

*Research Article***Diabetic Foot Infection: Predictors of Outcome****Mohamed R. Abdella, Ahmad Atiya and Emad Elsageer**

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**Abstract**

**Objective:** The aim of this study was to evaluate the affection of different predictors on the outcome of diabetic foot infection. **Patients and methods:** This study included 50 patients with diabetic foot infection that were admitted to The Department of General Surgery, Minia University Hospital between July 2017 to July 2018. **Results:** Fifty patients were submitted to the study 11 of them were females and 39 were males. Gender in our study was not found to be an important predictive factor for limb loss ( $P=0.444$ ). The age ranges between 40 and 70 with main age of  $59.1 \pm 7.6$  years, patients who underwent major amputations were older. There was a significantly higher number of smokers in the metatarsal and major amputation group. Patients underwent major amputations had higher Wagner score and lower ABI than other patients with the  $p = 0.000$  in both. As regard laboratory data obtained from the patients, all were significant except random blood sugar and bleeding profile. **Conclusion:** Outcome of diabetic foot infection is not equal in all patients and is affected by different predictors which make a great change in final results. We studied some of them and still there are more predictors as duration of diabetes, type of its control, and time between onset of diabetic foot lesion and its presentation which can be fulfilled in other studies in the future.

**Keywords:** Predictors, Diabetic foot, Infection**Introduction**

Diabetic patients are more susceptible for limb amputations 20 times more than those who do not suffer from this disease and about 70% of limb amputations happen to diabetic patients. Foot disorders are a major source of morbidity and a leading cause of hospitalization for persons with diabetes.<sup>(1)</sup>

Vascular disease, abnormalities in blood flow distribution, peripheral neuropathy (PN), autonomic neuropathy, physical stress and infection are the major factors involving the pathogenesis of foot problems in diabetic patients.<sup>(2)</sup>

Foot infections are a common and serious problem in persons with diabetes. Diabetic foot infections typically begin in a wound, most often a neuropathic ulceration.<sup>(3)</sup>

Foot infections in patients with diabetes are difficult to treat because these individuals have impaired micro vascular circulation, which limits the access of phagocytes to the infected area and results in a poor concentration of antibiotics in the infected

tissues. In addition, diabetic individuals can not only have a combined infection involving bone and soft tissue called fetid foot, a severe and extensive, chronic soft-tissue and bone infection that causes a foul exudates, but they may also have disease that involves the large vessels, as well as micro vascular and capillaries that results in peripheral vascular disease.<sup>(4)</sup>

In general, foot infections in persons with diabetes become more severe and take longer to cure than do equivalent infections in persons without diabetes.<sup>(5)</sup>

Foot ulcer is the main cause of lower limb amputation, It develops in approximately 10% of patients with diabetes at one time or another.<sup>(6)</sup> Foot disorders are the leading cause of hospitalization among such patients, about 7% of diabetics with foot ulcers required hospitalization, which has astronomical cost.<sup>(7)</sup>

About 80% percent of lower-limb amputations in patients with diabetes are preceded by foot ulceration. The most common cause of admission of diabetic patients to hospitals is to treat the infected diabetic foot.<sup>(A)</sup>

### Patients and Methods

Fifty patients were presented to El- Minia university hospital between July 2013 and July 2014. Their ages ranged between 40 and 70 years old, were suffering from diabetic foot infection and were subjected to intervention evaluation of potential predictors of the outcome of diabetic foot infections after approval of the study protocol by the Local Ethical Committee and obtaining written fully informed patients' consent. Personal history especially age, sex and smoking, general examination especially nutrition and chronic diseases, description of the foot lesion which were classified according to the Wagner classification as grade 1 Ulcerated skin and subcutaneous tissue, grade 2 Deeper lesions that could penetrate to tendon, bone or joint capsule (there is as yet no abscess or osteomyelitis), grade 3 Deep tissues are involved, abscess, osteitis or osteomyelitis are present. Grade 4 Local gangrene, and grade 5 diffuse gangrene

Vascular condition of the limb by palpation of the peripheral pulsations, arterial ultrasonographic examination of affected limb was done for all examined patients, Ankle Brachial index was done to all patients using a handheld Doppler. Patients with absent or reduced pedal pulses or ABI < 0.9 underwent conventional Doppler examination and angiography and revascularization procedure was done to the ischemic patients. X-ray was done to evaluate the shape & condition of the foot bone. culture taking, and laboratory findings were evaluated for all patients in the form of complete blood picture (hemoglobin, white cells, PMNs and platelets), glycosylated hemoglobin, random blood sugar, creatinine, urea, ALT, AST and bleeding profile (INR, Pt).

