*Biomedical Research 2017; 28 (22): 10186-10190* *ISSN 0970-938X*
*www.biomedres.info*

# Analysis on distribution, drug resistance and risk factors of multi drug resistant bacteria in diabetic foot infection.

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## Abstract

**Objective: To investigate the distribution, drug resistance and risk factors of Multi Drug Resistant Bacteria in diabetic foot infection (MDRMs), so as to provide reference for clinical prevention and treatment.**

**Methods: 96 cases of patients with diabetic foot infection were collected, and detection of pathogenic bacteria at infection site as well as analysis of drug sensitivity were conducted. 24 cases of MDRMs occurrence were seen as case group, and 32 cases of sensitive bacterial infection as control group, between which the comparative analysis of clinical data were conducted.**

**Results: The main MDRMs have a more serious resistance to common antibacterial drugs, and *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacteriaceae* are relatively sensitive to meropenem, *Pseudomonas* and *Enterobacteriaceae* are relatively sensitive to aztreonam; the results of single factor and multi factor analysis showed that long-term use of antibiotics (OR: 1.747; 95% CI: 1.302~2.349), combination with osteomyelitis (OR: 4.287; 95% CI: 1.613~10.865), neural ischemic wound (OR: 1.238; 95% CI: 1.164~1.384 ), >2 times/y in hospital due to the same wound (OR: 1.953; 95% CI: 1.236~8.791) were independent risk factors that cause the occurrence of MDRMs (P<0.05).**

**Conclusion: When patients with diabetic foot infection are combined with MDRMs infection, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and others are the most common. General resistance to a variety of cephalosporins, long-term use of antibiotics, combination with osteomyelitis, neural ischemic wound, >2 times/y in hospital due to the same wound are independent risk factors for the occurrence of MDRMs.**

**Keywords:** Diabetic foot, Multi drug resistant bacteria, Risk factors, Infection.

*Accepted on December 11, 2017*

## Introduction

Diabetic Foot (DF) is a common complication of diabetes, while the factors such as poor glycemic control in diabetes, longer course of disease, etc. exist, diabetic foot infections is prone to generate [1]. Foot wounds are an increasingly common problem in people with diabetes and now constitute the most frequent diabetes-related cause of hospitalization [2]. People with diabetes have about a 25% chance of developing a foot ulcer in their lifetime, about half of which are clinically infected at presentation [3]. Peripheral vascular disease and nerve abnormalities at lower limbs' far-end extremity of patients will appear, of which the main clinical symptoms is foot ulcer. After diabetic foot occurs, wound healing is not easy, which has a great impact on patients' quality of life. These diabetic foot infections are associated with poor clinical outcomes for the patient and high costs for both the patient and the health care system [4]. Patients with a DF have a 50-fold increased risk of hospitalization and 150-fold increased risk of lower extremity amputation compared with patients with diabetes and no foot infection [5]. In the recent years in clinic, diabetic foot infected by Multi Drug Resistant Bacteria (MDRMs) are not uncommon [6], which increased year by year, and long-term repeated MDRMs infection has become a major cause of amputation in patients with diabetic foot. Some studies reported that staphylococcus aureus is, by far, the most frequent pathogen isolated in diabetic foot infections either as the sole isolate or as a component of mixed infection [7]. Of major concern is the increasing incidence of Methicillin-Resistant *S. aureus* (MRSA) [8-10]. In order to investigate the distribution, drug resistance and risk factors of multi drug

resistant bacteria in diabetic foot infection, so as to provide reference for clinical prevention and treatment, the detection and analysis of MDRMs pathogen in patients with diabetic foot admitted to hospital in recent years were conducted in this study, which is reported as follows now.

## Materials and Methods

### *Clinical data*

96 cases of patients with diabetic foot infection admitted to hospital from January 2008 to June 2013 were selected as research object, including 53 cases of male patients, and 43 cases of female; aged 32~72 y old with the average (63.21 ± 6.43 y old). The detection of pathogenic bacteria at infection site as well as analysis of drug sensitivity were conducted, and 24 cases of MDRMs occurrence were seen as case group, 32 cases of sensitive bacterial infection as control group.

### *Strains culture and identification*

When patients were admitted to hospital, secretions at the infection site of diabetic foot were sampled and deep abscess could be gotten by sterile needle or at the time of debridement. The specimen were injected into culture medium for bacteria culture and identification and VITEK 32 automatic bacteria identification instrument (French bioMerieux company)was adopted for identification of pathogenic bacteria, and Kirby-Bauer (K-B) method (China, BIO-KONT)was used for drug sensitivity test.

### *Statistical analysis*

SPSS16.0 software was adopted for statistical analysis, and $\chi^2$ test was adopted for count data, measurement data was expressed by the mean ± standard deviation, and t-test was conducted. $\chi^2$ test was adopted for single factor analysis, non-conditional multi factors logistic regression analysis was used for multi factors analysis, and $P<0.05$ was seen as statistically significant difference.

