Pruritus in Diabetes Mellitus: Investigation of Prevalence and Correlation With Diabetes Control

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Three hundred diabetic and 100 nondiabetic hospital outpatients (both groups of comparable age and sex distribution) were assessed for the presence of generalized and localized pruritus. Pruritus vulvae was significantly more common in diabetic women (18.4%) than in controls (5.6%) and was significantly associated with poor diabetes control (mean glycosylated hemoglobin level <12%). Other forms of localized pruritus were equally common in diabetic and nondiabetic patients, regardless of glycosylated hemoglobin levels. Generalized pruritus was present in 14 diabetic patients, but in 5 cases the symptom was ascribed to intercurrent illness or drug administration. Thus, generalized pruritus without apparent cause was present in only 8 diabetic patients (2.7%) and was not significantly more common than in nondiabetic patients. It is doubtful if diabetes mellitus per se should be regarded as a cause of generalized or localized pruritus, other than pruritus vulvae. DIABETES CARE 1986; 9:273–75.

It is generally accepted that diabetes mellitus is a cause of generalized pruritus.[1–3] Most articles on the subject refer to the study of Greenwood,[1] who reported a prevalence of 3% of generalized pruritus in 500 patients with diabetes mellitus. More recent workers have emphasized that the association is uncommon but have not attempted to ascertain a prevalence of generalized pruritus in a comparable nondiabetic population.[4–7] Moreover, there exist only anecdotal accounts of the relationship between generalized itch and the quality of diabetes control as judged by random blood glucose estimations or presence of glycosuria;[8,9] no study has related the symptom to a more reliable or longer-term indicator of glycemia such as glycosylated hemoglobin.[10,11] We now report a study in which we have determined the prevalence of localized and generalized pruritus in a diabetic outpatient population, related the symptom to degree of diabetes control as judged by glycosylated hemoglobin concentration, and compared the findings with those in a comparable nondiabetic population.

PATIENTS AND METHODS

Patients. Three hundred diabetic outpatients attending the clinic at Glasgow Royal Infirmary for routine review were asked if they had suffered from itch within the preceding 3 mo. One hundred forty-two men (47% total) and 158 women (53%), mean age 56 yr (range 15–85 yr), were interviewed; women were asked specifically about pruritus vulvae. For the purpose of the study, generalized pruritus was defined as pruritus affecting more than one major body area: head and neck, trunk, or limbs. All patients were seen by two observers (J.B.N. and A.M.).

For comparative purposes a control population of 100 hospital outpatients, comparable in age and sex distribution to the diabetic group, was also assessed for the presence of itch. Forty-six (46%) were men and 54 (54%) were women, mean age 55 yr (range 16–82 yr). These patients were attending the Ophthalmology Clinic at the Infirmary and were known to be nondiabetic at the time of the study.

Investigations. Patients with generalized pruritus were investigated in an attempt to determine an underlying cause for the symptom. Full history was obtained and clinical examination performed. To exclude diabetic autonomic neuropathy as a contributory cause of pruritus (by the induction of anhydrosis or oligohydrosis), the following simple tests of autonomic nerve function were performed: blood pressure was measured in the supine and erect postures (a fall of ≥30 mmHg in systolic blood pressure considered significant); and variation in heart rate during deep breathing, at a rate of 6 breaths/min, was examined by an electrocardiogram (a difference of ≤10 beats/min between the maximum and minimum heart rates considered abnormal). Venous blood was withdrawn for estimation of plasma urea and electrolytes, liver function tests, hemoglobin, erythrocyte sedimentation rate,

TABLE 1
Clinical characteristics of 13 diabetic patients with generalized pruritus

Patient no.	Age (yr)	Therapy	Duration of diabetes	GHb*	Cause of pruritus
1	60	Glibenclamide	6 mo	8.1	†
2	52	Diet	10 yr	8.6	†
3	34	Insulin	2 yr	11.2	†
4	50	Insulin	5 yr	9.8	†
5	53	Glibenclamide	1 yr	13.3	†
6	75	Metformin	6 mo	12.3	†
7	57	Glibenclamide	2 mo	11.8	†
8	64	Metformin	4 yr	12.7	†
9	80	Insulin	3 mo	12.8	Ichthyosis
10	68	Chlorpropamide	5 mo	10.7	Iron deficiency anemia
11	60	Glibenclamide	2 yr	10.2	Psoriasis
12	64	Chlorpropamide	18 mo	11.5	Eczema
13	21	Insulin	4 mo	8.2	Iron deficiency anemia

*Glycosylated hemoglobin.
†Not found.

glucose, glycosylated hemoglobin, serum iron and iron binding capacity, and thyroid function tests. Patients with pruritus confined to the vulva were asked to attend for clinical examination including perineal inspection and vaginal swab. Blood was obtained for estimation of glycosylated hemoglobin concentration. Further investigations were not pursued in patients with other forms of localized pruritus.

Blood for measurement of glycosylated hemoglobin concentration was taken from all other diabetic patients who did not offer a history of pruritus. Glycosylated hemoglobin was measured by a standard automated colorimetric method as previously described,[12] the normal range in our nondiabetic population being 3–9%. Findings in the nondiabetic and diabetic groups were analyzed statistically by Student's t test, using Yate's correction for small samples where appropriate. However, the analysis of small subgroups within either the diabetic or the nondiabetic patients was by a nonparametric test (the Wilcoxon rank-sum test).