After hospital admission all patients underwent primary surgical operation according to the degree of their foot condition ranging from simple foot debridement, toe or more than one toe amputation, metatarsal amputation or directly below or above knee amputation. Ischemic patients underwent vascular intervention by the vascular surgeons before they have their foot operations.

We consider infection to be present in the examined patients when the wound has purulent secretions or at least two of the following: redness, pain, tenderness, indurations, warmth, lymphangitis, foul smell, or gas formation. culture taking from all patients after admission to hospital and after first debridement. Samples were obtained by deep-needle aspiration, bone biopsy or curettage of the ulcer.

After primary operation all patients stay in our hospital for daily dressing, wound observation and taking medications. Patients whom wounds were improved were discharged and followed up at the outpatient clinic. Other patients underwent further operations according to their foot conditions. Some patients had one operation others had more than one according to the condition.

Treatment consisted of daily wound care, bed rest, special materials used to avoid putting pressure on the affected area when ambulating, parenteral antibiotics and debridement or amputation (minor or major) when indicated. Wound debridement was performed routinely to remove extensive callus and necrotic tissue (Fig. 1).

Infected diabetic foot ulcer was defined according to the Infectious Diseases Society of America guidelines as the presence of purulent wound drainage or  $\geq 2$  designated systemic or local inflammatory findings.

Antibiotics were started as empirical parenteral treatment covering gram +ve, gram -ve and anaerobic organisms; change in antimicrobial regimen was guided by culture results and clinical

follow-up. Parenteral antibiotic treatment was followed by prolonged oral therapy.

Follow up was done after hospital discharge where all patients were observed at the diabetic foot outpatient clinic weekly for the next 3 months.



**Fig. (1): patient underwent midfoot debridement.**

### Results

In our study on 50 patients with diabetic foot infection admitted to our hospital 10 patients started with foot debridement operation, 20 patients started with toe or more amputation, 2 patients started with metatarsal amputation, 2 patients started with major amputation (below or above knee) and 16 patients started with vascular intervention operation while the final

results of these 50 patients were: 13 patients ended with debridement, 22 patients ended with toe or more amputation, 7 patients ended with metatarsal amputation and 9 patients ended with major amputation (below or above knee).

Fifty patients were submitted to the study 11 of them were females and 39 were males (Table 1).

**Table (1):** Comparative study between outcome and gender using Chi square Test ( $\chi^2$ ).

			Category				$\chi^2$	P	Sig.
			Debridement	Toe(s) amputation	Metatarsal amputation	Major amputation			
Sex	Males	N.	11	16	6	6	3.004	0.484	NS
		%	84.6%	72.7%	100.0%	77.7%			
	Females	N.	2	6	0	3			
		%	10.4%	27.3%	0.0%	33.3%			

The age ranges between 40 and 70 with main age of  $59.1 \pm 7.7$  years, patients Who underwent major amputations were older (Table 2).

**Table (2):** Comparative study between different outcomes and age using One way ANOVA Test (F).

		N	Mean	SD	F	P	Sig.
Age	Debridement	13	58.10	4.997	2.479	0.027	S
	Toe(s) amputation	22	57.09	7.849			
	Metatarsal amputation	6	60.17	9.600			
	Major amputation	9	64.78	7.102			

As regard special habits, there was a significantly higher number of smokers in the metatarsal and major amputation group (Table 3).

