Skin Surface pH in Intertriginous Areas in NIDDM Patients

Possible correlation to candidal intertrigo

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OBJECTIVE — To compare skin surface pH and moisture in intertriginous areas in diabetic patients and healthy control subjects and to study the relationship between these parameters and candidal infection.

RESEARCH DESIGN AND METHODS — We measured the skin surface pH and moisture in the axillary, inframammary, inguinal, and forearm skin with a pH meter with a flat-glass electrode and skin corneometer. The subjects were 50 NIDDM patients from the diabetic outpatient clinic at Beilinson Medical Center, Petah Tiqva, Israel, and 40 healthy control subjects from hospital personnel. The main outcome measures were skin surface pH, skin moisture, and skin culture for *Candida*.

RESULTS — Skin pH in the inguinal and axillary regions was significantly higher in diabetic patients compared with healthy control subjects ($P < 0.0001$), whereas no difference was noted in the forearm. In the inframammary region, diabetic women had significantly higher pH than nondiabetic women ($P < 0.01$). No difference was noted in men in this region. Six patients (12%) had candidal infection in intertriginous areas.

CONCLUSIONS — Our study indicates that in intertriginous regions, skin surface pH of diabetic patients is significantly higher than in normal control subjects and implies the significance of skin pH as a possible factor promoting host susceptibility to skin candidal infection.

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NIDDM, NON-INSULIN-DEPENDENT DIABETES; BMI, BODY MASS INDEX; ANOVA, ANALYSIS OF VARIANCE.

It is widely accepted that candidal skin infections are more prevalent in diabetic patients (1,2). The mechanism by which diabetes increases host susceptibility to candidiasis is not clear (3). One of the factors that contributes to candidal growth is environmental pH (4). No published data are available on skin pH in diabetic patients. The skin pH in normal adults is acidic and ranges between 4 and 6 (5,6). The importance of skin acidity in preventing infections was demonstrated in 1942 by Arnold (7) and is still generally accepted (8). Skin acidity is considered a product of lactic acid, amino acids in sweat secretions, sebum, and protein substances of the stratum corneum (5). Skin pH values vary in different body areas, apocrine and urogenital folds have a higher pH (9). Skin pH is higher in females (5,10) and also depends on skin humidity (9). An important predisposing factor for intertriginous candidal infection is increased skin humidity caused by occlusion, maceration, and sweating (11).

The purposes of this study were as follows: *1*) to compare skin pH and moisture in NIDDM patients with those in nondiabetic control subjects by using planar electrode and skin corneometer; *2*) to examine whether skin pH in diabetes affects host susceptibility to skin candidal infection; *3*) to investigate the relationship between moisture and pH of the skin; and *4*) to correlate skin surface pH in NIDDM patients with metabolic control and with microvascular complications (proliferative diabetic retinopathy and diabetic nephropathy).

RESEARCH DESIGN AND METHODS

— Fifty NIDDM patients, 27 men and 23 women, 32–76 yr of age, (mean age: 56 yr) participated in the study. Of the patients, 23 were treated with insulin, 25 were treated with oral hypoglycemic drugs, and 2 were treated with diet only. Forty nondiabetic volunteers, 22 men and 18 women, 28–77 yr of age (mean age: 53 yr), served as control subjects.

Table 1—*Skin surface pH in four body sites in NIDDM patients compared with control subjects*

	Skin surface pH			
	NIDDM patients		Control subjects	
	Men	Women	Men	Women
n	27	23	22	18
Axilla*	6.84 ± 0.17	7.18 ± 0.18	5.84 ± 0.1	5.99 ± 0.11
Inframammary†	5.59 ± 0.12	6.53 ± 0.15	5.54 ± 0.1	5.83 ± 0.17
Inguinal*	6.89 ± 0.09	7.10 ± 0.17	6.22 ± 0.13	6.22 ± 0.16
Forearm‡§	5.01 ± 0.11	5.52 ± 0.13	5.06 ± 0.11	5.62 ± 0.12

Data are means ± SE.
*$P < 0.0001$, NIDDM patients vs. control subjects; NS, men vs. women.
†$P < 0.01$, NIDDM patients vs. control subjects; $P < 0.0001$, men vs. women.
‡NS, NIDDM patients vs. control subjects; $P < 0.0001$, men vs. women.
§$P < 0.002$, forearm vs. other regions.

