Epidemiological Insights into Diabetic Foot Amputation and its Correlates: A Provincial Study

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ABSTRACT

BACKGROUND: Diabetic foot ulcer and potential subsequent lower extremity amputation are major complications of diabetes mellitus and are also prominent morbidity factors that could affect patients' quality of life.

OBJECTIVES: This study aimed to assess the prevalence of diabetic foot amputation and explore correlates of amputation cause and type among subjects with diabetes mellitus in Tehran, Iran.

METHODS: A descriptive cross-sectional study was conducted to assess the demographic, sociological, and clinical characteristics of subjects who had undergone lower extremity amputation due to diabetic foot ulcers, from 2011 to 2020, in two educational medical centers in Tehran, Iran. We examined the medical records of 4676 individuals who were admitted to Shariati and Sina hospitals due to diabetic foot issues. Information related to patient demographics (age, gender, marital status), social factors (education level, insurance), and clinical data (medical history, laboratory results, and characteristics of diabetic foot ulcers) was collected for subjects who had undergone lower extremity amputation due to diabetic foot ulcer. The collected data was reported using average values, standard deviations and proportions and analyzed using statistical tests.

RESULTS: During one decade, 882 out of 4676 (18.8%) patients with diabetic foot ulcers underwent lower extremity amputations of various types in Sina and Shariati hospitals in Tehran, Iran. Of these, 692 (14.5%) were included for further analysis in the study and the rest were excluded due to lack of sufficient recorded data. About 75.9% of the study population was male, and the average age including both sexes was 60 years. About 92.7% were married, and on average, subjects had been afflicted with diabetes mellitus for 15.1 years. Statistical analysis using Pearson's chi-square test showed there was a significant association between the treatment regimen for diabetes mellitus and the type of amputation ($P = .01$), as well as between the duration of the disease and the cause of amputation ($P = .01$) and its type ($P = .04$).

CONCLUSION: diabetes mellitus related treatment regimen and duration of disease are significantly associated with amputation cause and type.

PLAIN LANGUAGE SUMMARY

Understanding Why and How Diabetic Patients Lose Their Feet: A Study from Tehran, Iran

This study explored patients with diabetes in Tehran, Iran, experience foot problems leading to amputation. We looked at the records of 4676 patients over a decade, finding that 18.8% had lower limb amputations. Key factors included treatment methods for diabetes and the duration of the disease, significantly impacting the cause and type of amputation. These insights can guide better care to prevent such serious complications in patients with diabetes.

KEYWORDS: Diabetes mellitus, diabetic foot, foot ulcer, amputation, Iran

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Research Highlights

- Osteomyelitis was the most common amputation cause (36.4%)
- Toe amputation was the most prevalent amputation type (34.5%).
- The most prevalent wound class and wound site categories were forefoot (72%) and ischemia (49.7%), respectively.
- The incidence of amputations per year fluctuated considerably, with noticeable rises in 2015 and 2020.
- Duration of disease had a significant association with amputation type ($P = .04$) and cause ($P = .01$).
- The most common diabetes mellitus treatment regimen was insulin (51.87%), and the category of treatment regimen was significantly associated with amputation type ($P = .01$).

Introduction

Diabetes Mellitus (DM) is a prevalent disease worldwide, affecting 463 million adults (20-79 years old). More than 95% of all adults with DM have type 2 diabetes mellitus (T2DM), and this proportion is increasing in most countries.[1,2] Several complications can follow DM. Worldwide, these include cardiovascular diseases (32%),[3] diabetic eye disease (35)%,[4] CKD (25%-36%),[5] and diabetic foot ulcers (DFU) (19-34%).[6]

Diabetic foot ulcers account for a large portion of hospitalizations for patients with diabetes, and lower extremity amputation is a prevalent consequence of DFU. Diabetic foot prevalence in the Middle East varies between 2.7% and 12%.[7,8] The estimated rate of foot amputation in patients with diabetes in the Middle East region is approximately high. The pooled prevalence of amputation rate in patients with DFU was 33% in the region.[9]

In Iran, the prevalence of diabetic foot among T2DM patients in 2019 was 3% (95% CI: 1%-5%).[10] Late diagnosis or inadequate management can lead to the need for lower extremity amputation. The prevalence of lower limb amputation in Iran is 1.2% to 13.7% in patients with DM, and amputation occurs in 34.7% to 49.65% of patients with diabetic foot ulcer.[11-13]

