

Diabetes Mellitus in Hopi and Navajo Indians

Prevalence of Microvascular Complications

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SUMMARY

In a cross-sectional study of Hopi and Navajo Indians with non-insulin-dependent diabetes mellitus, we found vascular complications to be strongly related to the duration of diabetes. In patients with diabetes of at least 10 yr duration, retinopathy was found in 57%, nephropathy in 40%, peripheral neuropathy in 21%, and peripheral vascular disease in 28%. For the Hopi and Navajo, the duration-specific prevalence rates of microvascular disease were very similar to prevalence rates found in many other populations. Thus we question the concept, based on reports in the late 1960s, that the Hopi and Navajo Indians have hyperglycemia as an isolated chemical abnormality unaccompanied by other manifestations of diabetes mellitus. DIABETES 32:894-899, October 1983.

In the late 1960s, the definitive articles on diabetes mellitus in Hopi and Navajo Indians described a remarkable lack of microvascular complications in these two tribes.^{1,2} Saiki and Rimoin² stated that "abnormal glucose tolerance appears to be a relatively isolated, benign chemical abnormality in the Navajo." Unfortunately, this information continues to prevail as the standard reference for microvascular complications in these two Indian tribes,^{3,4} often fostering a "benign neglect" attitude in the physicians who care for these diabetic patients.

We have conducted a cross-sectional study of 137 diabetic patients (77 Hopi and 60 Navajo) followed in our diabetic clinic with specific reference to microvascular complications.

METHODS

The Hopi and Navajo Indians live in northeastern Arizona. The Navajo tribe, numbering approximately 150,000, are Athabascan, being related to the Apaches of Arizona and the Haida Indians of Canada and Alaska. The Hopi, numbering approximately 7000, are Aztec-Tanoan, a Pueblo tribe, and are related to the Pima of south-central Arizona. The two

tribes are completely distinct socially, culturally, and historically, even though the smaller Hopi reservation is surrounded by the larger Navajo reservation. There is little intermarriage between the two tribes. The United States Public Health Service Hospital at Keams Canyon, Arizona, serves both tribes, caring for most of the 7000 Hopi and nearly 6000 Navajo.

The subjects of this report were all the Hopi or Navajo Indians known to have diabetes mellitus, and cared for by the authors from July 1, 1979, to June 30, 1980, at the Keams Canyon Indian Health Service Hospital, Keams Canyon, Arizona.

One hundred thirty-seven patients were evaluated (77 Hopi and 60 Navajo), and data were abstracted from their hospital records. All diagnoses of diabetes were confirmed by a fasting plasma glucose concentration ≥ 140 mg/dl. The duration of diabetes was calculated as the length of time from the initial diagnosis of diabetes until January 1, 1980, the midpoint of the study period.

All patients had careful histories and physical examinations performed by one of the authors (R.R., H.M., or M.B.). Heights and weights were recorded, and from these the body mass index was calculated as wt/ht^2 in kg/m^2 . A body mass index ≥ 27 kg/m^2 in men or ≥ 25 kg/m^2 in women has been suggested as a definition of obesity.⁵ Nephropathy was defined as proteinuria ≥ 1 by dipstick (Multistix, Ames Division, Miles Laboratories, Inc., Elkhart, Indiana) and/or a serum creatinine concentration ≥ 2.0 mg/dl. Twenty-four-hour quantitative analyses for proteinuria were not done routinely.