## Results

### *Detection rate of MDRMs*

In 96 cases of patients, 56 cases of secretion culture in diabetic foot infection were positive with the rate of 58.33%, and 24 cases with positive MDRMs accounted for 42.86%, 32 cases of sensitive bacteria accounted for 61.14%. The differences of age, gender, blood pressure, disease course between the two groups were not significant, as seen in Table 1.

***Table 1.*** *Comparison of the clinical data between the two groups ($\bar{x}$ ± s).*

| Items | | Case group (n=24) | Control group (n=32) |
|---|---|---|---|
| Gender (case) | Male | 16 | 20 |
| | Female | 8 | 12 |
| Age (y old) | | 63.27 ± 6.40 | 63.18 ± 6.48 |
| Disease course (y) | | 11.87 ± 8.34 | 12.01 ± 7.49 |
| Glycosylated hemoglobin (%) | | 8.10 ± 1.83 | 8.03 ± 1.97 |
| Blood pressure | Diastolic pressure (mmHg) | 88.97 ± 18.65 | 90.02 ± 16.80 |
| | Systolic pressure (mmHg) | 132.42 ± 36.77 | 130.04 ± 34.88 |

### *Distribution of MDRMs*

A total of 36 strains of bacteria were isolated in case group, and MDRMs distribution and constituent ratios were seen in Table 2.

***Table 2.*** *Constituent ratios of the multidrug-resistant bacteria (%).*

| Nosophyte | Strains | Constituent ratios |
|---|---|---|
| *Staphylococcus aureus* | 17 | 47.22 |
| *Pseudomonas aeruginosa* | 10 | 27.78 |
| *Enterobacteriaceae* | 6 | 16.67 |
| *Acinetobacter* | 2 | 5.55 |
| *Enterococcus* | 1 | 2.78 |
| Total | 36 | 100.00 |

### *Drug resistance rate of MDRMs*

Drug resistance rate of main MDRMs to antibacterials is shown in Table 3.

### *The risk factors for MDRMs occurrence in diabetic foot infections*

The results of single factor analysis showed that long-term use of antibiotics, combination with osteomyelitis, neural ischemic wound, >2 times/y in hospital due to the same wound were single risk factors that cause the occurrence of MDRMs ($P<0.05$), as shown in Table 4. Non-conditional multi factors logistic regression analysis also showed that long-term use of antibiotics (OR: 1.747; 95% CI: 1.302~2.349), combination with osteomyelitis (OR: 4.287; 95% CI: 1.613~10.865), neural ischemic wound (OR: 1.238; 95% CI: 1.164~1.384), >2 times/y in hospital due to the same wound (OR: 1.953; 95% CI: 1.236~8.791) were independent risk factors of MDRMs occurrence ($P<0.05$), as seen in Table 5.

***Table 3.*** *Drug resistance rates of the major species of multidrug-resistant bacteria (%).*

| Antibacterials | *Staphylococcus aureus* (n=17) | *Pseudomonas aeruginosa* (n=10) | *Enterobacteriaceae* (n=6) |
|---|---|---|---|

| | Strains | Drug resistance rate | Strains | Drug resistance rate | Strains | Drug resistance rate |
|---|---|---|---|---|---|---|
| Oxacillin | 17 | 100 | - | - | - | - |
| Ampicillin | - | - | - | - | 6 | 100 |
| Cefazolin | 17 | 100 | - | - | - | - |
| Cefotaxime | - | - | 5 | 50 | 5 | 83.33 |
| Cefalotin | - | - | - | - | 6 | 100 |
| Cefatriaxone | - | - | 8 | 80 | 6 | 100 |
| Cefoperazone | - | - | 6 | 60 | 5 | 83.33 |
| Ceftazidime | - | - | 8 | 80 | 6 | 100 |
| Cefepime | - | - | 6 | 60 | 4 | 66.67 |
| Meropenem | 4 | 23.53 | 3 | 30 | 1 | 16.67 |
| Ciprofloxacin | 15 | 88.24 | 5 | 50 | - | - |
| Levofloxacin | 16 | 94.12 | 8 | 80 | 5 | 83.33 |
| Aztreonam | - | - | 2 | 20 | 1 | 16.67 |
| Ampicillin/sulbactam | 17 | 100 | 8 | 80 | - | - |
| Piperacillin/sulbactam | - | - | 5 | 50 | 6 | 100 |
| Azithromycin | 16 | 94.12 | - | - | - | - |
| Fosfomycin | - | - | - | - | 4 | 66.67 |
| Clindamycin | 17 | 100 | - | - | - | - |

