Bacteria Patterns in Infected Diabetic Foot: Is There a Surgical Implication?
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ABSTRACT
Background: The number of patients suffering from diabetes and its complications in the world is doubling every 10-15 years. Apart from development of retinopathy, nephropathy, and diabetic-induced atherosclerotic changes in high caliber arteries. Critical ischemia with gangrenous changes of the lower limb has occurred quite often as a result of micro-angiopathy.
Objective: This study aimed to investigate the bacterial spreading and related outcomes of treatment in 81 patients with diabetic foot complicated by infection.
Materials and methods: A retrospective study based on the analysis of the patients medical records from the hospital database. The bacteriological analysis of the tissues from infected wounds, obtained during surgical debridement or amputation, were conducted in all patients. Microbiological investigations of the the contents of an aerobic and anaerobic bacterial flora in the wounds were compared and analyzed in all cases considered suitable for this study.
Results: Analysis of microbial spreading revealed growth of bacteria in all diabetic foot wounds. Associations of aerobes with anaerobes were found in 89.9 % of the cases. Escherichia coli was the dominating agent among anaerobes (22%), leading to development of infectious process and distributed in a proximal direction along synovial-tendon sheets of the foot.
Conclusion: Aggressive debridement of necrotized tissues, including proximal and distal parts of tendons up to 5 cm within the limits of healthy looking tissues may disrupt further spreading of purulent infection and lead to favorable outcome.
Keywords: diabetic foot, diabetic infection, diabetic complications, bacterial spreading.

INTRODUCTION
Currently diabetes mellitus is one of the major problems of modern endocrinology. The number of patients suffering from this condition and its complications in the world is doubling every 10-15 years.1,2 Apart from development of retinopathy, nephropathy, and diabetic-induced atherosclerotic changes in high caliber arteries. Critical ischemia with gangrenous changes of the lower limb has occurred quite often as a result of micro-angiopathy.3,4 The attention of the surgeons first of all is attracted by the fast development of necrotizing processes in distal foot associated with a virulent infection which leads to high morbidity and mortality. Among some major reasons in development of this complication are late detection of diabetes, the aggressiveness of the disease, lack of dynamic self-assessment, and poorly controlled hyperglycemia.5,6 As a result of critical ischemia concerning gangrene of the lower extremity, more than 200,000 high amputations performed annually in the world. According to the World Health Organization data, from 45 up to 70% of non-traumatic amputations of the lower extremity are made for patients with diabetes mellitus.7
A leading role in the development of a necrotic process in diabetic foot has fast spreading of infection in a proximal direction in conditions of angiopathy and neuropathy. However, mechanisms and pathways of distribution of infection in foot and shin are not clear and poorly understood.8,9 The aims of this study were to analyze the diabetes related infections and investigation of possible correlations with the rate and level of amputations. We believe that a better understanding of the problem could increase the effectiveness of surgical treatment of diabetic foot.
Also, the identification of bacterial patterns in complicated infected diabetic foot and their possible surgical implications?

MATERIALS AND METHODS
This retrospective study was based on the data obtained from the Department of Surgery at King Khaled Hospital in Al Kharj city with population in the region over 650,000 people. Medical records of 81 patients admitted from 2010 to 2015 with
complicated diabetic foot wounds, who received surgical treatment were reviewed. Microbiological studies were conducted on all patients after the specimens were collected from the infected wounds. According to the hospital microbiology department specimen collected before necrotic tissues were debrided. Microbiological study also included biopsy from the exposed tendons adjacent to the wound. Cultures were processed by standard procedures in the microbiology laboratory for gram stains and antibiotic sensitivity. The results of microbiological studies were collected and analyzed from the patient’s medical records.

Excel 2016 computer software was used for statistical calculations in this study. Correlation of finding with P value < 0.05 was considered as significant. The access to the patient’s records for this retrospective study was approved by the King Khaled Hospital, which is a major teaching for the College of Medicine at the Prince Sattam bin Abdulaziz University, Al Kharj, Saudi Arabia.

RESULTS
The breakdown of analysis of aerobic microorganisms shown that Pseudomonas aureginosa were isolated more often among aerobic bacteria counting for 59%, followed by Staphylococcus aureus 30% and Acient baumannii 11% respectively as shown in Table (1).

