)	Yes No. (%)		
Dry gangrene			7.79	0.005*
No	46 (18.6)	201 (81.4)		
Yes	8 (7.2)	103 (92.8)		
Wet gangrene			12.96	<0.001*
No	51 (19)	217 (81)		
Yes	3 (3.3)	87 (96.7)		
Gas gangrene			0.77	0.379
No	51 (15.6)	276 (84.4)		
Yes	3 (9.6)	28 (90.3)		
Site of admission			26.68	<0.001*
ER	36 (12.2)	260 (87.8)		
Not applicable	5 (83.3)	1 (16.7)		
Outpatient	13 (23.2)	43 (76.8)		
Cause of amputation			72.92	<0.001*
Critical ischemia	0 (0.0)	24 (100)		
Infection	3 (1.7)	177 (98.3)		
Not applicable	49 (35)	91 (65)		
Trauma	2 (14.3)	12 (85.7)		

ER: emergency room.

Table 4
Relationship between type of amputation and clinical and laboratory data.

Variable	Amputation type			χ^2	p-value
	Minor No. (%)	Major No. (%)	Both No. (%)		
Duration of diabetes	14.63 ± 6.51	19.29 ± 10.85	17.08 ± 8.08	2	0.494
White blood cell count	14.14 ± 7.16	20.22 ± 14.13	17.28 ± 6.69	2	<0.001
Hemoglobin	10.4 ± 2.2	9.22 ± 2.78	9.21 ± 2.14	2	<0.001
HbA_{1c}	10.23 ± 6.63	8.7 ± 2.47	8.29 ± 2.12	2	0.009
Type of diabetes				5.88	0.208
Type 1	19 (35.8)	21 (39.6)	13 (24.5)		
Type 2	91 (40.4)	85 (37.8)	49 (21.8)		
Oral hypoglycemic agents				11.56	0.021
No	27 (33.8)	27 (33.8)	26 (32.5)		
Yes	63 (44.1)	54 (37.8)	26 (18.2)		
Insulin treatment				11.37	0.023
No	30 (35.3)	39 (45.9)	16 (18.8)		
Yes	73 (41.5)	58 (33)	45 (25.6)		

insulin ($p < 0.05$). Furthermore, these participants who had undergone amputation had an increased white blood cell (WBC) count and HbA_{1c} level (Table 4).

Participants with lower mean hemoglobin and higher mean creatinine levels constituted a significantly higher percentage of those who died ($p < 0.05$), as did those who had cardiovascular disease, hypertension, chronic kidney disease, or more than one chronic disease ($p < 0.05$) (Table 5).

4. Discussion

Despite lower limb amputation being the most unpleasant consequence of diabetic foot, there have been no recent studies in Saudi Arabia that address the pattern and type of amputation. Our study was designed to determine the pattern and type of amputations performed on patients with diabetic foot in a tertiary hospital in Saudi Arabia.

Our findings demonstrated that 84.9% of the patients underwent amputation, 40.1% of which were major amputations. Of these, infection was the most common cause of amputation. As reported in our study, high HgA1c level, WBC count, and duration of diabetes were highly predictive of the attempt and frequency of amputation rate. Similarly, patients with low hemoglobin and high creatinine levels had a higher mortality rate.

The mean age of the participants in this study was 63 years, which is consistent with that found in other studies from different countries [12,13]. In contrast, a mean age of 56 years was found in multicenter observational studies in two different countries (from India and Nigeria) [11,14]. This might be due to the remarkable development in health services and primary healthcare centers distributed throughout Saudi Arabia over the last decade.

Similar to the findings of other studies, there was a predominance of men over women in the present study [13]. It is possible that women have superior diabetic foot awareness, knowledge, and attitudes than men; they have also been found to be less susceptible to diabetic foot according to a cross-sectional study in Saudi Arabia [15]. Non-Saudis represented the majority of our sample, which was related to the eligibility criteria of patient admission to other hospitals in the city.

The most common presentation among the participants in our study who underwent amputation was gangrene followed by chronic foot ulcers, which is consistent with the findings of other studies [16]. Similar results were obtained in other studies as the most prevalent cause of amputation was infection followed by ischemia. Additionally, almost

Table 5
Relationship between death among all participants and their characteristics and clinical and laboratory data.