The patients were referred from the Diabetic Outpatient Clinic of Beilinson Medical Center. A thorough medical history was taken, including the following data: age, sex, diabetes duration, hypoglycemic agents, and BMI (weight/height^2 in kg/m^2). All the diabetic patients were examined for skin infections. Data on microvascular complications were obtained from patients files as follows: creatinine levels, microalbuminuria, and fundoscopic eye examination.

The blood glucose control was assessed by HbA_{1c} and fructosamine.

In 15 diabetic patients, blood gases were drawn to evaluate blood pH in correlation to skin pH.

All examinees were instructed to refrain from washing their body with soap, from using detergents, and from applying cosmetics 1 day before the test to eliminate the effect of these substances on skin pH and moisture.

Experiments were conducted in an environmentally controlled room at a constant temperature of 22 ± 1.5°C and a humidity level of 35%. All patients lay supine for an acclimatization period of 45 min.

pH measurements

A pH meter (pH 900M, Courage and Khazaka Electronie, Cologne, Germany) with a flat-glass electrode was used to measure skin pH. The pH meter was calibrated before use each day of examination according to the manufacturer's instructions. Three measurements were recorded on every site bilaterally as was the mean value on the forearm, axilla, inframammary, and inguinal areas.

Skin moisture measurement

A corneometer (CM-820 PC Courage and Khazaka Electronie, Cologne, Germany) was used to register the electrical capacitance of the skin surface as an indicator of stratum corneum moisture, according to the manufacturer's guidelines (12). Skin moisture measurements were recorded in the same manner as pH measurements.

Investigation for candidal flora

Skin samples for *Candida* were taken from the diabetic patients. Swab smears from axilla, inframammary, and inguinal areas were innoculated on Sabouraud dextrose agar containing chloramphenicol (Hylab, Kirayt Weizman, Israel) and cultured for 7 days at 28°C. The identification of the yeasts in the positive culture was based on carbohydrate assimilation using the API-20 C AUX system (Bio Merieux Sa, Lyon, France), morphology on cornmeal agar germ tube formation, and sensitivity to cycloheximide.

Statistical analysis

Two-way ANOVA was used to compare NIDDM patients and healthy control subjects and to compare men and women. Multiple regression was used to study the differences in pH and moisture within the group of NIDDM patients. The dependent variables were age, sex, duration of diabetes glucose levels, HbA_{1c}, and BMI (<25 or >25 kg/m^2), and the presence or absence of *Candida*. Multiple regression was used to study the relationship between candidal infection and sex, age, duration of diabetes, glucose levels, HbA_{1c}, BMI, treatment, and microvascular complications.

RESULTS— Table 1 summarizes the results of skin surface pH in diabetic patients compared with healthy control subjects. Skin surface pH in the axillary and inguinal regions in NIDDM patients was significantly higher than in healthy control subjects ($P < 0.0001$). In diabetic women, but not in men, skin surface pH in inframammary regions was significantly higher than in healthy control subjects ($P < 0.01$). No difference was noted in skin forearm pH between patients and healthy control subjects.

The pH in the inframammary region was higher in women than in men only in the diabetic group ($P < 0.0001$), whereas the pH in the forearm was higher in women than in men in both groups ($P < 0.0001$). Inguinal pH was higher in women with BMI >25 kg/m^2 (7.39 ± 0.19, 15 women) compared with women with BMI <25 kg/m^2 (6.57 ± 0.25, 8 women; $P < 0.02$). Such a difference was not found in men, in whom the respective values were 6.89 ± 0.09 (18 men) and 6.9 ± 0.19 (9 men).

Table 2 summarizes the results of skin moisture. No significant differences were observed in skin moisture between NIDDM patients and healthy control subjects. No correlation was found be-

Table 2—*Skin moisture in four body areas in NIDDM patients compared with healthy control subjects*

	NIDDM patients		Control subjects	
	Men	Women	Men	Women
n	27	23	22	18
Axilla*	109.8 ± 3.1	117 ± 1.85	102.3 ± 4.3	115.2 ± 1.3
Inframammary*	104.5 ± 3.4	114.7 ± 3.2	98.7 ± 4.2	112.8 ± 2.8
Inguinal†	108.3 ± 3	109.8 ± 3	107 ± 2.6	102.3 ± 3.6
Forearm†‡	102.9 ± 3	103.5 ± 2.8	99.5 ± 3.9	95.1 ± 3.3

Data are means ± SE.
*NS, NIDDM patients vs. control subjects; $P < 0.001$, men vs. women.
†NS, NIDDM patients vs. control subjects; NS, men vs. women.
‡$P < 0.02$, forearm vs. other regions.

tween skin moisture and skin surface pH. Forearm moisture was significantly lower than other regions ($P < 0.02$). Axillary and inframammary moisture was significantly higher in women ($P < 0.001$), whereas the other two regions did not show sex variations.

