

Odontogenic infection involving the secondary fascial space in diabetic and non-diabetic patients: a clinical comparative study

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Abstract (J Korean Assoc Oral Maxillofac Surg 2013;39:175-181)

Objectives: This retrospective study was performed to evaluate the clinical impact of diabetes mellitus on the prognosis in secondary space infection.

Materials and Methods: Medical records, radiographic images, computed tomography, and microbial studies of 51 patients (25 diabetic patients and 26 non-diabetic patients) were reviewed. Patients were diagnosed as secondary fascial space infections with odontogenic origin and underwent treatment at Chonnam National University Hospital, in Department of Oral and Maxillofacial Surgery, from January 2007 to February 2009.

Results: Compared to patients without diabetes, patients with diabetes were presented with the following characteristics: older age (diabetic patients: 62.9 years, non-diabetic patients, 47.8 years), more spaces involved (diabetic patients, 60%; non-diabetic patients, 27.3%), more intense treatment, longer hospitalization (diabetic patients, 28.9 days; non-diabetic patients, 15.4 days), higher white blood cell and C-reactive protein values, higher incidence of complication (diabetic patients, 40%; non-diabetic patients, 7.7%), and distinctive main causative microorganisms.

Conclusion: These results suggest that the prognosis of diabetic patients is poorer than that of non-diabetic patients in secondary space infections since they had greater incidence rates of involved spaces, abnormal hematologic findings, more complications, and additional procedures, such as tracheostomy.

Key words: Diabetes mellitus, Diabetes complications, Bacterial infections, Abscess, Cellulitis

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I. Introduction

Diabetic mellitus (DM) can cause diabetic coma, hypoglycemia shock, retinopathy of the eye, macular edema, coronary disease, peripheral vascular disease, and cerebrovascular disease¹. Patients with DM have higher risk of infection^{2,3} due to their abnormal phagocytosis, persistent reduction of blood flow, and cell-mediated immune abnormalities typical of diabetic patients⁴. The World Health Organization classified diabetes as a cause of secondary immune deficiency⁵.

According to Delamaire et al.⁴, diabetic patients were more

susceptible to complications or infections of the blood vessels because of the functional alteration of the polymorphonuclear leukocytes in diabetic patients. Moreover, diabetic patients are reported to have problems with chemotaxis, phagocytosis, and bactericidal function, with gram-negative bacilli species as the main causative infectious bacteria in the oral cavity⁶.

There are two routes of infection in the oral and maxillofacial area: one is the route via the root apex, and the other is the route via the deep periodontal pocket. The fascial spaces that could be directly affected by odontogenic infections are called 'primary spaces', and they include canine, infratemporal, buccal, submental, submandibular, and sublingual spaces. Failure to control the infections may cause them to spread to secondary spaces including temporal, masseteric, pterygo-mandibular, lateral pharyngeal, retropharyngeal, and pre-vertebral spaces⁷. It is difficult to treat patients who have these space infections without drainage of purulent exudates, since those are connected to primary spaces and are surrounded by connective tissues that have poor blood supply. If the infections of diabetic patients spread to secondary spaces,

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they would be more severe, with the patients suffering from more complications; hence the difficulty of treatment and the need for much longer treatment period compared to patients without systemic diseases⁶.

Beck et al.⁸ reported that secondary fascial space infections can cause life-threatening complications in patients with weakened immunological functions such as diabetic patients. On the other hand, Chen et al.⁹ noted how diabetic patients normally have unique clinical features in the oral and maxillofacial areas compared to non-diabetic patients. Note, however, that there are not enough clinical studies on the difference between DM patients and non-DM patients in the treatment of fascial infection with odontogenic origin in the maxillofacial area. Therefore, this study was conducted to evaluate clinically the impact of DM on the prognosis of secondary fascial space infection.