Peripheral neuropathy was defined as any subjective complaints of paresthesias in the feet, absent deep tendon reflexes of the knees or ankles, absent position or vibratory sensation of the feet, or alteration of sensation to pinprick of the feet in a "stocking" distribution. Peripheral vascular dis-

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TABLE 1
Hopi and Navajo Indian patients with diabetes treated at the Indian Health Service Hospital, Keams Canyon, Arizona

| Age (yr) | Sex | Hopi | | | | Navajo | | | | Total | | | |
|----------|-----|-----------------|------------------------|-------|-----------|-----------------|------------------------|-------|----------|-----------------|------------------------|-------|----------|
| | | Number examined | Diabetes duration (yr) | | BMI* mean | Number examined | Diabetes duration (yr) | | BMI mean | Number examined | Diabetes duration (yr) | | BMI mean |
| | | | Mean | Range | | | Mean | Range | | | Mean | Range | |
| 20-39 | M | 2 | 3.3 | 1-6 | 30 | 0 | — | — | — | 2 | 3.3 | 1-6 | 30 |
| | F | 2 | 8.5 | 3-14 | 29 | 3 | 2.3 | 1-4 | 30 | 5 | 4.8 | 1-14 | 30 |
| 40-59 | M | 11 | 8.0 | 0-20 | 27 | 10 | 2.3 | 0-5 | 27 | 21 | 5.3 | 0-20 | 27 |
| | F | 15 | 6.1 | 1-14 | 31 | 21 | 5.9 | 1-30 | 29 | 36 | 6.0 | 1-30 | 30 |
| 60-79 | M | 8 | 9.4 | 3-15 | 27 | 10 | 5.4 | 1-18 | 27 | 18 | 7.2 | 1-18 | 27 |
| | F | 33 | 8.6 | 1-23 | 28 | 15 | 9.1 | 0-22 | 27 | 48 | 8.8 | 0-23 | 28 |
| 80-99 | M | 2 | 9.5 | 5-14 | 28 | 0 | — | — | — | 2 | 9.5 | 5-14 | 28 |
| | F | 4 | 20.4 | 18-23 | 24 | 1 | 16 | 16-16 | 29 | 5 | 19.5 | 16-23 | 25 |
| Total | | 77 | 8.6 | 0-23 | 28 | 60 | 6.0 | 0-30 | 28 | 137 | 7.5 | 0-30 | 28 |

*BMI = body mass index, an estimate of obesity, computed as wt/ht² in kg/m².

ease was inferred from any amputation of a lower extremity, absent dorsalis pedis or posterior tibial pulses, a history of intermittent claudication, or skin ulcers and infections of the lower extremities.

The eyes of all patients were examined by a single observer (J. McV.) with a direct and an indirect ophthalmoscope through dilated pupils. The presence of retinal exudates, microaneurysms, hemorrhages, and neovascularization was recorded. In most cases the examiner was aware that the patient had diabetes, but was unaware of the disease duration or other clinical features. The presence of retinopathy was not determined in three subjects, two of whom did not receive an eye examination during the study period, and one of whom had cataracts preventing visualization of the fundi.

Results were analyzed by standard statistical methods, including chi-square tests and linear discriminant functions.⁶ The difference in prevalence rates of retinopathy between Hopi and Navajo patients was assessed, controlling for confounding by the duration of diabetes by the method of Mantel and Haenszel.⁷

RESULTS

The mean values of the duration of diabetes and body mass index of the 137 diabetic patients are shown by age, sex, and tribe in Table 1. The mean duration of known diabetes was 7.5 yr, ranging from 0 (new diagnosis) to 30 yr. Twenty-three percent of the patients had been treated without the

use of hypoglycemic drugs, 40% had received oral hypoglycemic drugs, and 37% had received insulin, as shown in Table 2. Nearly all insulin-treated patients received one daily injection of NPH insulin.

Diabetic patients from both tribes had similar prevalence rates of retinopathy after stratifying for the duration of diabetes. There was little difference between Hopi and Navajo patients in the duration-specific retinopathy rates, as shown in Table 3 ($\chi^2 = 0.51$, $df = 1$, NS, controlling for duration).⁷ Prevalence rates are shown in Table 4 for specific retinal lesions. In this and in subsequent tables, the results from the two tribes were similar and were pooled. Exudates and hemorrhages (including microaneurysms) were strongly related to diabetes duration (exudates: $\chi^2 = 10.1$, $df = 3$, $P < 0.025$; hemorrhages: $\chi^2 = 14.0$, $df = 3$, $P < 0.005$). The presence of any element of retinopathy increased from 19% among those with known duration <2 yr to 57% in those with ≥ 10 yr of known diabetes ($\chi^2 = 14.6$, $df = 3$, $P < 0.005$). Neovascularization was much less frequent, being observed in only 4% of the subjects, too few to allow analysis by the duration of diabetes.

