



**ANTIMICROBIAL ACTIVITY OF ASPERGILLUS GLIOTOXIN ON *S. AUREUS* IN  
DIABETIC'S PATIENT'S TYPE-2**

Anaam F.\*<sup>1</sup>, Eptissam Y. Pirko<sup>2</sup>, Adawia F. Abaas<sup>3</sup> and Burooj M. Razooqi Al-Aajem<sup>4</sup>

<sup>1</sup>Assistant Prof., (PhD.) Department of Microbiology, College of Science.

<sup>2</sup>Assistant Lecture, (PhD.) Department of Microbiology, College of Medicine.

<sup>3</sup>Lecture, (PhD.) Department of Microbiology, College of Medicine.

<sup>4</sup>Assistant Prof., (M.Sc.) Department of Microbiology, College of Medicine, Diyala University, Diyala, Iraq.

\*Corresponding Author: Anaam F.

Assistant Prof., (PhD.) Department of Microbiology, College of Science.

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**ABSTRACT**

**Background:** Diabetes mellitus is a serious public health problem, *S. aureus* is the most common bacteria isolated from ulceration of diabetic patients, and increase the risk of *S. aureus* carriage in patients with diabetes may reflect association between diabetes and bacterial carriers. **The aim of the study** was to estimation rate of *S. aureus* carrier in diabetic's patients type-2 and determine antimicrobial effect of Gliotoxin on previous bacterial carriage in type-2 diabetes. **Patients and Methods:** The study was conducted on 450 diabetics' patients, attended the out patients clinic in Baquba Teaching Hospital, their ages ranged from 15-65 years, with mean age of 36.15, who were randomly selected, during the period from May 2016 to April 2017, patients were classified into two groups according to type of diabetes, group1 included: 184 with type1-diabetes, and group2: included 266 with type2-diabetes, 97 patients with foot ulcers. Swabs were taken from anterior nares, toe and axillae for each diabetic patient type-2, identified based on standard bacteriological methods. Using Kirby-Bauer method for detection antibacterial effect of Gliotoxin. **Results:** The results showed rates of bacterial carriage in anterior nares of type-2 diabetic patients without complications were (11.4%), (4.4%), respectively for *S. aureus* and *MRSA*, in type-2 diabetes with complications were (8.6%), (2.1%) respectively for *S. aureus* and *MRSA*. The study showed the *Aspergillus fumigatus* Gliotoxin was effective against *S. aureus* and *MRSA* carrier in diabetics patients type-2 with foot ulcer, for *S. aureus* inhibition diameter was (20.50, 16.40, 12.20) mm for different concentrations of Gliotoxin, to *MRSA* was (8.25, 6.1, 4.20) mm. Its antibacterial effect was directly proportional with its concentration According to the values of MIC & MBC, the results revealed that the Gliotoxin of *Aspergillus fumigatus* were more effective as antibacterial agent against *S. aureus* and *MRSA*. **Conclusion:** Increasing rate of *S. aureus* carrier in diabetic patient's type-2 which lead to a significantly increased risk of bacterial infections. Gliotoxin was effective as antibacterial agent against *S. aureus* in type-2 diabetes.

**KEYWORDS:** Diabetes type-1, diabetes type-2, *S. aureus* nasal carriage, *Aspergillus fumigatus*, Gliotoxin (GT).

**INTRODUCTION**

Diabetes mellitus is a serious public health problem in worldwide.<sup>[1]</sup> Infections with diabetes are one of the leading causes of human mortality. It represents a severe complication of diabetes and the most common cause of diabetes associated hospital admissions.<sup>[2]</sup> Diabetes is a chronic infection occurs when pancreas yield in sufficiently amount of insulin and may when the body cannot efficiently use the insulin.<sup>[3]</sup> *S. aureus* are the most common bacteria isolated from ulceration of diabetes<sup>[4]</sup>, chronic leg ulcers affect 1-2% of the general population and are related to increased morbidity and health costs.<sup>[5]</sup> The pathology resulting from *S. aureus* infections is of great importance due to growing resistance to antimicrobial agents.<sup>[6,7]</sup> Multiple studies

have also detected the presence of bacteria and the polymicrobial nature of chronic, non-healing wounds, and the frequency of *S. aureus* infections has to be high.<sup>[8,9]</sup> *S. aureus* is able to produce biofilms and to express antimicrobial resistance and a variety of virulence factors such as surface proteins, endotoxins, and exoenzymes which enhances its virulence.<sup>[10]</sup> The increased carriage in patients with diabetes may reflect association between diabetes and risk factors found in the general population such as, bacterial carriers among diabetic patients.<sup>[11]</sup> The increasing association of multi-drug resistant bacteria with diabetic foot ulcers is the most problem. Initial therapy of diabetic foot infections is frequently fastidious because reliable culture data is lacking.<sup>[12]</sup> *Aspergillus fumigatus* is known to produce

various mycotoxins including Gliotoxin, that is an alkaloid with a low molecular size, and possess number of immunosuppressive activities.<sup>[13]</sup> Antimicrobial activity cytokine release by leukocytes and T-lymphocyte-mediated cytotoxicity it is genotoxic and also causes apoptosis in macrophages. That is biologically active secondary metabolites causing serious risks for human and animal health.<sup>[13]</sup>