II. Materials and Methods

1. Patients

The medical records of 51 patients diagnosed with secondary fascial space infections and treated at Department of Oral and Maxillofacial Surgery in Chonnam National University Hospital (Gwangju, Korea) from January 2007 to February 2009 were reviewed. The patients were divided into two groups: DM group and non-DM group. Patients with previous history of DM and without previous history of DM but had fasting plasma glucose level of over 126 mg/dL were classified under the DM group. Other patients who had no previous medical history and whose fasting plasma glucose level was under 126 mg/dL were classified under the non-DM group. Note, however, that we reclassified the suspected diabetic patients with an additional glucose tolerance test. At least 25 of the patients had DM, and 26 had no DM. In the DM group, 10 were male and 15 were female. In the non-DM group, 10 were male and 16 were female. All of the patients received treatment while they were hospitalized.

Investigation was done on the age of the patients, type of diffused space, type of antibiotics, duration of drug administration, number of surgical operations and tracheostomy, clinicopathological test, complications, period of hospitalization, and microorganism involved using the patients' medical records, radiography, and computed tomography (CT) between the two groups. When more than 2 spaces were involved, the case was classified as multiple secondary space infection.

2. Diagnosis of secondary fascial space infection

1) Hematologic examination

Indicators such as white blood cell (WBC), C-reactive protein (CRP), and body temperature were chosen to evaluate the extent of inflammation on the relevant patients.

2) Radiographic examination

Iopromide (Ultravist; Bayer Korea Ltd., Seoul, Korea) was used as contrast media for facial CT with enhancement. The same examiner read the CT images and performed diagnosis. (Fig. 1, Table 1)

3. Surgical procedures

We performed tracheotomy or intubation for emergency patients with dysphagia, dyspnea, and reduced oxygen saturation to secure the patients' airway. For patients who are not in emergency state, we did antibiotic and fluid therapy first, and then took CT to confirm the localization of the abscess. After that, we performed incision and drainage (I&D) with the insertion of thoracic catheters. During the procedure, we took pus cultures and selected the most specific antibiotics based on the result. The inserted tubes were replaced every 2-3 days. The silastic catheter was replaced with thoracic catheter in accordance with the extent of pus drainage. As radical therapy, root canal therapy or tooth extraction was carried out in case of tooth-origin infections.

We regarded the termination of treatment or time of discharge as the moment patients' clinical symptoms improved, with normal inflammation level in the serum laboratory test and complete treatment of involved microorganisms.

4. Bacterial culture test

Amoxicillin/clavulanic acid (Augmentin; Ilsung Pharmaceuticals Co. Ltd., Seoul, Korea) was the drug of choice as empirical antibiotics. Clindamycin (Fullgram; Samjin Pharmaceuticals Co. Ltd., Seoul, Korea) or astromycin sulfate (Fortimicin; Yungjin Pharmaceuticals Co. Ltd., Seoul, Korea) was subsequently used according to the result of a serum laboratory test. During I&D, we took the drained pus using sterile agar gel transport swabs without charcoal (Copan Italia S.p.A., Brescia, Italy). Susceptibility to various antibiotics (β -lactam, aminoglycoside, lincosamide, cephalosporin, and quinolone) was evaluated by measuring the "minimal inhibitory concentration (MIC)" of bacteria cultured for 4-5