The mortality rate and morbidity cost of DFU amputation are also considerable, with 5-year mortality rates after amputation being around 40%.[14] Diabetic foot disease accounted for ~20.5 million YLDs in a 2015 systematic review, ranking in the top-10 conditions for numbers of YLDs caused.[15] Diabetic foot ulceration, and potential subsequent limb amputation and postural instability can have serious quality of life and psychosocial consequences, including depression. Access to medical services, better assessment methods tailored to DFU, and possible new therapeutic strategies can help reduce these effects.[16,17]

Risk factors for DFU amputation include male gender, ulcer duration greater than 1 month, peripheral vascular disease, Wagner grade 4 or higher, proteinuria, leukocytosis, wound infection, elevated HbA1c, magnesium, and platelet levels, and osteomyelitis.[18,19] Cardiovascular risk factors are also associated with diabetic peripheral neuropathy and therefore, DFU; these include elevated triglyceride levels, body mass index (BMI), smoking, and hypertension. Reliable glycemic control is the primary strategy in preventing the need for diabetic foot amputation.[20]

Most importantly, lower extremity amputation can be avoided in many cases with a more precise and aggressive therapeutic regimen. A well-defined healthcare program for DFU with structured outpatient and inpatient guidelines, and with knowledge of risk factors associated with lower extremity amputation, tailored to the healthcare system of each country is key to reducing the morbidities and costs of diabetes mellitus.

The purpose of this study is to describe the prevalence of diabetic foot amputation and the factors associated with amputation type and cause in two educational medical centers in Tehran, Iran. Sufficient epidemiological data is necessary to promote public health decision-making and potential future research in Iran.

Methods

Setting

The setting of the study was the hospital wards in which patients with foot problems related to diabetes mellitus were admitted, such as surgery, orthopedics and internal medicine (endocrine) wards of Shariati and Sina hospitals in Tehran from 2011 to 2020.

Participants

The study population were patients with diabetes of all ages and of both genders who had undergone lower extremity amputation due to DFU, in two major referral specialty hospitals affiliated with Tehran University of Medical Sciences in Tehran.

Sampling

Medical document archives, both digital (HIS system) and paper versions, were searched for patients admitted with DM-related foot lesions and ulcers. For each hospital, medical archives supervisors were contacted after receiving the ethics code; for some patients the data available was in digital form, while for others only medical documents were available, requiring manual data extraction, which was carried out by trained nurses. Medical records of all patients with DFU were extracted, and all files related to patients who had undergone lower extremity amputation due to DFU were selected (n = 882), including both type 1 and type 2 DM. Among these, patients with more than >20% of their data variables missing (n = 190) were excluded, and the rest (n = 692) were included for further

detailed analysis. Each patient was assigned a 5-digit ID code, which represented hospital of admission and year of admission with the last 3 digits used as an anonymous personal ID.

Variable definitions

Demographic data included age, sex, marital status and education level. Sex was assigned as male or female, marital status was assigned as single or married, and education level was assigned as uneducated (illiterate), below college or above college level. Previous history of hypertension, myocardial ischemia, stroke, retinal vascular involvement and renal disease were also recorded as yes or no fields in the questionnaire.

Medical information started with duration of disease and DM treatment regimen. Duration of disease was measured in years and categorized into less than 10, 10 to 20, and more than 20 years. Lab data recorded were Hemoglobin A1c level, serum creatinine, white blood cell (WBC) levels, red blood cell (RBC) levels, C-reactive protein (CRP), and right and left ankle-brachial index. All medical and lab workup data was obtained before any LEA surgery. Hemoglobin A1c (HbA1c) levels indicate the excess sugar in the bloodstream, and are used to estimate the 3-month average of blood sugar level. CRP is a pentameric protein found in blood plasma, whose circulating concentrations rise in response to inflammation. It is an acute-phase protein of hepatic origin. Serum creatinine is an important prognostic marker in diabetes mellitus, and was measured in mg/dL. Ankle-brachial index (ABI) is the ratio of the systolic blood pressure measured at the ankle to that of the brachial artery; ABI values of 1.0 to 1.4, 0.91 to 0.99, and $\leqslant$0.90 indicate no blockage, borderline blockage, and peripheral artery disease (PAD), respectively.[21,22]

