

Risk factors associated with lower extremity amputation in Sudanese individuals with diabetes: The need for improvement in primary health care system

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ABSTRACT

Background: Lower extremity amputation (LEA) in individuals with diabetes is a serious health issue with a considerable physical and social burden. The aim of this study was to assess the prevalence and risk factors associated with LEA in diabetic foot ulcer (DFU) patients. **Materials and Methods:** This was a cross-sectional health facility-based study that recruited 315 diabetes individuals with foot ulcers from the diabetes center in Khartoum, Sudan. Direct interviewing of subjects was used to obtain data, using a standardized validated questionnaire. Chi-square and logistic regression analysis were used in data analysis. **Results:** 69.5% of the diabetic participants were aged 50 years old or more, and 71.1% were males. Most of the subjects (48.2%) were diabetics for a duration of >10 years, while more than one third (37.5%) of them were diabetic for 5–10 years. The majority (89.5%) had type 2 DM, while only 10.5% were type 1 DM. Two hundred forty-five patients had a left lower foot ulcer; 55.1% of the patients' ulcers were present in the toes, while 21.6% were in the foot sole. The overall prevalence of lower limb amputation was 17.1%. Individuals with diabetes patients with LEA had a higher incidence of hypertension ($P = 0.000$), retinopathy ($P = 0.000$), nephropathy ($P = 0.002$), ulcer size >2.5 cm ($P = 0.000$), and neuropathy ($P = 0.000$) through Chi-square analysis. Furthermore, logistic regression analysis showed that amputation was significantly associated with retinopathy ($P = 0.000$), size of ulcer ($P = 0.000$), and neuropathy ($P = 0.016$). **Conclusion:** The overall prevalence of LEA was 17.1%. The primary risks factors associated with amputation were presence of neuropathy and ulcer size >2.5 cm. Presence of retinopathy predispose diabetic individuals to amputation. Amputation is associated with disability and psychological problems; therefore, there is an urgent need for more improvement in preventative measures and primary health care system in low resource setting country like Sudan in order to decrease diabetes complications, especially patient's education about diabetes management by primary care physicians.

Keywords: Amputation, diabetes, foot ulcer, primary care, retinopathy, Sudan

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Introduction

Diabetic foot is one of diabetes complication that can be associated with recurrent hospital admission.^[1] The lifetime

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incidence of developing diabetic foot ulcer (DFU) can reach 25%.^[2] Different factors and causes can lead to DFU, such as uncontrolled diabetes may lead to neuropathy and minor trauma can be associated with delayed healing. Furthermore, deformity, high plantar pressures, and peripheral arterial disease (PAD) can also lead to DFU.^[3]

Importantly, lower extremity amputation (LEA) is always one of the feared complications of DFU, and it was estimated that 85% of amputation in diabetic patients are preceded by a foot ulcer.^[4] The pathway to LEA is multifactorial, involving many risk factors which include duration of diabetes mellitus,^[5,6] previous amputation,^[7] poor glycemic control, hypertension,^[8] nephropathy, dyslipidemia, PAD, retinopathy, peripheral neuropathy, osteomyelitis, and wound severity.^[9-11] In terms of clinical management, thorough and systematic evaluation and classification of a foot ulcer are necessary for the appropriate treatment.^[12] Furthermore, with adequate foot care and education of people with diabetes, amputation can be prevented.

Almobarak *et al.*^[13] showed that the prevalence of DFU in Khartoum, Sudan was 18.1%. Also, Ahmed *et al.*^[14] showed that only 46.7% of Sudanese individuals with diabetes had good knowledge about diabetic foot self-care, suggesting that a large proportion of the diabetes population lacked the necessary knowledge and awareness, which could be a contributing factor to the high prevalence of DFU (18.1%). Although the prevalence of DFU is high among Sudanese diabetic patients,^[13] knowledge about the sequelae of DFU, which is often LEA, remains unknown. Therefore, this study aims to assess the prevalence and risk factors associated with LEA among Sudanese individuals with diabetes with foot ulcers.

Research Design and Methods

Study subjects

The study was conducted in Khartoum North diabetes center. The study population was individuals with diabetes who attended for treatment for DFU with and without amputation, between 1st of July 2016 and 30th of July 2018. This was a cross-sectional health facility-based study. The Khartoum state provided health insurance coverage for individuals with diabetes. The study's inclusion criteria included adult individuals with diabetes aged ≥ 18 years of both sexes with foot ulcers who consented to participate in the study. Exclusion criteria were non-diabetic patients who underwent amputation, individuals diagnosed with diabetes for ≤ 6 months, patients with uncompleted medical records, and participants who did not consent to participate.