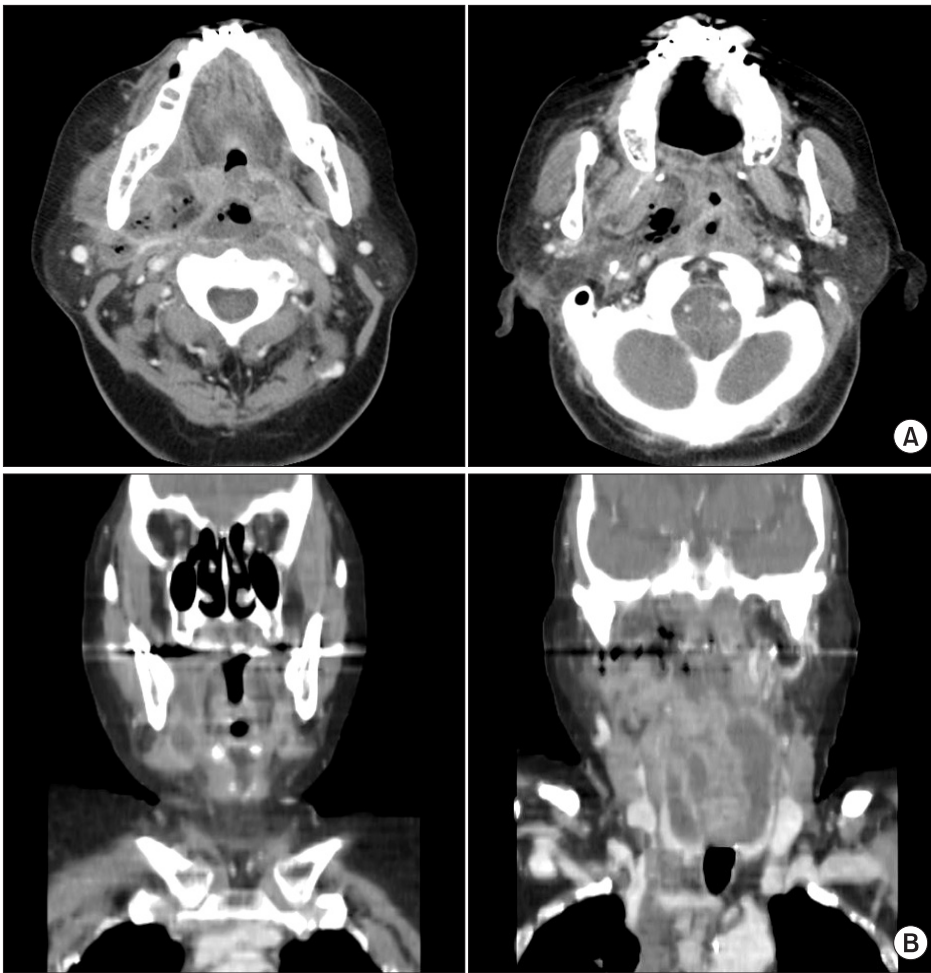


Fig. 1. A. Axial view of computed tomography (CT) scans disclose the fascial space of pterygomandibular, parapharyngeal, retropharyngeal, and submandibular space. B. Coronal view of CT scans show widened spaces.
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Table 1. Classification of primary and secondary spaces

Primary space	Secondary space
Canine space	Parapharyngeal space
Buccal space	Temporal space
Infratemporal space	Submasseteric space
Buccal space	Infratemporal space
Submental space	Pterygomandibular space
Sublingual space	
Submandibular space	

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days, after which the specific antibiotics were selected.

5. Statistical analysis

Statistical analysis of each numeral value of the clinical similarity in diabetes and non-diabetes patients was performed using t-test (SPSS program ver. 12.0; SPSS Inc., Chicago, IL, USA).

III. Results

1. Age distribution

The patients' average age was 62.9 years (range, 23-79 years) in the diabetic group and 47.8 years (range, 13-72 years) in the non-DM group. This suggests that the DM group was much older than the non-DM group ($P>0.05$).

2. Involved fascial spaces

The masseteric, pterygomandibular, and temporal spaces were the secondary spaces that were mainly involved. Note that 15 patients in the DM group (60.0%) had multiple secondary space infections spreading to more than 2 secondary spaces, which was double that observed in the non-DM group (30.0%).(Table 2, $P<0.05$) We could observe more than 2 involved spaces - sometimes up to 5 spaces - in the DM group, but mostly 2 spaces in the non-DM group, with 2 of them having 3 space infections.(Table 3)

3. Types of antibiotics, duration of drug administration, and number of operations

The mean number of antibiotics prescribed was 3.8 in the DM group (range, 2-5) and 3.1 in the non-DM group (range, 2-4). The mean duration of intravenous administration of antibiotics in the DM and non-DM groups was 23.8 days (range, 7-62 days) and 13.8 days (range, 4-28 days), respectively. The mean duration of oral administration after intravenous administration in the DM and non-DM groups was 17.8 days (range, 7-8 days) and 9.4 days (range, 7-17 days), respectively. The mean number of surgical procedures

performed in the DM and non-DM groups was 1.6 (range, 0-6) and 0.9 (range, 0-1), respectively.(Table 4, $P<0.05$)

4. Hematologic examination

During the treatment period, the WBC and CRP levels increased at the time of admission and preoperative and postoperative states of the patients but became almost normal at the time of completion of treatment in both DM and non-DM groups. All of those levels were higher in the DM group compared to the non-DM group.(Table 5, $P>0.05$)