No correlation was found between blood pH levels and skin surface pH in NIDDM patients. Within the group of NIDDM patients, neither pH nor moisture showed a correlation to HbA_{1c} levels.

Candidal skin infections

In 6 of 50 NIDDM patients (5 women, 1 man), cultures grew *Candida*. Five of the patients with positive cultures had a clinical diagnosis of intertrigo, and one woman had pruritus vulvae (patient no. 3 in Table 3). In patients with no clinical evidence of *Candida*, no growth of *Candida* was seen. The positive isolates were *Candida albicans* in three patients, *Candida glabrata* in two patients, and *Candida parapsilosis* in one patient. The sites where *Candida* was cultured are shown in Table 3.

No significant differences in skin pH or moisture were found between diabetic patients with candidiasis and those without (Table 4).

Patients with no candidal infection had mean ± SE HbA_{1c} levels of 10.6 ± 0.4, whereas patients with candidal infection had 12.9 ± 1.1. This difference was not statistically significant because of the small number of patients with candidal infection. No correlation was found between candidal infection and diabetes control, microvascular complications, age, duration of diabetes, or treatment. The presence of candidal infection was frequent in women ($P < 0.05$) and correlated with BMI ($P < 0.003$).

CONCLUSIONS— In this study, NIDDM patients had a significantly higher pH in intertriginous areas, and 12% of them had intertrigo *Candida*. It is tempting to speculate that the increase of candidal infection is caused by intertriginous alkalinity. The correlation between skin surface pH and candidal growth has not been investigated yet. Odds (4) reviewed all the reports on the effect of pH on candidal growth and suggested that pH per se is unlikely to affect the rate of growth or survival of *Candida albicans*. However, pH can affect the morphological form of *Candida albicans*, and this may affect the ability of the fungus to adhere to and invade the host (4). The hypha form is the initial invader into host tissue, and this form grows optimally in pH >6.5 (13). Other factors must affect risk for candidal intertrigo, such as a high skin moisture in NIDDM patients achieved by maceration, occlusion, and sweating (14). Higher moisture levels in intertriginous areas in both NIDDM patients and control subjects were found, but no differences were found between patients with or without candidal infection, nor was a correlation found between skin moisture and skin surface pH in diabetic patients. Other possible factors are the impaired immunological status and complement activation in diabetic patients as sequellae of high glucose (3).

Several explanations exist as to why the skin surface pH is higher in intertriginous areas of diabetic patients. Intertriginous areas are humid and moist

Table 3—*Sites where Candida was cultured*

	Patient no.					
	1	2	3	4	5	6
Axilla	+			+	+	+
Inframammary	+	+				
Inguinal	+	+	+		+	+

Table 4—*Skin surface pH in NIDDM patients with and without candidiasis*

	NIDDM with candidiasis skin pH	NIDDM without candidiasis skin pH
n (M/F)	6 (1/5)	44 (26/18)
Axilla*	7.21 ± 0.3	6.96 ± 0.13
Inframammary (women only)*	6.72 ± 0.31	6.47 ± 0.17
Inguinal*	7.11 ± 0.21	6.97 ± 0.09
Forearm*	4.98 ± 0.18	5.2 ± 0.1

Data are means ± SE.
*NS.

with many sweat glands, mainly apocrine, which are innervated by sympathetic nerves. Skin humidity elevates skin surface pH (9), but no correlation between skin moisture and skin surface pH in diabetic patients was demonstrated.

Another explanation for a higher skin pH in diabetic patients is lactic acid. Thurmon and Ottenstein (15) demonstrated that lactic acid is mainly responsible for the acidity of sweat. They also found that in axillary areas, where sweat is preponderantly apocrine, the lactic acid content is lower than in eccrine areas. Kandhari et al. (16) found that diabetic patients tended to have decreased levels of skin lactic acid in their legs, the lower levels being found mostly in diabetic patients with infections. This explanation is slightly problematic: it means that less substrate sugar reaches the skin surface, a finding that contradicts the high skin-to–blood glucose ratio found in diabetic patients (17).

Note that areas of skin with high pH coincide with areas of hyperkeratosis and papillomatosis in insulin-resistant states, such as obesity and overt acanthosis nigricans. This fact can point to a common cause either through hyperinsulinemia or through other growth factors associated with these states, such as epidermal growth factor and transforming growth factor–α (18).

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