Ulcer laterality was recorded as left, right or both feet, and anatomic site as forefoot, midfoot, or heel. DFUs were classified as ischemic, neuroischemic, neuropathic, venous, or Charcot joint. Ischemic DFUs were defined as ulcers occurring in the presence of PAD, neuropathic DFUs were defined as ulcers occurring with neuropathy (assessed via history and physical examination), and neuroischemic DFUs were defined as ulcers concurrent with both ischemia and neuropathy,[23,24] according to the latest guidelines available at the time of analysis (the definitions have not changed as of 2023). Amputation sites included below knee, above knee, ray, toe, Charcot arthropathy, and Lisfranc. Causes of amputation included Wagner grades 4 or 5,[23] osteomyelitis and Charcot arthropathy. Amputation types included toe amputation (resection of phalanges), below knee amputation (transection of tibia and fibula), ray amputation (resection of metatarsals and associated toes), Lisfranc amputation (resection of tarsometatarsal joints), above knee amputation (transection of femur), and Chopart amputation (disarticulation at the talonavicular and calcaneocuboid level).[25-27]

Glycemic control was a key variable and was categorized as good control (HbA1c $\leqslant$ 7%) and poor control (HbA1c $>$ 7%) according to the latest American Diabetes Association guidelines at the time of data analysis[28]; an A1c level of $\leqslant$7% is the recommended target level in the 2023 version of the guideline as well.[29]

Duration of disease, possible later patient expiration, and potential foot necrosis, gangrene and trauma related to DFU were also recorded.

Measurements

Demographic data, past and present medical history, information about diabetes and any complications were recorded using valid questionnaires. The last part of the questionnaire was specifically related to the traits of subjects' diabetic foot ulcer and amputation.

Two questionnaires were used, one for demographic data and one for medical data and history. Demographic data recorded included age, sex, marital status, education, insurance, employment and smoking, recorded as responses in the questionnaire. Employment and (current) smoking were defined as yes/no responses stated by the patient in the questionnaire.

HbA1c was measured in our study in percentage, using measurement kits from Pars Azmun™ and Pishtaz Teb™. CRP and serum creatinine were measured using automated analyzers, in the units of μg/mL and mg/dL, respectively. WBC levels were measured using automated counters, in *cell* /μL.

Data collection

Medical records of patients with foot lesions due to diabetes mellitus, both in paper and digital form, in the 10 years of 2011 to 2020, were extracted for data. Ankle-brachial index and HbA1c levels were missing from some files but were not used as exclusion criteria. The questionnaires were then used to extract data from the files. In the case of HbA1c levels measured serially, the last measurement before amputation was recorded.

Statistical analysis

Statistical analysis was performed using SPSS software (version 16.0). Categorical variables were reported as [n (%)] values and quantitative variables were reported as [mean ± standard deviation] values.

Associations between select categorical variables and outcome variables (namely, amputation type and cause) were analyzed using Pearson chi-square tests. *P*-values less than .05 were considered to be statistically significant. Due to various amounts of missing values for each variable, percentages stated in the text are adjusted for missing values, but non-adjusted percentage values are also available in Tables 1 and 2.

Table 1. Demographic and clinical characteristics of the study population (N = 692).

AGE	MEAN ± SD	60.95 ± 10.782	
VARIABLE	CATEGORY	N (%)	FREQUENCY ADJUSTED FOR MISSING VALUES (%)
Gender	Male sex	525 (75.9)	75.9
Marital status	Married	635 (91.8)	92.70
	Single	50 (7.2)	7.29
	Missing	7 (0.1)	-
Insurance	Yes	647 (93.5)	93.50
	No	45 (6.5)	6.50
Employment	Missing	372 (53.8)	-
	No	216 (31.2)	67.50
	Yes	104 (15)	32.50
Education	Missing	572 (82.7)	-
	No education	60 (8.7)	50.00
	Up to high school	40 (5.8)	33.33
	Diploma	16 (2.3)	13.33
	Higher education	4 (0.6)	3.33
Hypertension	Yes	381 (55.1)	63.03
	No	196 (28.3)	33.96
	Missing	115 (16.6)	-
Smoking	No	346 (50)	66.66
	Yes	173 (25)	33.3
	Missing	173 (25)	-
Treatment regimen	Insulin	359 (51.87)	51.87
	Oral agents	251 (36.27)	36.27
	Both	82 (11.84)	11.84
History of myocardial infarction	Yes	330 (47.7)	58.61
	No	233 (33.7)	41.38
	Missing	129 (18.6)	-
History of cardiovascular accidents and/or strokes	No	369 (53.2)	83.48
	Missing	250 (36.1)	-
	Yes	73 (10.5)	16.51
History of renal disease	No	326 (47.1)	64.81
	Missing	189 (27.3)	-
	Yes	177 (25.6)	35.18
Retinal vascular involvement	No, n (%)	336 (48.6)	69.42
	Missing, n (%)	208 (30.1)	-
	Yes, n (%)	148 (21.4)	30.57