5. Tracheotomy and complication

The tracheotomy ratio was higher in the DM group (20%, 5 people) compared to the non-DM group (3.8%, 1 person) ($P<0.05$). The complication ratio was 40.0% (10 people) and 7.7% (2 people) in the DM and non-DM groups, respectively ($P<0.05$). The major complications were airway obstruction, sepsis, cavernous sinus thrombosis, trismus, skin defect, scar contraction, and hypoesthesia.(Table 6)

6. Duration of hospitalization

The mean duration of hospitalization was 28.9 days in the

Table 2. Distribution of secondary spaces

Fascial space	DM	Non-DM	Total
Parapharyngeal space	0 (0)	4 (15.4)	4
Temporal space	2 (8.0)	4 (11.5)	6
Submasseteric space	4 (16.0)	6 (23.1)	10
Pterygomandibular space	4 (16.0)	4 (15.4)	8
Extended space*	15 (60.0)	8 (30.0)	23
Total	25 (100)	26 (100)	51

(DM: diabetes mellitus)

*Two or more involved spaces, $P<0.05$.

Values are presented as number (%) or number only.

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Table 3. Number of extended spaces

Number of extended space	DM	Non-DM	Total
2	6	6	12
3	5	2	7
4	2	0	2
≥5	2	0	2
Total	15	8	23

(DM: diabetes mellitus)

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Table 4. Count of antibiotics and surgery

Number of treatment	DM	Non-DM
Antibiotics used	3.8 (2-5)	3.2 (2-4)
I&D*	1.6 (0-6)	0.9 (0-1)

(DM: diabetes mellitus, I&D: incision and drainage)

* $P<0.05$.

Values are presented as mean (range).

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Table 5. Comparison of WBC and CRP in the diabetic and non-DM groups

	DM				Hospitalization	Non-DM		
	Admission	Before operation	After operation	Discharge		Before operation	After operation	Discharge
WBC* (/mm ²)	16,250 (10,110-25,340)	17,280 (11,230-26,740)	14,320 (9,800-22,300)	7,520 (3,400-14,340)	12,320 (9,840-22,380)	13,560 (9,840-23,350)	11,420 (9,640-23,440)	7,830 (4,320-14,560)
CRP* (mg/dL)	18.4 (6.4-48.0)	16.6 (5.8-47.2)	14.8 (5.5-48.2)	0.49 (0.3-2.8)	14.2 (3.4-42.0)	13.4 (3.1-40.2)	10.2 (2.5-41.2)	0.44 (0.3-2.1)

(WBC: white blood cell, CRP: C-reactive protein, DM: diabetes mellitus)

* $P<0.05$, WBC and CRP values were higher in DM except at the discharge.

Each level shows the average of the maximal levels during that period.

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Table 6. Complications of secondary space abscess patients

Complication	DM	Non-DM
Airway obstruction	2 (8.0)	0
Sepsis	1 (4.0)	0
Scar contraction	2 (8.0)	0
Skin defect	1 (4.0)	0
Trismus	2 (8.0)	2 (7.7)
Cavernous sinus thrombosis	1 (4.0)	0
Hypoesthesia	1 (4.0)	0
Death	0	0
Total	10 (40.0)	2 (7.7)

(DM: diabetes mellitus)

Values are presented as number (%).

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DM group (range, 7-88 days) and 15.4 days (range, 4-35 days) in the non-DM group ($P>0.05$).

7. Main causative microorganism

Klebsiella pneumoniae, *Staphylococcus* species, and *Candida* were the main causative organisms in the DM group.(Table 7)

IV. Discussion

Infections occur when there is a disruption of the balance between the human defense mechanism and bacterial infection mechanism. The more significant factor of the two is human defense mechanism, i.e., local immunity, humoral immunity, and cellular immunity¹⁰. Local immunity includes mechanical defense by the surface or mucous membrane of the host itself and defense of normal flora of skin, suppressing the growth of other infectious bacteria. Humoral immunity, a non-cellular immune system, includes the immune system by the complement or immunoglobulin and mainly exists in the serum or exudates. Cellular immunity means the immune system phagocytosis by phagocytes, such as polymorphonuclear lymphocytes, monocytes, and macrophages.