Nephropathy, peripheral neuropathy, and infections or amputations of the lower extremities were also strongly related to the duration of diabetes. These lesions were common in those who had had diabetes ≥ 10 yr (Table 5).

The relationships of the complications of diabetes with the duration, age, sex, obesity, and method of treatment are

TABLE 2
Type of therapy for diabetes by tribe and sex in American Indian patients at Keams Canyon, Arizona

| Tribe | Sex | Treatment | | | | | | Total no. |
|--------|------|-----------|----|-----------------------------|----|---------|----|-----------|
| | | No drugs | | Oral hypoglycemic medicines | | Insulin | | |
| | | No. | % | No. | % | No. | % | |
| Hopi | M | 4 | 17 | 10 | 43 | 9 | 39 | 23 |
| | F | 14 | 26 | 22 | 41 | 18 | 33 | 54 |
| Navajo | M | 5 | 25 | 5 | 25 | 10 | 50 | 20 |
| | F | 9 | 23 | 18 | 45 | 13 | 33 | 40 |
| Total | Both | 32 | 23 | 55 | 40 | 50 | 37 | 137 |

TABLE 3
Prevalence of retinopathy* by duration of known diabetes in Hopi and Navajo Indians

| Duration of known diabetes (yr)† | Hopi | | | Navajo | | | Total | | |
|----------------------------------|----------|--------------|----|----------|--------------|----|----------|--------------|----|
| | No. pos. | No. examined | % | No. pos. | No. examined | % | No. pos. | No. examined | % |
| <2 | 3 | 10 | 30 | 3 | 21 | 14 | 6 | 31 | 19 |
| 2-4 | 5 | 19 | 26 | 3 | 16 | 19 | 8 | 35 | 23 |
| 5-9 | 6 | 18 | 33 | 4 | 8 | 50 | 10 | 26 | 38 |
| ≥10 | 17 | 28 | 61 | 7 | 14 | 50 | 24 | 42 | 57 |
| Total | 31 | 75 | 41 | 17 | 59 | 29 | 48 | 134 | 36 |

*Retinopathy was defined as the presence of microaneurysms, hemorrhages, exudates, or neovascularization in either retina. Of the 137 patients shown in Tables 1 and 2, satisfactory retinal examinations were performed in 134.

†Fractional years are truncated to the lower full year.

shown in Table 6. When each variable was considered individually, only the duration of diabetes was significantly associated with nephropathy, peripheral neuropathy, and infection or amputation of the lower extremities. There were no important differences in age, sex, obesity (estimated by the body mass index), or type of treatment between patients with or without each of the types of complications.

The joint relationships of these variables with retinopathy were examined using a linear discriminant function.⁶ The duration of diabetes was the strongest discriminator between patients with and without retinopathy. None of the other variables was significantly associated with retinopathy, either singly (as shown in Table 6) or as additional contributors to the discriminant function. Similarly, in discriminating between those with or without nephropathy, peripheral neuropathy, or infections or amputations of the lower extremities, none of the other variables in Table 6 made a significant contribution after the duration of diabetes was considered.

