

ORIGINAL RESEARCH



## THE IMPACT OF TREATMENT WITH METFORMIN ON DIABETIC FOOT ULCER AMONG DIABETIC PATIENTS VISITING JORDANIAN ROYAL MEDICAL SERVICES

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### ABSTRACT:

**Introduction:** Diabetic foot is one of the common complications associated with diabetes. The treatment of metformin may help in reducing the prevalence of diabetic foot ulcer among diabetic patients.

**Study objectives:** To investigate the prevalence of diabetic foot ulcer among diabetic patients attending out-clinic patients at Jordanian Royal Medical Services and to investigate the impact of metformin treatment in the development of diabetic foot ulcer.

**Methodology:** A retrospective design was involved to collect data from files of diabetic patients. Study variables included some demographic variables such as gender and age; and clinical variables such as duration of diabetes, treatment with metformin, and the status of diabetic foot ulcer. Data were collected and entered into SPSS version 20 for analyzing purposes. Statistical analysis included descriptive features such as frequency, percentage, mean and standard deviation. The relationship between variables was examined using various statistical models such as Chi-Square test, One Way Anova, and Pearson's correlation. The significance was accepted if  $p \leq 0.05$ .

**Results:** Study included 62 diabetic patients; the mean age was  $56.95 \pm 11.98$  years. The males were 33 (53.2%), the duration of diabetes was  $7.5 \pm 5.86$  years; about 66% of patients were prescribed for metformin, the mean of metformin dose was  $1617.32 \pm 649.49$  mg, and the prevalence of DF was 8.1%. No significant relationships were observed between DF and each of gender and metformin use ( $p > 0.05$ ). Both One Way Anova Test and correlation test showed that DF was significantly associated with DF.

**Conclusion:** The present study showed that treatment by metformin is associated significantly with metformin dose and could help diabetic patients against developing DF.

**Keywords:** Diabetic foot (DF), Diabetes, Metformin, Ulcer.

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**INTRODUCTION:**

Diabetes is not a single disease, but it is a group of metabolic diseases and characterized by hyperglycemia and abnormal lipid metabolism, carbohydrates and insulin resistance and is considered as the main cause of death globally for non-communicable diseases<sup>1</sup>.

Epidemiological studies showed that about 382 million people were diagnosed to have DM in 2013 in global level and this number is expected to increase to 592 million cases worldwide<sup>2</sup>. Diabetes is associated with various complications such as cardiovascular complications, vascular insufficiency, renal damage, retinopathy and diabetic foot (DF). These complications lead to low quality of life of diabetic patients<sup>3</sup> and burden healthcare systems<sup>4-7</sup>.

DF is considered one of the most important complications of diabetics with large cost impacts and quality of life of the patients. DF is the main cause of non-traumatic amputation at global level<sup>4, 8</sup>. At the international level, the prevalence of DF has been estimated to range from 4.4 to 10.5%<sup>9</sup>.

The development of diabetic foot lesions is considered a complicated matter and requires the presence of three factors: neuropathy, peripheral vascular disease, and infection<sup>10-11</sup>.

Several studies have indicated to the mechanisms by which metformin lowers the risks of microvascular and macrovascular disease including reduced weight gain and hyperinsulinemia, enhancing the function of endothelial function, and fibrinolysis, and reduction of low grade inflammation, oxidative stress, and glycation<sup>12-14</sup>.

Patients with diabetes mellitus are more likely to need insulin treatment<sup>15</sup>. However, other studies

conducted in diabetic patients treated with insulin have revealed the potential of metformin to enhance glycemic control and to lower insulin needs and weight gain<sup>16-18</sup>.

**STUDY OBJECTIVES:** To investigate the prevalence of diabetic foot ulcer among diabetic patients attending out-clinic patients at Jordanian Royal Medical Services and to investigate the impact of metformin treatment in the development of diabetic foot ulcer.

**METHODOLOGY:** A retrospective design was conducted to collect data from files of diabetic patients. Study sample included 62 files of diabetic patients. Study variables included some demographic variables such as gender and age; and clinical variables such as duration of diabetes, treatment with metformin, and the status of diabetic foot ulcer. Data were collected and entered into SPSS version 20 for analyzing purposes. Statistical analysis included descriptive features such as frequency, percentage, mean and standard deviation. The relationship between variables was examined using various statistical models such as Chi-Square test, One Way Anova, and Pearson's correlation. The significance was accepted if  $p \leq 0.05$ .

**RESULTS:****Characteristics of study participants**

Data presented in table (1) indicated that there were 62 diabetic patients in the study. The mean age was 56.95±11.98 years. The frequency of gender revealed that males were 33 (53.2%) (Figure 1); the duration of diabetes was 7.5±5.86 years; metformin use was documented in about 66% of diabetic patients (Figure 2); the mean of metformin dose was 1617.32±649.49 mg, and the prevalence of DF was 8.1% (figure 3).