In diabetic patients, among the immunities above are disorders of cell-mediated immune system, phagocytosis, and supply of blood, causing increased infection¹¹. There were decreases in the ability of chemotaxis, phagocytosis, and cell destruction, which are factors of innate cellular immunity, and function of diabetic polymorphonuclear lymphocytes and diabetic monocytes in diabetic patients¹¹. Tanaka³ suggested that the function of neutrophil, such as chemotaxis or production of cytokines, is reduced under high blood sugar levels. Similarly, previous studies reported that diabetic

Table 7. Distribution of microorganisms

Bacteria group	DM (n)	Non-DM (n)
Aerobic bacteria		
<i>Acinetobacter baumannii</i>	2	1
<i>Pseudomonas aeruginosa</i>	1	1
<i>Enterobacter aerogenes</i>	1	0
Facultatively aerobic bacteria		
<i>Staphylococcus hominis</i>	1	0
<i>Staphylococcus epidermidis</i>	3	0
<i>Streptococcus constellatus</i>	0	4
<i>Streptococcus anginosus</i>	1	3
<i>Streptococcus viridans</i>	1	1
<i>Streptococcus mitis</i>	1	0
<i>Streptococcus oralis</i>	1	0
<i>Pneumoniae</i>	2	0
<i>Klebsiella pneumonia</i>	3	0
<i>Enterococcus faecalis</i>	2	0
<i>Enterobacter cloacae</i>	1	0
<i>Citrobacter freundii</i>	2	0
Coagulase-negative staphylococcus	0	3
Unidentified aerobic gram-positive bacilli	0	3
Fungi		
<i>Candida</i>	3	0
No growth	7	8

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patients are vulnerable to infections due to a decrease in the bactericidal effects of neutrophil, cellular immunity, and activity of complement under persistent high blood sugar levels. In addition, chronic diseases such as diabetes occur more often in older patients. In this study, the average age of the DM group was 62.9 years compared to 47.8 years in the non-DM group. These results were similar to other reported studies^{12,13}. Note, however, that aging influences the immune system, making the latter typically less responsive to infection; vaccination can be more responsive to inflammation¹⁴.

Lee et al.¹⁵ reported that 81.6% of odontogenic infection showed single fascial space involvement. In contrast, 23 patients exhibited more than two fascial space involvements. (Table 3) In the study of head and neck space infections of odontogenic origin by Rega et al.¹⁶, multiple-space infections were more common than single-space infections. Such discord may result from the latency in visiting the hospital. Note that the DM group had higher incidence of multiple fascial space infections than the non-DM group. This could be related to further progression to deep neck infection as reported by Huang et al.¹⁵.

Diabetic patients should be treated based on more stringent criteria due to their decreased immune function. Diabetes is reported to enhance inflammation in general by altering the myeloid and lymphoid functions^{17,18}. Chen et al.¹² cited

the need for closer observation and more active surgical treatments for diabetic patients who had deep neck infections since they have poorer prognosis than non-diabetic patients. In this study, the difference in the number of antibiotics was insignificant. Augmentin was administered as empirical antibiotic for patients with secondary space infections, with clindamycin and/or aminoglycoside added in severe cases. Antibiotics were administered every 8 hours to maintain MIC. Although Warnke et al.¹⁹ attempted to change the administration method from intravenous administration for 3 days to oral administration to treat abscesses, antibiotics were administered orally after an improvement in the aspects of physical inflammation and clinical features. Note, however, that the period of antibiotics administration and period of hospitalization were longer for diabetic patients, and they underwent more surgical intervention. These results can be said to be a reflection of persistent inflammation and delayed healing, which could be due to prolonged inflammatory response to cytokine dysregulation and enhanced fibroblast apoptosis by diabetes^{20,21}.