Table 1. Types of aerobic bacteria isolated from the infected diabetic wounds.

<table>
<thead>
<tr>
<th>Aerobes</th>
<th>Number of cases with isolated bacteria</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACIENT BAUMANNII</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td>PSEUDOMONAS AERUGINOSA</td>
<td>46</td>
<td>59</td>
</tr>
<tr>
<td>STAPHYLOCCUS AUREUS</td>
<td>23</td>
<td>30</td>
</tr>
<tr>
<td>Total</td>
<td>77</td>
<td>100</td>
</tr>
</tbody>
</table>

In 69 patients (89%) isolated aerobic bacteria were presented mostly by Staphylococcus aureus and Pseudomonas aureginosa (P<0.01).

Most frequently isolated anaerobic bacteria were E.Coli (22%), Proteus mirabilis (15.6%), Klebsiella pneumonia (12.5%) and Enteracoccus faecalis (12.5%). This could be attributed to the fact that gram-negative anaerobes were considered as the most aggressive pathogens. The representatives of anaerobes isolated from infected wounds are shown in Table (2).

Table 2. Type of an anaerobic bacteria isolated from the infected diabetic wounds.

<table>
<thead>
<tr>
<th>Anaerobes</th>
<th>Number of cases with isolated bacteria</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>ENTEROCOCCUS FAECALIS</td>
<td>8</td>
<td>12.5</td>
</tr>
<tr>
<td>ESCH. COLI</td>
<td>14</td>
<td>22</td>
</tr>
<tr>
<td>KLEBSIELLA</td>
<td>8</td>
<td>12.5</td>
</tr>
<tr>
<td>PNEUMONIA</td>
<td>5</td>
<td>7.8</td>
</tr>
<tr>
<td>MORGANELLA MORGANII</td>
<td>4</td>
<td>6.2</td>
</tr>
<tr>
<td>CITROBACTER</td>
<td>4</td>
<td>6.2</td>
</tr>
<tr>
<td>FREUNDII PROTEUS</td>
<td>10</td>
<td>15.6</td>
</tr>
<tr>
<td>MIRABILIS</td>
<td>4</td>
<td>6.2</td>
</tr>
<tr>
<td>SERRATIA</td>
<td>5</td>
<td>7.8</td>
</tr>
<tr>
<td>MARCESCENS</td>
<td>5</td>
<td>7.8</td>
</tr>
<tr>
<td>KLUYVERA INTERMEDIA</td>
<td>6</td>
<td>9.4</td>
</tr>
<tr>
<td>STAPHYLOCOCCUS S HAEMOLYTICUS</td>
<td>64</td>
<td>100</td>
</tr>
</tbody>
</table>

In majority of the cases (89.9%) associations of aerobic and anaerobic flora were found together, where isolated micro-flora consisted of two or more microorganisms.

Representation of isolated bacteria types in the wounds in the studied group of the patients are shown in Graph (1).
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**Figure (1):** Different types of bacteria

33 out of 81 patients had amputations of the limbs at the different levels due to progression of the infection and diabetic foot complications. The level of amputations is shown in (Graph 2). The number of isolated bacteria was correlated to the on the level of amputation. Above knee amputations (AKA) were performed in 3 patients (10.5% out of all amputations) where the combinations of more than three isolated aerobic and anaerobic cultures were identified with high prevalence of anaerobic cultures (p<0.05). 5 patients (15.1%) had below knee amputations where combination at least two aerobic and anaerobic bacteria was also identified.

**Figure (2):** Level of amputations

The mean duration of hospital stay was 21.44±17.7 days. The periods of hospital stay were also subdivided due to the severity of presentation and necessity to manage co-morbidities as shown in Table 3.
DISCUSSION

In the last decade, several studies of diabetic foot complications leading to limb amputation in DM patients have been reported. Diabetic foot in uncontrolled DM with poor tissue perfusion due to diabetic angiopathy is easily complicated by the fast spreading of bacteria, both aerobic and anaerobic in nature, which can be presented in forms of cellulitis, superficial and deep ulceration, development of partial tissues necrosis and gangrene. 11, 12

Diabetic foot is a common complication frequently presented with gangrene, which require minor or major amputations at different levels with high incidence.7

Production of gialuronidase, collagenase, fibrinolysin, elastase and other fermenting substances, produced by anaerobes lead to distraction and disintegration of the soft tissues. Thus, they create favorable environment for further growth and spreading of anaerobic infection. As the result of this spreading, fast progression of pathological process can be observed in the deep anatomical structures of foot and shin, which consequently lead to spreading of necrotizing process and unsatisfying surgical results with necessity for amputations13.