**Table (3):** Comparative study between outcome and special habit.

			Category			
			Debridement	Toe(s) amputation	Metatarsal amputation	Major amputation
Special H.	Non-smoker	N.	7	13	2	4
		%	53.8%	59.1%	33.3%	44.4%
	Ex-smoker	N.	3	0	1	1
		%	23.1%	22.7%	16.7%	11.1%
	Smoker	N.	3	4	3	4
		%	23.1%	18.2%	50.0%	44.4%

As regard the character of the lesion:

- 1- Site: patients were classified into 4 groups according to the site of the lesion (toe, forefoot, midfoot, hindfoot).
- 2- Discharge.
- 3- Ischemia and ABI.
- 4- Osteomyelitis in foot X- rays.

There was a higher incidence of ischemia and osteomyelitis in major amputation groups ( $p=0.016$ ) and ( $p=0.009$ ) respectively (Table 4 & 5).

**Table (4):** Lesions characteristics of studied patients

Lesion characteristics		N.	Percent (%)
Site of lesion	Forefoot	19	38.0
	Midfoot	3	6.0
	Hindfoot	0	10.0
	Toe	23	46.0
Discharge		24	48.0
Ischemia		8	16.0
Vascular operations		6	12.0
Osteomyelitis		10	20.0

\* N.B. 7 of all patients underwent revascularization operations.

**Table (5):** Comparative study between outcome and lesion characteristics using Chi square Test (X<sup>2</sup>)

			Category	X <sup>2</sup>	P	Sig.			
			Debridement	Toe(s) amputation	Metatarsal amputation	Major amputation			
Discharge	Yes	N.	4	11	4	0	2.620	0.478	NS
		%	30.8%	50.0%	66.7%	50.6%			
Ischemia	Yes	N.	0	2	2	4	10.017	0.016	S
		%	0.0%	9.1%	33.3%	44.4%			
Vascular op.	Yes	N.	0	2	2	2	0.420	0.087	NS
		%	0.0%	9.1%	33.3%	22.2%			
Osteomyelitis	Yes	N.	0	7	3	0	9.048	0.009	HS
		%	0.0%	31.8%	50.0%	50.6%			
Site of lesion	Forefoot	N.	0	6	4	4	13.646	0	NS
		%	38.0%	27.3%	66.7%	44.4%			
	Midfoot	N.	1	1	0	1			
		%	4.7%	4.5%	0.0%	11.1%			
	Hindfoot	N.	3	0	0	2			
		%	23.1%	0.0%	0.0%	22.2%			
	Toe	N.	4	10	2	2			
		%	30.8%	68.2%	33.3%	22.2%			

Patients underwent major amputations had higher Wagner score and lower ABI than other patients with the p = 0.000 in both (Table 6 & 7).

**Table (6):** ABI and Wagner score of studied patients

	Mean	SD	Range	
			Minimum	Maximum
ABI	0.9	0.2	0.3	1.1
Wagner score	2.7	1.1	1.0	5.0

**Table (V):** Comparative study between different outcomes and ABI and Wagner score using One way ANOVA Test (F)

		N	Mean	SD	F	P	Sig.
<b>ABI</b>	<b>Debridement</b>	13	0.980	0.0801	7.927	0.000	HS
	<b>Toe(s) amputation</b>	22	0.900	0.1718			
	<b>Metatarsal amputation</b>	6	0.717	0.2808			
	<b>Major amputation</b>	9	0.733	0.2449			
<b>Wagner score</b>	<b>Debridement</b>	13	1.79	0.947	11.179	0.000	HS
	<b>Toe(s) amputation</b>	22	2.73	0.703			
	<b>Metatarsal amputation</b>	6	3.77	0.816			
	<b>Major amputation</b>	9	3.44	1.014			

As regard laboratory data obtained from the patients, all were significant except random blood sugar and bleeding profile (Table ^ & 9).