DISCUSSION

The microvascular complications of diabetes in the Hopi and Navajo Indians were similar to those reported in patients of other racial or ethnic groups. Diabetic retinopathy, in particular, has a remarkably similar relationship to the duration of diabetes in several populations, as shown in Figure 1. The duration-specific prevalence rates of retinopathy for the Hopi and Navajo from Table 3 are plotted in Figure 1 and compared with rates from other populations. Fifty-seven percent of our patients with ≥10 yr of known diabetes had retinopathy. The prevalence rates of retinopathy in 890 Pima Indians with diabetes were determined by methods⁹ almost identical

to those of the present study. Rates of retinopathy according to the duration of diabetes are also shown from English,⁹ Swedish,¹⁰ and Japanese¹¹ studies. The results of all five studies are similar, except that the rates in the Pima tend to be lower for a given duration of diabetes. The Pima study included many subjects diagnosed through extensive routine screening procedures as well as those seeking medical care. In contrast, the other studies, which are based entirely on diabetes clinic patients, may have selected patients with more advanced disease. Because the Pima population has participated in a longitudinal diabetes study since 1965,¹² it is unlikely for a Pima to have undiagnosed diabetes for several years, as could have occurred in the other studies. In addition to these five studies, other investigators have reported similar findings, but the duration groups reported were not sufficiently comparable to those of the present report for inclusion in Figure 1. In a study of Japanese diabetic patients in Hiroshima and diabetic patients of Japanese descent living in Hawaii, the retinae were examined with a direct ophthalmoscope through dilated pupils as in the present study.¹³ Among these Japanese patients with diabetes of 10-19 yr duration, retinal microaneurysms or hemorrhages were found in 57% of subjects in Hiroshima and 55% of subjects in Hawaii, similar to the prevalence of 57% in Hopi and Navajo subjects with diabetes ≥10 yr duration (Table 4).

In Hopi and Navajo patients who had known diabetes ≥10 yr, 57% had retinopathy, 40% had nephropathy, 21% had peripheral neuropathy, and 28% had either amputations or peripheral vascular disease (Table 5). These findings illustrate the universal nature of diabetic retinopathy and other

TABLE 4
Prevalence of retinal lesions by duration of known diabetes in Hopi and Navajo Indians. The data for both tribes are combined

| Duration of known diabetes (yr) | No. examined | Exudates | | Microaneurysms or hemorrhages | | Neovascularization | | Any retinopathy | |
|---------------------------------|--------------|----------|----|-------------------------------|----|--------------------|----|-----------------|----|
| | | No. | % | No. | % | No. | % | No. | % |
| <2 | 31 | 4 | 13 | 5 | 16 | 1 | 3 | 6 | 19 |
| 2-4 | 35 | 5 | 14 | 7 | 20 | 0 | 0 | 8 | 23 |
| 5-9 | 26 | 7 | 27 | 9 | 35 | 3 | 12 | 10 | 38 |
| ≥10 | 42 | 17 | 40 | 22 | 52 | 2 | 5 | 24 | 57 |
| Total | 134 | 33 | 25 | 43 | 32 | 6 | 4 | 48 | 36 |

TABLE 5

Prevalence of nephropathy, neuropathy, and lower extremity amputation by duration of known diabetes in Hopi and Navajo Indians. The data for both tribes are combined

| Duration of known diabetes (yr) | No. examined | Nephropathy* | | Peripheral neuropathy | | Lower extremity infections, amputation, or evidence of peripheral vascular disease | |
|---------------------------------|--------------|--------------|----|-----------------------|----|--|----|
| | | No. | % | No. | % | No. | % |
| <2 | 32 | 3 | 9 | 1 | 3 | 2 | 6 |
| 2-4 | 36 | 12 | 33 | 4 | 11 | 1 | 3 |
| 5-9 | 26 | 10 | 38 | 4 | 8 | 3 | 12 |
| ≥10 | 43 | 17 | 40 | 9 | 21 | 12 | 28 |
| Total | 137 | 42 | 31 | 16 | 12 | 18 | 13 |

*Proteinuria (≥1 by dipstick) or serum creatinine concentration ≥2.0 mg/dl.