Variable	Death		χ^2	p-value
	Yes No. (%)	No No. (%)		
Age	66.11 ± 14.86	63.35 ± 13.96	1.45	1.46
Sex			0.001	0.969
Women	25 (20.8)	95 (79.2)		
Men	50 (21)	188 (79)		
Nationality			0.6	0.437
Non-Saudi	49 (22.3)	171 (77.7)		
Saudi	26 (18.8)	112 (81.2)		
Duration of diabetes	24.6 ± 9.39	16.3 ± 8.13	0.05	0.050
White blood cell count	18.01 ± 10.64	16.55 ± 10.54	0.117	0.238
Hemoglobin	9.04 ± 1.91	110.02 ± 2.59	2.81	0.005
HbA_{1C}	8.62 ± 2.107	9.458 ± 4.87	1.08	0.279
C-reactive protein	156.11 ± 74.51	140.6 ± 93.59	0.93	0.353
Creatinine	271.59 ± 236.42	156.81 ± 1 68.51	5.52	<0.001
Chronic diseases				
Cardiovascular disease	36 (29.5)	86 (70.5)	8.18	0.004
Hypertension	66 (24.3)	206 (75.7)	7.51	0.006
Chronic kidney disease	26 (38.2)	42 (61.8)	15.14	<0.001

An older age and ICU admission were the main risk factors for death ($p < 0.05$) (Table 6); the mortality rate was 0.2, and there were 75 deaths among the participants.

Table 6
Multivariate logistic regression analysis of the independent predictors (risk factors) of death among all participants.

Variable	B	Wald	p-value	Odds ratio (95% CI)
Age	0.02	4.36	0.037	0.97 (0.95–0.99)
Sex	0.28	0.67	0.413	0.75 (0.37–1.49)
Nationality	0.19	0.33	0.561	1.21 (0.62–2.37)
Insulin use	0.35	0.74	0.390	0.7 (0.31–1.56)
White blood cell count	0.07	0.38	0.534	1.07 (0.85–1.34)
Hemoglobin	0.38	0.54	0.459	146 (0.53–4.06)
HbA_{1C}	0.2	0.23	0.630	1.22 (0.53–2.78)
ICU admission	2.55	46.56	<0.001	12.9 (6.19–26.9)
Amputation type	0.04	0.04	0.836	0.49 (0.27–0.87)

CI: confidence interval; ICU: intensive care unit.
P-values in bold font indicate significance.

half of the participants had peripheral vascular disease [11,17]. A possible explanation for this may be that peripheral vascular disease reduces tissue antibiotic concentration and increases colonization of multidrug-resistant microbes in diabetic foot wounds, leading to an increased risk of amputation [14].

Contrary to expectations, this study found a substantial difference in the percentage of participants who underwent amputation—more than three-quarters of our sample—compared with other international studies that reported amputation rates of 47% and 35% [12,14]. Even when compared to findings of previous national studies that report rates of 55% and 40% [18,19], our findings substantially differ. More than half of the participants in our study underwent major amputations, with above-knee amputation being the most common. The remaining participants underwent minor amputations, with the most common being transmetatarsal amputation. The differences in our findings compared to those of other studies can be attributed to multiple factors, such as most of our patients being admitted through the ER with late presentations. The observed delay in seeking medical care could be attributed to limited knowledge and negative health-seeking attitudes, including self-management and traditional care practices. Additionally, hospital-related factors such as eligibility criteria and a shortage of beds may have played a role.

Our study explored some of the predictors of lower limb amputation in patients with diabetes. It is widely acknowledged that HbA_{1c} is a crucial serum marker to monitor blood glucose control. Glycemic control is an important strategy to prevent the progression of diabetic peripheral neuropathy, which plays a role in the need for lower limb amputation [20].

Our findings revealed that the risk for lower limb amputation increased significantly with a high HbA_{1c} level. Studies have also shown that patients with poor glycemic control undergo a higher percentage of minor and major lower limb amputations [21]. This may be because a high HbA_{1c} level has a multifactorial effect in leading to lower limb amputation. One possible explanation is that the poorer the HbA_{1c} level, the greater the increase in apoptosis in diabetic wounds, which contributes to delayed wound healing. Another reason may be that a high HbA_{1c} level is related to peripheral arterial disease, which is a risk factor for lower limb amputation, in patients with diabetes [22,23].

It is not challenging to find an association between an increased WBC count and increased lower limb amputation frequency. Laboratory findings help to determine the severity of foot infections; thus, they can be used as diagnostic and prognostic indicators. A high WBC count is associated with poorer glucose metabolism and the presence of infections, such as osteomyelitis, which has been shown to be a strong predictor of amputation; therefore, these markers may indirectly predict the need for amputation [19,24].