**Table (^):** Baseline laboratory data of studied patients.

	Mean	SD	Range	
			Minimum	Maximum
Hemoglobin	11.6	1.8	7.9	10.6
<b>WBC</b>	13.3	0.4	4.7	27.0
<b>PNL</b>	71.8	12.7	33.0	90.6
<b>PLT</b>	363.2	176.4	167.0	1024.0
<b>Creatinine</b>	1.2	1.1	0.0	8.2
<b>BUN</b>	47.4	26.1	12.0	148.0
<b>Alt</b>	19.9	18.4	2.0	110.0
<b>Ast</b>	20.8	14.4	3.0	76.0
<b>Albumin</b>	3.4	0.0	2.4	4.0
<b>RBS</b>	284.7	114.7	113.0	714.0
<b>A1c (%)</b>	10.3	2.0	6.0	10.0
<b>INR</b>	1.3	0.3	1.0	2.2
<b>PT</b>	17.3	3.0	12.0	31.0

**Table (9):** Comparative study between different outcomes and baseline laboratory data using One way ANOVA Test (F)

		N	Mean	SD	F	P	Sig.
<b>Hemoglobin</b>	<b>Debridement</b>	13	12.73	1.383	3.091	0.036	S
	<b>Toe(s) amputation</b>	22	11.03	1.942			
	<b>Metatarsal amputation</b>	7	11.00	1.001			
	<b>Major amputation</b>	9	10.46	1.744			
<b>WBC</b>	<b>Debridement</b>	13	10.423	3.3750	0.121	0.004	S
	<b>Toe(s) amputation</b>	22	12.709	4.2309			
	<b>Metatarsal amputation</b>	7	14.720	9.7840			
	<b>Major amputation</b>	9	18.309	3.3190			
<b>PNL</b>	<b>Debridement</b>	13	72.931	7.9089	7.809	0.001	HS
	<b>Toe(s) amputation</b>	22	70.990	13.7094			
	<b>Metatarsal amputation</b>	7	70.417	9.9907			
	<b>Major amputation</b>	9	83.922	7.1277			
<b>PLT</b>	<b>Debridement</b>	13	200.38	71.111	0.009	0.002	HS
	<b>Toe(s) amputation</b>	22	377.40	174.789			
	<b>Metatarsal amputation</b>	7	304.83	48.807			
	<b>Major amputation</b>	9	023.00	229.710			

**Table (9):** Continued.

		N	Mean	SD	F	P	Sig.
<b>Creatinine</b>	<b>Debridement</b>	13	0.884	0.2231	2.041	0.012	HS
	<b>Toe(s) amputation</b>	22	1.002	0.0878			
	<b>Metatarsal amputation</b>	7	1.300	0.9704			
	<b>Major amputation</b>	9	2.107	2.3170			
<b>BUN</b>	<b>Debridement</b>	13	30.08	9.278	7.404	0.000	HS
	<b>Toe(s) amputation</b>	22	40.91	18.948			
	<b>Metatarsal amputation</b>	7	04.33	29.091			
	<b>Major amputation</b>	9	77.77	34.939			
<b>Alt</b>	<b>Debridement</b>	13	17.92	11.079	4.096	0.049	S
	<b>Toe(s) amputation</b>	22	14.36	7.939			
	<b>Metatarsal amputation</b>	7	30.33	22.777			
	<b>Major amputation</b>	9	29.11	34.302			
<b>Ast</b>	<b>Debridement</b>	13	18.92	12.874	0.046	0.030	S
	<b>Toe(s) amputation</b>	22	17.09	0.830			
	<b>Metatarsal amputation</b>	7	31.00	21.717			
	<b>Major amputation</b>	9	28.00	20.737			
<b>Albumin</b>	<b>Debridement</b>	13	3.010	0.0398	3.923	0.014	S
	<b>Toe(s) amputation</b>	22	3.040	0.4788			
	<b>Metatarsal amputation</b>	7	2.800	0.4278			
	<b>Major amputation</b>	9	3.177	0.0292			





Table (9): Continued.

		N	Mean	SD	F	P	Sig.
<b>RBS</b>	<b>Debridement</b>	13	200.38	102.773	1.223	0.312	NS
	<b>Toe(s) amputation</b>	22	271.00	114.707			
	<b>Metatarsal amputation</b>	6	319.83	108.836			
	<b>Major amputation</b>	9	337.33	92.121			
<b>A/c (%)</b>	<b>Debridement</b>	13	8.977	1.8180	11.130	0.002	S
	<b>Toe(s) amputation</b>	22	10.218	2.0763			
	<b>Metatarsal amputation</b>	6	10.917	3.4149			
	<b>Major amputation</b>	9	12.267	2.0913			
<b>INR</b>	<b>Debridement</b>	13	1.284	0.329	0.003	0.782	NS
	<b>Toe(s) amputation</b>	22	1.340	0.2411			
	<b>Metatarsal amputation</b>	6	1.373	0.3334			
	<b>Major amputation</b>	9	1.420	0.1908			
<b>PT</b>	<b>Debridement</b>	13	10.769	2.4068	0.477	0.700	NS
	<b>Toe(s) amputation</b>	22	17.191	2.1071			
	<b>Metatarsal amputation</b>	6	17.017	7.8110			
	<b>Major amputation</b>	9	16.489	1.0696			

