

Pattern of Bacteria and Fungi Growth in the Non-Insulin Dependent Diabetes Mellitus' Toe Webs

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Objectives: To assess the growth of bacteria and fungi in the Non Insulin Dependent Diabetes Mellitus (NIDDM) toe webs and to correlate with the glycemetic control and to frequent feet washing.

Methods: Sixty one NIDDM patients (28 males, 33 females) with a mean age of 51.7 years, and mean diabetes duration of 7 years (0.5-30 years). Compared with 29 non-diabetic healthy subjects as a control group with mean age 45.5 years, were randomly selected, evaluated and examined in the Endocrine Clinic - KHMC for skin peripheral pulse status.

Skin scrapings were taken from both 4th toe webs regardless of the presence or absence of any lesion. These were cultured on Sabouraud's dextrose and blood agar media. Grain stain and lactophenol cotton blue stain were also obtained. Venous blood for blood sugar and HbA_{1c} was also extracted. HbA_{1c} was considered as a measure of control. Levels < 7% were considered good control, 7.1-9.5 % fair control, > 9.5% poor control.

Results: In the NIDDM group, there were 21 (34.4%) patients with superficial skin lesions over the fourth toe web, 28 (45.9%) were having absent tibialis posterior and dorsalis pedis pulses bilaterally and 5 unilaterally. 55.7% were having associated diseases and 80.33% were using frequent foot washings for religious purposes. Seventeen patients were having good control of their diabetes, 29 fair control and 15 with poor control. The mean HbA_{1c} was 8.68 + 1.16 (+ SD).

In the control group 2 were having skin lesions and 75.86% were using frequent foot washings. %7.4% of the diabetic sample were having positive cultures, gram positive cocci, candida albicans, mixed growth of gram positive and negative, gram negative cocci and dermatophytes in decrescendo manner were obtained (19.7%, 14.7%, 13.2%, 4.9%, 4.9% versus 6.9% in the control group (Candida Albicans 100%) P < 0.05. All patients with poor glycemetic control were having positive cultures, versus 41.7% with fair control and 47% with good glycemetic control P < 0.001.

None of the patients with dermatophytes were having intact skin, while 55% of patients with candida were having superficial lesions.

Positive cultures with normal skin occurred in 27,9% in NIDDM group versus 6.9% in control group, and with toe web lesions in 29.5% in NIDDM group, versus none in control group P < 0.05. 61.2% of feet washers in NIDDM group have positive cultures versus 4.5% in control group.

Conclusion: Diabetic patients have higher carriage rates of both bacteria and fungi which increase with skin breakdown. Susceptibility to infection is increased by poor glycemetic control. Diabetes does not predispose to the carriage of dermatophytes in the toe webs of normal appearance. Frequent feet washing predispose more to infection in diabetics and needs special attention.

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Cutaneous lesions to which diabetics are more susceptible include bacterial and fungal infections and it may provide a clue to the presence of the condition. Infections are more common in diabetics than non-diabetics due to impaired immunity i.e., impaired neutrophilic chemotaxis and phagocytosis¹, peripheral vascular disease and neuropathy² particularly when diabetes is poorly controlled. Despite the great improvement in antibiotics, insulin therapy and better methods of control and education, nevertheless infection still accounts for much morbidity and mortality in diabetics³, more so in developing countries.

Bacterial infection may be the presenting feature of diabetes mellitus (DM). It commonly occurs in the intertrigo areas. The limb may be threatened and rigorous intravenous antibiotics therapy may be required⁴. Fungal infections particularly candidiasis is a common yeast infection in diabetics which may infect any area of the skin. Tinea infection may occur in any part of the body, but the feet are the most common sites. This epidermophyte which causes harmless annoyance in most people, can in diabetics lead to serious infection¹. The organisms break the defensive integumentum and secondary infection can occur.

Like the rest of the skin, the toe webs are normally populated by a variety of microbes⁵, but dermatophytes are not considered part of Dermal skin flora^{6,7}, although some authors do⁴. Many studies, however, showed a significant growth of aerobes, anaerobes and fungal infections in diabetic foot with ulcerations⁸ 81%.¹⁷, but none have been done without preexisting foot lacerations or ulcerations, and in correlation to glycemic control. Feet washing; a religious ritual habit, which exposes the feet (webs) to more wet media may increase the risk of infection if not dried properly.