Ethical approval

Ethical approval was obtained from the faculty of Medicine, University of Medical Sciences and Technology, Khartoum, Sudan (IRB 00008868) and date was 3/12/2017.

Questionnaire (Study variables and outcome endpoints)

The data was collected through direct interviewing of the participants by medical doctor using a validated questionnaire. The questionnaire comprised of closed-ended questions that covered the following: sociodemographic factors of participants, diabetes information, anatomical area of foot ulcers, and presence or absence of foot amputation.

Data analysis

Descriptive statistics of frequency and percentages were used to summarize data on sociodemographic factors, diabetes information, and areas of foot ulcers. For statistical analysis, we have divided the cohort into those with amputation and non-amputation groups. Chi-square and logistic regression tests were used to assess the risk factors associated with diabetic foot amputation. Statistical analysis was performed by the statistical package for social science (SPSS, version 26).

Results

Baseline sociodemographic characteristics

Among the 315 diabetic participants with foot ulcers, 69.5% were aged above 50 years and 71.1% were males. The majority of the patients (70.5%) had jobs that did not pose a risk for injury, while 29.5% of the participants had a risk for occupational injury. Participants registered with the diabetes center and enrolled in the study were from the following regions: Omdurman (30.2%), Bahri (25.7%), Khartoum (23.5%), and outside Khartoum State (20.6%). About two-thirds of the participants (61.6%) had health insurance [Table 1]. More than one-third of the participants (37.5%) were diabetic for 5–10 years, while 14.3% lived with diabetes for < 5 years and 48.2% lived with diabetes for > 10 years. The majority (89.5%) had type 2 DM, while only 10.5% had type 1 DM [Table 2]. Seventy patients had a right foot ulcer. The most common ulcer locations were toes (38.6%), sole (31.4%), and heel (12.9%). On the other hand, 245 patients had a left foot ulcer; 55.1% of these patients' ulcers were present in the toes, while 21.6% were in the sole [Table 3].

Risk factors associated with amputation

Importantly, the overall prevalence of amputation was 17.1% (11.1% minor and 6% major amputation). We have used Chi-square test to assess for the significant of risk factors among those patients with and without amputation. Gender, age, duration of diabetes, type of diabetes, smoking and chewing tobacco were not significantly associated with amputation [Table 4]. Through Chi-square statistical analysis, DFU patients with LEA were significantly more hypertensive ($P = 0.000$), with an increase in size of ulcer 2–5 cm ($P = 0.000$), different causes of ulcer ($P = 0.009$). Also, LEA patients presented with more diabetic complications that included retinopathy ($P = 0.000$), nephropathy ($P = 0.002$), ischemic heart disease ($P = 0.000$), and neuropathy ($P = 0.000$) [Table 4] compared to diabetic patients that didn't undergo LEA. Logistic regression analysis showed

Table 1: Socio-demographic characteristics of respondents in Khartoum North Diabetes center , Sudan, (n=315)

Variables	Frequency (n)	Percentage
Age group		
18-30 years	10	3.2
31-50 years	86	27.3
>50 years	219	69.5
Gender		
Male	224	71.1
Female	91	28.9
Occupation		
Job with injury risk (Jobs involving extensive manual material handling or vehicular operations)	93	29.5
Job without injury risk	222	70.5
Residence		
Bahri	81	25.7
Khartoum	74	23.5
Omdurman	95	30.2
Outside Khartoum State	65	20.6
Socioeconomic status		
Low	153	48.6
Moderate	161	51.1
High	1	0.3
Health insurance		
Yes	194	61.6
No	121	38.4

Table 2: Clinical characteristics (diabetic information) of DFU patients in Khartoum North Diabetes center , Sudan, (n=315)

Variables	Frequency (n)	Percentage
Duration of diabetes		
1-4 years	45	14.3
5-10 years	118	37.5
11-15 years	58	18.4
16-20 years	42	13.3
>20 years	52	16.5
Type of diabetes		
Type 1	33	10.5
Type 2	282	89.5

Table 3: Ulcers locations in DFU patients in Khartoum North Diabetes center , Sudan (n=315)