complications of diabetes. The development of these complications is strongly dependent on the duration of diabetes, but appears not to depend on racial or geographic characteristics. The present finding of little relationship of retinopathy to age, after duration has been taken into account, is consistent with previous findings in adults.⁸⁻¹⁰

It is difficult to reconcile these findings with previous reports that hyperglycemia in the Hopi and Navajo was unaccompanied by microvascular complications typical of diabetes.^{1,2} Saiki and Rimoin² found retinopathy in 7%, albuminuria in 21%, and peripheral vascular disease in 4% of Navajo patients with diabetes, although they did not present rates of vascular complications as a function of the duration of diabetes. In their study of complications in 101 Hopi and Navajo diabetic patients using clinical criteria similar to those of the present report, Prosnitz and Mandell¹

found only 2 people with retinopathy, but 19 with nephropathy, 8 with peripheral neuropathy, and 2 with peripheral vascular disease. The prevalence of complications was related to the duration of diabetes. Thus the prevalence of retinopathy was quite low in these earlier studies. It is possible that the prevalence of diabetes has increased substantially since 1967 or 1968 when these papers were published, as diabetes prevalence may have increased in other populations,³ including another American Indian tribe, the Pima.^{14,15} If these studies were performed during a period of an explosive increase in the incidence of diabetes, very few subjects might have had diabetes long enough to develop microangiopathy. Alternatively, in the earlier studies the low prevalence of retinopathy (which was more strikingly different from our study than were prevalence rates of the other complications) might be partly due to differences in eye

TABLE 6

Associations of complications of diabetes with characteristics of the Hopi and Navajo Indian patients

| | Any retinopathy | | Nephropathy | | Peripheral neuropathy | | Lower extremity infections, amputation, or evidence of peripheral vascular disease | |
|--|-----------------|-------|-------------|------|-----------------------|-------|--|-------|
| | No | Yes | No | Yes | No | Yes | No | Yes |
| No. subjects* | 85 | 47 | 94 | 41 | 120 | 15 | 118 | 17 |
| Mean diabetes duration (yr) | 6.1 | 10.2† | 6.8 | 9.3‡ | 7.1 | 11.5‡ | 6.9 | 12.4† |
| Mean age (yr) | 59 | 62 | 59 | 63 | 60 | 64 | 60 | 64 |
| Percentage of female subjects | 69 | 66 | 68 | 68 | 70 | 53 | 68 | 71 |
| Mean BMI§ | 29 | 27 | 28 | 28 | 28 | 28 | 28 | 27 |
| Percentage distribution of diabetes drug use | | | | | | | | |
| None | 27.0 | 14.9 | 25.5 | 19.5 | 25.8 | 6.7 | 26.3 | 5.9 |
| Oral | 36.5 | 46.8 | 38.3 | 43.9 | 39.2 | 46.7 | 38.1 | 52.9 |
| Insulin | 36.5 | 38.3 | 36.2 | 36.6 | 35.0 | 46.7 | 35.6 | 41.2 |

*Totals are less than the 137 subjects in the full study because values of some variables were unavailable for a few subjects.

†P < 0.001, ‡P < 0.05: significance of difference in this variable (without regard for other variables) between subjects with and without the complication.

§Body mass index, or wt/ht² in kg/m².