We found a significant relationship between the duration of diabetes and an increased rate of both minor and major lower limb amputation. This corroborates the concept that chronic diabetes complications—such as atherosclerotic disease, immune alterations, and peripheral neuropathies—increase in incidence and severity over the course of the disease [25]. Moss et al. also found that the frequency of amputation increases with the duration of diabetes; however, these authors did not distinguish between the rates of major and minor amputations as we did in our study [26].

Although the risk of hypertension in patients with diabetes is reported to be twice that in those without diabetes [27], we failed to find any association between amputation and hypertension. These data suggest that hypertension may be an important factor that affects the prognosis of patients with DFUs. Nonetheless, it is still necessary for patients with DFUs to have adequate blood pressure control, as hypertension may lead to adverse cardiovascular and cerebrovascular events.

Previous studies have reported a 5-year and a 10-year mortality rate of up to 51% and 49%, respectively [28,29]. In the current study, the 7-year mortality rate was 20%, which is lower than the findings of most other studies—except for a few, including that by Pinto et al., which reported a mortality rate of only 13.7% [30]. This lower mortality rate could be explained by the multidisciplinary approach followed at our center. Similarly, the findings of a lower mortality rate from a study in France could also be explained by the advanced care provided in cases of DFUs at their multidisciplinary foot care units [31]. In a study by Young et al., the mortality rate decreased from 48% to 26.8% after introducing a strategy of aggressive control of cardiovascular risk management [32].

Most of the deceased patients in our study had previously undergone amputations (88%). This finding is similar to that of several other studies, and shows that the worst survival rates occur among patients who undergo lower-extremity amputations, and this is considered to be a significant predictor of both all-cause and cardiovascular mortality [29,33].

The participants in our study died at an earlier age (66.11 years) than expected in the population, which is consistent with the findings of a previous study [29]. Many studies have found that male patients with DFUs have significantly higher mortality rates than female patients [29,33]. However, in our study, we found a non-significant difference in mortality between male and female patients (21% and 20.8%, respectively); a similar finding was also reported in another study in Australia [34].

Low hemoglobin and high serum creatinine levels were strongly associated with mortality in our study, and this could reflect the severity of the disease in our participants—either due to poor control of the

disease or the fact that more than half of our participants were non-Saudi, which led to a delay in management due to eligibility issues. For the same reason, we could explain why ICU admission was found to be a predictor of mortality. In addition, we found strong association between the duration of diabetes and mortality rate, which is considered one of the known risk factors for mortality among patients with diabetes [33].

Increased creatinine levels in deceased patients reflect an advanced status of renal impairment; therefore, not surprisingly, the most common comorbidity associated with death in our participants was chronic kidney disease, which has been proven in multiple populations to be one of the greater risk factors for all-cause mortality [33,34].

Our study has a few limitations. First, selection bias was introduced given that this was a retrospective analysis and involved only hospitalized patients, which negatively impacts the external validity of our findings. Second, since this was an observational study that relied on secondary data from hospital records, there were various cases of incomplete data. Third, we were unable to predict the outcomes of patients who were discharged from the hospital after lower limb amputation and were lost to follow-up.

5. Conclusion

This study demonstrates that diabetic foot complications are a serious health problem, especially in our society, as most of our participants underwent amputations. Gangrene was identified as the most common presentation. A high WBC count and HbA_{1c} level were significant predictors of amputation in participants with DFUs; once infection occurs, the risk of diabetic foot-related amputation rapidly increases. Interestingly, we found a relatively low mortality rate. Nonetheless, premature death was identified among the participants; therefore, strategies to control risk factors are required. Although the risk factors for DFU are difficult to control, knowledge of these factors and more control are critical to prevent amputation. This can be achieved by establishing multidisciplinary teams for more holistic management. However, their role should be further investigated.

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Ethical approval

Unit of Biomedical Ethics at King Abdulaziz University issued approval (Reference No 465–20). The Research Ethical Committee (REC) recommended granting permission of approval to conduct the project.

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Author contribution

Abdullah Almohammadi: study concept, study design, data collection, data analysis, writing the paper. Maryam Alnashri: study concept, study design, data collection, data analysis, writing the paper. Rawan Harun: study concept, study design, data collection, data analysis, writing the paper. Sarah Alsamiri: study concept, study design, data collection, data analysis, writing the paper. Dr. Maram Alkhatieb: study concept, study design, data analysis, direct supervision.

Consent

The requirement for informed consent was waived owing to the retrospective nature of the study.

Registration of research studies

Name of the registry: clinicaltrials.gov
Unique Identifying number or registration ID: NCT05123157
Hyperlink to your specific registration (must be publicly accessible and will be checked): https://clinicaltrials.gov/ct2/show/NCT05123157

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Declaration of competing interest

None.

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