**Table 1: Characteristics of study participants**

Variable	Description
Age (M±SD) years	56.95±11.98
Gender (N, %):	
- Males	33 (53.2%)
- Females	29 (46.8%)
Duration of diabetes (M±SD) years	7.5±5.86
Metformin use (N, %):	
- Yes	41 (66.1%)
- No	21 (33.9%)
Metformin dose (M±SD) mg	1617.32±649.49
Diabetic foot (N, %):	
- Yes	5 (8.1%)

- No	57 (91.9%)
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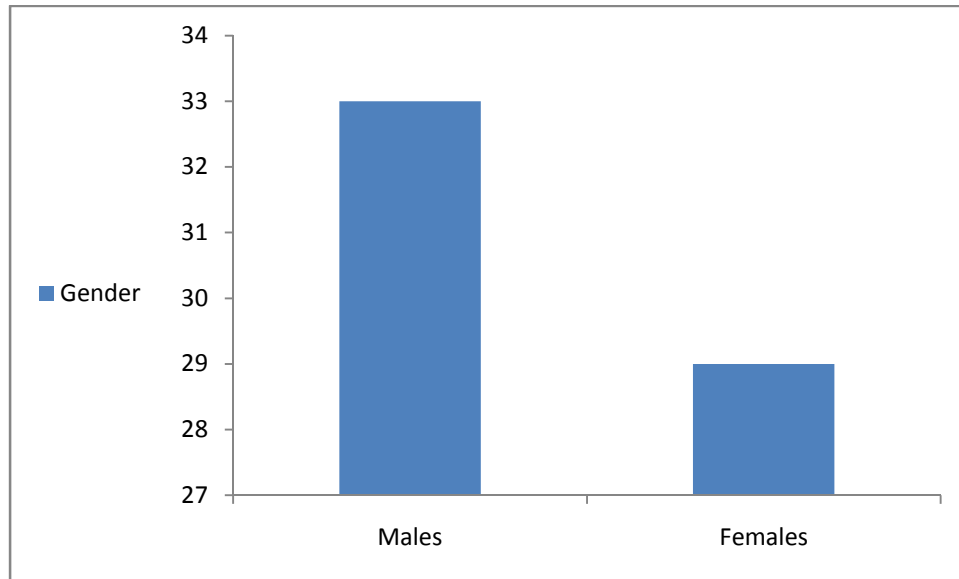


Figure 1: Frequency of diabetic patients by gender

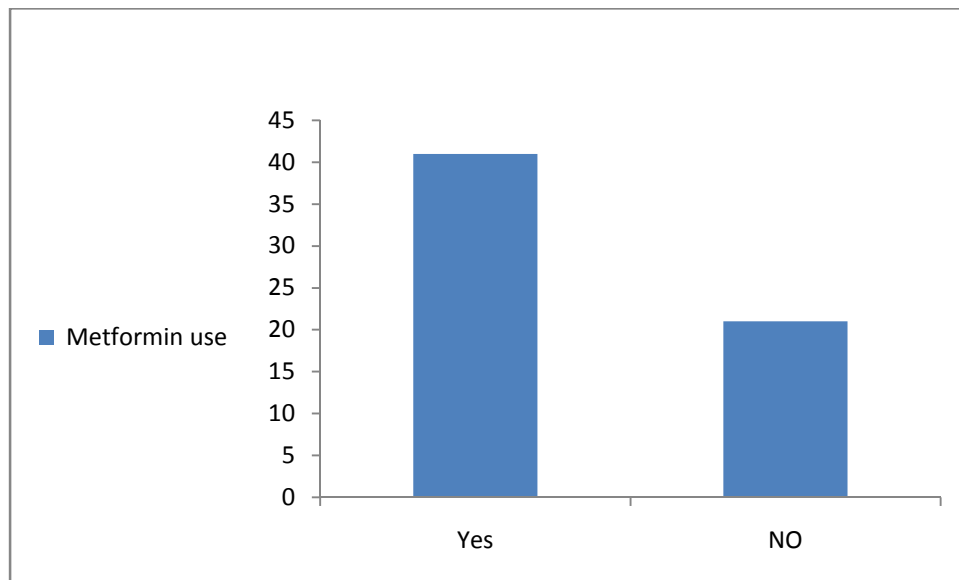
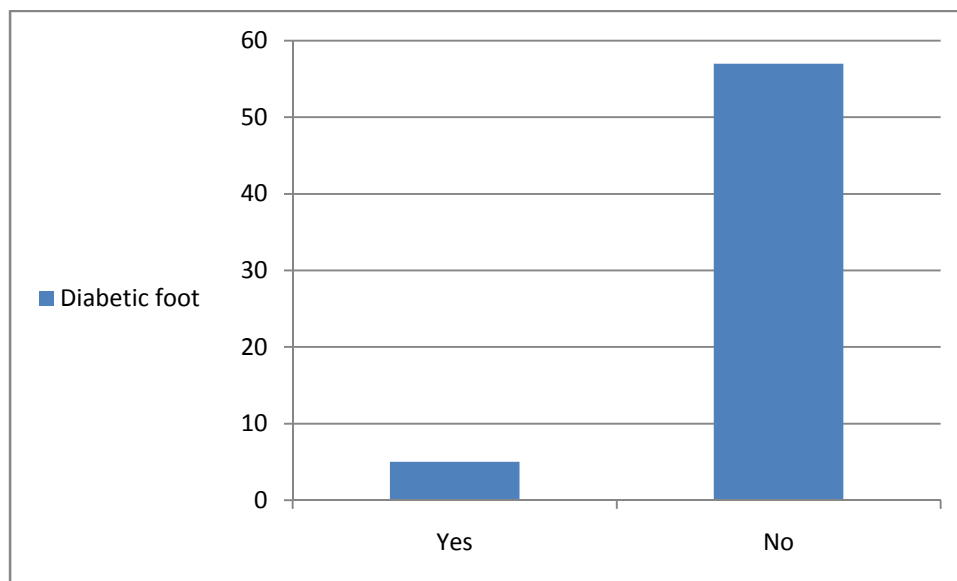