All patients had culture and sensitivity test , the results had been classified into 3 groups: Gram -ve organisms, Gram +ve organisms and mixed organisms (Table 10 & 11).

Table (10): Culture findings of studied patients.

		N.	Percent (%)
<b>Culture gram</b>	<b>Gram +ve</b>	13	26.0
	<b>Gram -ve</b>	30	60.0
	<b>± growth (mixed)</b>	7	14.0

Table (11): Organism distribution in culture of studied patients.

		N.	Percent (%)
<b>Culture organism</b>	<b>bacilliklebs.</b>	0	0.0
	<b>bacilliklebs. proteus</b>	2	4.0
	<b>bacilliproteus, ecoli</b>	1	2.0
	<b>bacilliproteus ,psudo.</b>	1	2.0
	<b>bacilliecoli</b>	7	14.0
	<b>bacilliecoli, klebs</b>	1	2.0
	<b>bacilliecoli, psudo.</b>	3	6.0
	<b>bacilliklebs.</b>	6	12.0
	<b>bacillipsudomonus</b>	3	6.0
	<b>bacillipsudomonus, klebs.</b>	1	2.0

	cocci	13	26.
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## Discussion

In our study we found that debridement was the first and most important step in healing of diabetic foot infection by removal of all non-viable and infected tissue (including bone) in some cases from open wounds, also surrounding callosities, until a new border of healthy, bleeding soft tissue and this matches with Berm et al., who mentioned that extensive sharp excision debridement has five aims (removes local contaminated bacteria, stimulates healing, documents the absence of hyper keratotic tissue and tumor, decreases local infection and assesses depth of infection in addition to any potential penetration into bones and joints and along tendon sheaths).<sup>(4)</sup>

Cultures should be obtained not to diagnose the infection, but to determine which organism is causing the clinically diagnosed infection in order to aid in antibiotic selection. After removing overlying necrotic debris, specimens should be obtained from the wound base or deeper tissues for culture. Specimen for culture should not be taken from undebrided wounds or from wound drainage due to poor correlation with deep cultures.<sup>(11)</sup>

Our study examined whether or not certain baseline personal, clinical and laboratory features can predict the risk for overall and major amputations in a diabetic foot infection episode.

It was shown that limb ischemia, ABI, osteomyelitis, presence of gangrene (Wagner score) were major independent predictors of overall and major amputations. In concordance with our results, previous studies by Reiber et al.,<sup>(11)</sup> Mayfield et al.,<sup>(17)</sup> and Flores et al.,<sup>(17)</sup> also showed that limb ischemia, ABI and osteomyelitis are associated with an increased risk for amputation.

Eneroth et al., found that limb ischemia was an independent risk factor for amputation.<sup>(14)</sup> Diamantopoulos et al., showed that limb ischemia was the major factor

associated with worse outcome in diabetic foot infections. And the relationship between major amputation rate and the presence of limb ischemia was very strong.<sup>(19)</sup>

Our study show that low ABI is a major predictor factor associated with worse outcome in diabetic foot infections, similar to findings by and Hamalainen et al.,<sup>(13)</sup> and Pittet et al.,<sup>(16)</sup> which showed that patients with  $ABI < 0.7$  (indicating vasculopathy) underwent major amputations more frequent, in comparison with patients with  $ABI \geq 0.7$ . The  $ABI < 0.7$  was found to be highly significant in predicting limb loss ( $P = 0.000$ ).