Ulcer Location	Right foot (n=70)		Left foot (n=245)	
	Frequency (n)	Percentage	Frequency (n)	Percentage
Toes	27	38.6	135	55.1
Head of metatarsal	2	2.9	13	5.3
Medial aspect	4	5.7	13	5.3
Lateral aspect	5	7.1	10	4.1
Heel	9	12.9	12	4.9
Ankle	1	1.4	9	3.7
Sole	22	31.4	53	21.6
Total	70	100.0	245	100.0

that retinopathy, the ulcer's size, and neuropathy had a statistically significant association with amputation [Table 5]. In fact, retinopathy was more likely to be associated with an eight-fold increase in amputation risk ($P = 0.000$). Similarly, the increased size of the ulcer by more than 2.5 cm was likely to increase the risk of amputation by 5.5 times ($P = 0.000$). Also, neuropathy was significantly associated with amputation ($P = 0.016$, OR 1.2) [Table 5]. Overall, the data suggest that retinopathy, size of the ulcer >2.5 cm, and neuropathy are independent predictors of foot amputation in diabetics.

Discussion

We report in the current study that 17.1% of the 315 participants with DFU had an amputation. The amputation group had a higher incidence of person and limb specific risk factors that include hypertension, retinopathy, nephropathy, ulcer size >2.5 cm, and neuropathy. Furthermore, independent predictors of the amputation outcome were retinopathy, the size of the ulcer >2.5 cm, and neuropathy.

Morbach *et al.*, showed that amputation prevalence was 15.4%, while Lipsky *et al.*, showed amputation prevalence of 21.4%. The prevalence of amputation in this study was 17.1% and this was comparable with previous two studies by Morbach and Lipsky *et al.*^[15,16] On the other hand, the prevalence of amputation among DFU patients in China was lower than our reported value^[17] (Wang *et al.* 2016). The discrepancy between the findings can be attributed to various factors such as genetic profile differences, diabetes care/management, and early intervention. Retinopathy is among the most common microvascular complications of diabetes. The associative link between retinopathy and the increased risk of DFU is well established.^[18-20] Furthermore, an Australian retrospective study identified diabetic retinopathy as the most associated risk factor with amputation among DFU patients via Chi-square and logistic regression analysis.^[21] Similarly, we found that retinopathy was the strongest predictor of amputation in DFU patients. Strikingly, DFU patients who had retinopathy were eight times more likely to be amputated. Given the high associative relationship, retinopathy can serve as a marker for the amputation burden. It is worth noting that Pemayun *et al.* reported no association between amputation and retinopathy.^[22] The conflicting finding could be because of differences in the methodology of the studies since our study was a cross-sectional study, whereas the study conducted by the Pemayun *et al.* was a case-control study.

It worth mentioning that infection in DFU are likely to have preceded 85% of amputations in diabetic patients.^[4] Also, several studies had shown that large ulcer size increase the risk of amputation.^[23-25] We report that ulcer size of >2.5 cm was significantly associated with amputation through both Chi-square test and regression analysis. The association of amputation with ulcer size was of the second-highest magnitude. As expected, patients were more prone to develop ulcers in toes and soles as diabetic foot insensitivity that occurs before ulcer formation

Table 4: Risk factors associated with amputation using Chi-square test

Variable	Amputation %		P
	Not Amputated	Amputated	
Gender			
Males	81.3%	18.8%	0.297
females	84.6%	15.4%	
Age			
18-30 years	80.0%	20.0%	0.054
31-50 years	90.7%	9.3%	
>50 years	79%	21%	
Duration of diabetes			
Newly diagnosed	86.7%	13.3%	0.206
5-10 years	86.4%	13.6%	
11-15 years	77.6%	22.4%	
16-20 years	83.3%	16.7%	
>20 years	73.1%	26.9%	
Type of diabetes:			
Type 1	78.8%	21.2%	0.366
Type 2	82.6%	17.4%	
Cause of ulcer			
unknown	72.7%	27.3%	0.009
sharp injury	88.6%	11.4%	
tight shoes	93.8%	6.3%	
cellulitis	75.5%	24.5%	
thermal (temperature) factor	76.2%	23.8%	
Size of ulcer			
<2 cm	100.0%	0.00%	0.000
2-5 cm	88.6%	11.4%	
>5 cm	51.7%	48.3%	
Ischemic heart diseases			
yes	41.2%	58.8%	0.000
no	87.1%	12.9%	
Nephropathy			
Yes	46.2%	53.8%	0.002
No	83.7%	16.3%	
Retinopathy			
Yes	64.8%	35.2%	0.000
No	94.1%	5.9%	
Hypertension			
Yes	60.8%	39.2%	0.000
No	86.3%	13.7%	
Smoking			
Yes	88.1%	11.9%	0.128
No	80.9%	19.1%	
Chewing tobacco			
Yes	77.9%	22.1%	0.144
No	83.8%	16.2%	
Neurological presentations			
neuropathy	89.9%	10.1%	0.000
loss of muscles reflex	73%	27%	
pain	64.2	35.8	