In this prospective comparative study, we tried to assess the pattern of bacteria and fungi growth in NIDDM patients and to correlate with the glycemic control and with frequent foot washing on the diabetics' feet.

METHODS

Sixty one patients NIDDM with mean age 51.7 year (31-70) were randomly selected at the Endocrine Clinic at King Hussein Medical Centre (KHMC) from December 1996 to March 1997. They were 28 males and 33 females. A comparative control group of 29 non-diabetics healthy subjects with mean age of 45.6 years (24-63) were also asked to participate.

Both groups (NIDDM and control group) were evaluated and examined for their feet skin status, mainly the fourth toe webs for scaling, macerations, discoloration and vesiculation, peripheral pulses, clinical evidence of peripheral neuropathy (pinprick, vibration and position senses) and for any associated lesions or conditions. Each group was subdivided to two groups according to frequency of foot washing or not. Fifty patients were treated by oral hypoglycemic agents, 10 were on insulin because of secondary failure and one on diet alone. Venous blood for glucose and glycosylated hemoglobin (HbA_{1c}; reference range 4.2-6.2%) was also extracted from NIDDM group. HbA_{1c} was considered as a measure of control; levels < 7% were considered good control, 7.1-9.5% fair control, > 9.5% poor control.

All members of both groups were then scrapped at the 4th toe webs bilaterally regardless of the presence or absence of skin lesions. These scrappings were subjected to Gram stain and lactophenol cotton blue stain after treatment with potassium hydroxide, and were cultured on Sabouraud's dextrose and blood agar media (500 ml distilled water, 20 gm glucose, 5 gm peptone,

10 gm agar and 5 gm chloramphenicol) for 48 hours. The germ tube test was employed for Candida identification. Identification and culture results were obtained by the same microbiologist.

Statistical analysis was performed by χ^2 , Fisher exact test, difference between two percentages and z static test.

RESULTS

The clinical status and findings of both groups, associated diseases are shown in Tables 1 and 2. 80.3% were using frequent foot washings with no proper intertrigo drying in NIDDM group, and 75.8% in the other group.

Table I. Demographic and clinical characteristics

Parameter	NIDDM group n=61 n(%)	Control group n=29 n(%)
Previous foot infection	10(16.4%)	0
Associated diseases*	34(55.07%)	0
Frequent foot washing	49(80.3%)	22(75.8%)
Peripheral neuropathy	19(31.3%)	0
Foot exam = intact	40(65.6%)	27(93.1%)
Skin lesion = superficial	21(34.4%)	2(6.9%)
Peripheral vascular disease		
Bilateral	28(45.9%)	0
Unilateral	5 (8.2%)	0

* See table 2 for associated diseases.

Table 2. Association with other conditions in NIDDM group (55.7%)

	Hypertension	Hyperlipidemia	Hypothyroid	CVA	Psychosis
n	13	6	3	2	2
	DVT (old)	Hyper PRL	MS + MVR	TIA	Obesity
n	2	1	2	1	2

Seventeen patients of the diabetics were having good control of their DM. Mean HbA_{1c} (+ SD) 5.97%+ 1.09. Fair control was present in 29 patients with mean HbA_{1c} 8.14%+ 0.685, and 15 patients with poor control with mean HbA_{1c} of 11.93% + 1.7. An overall HbA_{1c} mean value of 8.68%+ 1.16. 57.4% of NIDDM group were having bacterial or fungal growth (positive cultures) versus 6.9% in the control group (95% confidence interval CI:34.73, 66.27 corresponding to P < 0.05).

The distribution of specific causative agents in relation to skin status in both groups is shown in Table 3. Comparing these results (positive cultures) in the two groups, there was a statistically significant difference; 95% CI = 35.6 + 18.44; P < 0.05.