Our study demonstrated that in all the investigated cases with infected diabetic foot, 89% had isolated associations of aerobic and anaerobic bacteria. We observed from the amputated tissues, that the major role in the progressing of infection process belongs to gram-negative anaerobic pathogens, which are spreading in all directions along tendon-synovial structures of the foot. The domination of non-clostridia anaerobes can have place in poorly oxygenated soft tissues as a result of progressing ischemia due to diabetic angiopathy. The results of the microbiological studies justified compulsory usage of broad-spectrum antibiotic therapy.

Ying Huang (2016) found that there was non significant difference in the mean number of isolates per specimen between swabbing and deep tissue biopsy of diabetic foot ulcers of different grades14. To date, most researchers consider that the deep tissue biopsy is the best way for the identification of pathogens in diabetic foot infection.15

Findings of this study were in agreement with those of several studies, which reported that E. coli is considered the most common isolates in many gram-negative bacterial infections, and it is mostly susceptible to Amikacin. However, P. aeruginosa in the other studies, was found to be the third most common organism isolated from diabetic patients.16 Although the risk of missing Gram-negative bacteria remains relatively high, swab cultures together with the deep tissue biopsy appear to be very reliable for guiding the antibiotic treatment of diabetic patients, especially with wounds of grade 2 and above proposed by PEDIS system (IWGDF). 17

Patients with diabetes mellitus are more commonly presenting with severe infection. Such infections are likely to be hidden by deep fascia planes and spread undetected under normal looking skin. This fact may often appear misleading and results in delay of recognizing the extent of tissue bacterial involvement and inadequate debridement or amputation, which enhance to further morbidity. Thus, aggressive approach to surgical debridement via bigger and deeper incisions seems to be justifiable in conjunction with sensitive antibiotic therapy in consideration of poly-microbial nature of the diabetic foot infection. In terms of surgical component, we believe that this group of patients should have wider debridement of infected wound, including dissection of tendon-synovial structures of affected toes up to 5 cm within healthy tissues. This surgical approach should be carried out in light of supportive medical treatment to improve regional blood flow and topical oxygenation of tissues.

Long hospital stay for patients in this study was 21.44 +/- 17.7 days. This is a common problem in patients with diabetic foot complications due to difficulty to manage microbial infection compared to non-diabetic group due to poor tissue perfusion. Obviously attempts for conservative treatment causing delays in surgical decision making towards amputation. In addition, the slow healing factors remain and in some cases, higher amputations needed to achieve good stump healing18.

Table 3: Period of hospital stay.

<table>
<thead>
<tr>
<th>HOSPITAL STAY</th>
<th>MALE</th>
<th>PERCENTAGE</th>
<th>FEMALE</th>
<th>PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-5</td>
<td>26</td>
<td>53.1%</td>
<td>15</td>
<td>46.9%</td>
</tr>
<tr>
<td>6-10</td>
<td>10</td>
<td>20.4%</td>
<td>9</td>
<td>28.1%</td>
</tr>
<tr>
<td>11-20</td>
<td>10</td>
<td>20.4%</td>
<td>5</td>
<td>15.6%</td>
</tr>
<tr>
<td>21-30</td>
<td>3</td>
<td>6.1%</td>
<td>3</td>
<td>9.4%</td>
</tr>
</tbody>
</table>

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CONCLUSION
It is possible to conclude aggressive debridement of necrotized tissues, including proximal and distal parts of tendons up to 5 cm within the limits of healthy looking tissues may disrupt further spreading of purulent infection and lead to more favorable outcome. Preventive measures like primarily good glycemic control and appropriate foot care, well-adjusted antibiotic therapy and patient’s education may dramatically reduce incidence of amputations among Saudi patients with diabetic foot. Our study advocated that developing specialised diabetic centres working in conjunction with specialists in microbiology can minimise the negative outcome of diabetic foot complications and significantly reduce morbidity and mortality in diabetic population of Saudi Arabia.

REFERENCES