Table 2. DFU characteristics of the study population (N = 692).

VARIABLE	CATEGORY	N (%)	FREQUENCY ADJUSTED FOR MISSING VALUE (%)
Involved foot	Left	365 (52.7)	53.20
	Right	316 (45.7)	46.60
	Missing	6 (0.8)	-
	Both	5 (0.7)	0.70
Wound site	Forefoot	499 (72.1)	88.16
	Missing	126 (18.2)	-
	Midfoot	35 (5.1)	6.18
	Heel	32 (4.6)	5.65
Wound class	Ischemic	344 (49.7)	57.81
	Neuroischemic	205 (29.6)	34.45
	Missing	97 (14)	-
	Neuropathic	41 (5.9)	6.89
	Venous	5 (0.7)	0.84
Amputation type	Toe amputation	239 (34.5)	35.88
	Below knee	175 (25.3)	26.27
	Ray amputation	134 (19.4)	20.12
	Lisfranc	71 (10.3)	10.66
	Above knee	43 (6.2)	6.45
	Missing	26 (3.7)	-
	Chopart	4 (0.5)	0.60
Amputation cause	Missing	257 (37.1)	-
	Osteomyelitis	252 (36.4)	57.93
	Wagner grade 4	111 (16.0)	25.51
	Wagner grade 5	59 (8.5)	13.56
	Charcot arthropathy	13 (1.9)	2.98
Ischemia type	Missing	636 (58.7)	-
	Necrosis	26 (3.8)	46.42
	Gangrene	23 (3.3)	41.07
	Trauma	7 (1.0)	12.5
Number of involved toes	Missing	516 (74.6)	-
	2 toes	73 (10.5)	41.47
	3 toes	53 (7.7)	30.11
	4 toes	36 (5.2)	20.45
	5 toes	14 (2.0)	7.95

Results

Of 4676 patients with DM-related foot problems, 882 (18.8%) patients with amputation were assessed for this study, with 692 (14.5%) subjects' data being included and the rest excluded due to missing data. The most common amputation type was toe amputation (35.8%), and the least common type of amputation was Chopart amputation (0.6%).

Table 1 shows the baseline and the clinical characteristics of the study population. According to the results, most of the subjects were male (75.9%) and married (92.7%), and were under insurance cover (93.5%). Also, the majority of the subjects had hypertension (63.0%), used insulin as treatment for DM (51.8%), and were current smokers (66.6%). Of those who had occupation and education levels specified, most were unemployed (67.5%) and uneducated (50.0%); this could be caused by a sampling bias as most patients referring to public-sector educational hospitals are of low socio-economic status.

Table 2 lists the DFU characteristics of the included subjects. Most commonly, DFUs were in the forefoot (88.1%), of the ischemic wound class (57.8%), and resulted in toe amputation (35.8%). Very few subjects had diabetic foot problems in both of their feet (0.7%). Amputation cause, ischemia type and number of involved toes were the variables with the highest amount of missing data. Charcot arthropathy as a cause for amputation was rare and observed in less than 3% of the subjects.

Figure 1 shows the percentage of DFU-related admissions resulting in amputation per year, in both Sina and Shariati hospitals combined. The ratio of amputations to admissions fluctuated considerably, with notable increases in 2015 and 2020. Potential factors associated with these trends are mentioned in the Discussion section.