***Table 4.*** *Univariate analysis of the risk factors for diabetic foot infections caused by the multidrug-resistant bacteria and the infection rates (%).*

| Related factor | Case group (n=24) | | Control group (n=32) | | $\chi^2$ value | P value |
|---|---|---|---|---|---|---|
| | Case | Infection rate | Case | Infection rate | | |
| Long-term use of antibiotics | 23 | 95.83 | 13 | 40.63 | 18.21 | <0.05 |
| Combination with osteomyelitis | 17 | 70.83 | 5 | 15.63 | 17.53 | <0.05 |
| Combination with neuropathy | 22 | 91.67 | 28 | 87.5 | 0 | >0.05 |
| Combination with nephrotic | 21 | 87.5 | 26 | 81.25 | 0.07 | >0.05 |
| Combination with | 22 | 91.67 | 28 | 87.5 | 0.01 | >0.05 |
| retinopathy | | | | | | |
| Ulcer number>3 | 16 | 66.67 | 15 | 46.88 | 2.17 | >0.05 |
| Neural ischemic wound | 18 | 75 | 11 | 34.38 | 9.07 | <0.05 |
| >2 times/y in hospital due to the same wound | 17 | 70.83 | 7 | 21.88 | 13.42 | <0.05 |

***Table 5.*** *Multivariate analysis of the risk factors for diabetic foot infections caused by the multidrug-resistant bacteria.*

| Influencing factor | β | $s\bar{x}$ | Wald value | P value | OR value | 95% CI |
|---|---|---|---|---|---|---|
| Long-term use of antibiotics | 0.557 | 0.141 | 15.376 | 0.001 | 1.747 | 1.302~2.349 |
| Neural ischemic wound | 0.216 | 0.497 | 18.252 | 0.001 | 1.238 | 1.164~1.384 |

| | | | | | | |
|---|---|---|---|---|---|---|
| >2 times/y in hospital due to the same wound | 0.658 | 0.159 | 18.244 | 0.001 | 1.953 | 1.236~8.791 |
| Combination with osteomyelitis | 1.429 | 0.592 | 8.640 | 0.002 | 4.287 | 1.613~10.865 |

## Discussion

### *Distribution characteristic and resistance analysis of MDRMs in diabetic foot infection*

Diabetic foot is a common complication of diabetes, more prone to Infection, which leads to diabetic foot infections more pathogens [11]. Diabetic foot infection can be found in the situation of a longer disease course, poor glycemic control and so on, which is prone to repeated infection. Clinical reports have shown that pathogenic bacteria causing diabetic foot infections are widely distributed [12], and both gram positive bacteria and gram negative bacteria can be detected, among which gram positive bacteria detection rate of MDRMs in patients with diabetic foot infection is higher, and the reason may be related to the abuse of clinical broad-spectrum antibiotic, etc., resulting in gram positive bacteria detection rate of extended spectrum lactamases has increased year by year. This study showed that MDRMs in patients with diabetic foot infection admitted to hospital accounted for 42.86% of pathogenic bacteria, and 36 strains of bacteria were isolated, of which gram positive bacteria accounted for over 50.0% of MDRMs, which was similar to other studies [13] According to the results of drug susceptibility, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter* were higher on antimicrobial resistance rate, *Staphylococcus aureus*, *Pseudomonas aeruginosa, Enterobacter* spp. were relatively sensitive to meropenem, and *Pseudomonas* and *Enterobacteriaceae* were relatively sensitive to aztreonam.

### *The risk factors analysis of MDRMs in diabetic foot infection*

The study results showed that long-term use of antibiotics, combination with osteomyelitis, neural ischemic wound, >2 times/y in hospital due to the same wound were single risk factors that cause the occurrence of MDRMs ($P<0.05$), which was consistent with the clinical reports [14]. Because ineffective control from antibiotics of infection and antibiotics are often replaced, various antibacterial drugs are more used in patients with diabetic foot infection. The patients also take antibiotic for treatment by themselves before admission to hospital, increasing the appearance probability of drug-resistant bacteria. In order to prevent diabetes foot infection or diabetic foot has occurred before, part of patients take antibiotics by themselves, resulting in inducing drug-resistant gene mutation and multidrug resistance appearance. Occurrence of patients with diabetic foot infection can be easily combined with osteomyelitis, mainly because of metabolic disorders in diabetic patients, ischemic ulcer, long-term infection causing deep ulcer, resulting in destruction of bone. Once osteomyelitis occurs, pathogen in deep bone marrow is not easy to be removed, and osteomyelitis which is repeatedly delayed for healing has become the main cause of amputation for patients. The neuroischaemic wound are different with ordinary wound, and its occurrence is mainly due to blood vessel circulatory disturbance and neuropathy. In deep site of infection ulcer, relative ischemia and hypoxia condition exist, and the concentration of antibiotics is not satisfying in the deep site of infection, thus it is easy to induce the emergence of drug-resistant bacteria. >2 times/y in hospital due to the same wound is an single risk factor that cause the occurrence of MDRMs, the reason of which is long time hospitalization and recurrent ulcer infection increase the risk of cross infection in the patients, thus the prevention and control of cross infection for patients should be pay attention to in various nursing and treatment operation in the hospital.

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