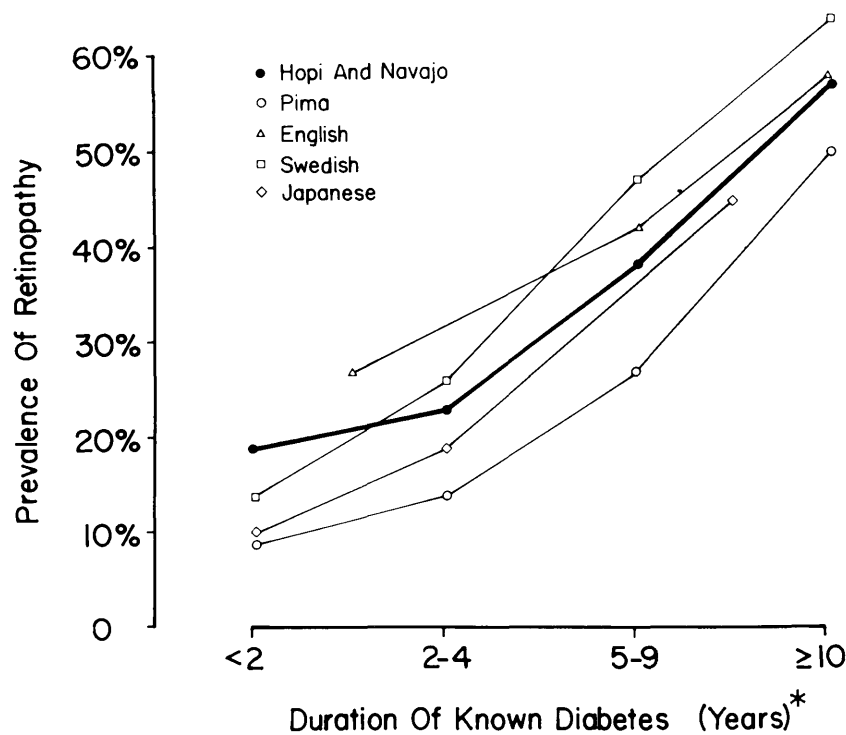


FIGURE 1. Prevalence of retinopathy (exudates, microaneurysms, hemorrhages, or neovascularization) according to duration of known diabetes in five populations. The Hopi and Navajo rates are from the present study. The Pima prevalence rates were estimated from the Pima Indian diabetes study as described previously⁸ and revised for this article by including additional data. The prevalence rates from an English diabetes clinic (restricted to patients diagnosed at age 30 yr or greater) were reported by Burditt et al.⁹ The Swedish rates are from Aarseth,¹⁰ and the Japanese rates are from Miki et al.¹¹ *Fractions of years are truncated to the lower full year. The duration groupings were not exactly as indicated on the abscissa in all populations. In the English study, the first point represents durations of 0-4 yr; in the Swedish and Japanese studies, the first point represents <1 yr and the second point 1-4 yr; in the Japanese study the last point represents ≥ 5 yr.

examination methods, which were not clearly described. In the present study the fundi were examined through dilated pupils allowing much better visualization than is usually possible through undilated pupils. Had we used more sensitive methods for detecting retinopathy, such as fundus photography or fluorescein angiography,¹⁶ the observed prevalence of retinopathy might have been even higher. Similarly, the prevalence of the other types of complications might have been higher if more sensitive methods had been used. Our methods were, however, similar to those of the previous studies in Hopi and Navajo Indians and in many other population groups.

The diabetic patients described by Prosnitz and Mandell¹ and by Saiki and Rimoin² were non-insulin-dependent, non-ketosis-prone, and obese, with their disease onset in adulthood. Our patients were very similar: non-insulin-dependent, non-ketosis-prone, and obese, with only four patients having the onset of diabetes at <30 yr of age (17, 25, 27, 29 yr).

In conclusion, diabetes in the Hopi and Navajo Indians is often accompanied by the retinopathy, nephropathy, peripheral neuropathy, and peripheral vascular disease that are typical of diabetes in other populations. The frequency of these complications is related to the duration of diabetes. The prevalence of diabetes in this population and of complications in all Hopi and Navajo diabetic subjects could not be estimated accurately because the study was conducted among patients attending a diabetes clinic. Among the patients with known diabetes, however, vascular complications clearly occurred with a similar direct relationship to the duration of diabetes as that previously reported in other racial groups. The suggestion that in some populations, such as the Hopi and Navajo Indians, hyperglycemia is an isolated

chemical abnormality unaccompanied by other diabetes manifestations must be seriously questioned.

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