Table 3 shows the baseline relevant medical history and lab data of the study population, with normal ranges for lab data according to the protocols of the kits utilized. Length of stay could vary greatly, with a minimum of 3 days and a maximum of 122. HbA1c was also above the recommended levels in most subjects, with a minimum of 5% and a maximum of 18%.

Table 4 displays the association between several key demographic and clinical factors and the important outcome variables of amputation type and cause, measured with chi-square tests. Significant associations were observed between DM treatment regimen and amputation type ($P = .010$), as well as between the duration of the disease and both amputation cause ($P = .017$) and type ($P = .043$). For further detail on the associated crosstabs and portion of missing data for each variable combination, please refer to Supplemental Material No. 1. In Table 5, we present a detailed breakdown of amputation causes and types versus DM treatment regimens, considering its key role as a modifiable factor.

Glycemic control is also another key variable in all treatment programs related to DM; its relation to the outcome variables is illustrated in Figure 2, with green showing subjects with good glycemic control and red showing subjects with poor glycemic control.

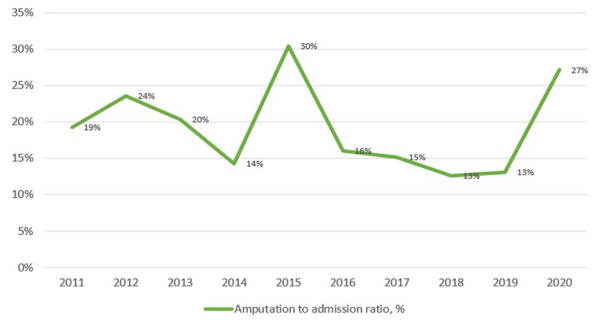

Figure 1. Percentage of DFU patients who underwent LEA each year in Shariati and Sina Hospitals, from 2011 to 2020.

Although statistically non-significant in this study, diabetes-related treatment regimen could also be a factor associated with amputation cause ($P = .190$) and amputation type ($P = .010$). Subjects on insulin also seem to be at a higher risk of below-knee amputation (Table 4).

Discussion

In this cross-sectional study, we studied the overall epidemiology and time trends in subjects with DFU who had undergone LEA, and observed fluctuating trend in the number of admissions and amputations over the years, along with several notable facts regarding the study population, including osteomyelitis being the most prevalent cause of amputation (57.9%), and toe amputation being the most prevalent amputation type (35.8%). The prevalence of LEA exhibited a downward trend from 2011 to 2014, and also 2016 to 2019, with a substantial increase in 2015 and 2020. These fluctuations in LEA rates highlight the dynamic nature of this issue and suggest the potential influence of external factors, such as healthcare policies or societal changes, which should be further investigated. One possible factor affecting this trend could be the initialization of specialized DFU care education workshops for the medical faculty of both of the medical centers contributing to the study, courtesy of a joint effort by the Department of Internal Medicine (Tehran University of Medical Sciences) and the Endocrine and Metabolic Disease Research Center (also affiliated with Tehran University of Medical Sciences). This could lead to more precise screening, diagnosis, and treatment programs, albeit a possible "increase" in the incidence of amputation events; but considering most amputations are of the toe amputation type, this could be indicative of an overall improvement in DFU care and limb salvage for DM patients.

The demographic and social characteristics of the study population, being mostly married (92.7%), and under insurance cover (93.5%) is probably reflective of the general population rather than a specificity of patients who have undergone LEA. Amputation prevalence is similarly higher in male patients in other countries as well, including Turkey[30] and China.[31] Evidence regarding the cause of this difference among males and females is inconclusive, even if the higher overall

Table 3. Study participant admission and paraclinical data (N = 692).

VARIABLE	MEAN ± SD	NORMAL RANGES
Length of stay in hospital (d)	17.66 ± 15.24	-
Duration of disease (y)	15.16 ± 8.53	-
Hb A1c	8.81 ± 2.09	⩽7%[a]
WBC	12 516 ± 6249.15	4500-11 000 /μL
CRP	78.84 ± 49.81	<10 mg/L
Creatinine	3.01 ± 2.83	0.8-1.3 mg/dL
ABI	0.986 ± 0.262	0.9-1.4

[a]The listed value is the HbA1c recommended goal in patients with diabetes mellitus, not the normal range for the general population.

Table 4. Correlations with amputation cause and type (N = 692).