Table 3. Distribution of positive cultures in each group with regard to specific organisms and relation to skin status

Specific organism n(%)	NIDDM group n=61 Control group n=29			
	Normal toe web n=40	Toe web lesions n=21	Normal toe web n=29	Toe web lesions n=2
Gram positive:				
Staph aureus	3(4.9%)	7(11.5%)	0	0
Staph.epidermd	1(1.6%)	0	0	0
B Hem.strep.B	1(1.6%)	0	0	0
Candida Albicans	4(6.6%)	5(8.2%)	2(6.9%)	0
Mixed growth	7(11.5%)	1(1.6%)	0	0
Gram negative				
proteus	0	2(3.3%)	0	0
Klebsiella	1(1.6%)	0	0	0
Dermatophytes	0	3(4.9%)	0	0
trichophytes				
mentagrophytes				
Total	17(42.5%)*	18(85.7%)	2(6.9%)	0
Sample total	35(57.4%)#	2(6.9%)		

* 95% CI = 21.77, 64.63; P<0.05 #

95% CI = 34.73, 66.27; P<0.05

All patients with poor glycemic control (n = 15) were having positive cultures (100%), while 41.4% of patients with fair control and 47% of patients with good control were having positive cultures (P<0.001) Fig. 1.

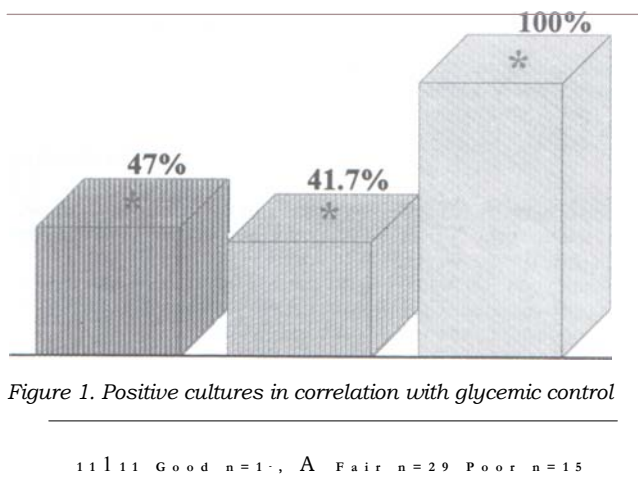


Figure 1. Positive cultures in correlation with glycemic control

Of the subgroup of frequent foot washers (n=49), 30 (61.2%) patients were positively cultured, compared with only one patient in the control group (4.55%) (95% CI = 56.68 + 16.18; P < 0.05). While for non-washers (n=12); 5 patients (41.6%) were having positive cultures vs. one in the control group (95% CI = 27.38 + 19.42; P < 0.05). Positive cultures in the patients with abnormal toe webs in NIDDM group were 18, while that of control group was zero (P < 0.05).

Intergroup comparison of positive cultures in washers versus non-washers in NIDDM group (61.2% vs 41.6%) was performed. The 95% CI was 3.98, 35.55 (P < 0.02) indicating an increased risk of infection. Although the fungal infection rate (19.67%) in the NIDDM group is higher than normal control group (6.9%), nevertheless this was of no statistical significance; [z static: 1.5689; P>0.124].

All patients with positive cultures for dermatophytes and 55% with candida albicans were having superficial 4th toe web lesions. For bacterial infection, 58.3% of gram positive, 66.6% of gram negative and only 12.5% of mixed growth were having abnormal superficial lesions toe webs [Table 3].

The incidence of bacterial infection is 0.54/100,000 population and for fungal infection is 0.28/100,000 population. An overall infection incidence is 0.83/100,000 versus 0.04/100,000 in the control subjects.

DISCUSSION

The fourth web was more commonly affected because of the natural occlusion of the toe webs leading to increased hydration which causes swelling and the development of multiple folds in the stratum corneum. This also leads to the accumulation of desquamated corneocytes on the surface of that stratum. Bacterial overgrowth is increased by the above mechanisms and heavy growth of bacteria with interaction with fungi is important in the development of interdigital infection. In our study, although the growth of fungal infection was not statistically significant in NIDDM group compared with control group, nevertheless it was of clinical significance. It has also demonstrated a higher growth of bacteria in diabetic patients. In contrast the study done by Aljabre et al" showed that diabetics have higher Gram negative and erythrosoma than dermatophytes in toe webs, our study showed a higher gram positive over growth followed by candida and mixed growth consistent with most other studies done in this regard".