Eneroth et al., Similar to our study reported that a diabetic foot wound exposing the bone was more likely to be associated with amputation and shows that deep infections and osteomyelitis were reported to be associated with threefold increased risk for amputation.<sup>(14)</sup>

A high Wagner grade was another strong predictor of the foot infection management outcome. Oyibo et al., reported that the Wagner grade significantly correlated with the risk of amputation.<sup>(14)</sup> Also, Calhoun et al., reported that increased Wagner grade was associated with a higher treatment failure. Ulcers of Wagner grades 4 and 5 denote the presence of local or diffuse gangrene, which are usually due to a combination of ischemia and infection. It is thus not surprising that grade 4 and 5 ulcers were very strongly associated with amputation in our study. Wagner classification, was an independent predictor of amputation.<sup>(14)</sup>

Through our study we found that several other baseline personal characteristics such as older age, and smoking were found to be associated with either overall or major amputations. It show a significant association between the age of the patient and overall and major amputations, similar to findings by Leung et al.,<sup>(17)</sup> and Santos et al.,<sup>(17)</sup> Which show that, thirty-eight

percent of patients older than age 70 suffered limb loss in comparison to 14.0% of patients younger than age 70 y. Patients older than age 70 were found to be a significant predictive factor for limb loss ( $P=0.026$ ).

Gender in our study was not found to be an important predictive factor for limb loss ( $P=0.484$ ). This is similar to findings by Miyajima et al.,<sup>(17)</sup> and Gurlek et al.,<sup>(18)</sup> ( $P=0.310$ ), although Hamalainen et al.,<sup>(14)</sup> showed otherwise, indicating that the male gender has a higher risk of undergoing lower extremity amputations.

Also our study shows that there is a significantly higher number of smokers in the metatarsal and major amputation group. J. Joseph Anderson et al., reported that smoker diabetic patients underwent more amputations, as well as more proximal amputations than those who did not smoke. The higher amount of smoking in pack years followed an increasing trend of more proximal amputations as well. ( $p=0.038$ ).<sup>(19)</sup>

Baseline laboratory predictors of overall and major amputation were evaluated by increased levels of WBC, PNL, PLT, creatinine, and glycosylated hemoglobin and decreased levels of hemoglobin and albumin were found to be associated with greater risk for overall amputations. We also found that baseline levels of WBC and PNL were related to outcome. In a prospective study, Lipsky et al., showed that elevated baseline levels of (WBC), PNL was associated with clinical treatment failure in diabetic foot infections treated with broad spectrum antibiotics.<sup>(11)</sup>

Leukocytosis was related to worse clinical outcomes in diabetic foot ulcer. A WBC count  $>12.0$  cells/ $\mu$ L was associated with increased risk for amputation.<sup>(17)</sup>

We also found that decrease the level of blood hemoglobin, was related to outcome of the diabetic foot infection and it can strongly predicted major amputation with ( $p=0.036$ ) Similarly, SenaYesil et al., found that decreased hemoglobin levels were associated with high amputation risk.<sup>(18)</sup>

Our study shows that high level of glycosylated hemoglobin in diabetic patients associated with increase the risk for major and over all amputations with ( $p=0.002$ ), Similar to our results, Andrea L.

et al., showed that diabetic foot wound outcome worse in patients with high blood glycosylated hemoglobin level more than in others with normal blood A<sup>1</sup>c.<sup>(19)</sup>

In concordance with our results, previous studies also showed that low serum albumin was reported to be associated with increased amputation risk.<sup>(17)</sup>

We also found that high Creatinine is a major predictor factor associated with worse outcome in diabetic foot infections, similar to findings Pittet et al.,<sup>(20)</sup> and Upchurch et al.,<sup>(21)</sup> showed a significant association between high Creatinine level of the patient and overall and major amputations. Limb loss occurred in 21.7% of patients with  $Cr \geq 100 \mu\text{mol/l}$ .  $Cr \geq 100 \mu\text{mol/l}$  was found, to be a highly significant predictive factor for limb loss ( $P=0.001$ ) elevated CRP levels and elevated Cr levels were useful in signalling severe infection and predicting limb loss.

However, a study by Santos et al., did not find Cr, glucose and WBC levels to be significant risk factors for major amputations.<sup>(17)</sup>

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