	AMPUTATION CAUSE*	AMPUTATION TYPE*
Gender	0.602	0.320
Marital status	0.414	0.658
Treatment regimen	0.199	**0.010**
Education	0.080	0.870
Duration of disease	**0.017**	**0.043**
Glycemic control	0.703	0.057

*Pearson's chi-square *P*-values are listed in the tables.
Bold numbers indicate statistically significant *P*-values.

prevalence of DFU in male patients is adjusted for; differences in joint mobility and the severity of neuropathic complications might play a role here.[32]

The prevalence of the different causes of LEA was different in our study compared to the available evidence. Osteomyelitis (57.9%) was the most common, followed by Wagner grade 4 (25.5%), grade 5 (13.5%), and Charcot arthropathy (2.9%); available evidence regarding the prevalence of these factors in developed countries states that "non-complicated" DFUs including Wagner grades 3 (37.6%), 4 (43.9%), and 5 are the most common, followed by osteomyelitis (20% in one study), and Charcot joint.[31,33-35] According to our findings, length of stay was prolonged in comparison to other studies.[36] HbA1c was also above the recommended levels in most subjects. According to most guidelines and available evidence, HbA1c plays a pivotal role in diabetic foot complications.[29,37] These findings all highlight a need for better standards of care for diabetes mellitus in the study population, and arguably, Iran.

Regarding the diabetic foot ulcer itself, there was no discrepancy between the right and left lower extremities, and very few subjects had both lower limbs involved. Most wounds were on the forefoot and of the ischemic type, which is different from other countries, such as China[31] and Pakistan.[38] Factors causing this difference could be an avenue of future research.

Due to most wounds being on the forefoot, most LEAs were also of the "toe amputation" type. This finding is similar to studies in Tanzania[38] and Malta.[39] Amputation level prevalence values observed in other studies varies, with the most common being transmetatarsal (31.1%), followed by toe (27.7%), and the least common Chopart joint (2.2%) in one study involving tertiary orthopedic hospitals in Brazil.[44] Various factors could cause this difference, including the epidemiological characteristics of DFU in different population, and the different guidelines regarding the surgery of DFUs utilized in different centers.

Limitations

The main limitation of this study is the inherent potential deficit of medical records when used as a source of data. Many subjects had one or several variables missing, and this could have potential effects on the overall composition of the data available for this study. The sample for this study was subjects admitted to Sina and Shariati hospitals in Tehran, which are major educational medical centers in Iran. Other sites in the country including those in smaller cities and rural areas, or the private care sector, could have varying epidemiological properties, due to possibly different DFU care protocols in different hospitals, discrepant levels of screening and care for DM and DFU across the country, cultural and educational factors

Table 5. DM-related treatment regimen versus amputation cause and amputation type.[a]

	AMPUTATION CAUSE, N (%)[B]				AMPUTATION TYPE, N (%)[B]					
	OSTEOMYELITIS	WAGNER GRADE 4	WAGNER GRADE 5	CHARCOT JOINT	TOE AMPUTATION	BELOW KNEE AMPUTATION	RAY AMPUTATION	LISFRANC AMPUTATION	ABOVE KNEE AMPUTATION	CHOPART AMPUTATION
Oral agents (%)	79 (31.3)	48 (43.2)	25 (42.3)	4 (30.7)	83 (34.7)	61 (34.8)	47 (34.3)	29 (40.8)	18 (41.8)	3 (75.0)
Insulin (%)	132 (52.3)	53 (47.7)	25 (42.3)	6 (46.1)	128 (53.5)	101 (57.7)	58 (43.2)	37 (52.1)	22 (51)	1 (25.0)
Both (%)	41 (16.2)	10 (9.0)	9 (15.2)	3 (23.0)	28 (11.7)	13 (7.4)	29 (21.6)	5 (7.0)	3 (6.9)	0 (0.0)
Total	252	111	59	13	239	175	134	71	43	4
Pearson chi-square *P*-value	.199				.010					

[a]Subjects with data available for both variables (n = 435 for amputation cause and treatment regimen, and n = 666 for amputation type and treatment regimen).
[b]The percentage values in each cell are calculated using the column's total.