RESULTS

Generalized pruritus. Thirteen diabetic patients complained of generalized pruritus (Table 1), the duration of the symptom varying from 2 mo to 10 yr. Nine of these patients were receiving oral hypoglycemic drugs, four were insulin treated, and one was treated by dietary means alone. No patient had evidence of autonomic neuropathy as judged by either of the simple tests of cardiovascular reflexes. In five patients an underlying (nondiabetic) cause for generalized pruritus was identified: two had iron deficiency anemia and one each suffered from ichthyosis, psoriasis, and eczema, respectively. Thus only eight diabetic patients (2.7%) were found to have no recognizable cause for generalized pruritus.

In the nondiabetic group, only one patient (1%) had generalized pruritus. No underlying cause for the symptom was ascertained. There was no statistical difference between diabetic and control populations with respect to the presence of generalized itch (Table 2).

The mean glycosylated hemoglobin level in diabetic patients with generalized pruritus (11.1 ± 1.8 SD) was marginally higher than in those without generalized pruritus (10.5 ± 3.4), but this difference was not statistically significant.

Localized pruritus. Of the 158 diabetic women, 29 (18.4%) had suffered from pruritus vulvae within the preceding 3 mo, the duration of the symptom varying from 2 wk to 6 yr. Fourteen of these patients were receiving oral hypoglycemic drugs, 11 were insulin treated, and four were treated by dietary means alone. Twenty-one women consented to perineal examination with vaginal swabbing. Six women had vulval rash, and there were nine positive vaginal swabs (seven for candida albicans, two for β-hemolytic streptococcal infection). Mean glycosylated hemoglobin in diabetic patients with pruritus vulvae (12.4 ± 2.4 SD) was significantly higher than the mean glycosylated hemoglobin of diabetic women without this symptom (10.0 ± 2.5, $P < .01$).

By contrast, only 3 of 54 women (5.6%) in the nondiabetic control group suffered from pruritus vulvae. All refused perineal examination and vaginal swabbing. The prevalence of pruritus vulvae in diabetic women was significantly higher than in the nondiabetic controls ($P < .05$).

The prevalence of other forms of localized pruritus was higher in the nondiabetic control group (10%) than in the diabetic group (7.7%, Table 2). This difference was not statistically significant.

DISCUSSION

In 1927, Greenwood[1] reported 16 patients (3.2%) with generalized pruritus in a series of 500 patients with diabetes mellitus. No attempt was made to relate the symptom to glycemic control of diabetes or to establish the prevalence of pruritus in a comparable nondiabetic population, but subsequently diabetes has frequently been cited as one cause of generalized pruritus in standard textbooks of dermatology.[2] More recent reviews have stressed that generalized pruritus is uncommon in diabetes and is rare as a presenting symptom.[4–7] Our own figure for the prevalence of generalized pruritus in a diabetic population (2.7%) is in close agreement with Greenwood's finding but does not differ statistically from that in a nondiabetic control group. Likewise the prevalence of other forms of localized pruritus (apart from pruritus vulvae) was comparable in both groups we studied, and we found no relationship between generalized pruritus and diabetes control as judged by glycosylated hemoglobin levels. All these factors would suggest that a diagnosis of diabetes mellitus per se should not be regarded as an adequate explanation for the complaint of generalized pruritus or of localized pruritus, with the exception of pruritus vulvae in diabetic women. It is notoriously difficult to define an underlying cause for generalized pruritus in many patients with this symptom: no less than 40% of the patients studied by Beare[8] were ultimately

TABLE 2
Prevalence of various forms of pruritus in a population of 300 diabetic hospital outpatients and a matched population of 100 nondiabetic outpatients

Symptom	Diabetic patients	Nondiabetic patients	Difference
Generalized pruritus (cause ascertained)	5/300 (1.7%)	0/100 (0%)	NS
Generalized pruritus (cause not determined)	8/300 (2.7%)	1/100 (1%)	NS
Pruritus vulvae*	29/158 (18.4%)	3/54 (5.6%)	$P < .05$
Other localized pruritus	23/300 (7.7%)	10/100 (10%)	NS

*Women only. NS, not significant.

considered to suffer from idiopathic prurigo, and we can offer no more satisfactory diagnosis for the majority of such cases in our own study. Fortunately the symptom usually resolves spontaneously with the passage of time.[8]

Pruritus vulvae has long been associated with diabetes in women, estimates of its prevalence varying from well below 10%[1,4,5] to ~50%.[9] Our study has again confirmed that pruritus vulvae is significantly more common in a treated diabetic population and is clearly related to poor diabetes control. This is in keeping with the clinical impression of most diabetes physicians and their patients, although the pathogenetic mechanism involved is obscure, because local application of glucose to the mucous membrane or the skin does not lead to pruritus.[3] It is worth emphasizing that significant infection was a comparatively uncommon cause of pruritus vulvae in our own patients, although the low rate of isolation of candida and other yeasts might reflect the intermittent use of antifungal agents.

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