Figure 2: Frequency of diabetic patients by metformin use



**Figure 3: frequency of diabetic foot by diabetic patients**

**The relationship between DF and study variables**

The relationship between diabetic DF and study variables was investigated based on Chi-Square test. The relationship between DF and gender was not

statistically significant ( $p=0.658$ ). The relationship between DF and metformin use was also investigated and it was not statistically significant ( $p=0.157$ ). A trend was observed in which all diabetic patients who developed DF were treated by metformin (table 2).

**Table 2: The relationship between diabetic foot and study variables (based on Chi-Square test)**

Variable	DF				P value
	Yes		No		
	N	%	N	%	
<b>Gender:</b>					<b>0.658</b>
- Males	2	6.1	31	93.9	
- Females	3	10.3	26	89.7	
<b>Metformin use:</b>					<b>0.157</b>
- Yes	5	12.2	36	87.8	
- No	0	0	21	100	

**Predictors of DF from study variables**

To determine the predictors of DF from study variable, One Way Anova Test was used. As shown

in table 3, there was no any significant relationship between DF and all study variables ( $p>0.05$ ), except metformin dose which was significantly associated with DF ( $p=0.05$ ).

**Table 3: Predictors of DF from study variables**

		Sum of Squares	df	Mean Square	F	Sig.
Age	Between Groups	8.476	1	8.476	0.058	0.810
	Within Groups	8740.379	60	145.673		
	Total	8748.855	61			
Gender	Between Groups	.095	1	.095	0.372	0.544
	Within Groups	15.340	60	.256		
	Total	15.435	61			
Duration	Between Groups	100.183	1	100.183	3.013	0.088
	Within Groups	1995.063	60	33.251		
	Total	2095.246	61			
Metformin use	Between Groups	.624	1	.624	2.823	0.098
	Within Groups	13.263	60	.221		
	Total	13.887	61			
Metformin dose	Between Groups	1829015.134	1	1829015.134	4.085	0.050
	Within Groups	17463789.744	39	447789.481		
	Total	19292804.878	40			

**Correlation between study variables:** The correlation between study variables was examined,

the only significant correlation was observed between DF and metformin dose ( $p=0.308$ ).

**Table 4: Correlation between DF and study variables**

Variable		DF	Age	Gender	Duration	Metformin use	Metformin dose
DF	Pearson Correlation	1	0.031	0.079	0.219	0.212	0.308
	Sig. (2-tailed)		0.810	0.544	0.088	0.098	0.050
	N	62	62	62	62	62	41

**DISCUSSION:** The present study was conducted to determine the prevalence of DF among diabetic patients and to investigate the impact of metformin treatment in the development of diabetic foot ulcer.

The results of this study showed that the prevalence of DF was 8.1%. Actually, this finding is consistent with other studies in which the prevalence of DF ranged from 4.4 to 10.5%<sup>9</sup>. Due to the considerations that diabetes has an increasing prevalence over the

time, and the impacts of DF from economic and quality of life<sup>4, 8</sup>, it is crucial to control diabetes to minimize these impacts.

The results of this study showed that DF was significantly associated with metformin dose ( $p=0.05$ ). This finding is consistent with other reported studies in literature. These studies put focus on the mechanisms by which metformin lowers the risks of microvascular and macrovascular disease

such as lowering weight gain and hyperinsulinemia, enhancing the function of endothelial function, and fibrinolysis, and reduction of low grade inflammation, oxidative stress, and glycation<sup>12-14</sup>. Other studies showed that other benefits of metformin treatment through enhance glycemic

control and to lower insulin needs and weight gain<sup>16-18</sup>.

**CONCLUSIONS:** The present study showed that treatment by metformin is associated significantly with metformin dose and could help diabetic patients against developing DF.

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