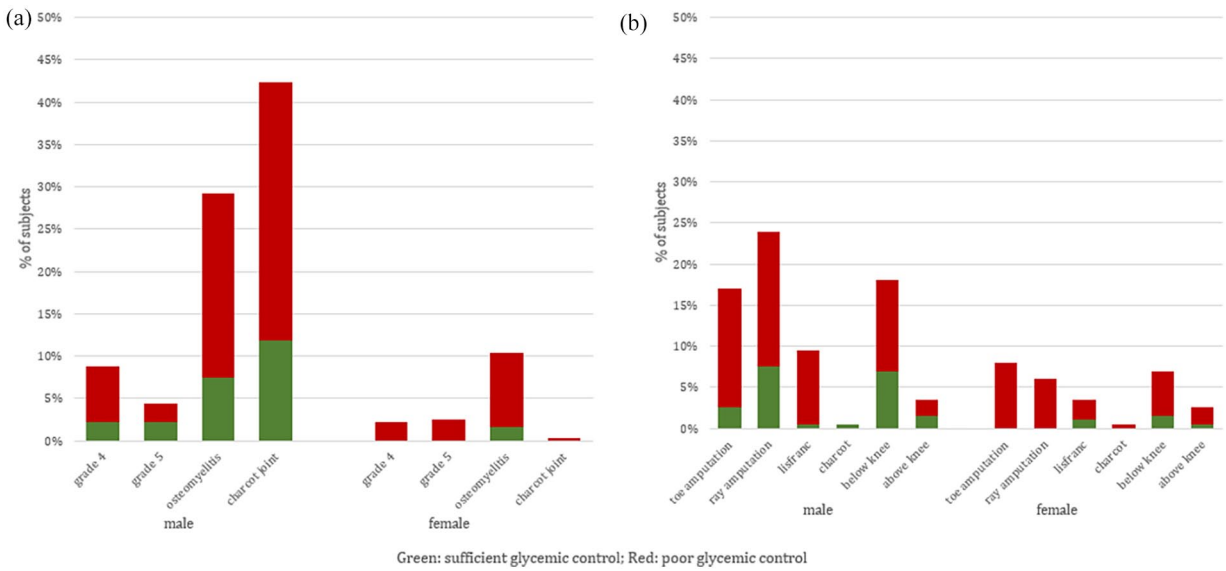

Figure 2. (a) Amputation cause, glycemic control, and gender and (b) amputation type, glycemic control, and gender. Green: sufficient glycemic control; Red: poor glycemic control.

causing patients not to refer for proper care, and even economic factors, although sufficient insurance cover seems to have mostly prevented this factor from playing a major role.

Conclusions

DM-related treatment regimen was significantly associated with amputation type, and duration of disease with both amputation cause and type. Also, the trend for the number of amputations per year fluctuated considerably, with a notable rise in 2020. The higher prevalence of osteomyelitis as a cause for LEA, and subpar levels of glycemic control compared to guideline standards are key findings, highlighting the need for further investigation and possible interventions aimed at reducing the incidence of LEA in patients with diabetes mellitus.

Declarations

Ethics approval and consent to participate

Approval for the study was given by the Research and Ethics Committee of the Endocrine & Metabolism Research Institute (IR.TUMS.EMRI.REC.1397.057), an affiliate of the Tehran University of Medical Sciences. Written informed consent forms (regarding the use of the patient's data for scientific research) were signed by all the subjects whose data was used in the study, at the time of their admission to the hospital. The anonymity of the data was emphasized in the consent forms, and the case of illiterate subjects, this information was explained by the head of the medical team (a specialist in orthopedics) to a suitable accompanying first-degree relative, and the form signed by that person. All measures necessary to ensure the privacy and safety of information found in subjects' medical files were taken. Data entries excluded the subjects' names, and instead used a 5-digit code as the ID for each patient.

Consent for publication

Not applicable.

Author contributions

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Availability of data and materials

The data that support the findings of this study are available on request from the corresponding authors, M.R.A. or M.S. The data are not publicly available due to restrictions by the governing body of the research, the Endocrine & Metabolism

Research Institute. The Institute did not allow public disclosure of the dataset due to concerns that individual privacy could be compromised and to adhere to local ethics regulations. Access to the raw data may be granted following review and approval of a request submitted to the Institute detailing how the confidentiality of personal data will be maintained.

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Supplemental material

Supplemental material for this article is available online.

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