often affects the plantar foot regions. However, it is unclear why more ulcers were formed on the left foot than the right one.

Importantly, we found that peripheral sensory neuropathy was 1.2 times more likely to be associated with predicted risk of amputation in DFU patients. Similar observation was also noted in Ethiopia (neuropathy was also associated with 1.6 times risk of amputation in DFU).^[20] Also, a German study

Table 5: Multivariate logistic regression analysis result of factors associated with amputation among diabetic foot ulcer patients in Khartoum North Diabetes center, Sudan, 2016-2018 (n=315)

Variables	B	S.E	Wald	P	Odd ratio (OR)
hypertension	0.427	0.442	0.931	0.335	1.532
Nephropathy	0.828	0.718	1.332	0.248	2.289
Retinopathy	2.120	0.511	17.226	0.000*	8.329
Size of ulcer (>2.5 cm)	1.713	0.418	16.796	0.000*	5.547
Neuropathy	0.165	0.068	5.834	0.016*	1.179

*Statistically significant, P≤0.05

had shown that diabetic polyneuropathy was a significant risk factor for amputation for type 2 diabetes patients with diabetic foot syndrome using Cox regression analysis.^[27] The associative relationship between neuropathy and amputation is likely because of high glucose-mediated damage to peripheral nerves that leads to the loss of foot protective sensation. The absence of foot sensation increases the predisposition to a foot injury and ulceration, and subsequently, an infection that can ultimately lead to amputation.^[28]

Limitations and strength

To our knowledge, the current study is the only study that characterized the determinants of LEA in patients with DFU in Sudan. The study is not without limitations. There is a selection bias, given the subjects were recruited from a single diabetic center, and hence may not be reflective of other regions in Sudan. So further multi-center studies are required. This was also a cross-sectional study and hence may not allow for the assessment of the temporal relationship between the potential risk factors and the end outcome.

Conclusion

The most significant factors associated with LEA were retinopathy, ulcer size, and neuropathy. Overall, we identified predisposing characteristics to amputation among DFU Sudanese patients. Identification of these risk factors can be utilized to develop an updated risk stratification system that would prove to be essential for decision making in terms of management and treatment protocol for Sudanese patients with diabetic feet in order to prevent or reduce LEA rates at institutional levels. More improvement in primary health system in Sudan will help to decrease diabetes complications. Primary care physicians are the first point of contact for patients with diabetes in rural and urban areas and their input in diabetes management will have substantial impact in decreasing risk of amputations. Importantly, the role of primary care physician in health education and foot care is extremely effective in empowering patients. There is an urgent need for more investment and improvement in primary health care system in Sudan, especially with diabetes management. Cheap and effective innovation like use of telemedicine especially during the COVID-19 pandemic can be used by primary care physicians to educate peoples in rural areas of Sudan. Amputation is associated with disability and psychological

problems; therefore, more preventative measures and health policies are needed. Optimization of diabetes control is serious challenge not only in Sudan but across developed and developing countries, which can contribute significantly in prevalence of amputation. Therefore, the input of primary care physicians is vital in vast and developing country like Sudan, in term of diabetes optimization and patient's education in feet protection.

Key points

- The prevalence of lower limb amputation was 17.1%.
- Risk factors were hypertension, retinopathy, nephropathy, ulcer size >2.5 cm, and neuropathy.
- Independent predictors of the amputation outcome were retinopathy, the size of the ulcer >2.5 cm, and neuropathy.
- The role of primary care physicians is extremely important in Sudan in term of patients' education about feet protection and diabetes control. Investment in primary care service and increasing numbers of primary care physicians with interest in diabetes may help significantly in decreasing the financial and psychological burdens associated with amputation in Sudan.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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