In this study, the DM group showed higher WBC level and CRP level in the blood at the time of treatment as well as more post-operative complications compared to the non-DM group. These results were consistent with the findings of previous studies^{12,13}. Thus, it is important to treat those patients in an active manner, such as active surgical incision, pus drainage, and use of empirical antibiotics. The result of our study is similar to that of a previous study of Huang et al.¹³, i.e., diabetic patients are vulnerable to deep neck infections, with much more complications and increase in the duration of hospitalization. In particular, tracheotomy and emergency I&D were required for 2 patients in the DM group due to the spread of infection to more than 5 spaces concerning airway obstruction. Tracheostomy and higher initial values of WBC and CRP suggest the severity of the infection, and they were significantly higher in the DM group. As complications, scar contraction and skin defect might be related to a wider extent of operation site and the delayed healing in diabetic patients. Cavernous sinus thrombosis was managed in consultation with the department of internal medicine. Huang et al.²² also reported low recovery rates among diabetic patients, which may have increased the number of complications. Deep neck infections may result in complications such as upper airway obstruction, descending mediastinitis, jugular vein thrombosis, venous septic emboli, carotid artery rupture, adult respiratory distress syndrome, septic shock, and disseminated intravascular coagulopathy²³. In our study,

the more frequently occurring complications were airway obstruction, scar contraction, and trismus. These results were consistent with the findings of previous studies^{22,23}.

Common odontogenic infections are usually associated with five or more types of bacterial strains - including both aerobic and anaerobic bacterial colonies - rather than just a single strain. Aerobic streptococcus is a predominant bacterial strain at the beginning of the infection, and anaerobic bacteria gradually increased as the infection became chronic²⁴. Warnke et al.¹⁹ reported that several bacterial strains formed colonies in 98% of patients with abscesses. *Viridans streptococcus* was the most common strain. According to Gilmer and Moody²⁵, the streptococci or staphylococci were observed in patients with acute dental infections in the early stage of infections. The proportion of anaerobic bacteria - *Klebsiella pneumonia* and *Streptococcus epidermidis* in our study - increased as the infection spread to secondary space or deep neck space. The type of bacterial growth differed between the DM group and non-DM group: *Klebsiella pneumoniae* in the DM group and *Streptococcus constellatus* in the non-DM group. We could observe fungal infections, such as *Candida* infection, in a group of diabetic patients.

Based on the result of this study and literature review, fascial space infections in diabetic patients tend to extend the secondary space and worsen. Korea is already an aging society and is expected to become an aged society in 2017²⁶, and almost 20% of the elderly (>60 years old) have DM²⁷. Therefore, oral hygiene care in elderly should be emphasized, especially among diabetic patients. Likewise, early diagnosis, strict control of blood sugar, empirical use of a wide range of antibiotics, and active surgical treatments are important.

V. Conclusion

In this study, we carried out image, physical, and clinical evaluations of 25 diabetic and 26 non-diabetic patients diagnosed with secondary space abscesses and treated at Department of Oral and Maxillofacial Surgery in Chonnam National University Hospital.

1. The average age of the DM group was 62.9 years (range, 23-79 years), which was higher than the non-DM group's 47.8 years (range, 13-72 years; $P>0.05$).
2. The rate of multiple secondary spaces infection of the DM group (60%) was higher than that of the non-DM group (27.3%, $P<0.05$).
3. The mean number of prescribed antibiotics was 3.8 (range, 2-5) in the DM group and 3.1 (range, 2-4) in the non-

DM group ($P>0.05$). The number of surgical operations performed was 1.6 (range, 0-6) in the DM group and 0.9 (range, 0-1) in the non-DM group ($P<0.05$).

4. The mean period of hospitalization of the DM group was 28.9 days (range, 7-88 days), which was longer than the non-DM group's 15.4 days (range, 4-35 days; $P>0.05$).

5. The values of WBC and CRP of the DM group were higher than those of the non-DM group during the treatment period ($P>0.05$).

6. The DM group recorded a 40.0% occurrence of complications, which was higher than the non-DM group's 7.7% ($P<0.05$). The tracheostomy rate of the DM group (20.0%) was also higher than that of the non-DM group (3.8%, $P<0.05$).

7. The results of bacteria cultivation indicated that the main causative microorganisms of diabetics were *Klebsiella pneumoniae* and *Staphylococcus* species.

These results suggest the need to treat diabetic patients as quickly as possible due to their high risk of infections.

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