**PATIENTS AND METHODS**

The study was conducted on 450 diabetic patients ascertained from a variety of sources, attended the out patients clinic in Baquba Teaching Hospital, their ages ranged from 15-65years, during the period from May 2016 to April 2017 in Baquba city in Iraq, patients were classified into two groups according to type of diabetes, group1 included: 184 with type 1-diabetes, and group 2: included 266 with type2-diabetes, 97patients with foot ulcer. Swabs were taken from anterior nares for each diabetic patient type-2, the specimens were inoculated on Blood agar and Mannitol salt agar plates by streaking methods for isolation of aerobic bacteria, incubated aerobically at 37C for 48 hour, the isolates were identified based on standard bacteriological methods.<sup>[14]</sup> Using Kirby-Bauer method for detection antibacterial effect of *Aspergillus fumigatus* Gliotoxin (GT) that performed and extraction with slight modifications with

50 ml of chloroform and extracts by thin layer chromatography technique (TLC) according to.<sup>[15]</sup>

**Statistical analysis:** This tool calculates the z score of the mean of a single sample.

**RESULTS**

The study was conducted on 450 diabetic patients ascertained from a variety of sources, attended the out patients clinic in Baquba Teaching Hospital, their ages ranged from 15-65years, during the period from May 2016 to April 2017 in Baquba city in Iraq. Patients were classified into two groups according to type of diabetes, group1 included: 184 with type 1-diabetes, and group2: included 266 with type2-diabetes, 97 patients with foot ulcers. Swabs were taken from anterior nares for each patient with type-2diabetes for detection bacterial carriers. The results as showed in table-1 explains rates of bacterial carriage in anterior nares of type-2diabetes without complications were 21(11.4%) and 4(2.1%) respectively for *S. aureus*, *MRSA*, rates of bacterial carriage in type-2 diabetes with complications were 16 (8.6%), 4(2.1%) respectively for *S. aureus*, *MRSA*, as explain in table-2. The study showed the *Aspergillus fumigatus* Gliotoxin was effective against *S. aureus* and *MRSA* carrier in diabetics patients type-2 with foot ulcer as in table-3, for *S. aureus* inhibition diameter was (20.50, 16.40, 12.20) mm for different concentrations of Gliotoxin, to *MRSA* was (8.25, 6.1, 4.20) mm.

**Table (1): The rate of *S. aureus*, *MRSA* carriage in anterior nares of diabetics patients type-2 groups.**

Bacteria Total no.185(100)	Type-2 diabetes without complication 62(33.5)	Type-2 diabetes with complication 34(18.5)	P value
<i>Staphylococcus aureus</i>	21(11.4)	16(8.6)	0.05
Methicillin Resistance <i>S.aureus</i>	8(4.4)	4(2.1)	0.06

**Table (2): Inhibition zone (mm) of Gliotoxin on *S.aureus* and *MRSA* carrier in type-2 diabetes.**

Bacteria	2mg/ml	4mg/ml	6mg/ml	8mg/ml
<i>Staphylococcus aureus</i>	20.50	16.40	12.20	16.0
Methicillin resistance <i>S.aureus</i>	8.25	6.1	4.20	8.2

**Table (3): Values of MIC and MBC of *Aspergillus fumigatus* Gliotoxin on bacteria isolated from type-2 diabetic patients.**

Bacteria	MIC	MBC
<i>Staphylococcus aureus</i>	2	4
Methicillin resistance <i>S.aureus</i>	4	6

**DISCUSSION**

Diabetes and it complications was chronic and non-healing due to several factors such as bacteria were the predominant pathogens in the diabetic infections especially ulcers<sup>[12]</sup>, our study revealed the high prevalence rate of bacterial carriage was observed especially in type-2 diabetes with foot ulcer. *S. aureus* was the most common bacteria of community and hospital-acquired infections that can cause morbidity and mortality, *S. aureus* nasal carriage vary between diabetic patients but increased in type-2 diabetes.<sup>[13]</sup> Increase risk of *S. aureus* and multidrug resistance bacteria especially *MRSA* carriage in patients with diabetes may association

with many factors such as obesity, old age, in appropriate previous antibiotics treatment and prolonged hospital stay, and state for several months.<sup>[15]</sup>

**CONCLUSION**

Increasing rate of *S. aureus* carrier in diabetic patient's type - 2 which lead to a significantly increased risk of bacterial infections. Gliotoxin was effective as antibacterial agent against *S. aureus* in type-2diabetis.

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