Patients who are used to washing their feet frequently for religious believes, with no proper drying are more prone to infections. This is due to increased interdigital moisture. The risk however is 13 folds higher in diabetics. This problem mandates special care and education for diabetics regarding their feet and prompt and aggressive intervention when early signs of infection appears, to avoid the drastic diabetic foot outcome. Dermatophytes were cultured in three patients who were having toe web lesions, and it seems that DM does not predispose to the growth of dermatophytes in normal skin. In contrast to dermatophytes, candida infected both groups and had a higher growth in diabetics with toe web lesions'. Although candida is considered a normal flora of the toe webs", we tend to believe that diabetes mellitus predisposes to skin candidal infection in as much as balanitis and vulvovaginitis.

CONCLUSION

We conclude that dermatophytes are not part of normal flora of the feet and DM does not predispose to the carriage of dermatophytes in the intact toe webs. Poor glycaemic control along with frequent foot washing without drying are of prime importance for the predisposition to bacterial and fungal infection. Foot infections are increased in diabetics regardless of the skin status. The feet of diabetic patients need special handling and care, particularly in patient with toe web lesions, which could be done by continuous education for proper pedicure and adequate glycaemic control.

REFERENCES

1. Wilson RM. Neutrophil function in diabetes. *Diabet Med* 1986;3:509-16.
2. Scapico FL. Foot infection in patients with diabetes mellitus. *J Am Podiatr Med Assoc* 1989;79:482-5.
3. Joseph WS, Axler DA. Microbiology and Antimicrobial therapy of diabetic foot infection. *Clin Podiatr Med Surg* 1990;7:467-81.
4. Edmond ME. The diabetic foot: pathophysiology and treatment. *Clin End & Metab* 1986;15:889-916.
5. Kozak GP, Krall LP. Disorders of skin. In: Marble A, Krall LP, Bradley RF, et al, eds. *Diabetes in Joslin's Diabetes Mellitus*. Lea & Febiger 1985:769-83.
6. Roberts SOB. Fungi and the skin. In: Champion RH, Gilman T, Rook AJ, et al, eds. *An introduction to the Biology of the skin*. Oxford: Blackwell Scientific Publication, 1970:206-22.
7. Midgley G, Clayton YM. Distribution of dermatophytes and candida spores in the environment. *Br J Dermatol* 1972;8:6977.
8. Kajetan M, Konkoly TM, Jeremenydy G. Experience with microbiological studies of the diabetic foot. *Or^y Hetil* 1995;136:2164-4.
9. Harris DR, Papa CM, Stanton R. Percutaneous absorption and the surface area of occluded skin. *Br J Dermatol* 1974;10:27-32.
10. Borrero E, Rossinin M, Jr. Bacteriology of 100 consecutive diabetic foot infection and in vitro susceptibility to Ampicillin/Sulbactam versus Cefoxitin. *Angiology* 1992;43:357-61.
11. Montes LF, Willborn WH. Anatomic location of normal skin flora. *Arch Dermatol* 1970;101:145-9.
12. Leyden JJ, Kligman AM. Interdigital athlete's foot: the interaction of dermatophytes and resident bacteria. *Arch Dermatol* 1978;114:1466-72.
13. Aljabre SHM, Alsultan A. Carriage of dermatophytes in the toe webs of adult non-insulin dependent diabetic patients. *Int Diabetes Digest* 1996;7:20-1.
14. Noble WC. Microbiology of specialised sites. In: *Microbiology of Human Skin*. London: Lloyd-Luk Medical Book. 2nd ed. 1981:339-59.
15. Golden EJ, Citron DM, Nesbet CA. Bacteriology and activity of 10 oral antimicrobial agents against bacteria isolated from causative cases. *Diabetes Care* 1996;19:638-41.
16. Asfar SK, Al-Arouj M, Al-Naki A, et al. Foot infections in diabetics: the antibiotic choice. *Can J Surg* 1993;36:170-2.
17. Ramani A, Ramani M, Shivanda PG, et al. Bacteriology of diabetic foot ulcers. *Indian J Pathol Microbiol* 1991;34:81-7.