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# Blood Pressure in Navajo Indians and Its Association With Type 2 Diabetes and Renal and Cardiovascular Disease

*Wendy Hoy, Amy Light, and Donald Megill*

**In mid-1990 we evaluated blood pressure and its associations in 366 nondiabetic adult Navajos and 400 Navajos with type 2 diabetes attending Indian Health Service outpatient clinics in Tuba City, Arizona. In nondiabetics, systolic blood pressure (SBP) rose with increasing age while diastolic blood pressure (DBP) fell; 13.4% had hypertension by diagnosis or treatment. Female nondiabetics had lower blood pressures than males. SBP and DBP correlated with age, body mass index (BMI), and urinary albumin excretion (UAE). Hypertension was associated with a sixfold increase in nephropathy, a threefold increase in renal insufficiency, and an almost sixfold increase in cardiovascular disease.**

**Diabetics had higher blood pressures than age- and sex-matched nondiabetics; 58.4% had hypertension by diagnosis or treatment, and, in spite of widespread antihypertensive treatment, blood pressures in almost 50% were suboptimal from the perspectives of cardiovascular and renal protection. Blood pressures of female diabetics were similar to those of males. Blood pressures correlated with age, BMI, and increasing UAE. Rates of nephropathy and cardiovascular disease were much higher in diabetics than nondiabetics, and within the diabetic population hypertension was associated with a greater than threefold increase in nephropathy, an eightfold increase in renal insufficiency, a fivefold increase in peripheral and cerebrovascular disease, and more than doubling of the rate of heart disease.**

**The relationships of blood pressure to renal and cardiovascular disease suggest similar mechanisms in nondiabetics and diabetics, with diabetes contributing an accentuated susceptibility. Albuminuria and cardiac disease are generated at "subhypertensive" blood pressures, while established hypertension appears to drive overt renal, cerebrovascular, and peripheral vascular disease, and to further increase heart disease risk. Assuming a causal association, vigorous control of hypertension should powerfully reduce renal, cerebrovascular, and peripheral vascular disease in the Navajo population. Prevention of microalbuminuria and heart disease probably requires broadly based risk factor modification in the entire community. Am J Hypertens 1994;7:321–328**

KEY WORDS: **Blood pressure, hypertension, renal disease, cardiovascular disease, Navajo Indians.**

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This work is dedicated to the memory of Dr. Donald Megill.

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American Indians, like many populations "in epidemiologic transition,"[1] are experiencing increasing rates of obesity, hypertension, and type 2 diabetes that were almost nonexistent in their predecessors.[2–5] This syndrome is attributed to changes in diet and activity superimposed on a genetic predisposition,[6] and is mediated in part by insulin resistance or hyperinsulinemia.[6,7] Complications are heart disease, stroke, amputations, renal disease and renal failure, visual impairment, and premature mortality.[8–14] In 1989, diabetes and hypertensive disease were the leading causes of outpatient visits to the Indian Health Service (IHS) for ages 45 to 64 years and 65+ years, and circulatory disorders featured prominently.[15] Death rates from diabetes among Indians nationwide in 1987 were 2.4 times those of the U.S. aggregate.[8] Diseases of the heart were the leading cause of death for Indian males and females, at an adjusted rate of 142.8/100,000 (ratio to U.S. aggregate rates 0.8), and cerebrovascular disease was the fourth leading cause. Diabetics have the highest rates of these cardiovascular complications, but they are also increasing in nondiabetics.[11,12]

The Navajo Indians are the largest Native American tribe, with an estimated 1992 population of 201,583.[16] Most live on the 25,000-square-mile Navajo reservation, which encompasses parts of northwestern New Mexico, northeastern Arizona, and southern Utah. Of Athabascan origin, they are descended from more recent trans-Bering migrations than the Mesoamerican Indians of the Hohokum and Anasazi cultures, and probably moved into the Southwest within the last 400 years.[9] Their population growth rate is high (2.8% per year); 50.4% of Navajos are less than 20 years old, and only 19.7% are 40 years of age or older.[17]

Obesity, diabetes, hypertension, and cardiovascular disease were rare among Navajos in the 1930s,[5] but are now major health problems. Navajos are becoming heavier and most adults are now overweight.[2,9] Diabetes was detected in 17.2% of Navajos aged 20 to 74 years in a regional 1989 to 1990 study, 2.5 times the rate of the general U.S. population.[18] Although normal blood pressures for Navajos have not been defined, rates of hypertension by usual standards are rising and it is especially common among diabetics.[19,20] Heart attacks have increased, with an especially precipitous rise since the late 1970s,[9,12,21] and heart disease is now the leading cause of death after accidents (73.7/100,000).[16] Amputations have increased, at least among diabetics, to a 1987 rate similar to that of U.S. diabetics in general.[9] Diabetic retinopathy is common.[22] Diabetic end stage renal disease (ESRD) has risen dramatically,[23] with a compound annual increase of about 12% in new cases coming to treatment from 1986 to 1990, and a crude incidence rate in 1990 of 225 per million (pm) compared with 33 pm for the U.S. aggregate for types 1 and 2 diabetes combined (W.E. Hoy, unpublished data).[13,23]

In this report we describe blood pressures of Navajo adult clinic patients, without and with type 2 diabetes, and evaluate its relationship to renal and cardiovascular disease.

## METHODS

In mid-1990, we collected information on more than 400 nondiabetic Navajo Indians attending Medical Clinic at the IHS hospital in Tuba City, Arizona, and on more than 400 Navajos with type 2 diabetes attending Diabetes Clinic at the same facility. These diabetics represent a third of the estimated 1200 diabetics at that Service Unit. Diabetes is diagnosed in the IHS by National Diabetes Data Group criteria,[24] as measured on the annual physical examination recommended for all Indians ≥ 18 years old. The first eight subjects who attended the clinic each day were included until the samples were complete. This report focuses on subjects 20 years of age and older, 366 nondiabetics and 400 diabetics. ESRD patients, whose care is largely rendered in the dialysis unit, were not among the study subjects.

We recorded blood pressure and weight at that visit, measured albumin concentration on a random urine specimen, and reviewed every medical record. Urinary albumin levels were measured with the portable Beckman Immunochemistry System (ICS), by a nephelometric technique using monoclonal antialbumin antibody, which is sensitive to albumin concentrations as low as 1 mg/L (1 μg/mL). Creatinine concentrations were measured by autoanalyzer on the same urine specimen. The albumin/creatinine ratio on a random urine sample has been validated as an epidemiologic tool in several population-based studies of renal disease.[25–31] This ratio rarely exceeds 10 mg/g in healthy young normal subjects,[29] with a median of 6 mg/g (Endocrine Sciences), but levels < 20 mg/g are considered potentially normal. Levels of 20 to 299 mg/g, or "microalbuminuria," indicate abnormal glomerular permeability or early renal disease, which predicts clinical nephropathy in type 2 diabetics[31,32] and predicts increased cardiovascular mortality in diabetics and nondiabetics.[32–35] Levels ≥ 300 mg/g, or "overt" albuminuria, indicate established nephropathy; a *protein*/creatinine ratio ≥ 1000 mg/g in Pima diabetics has been termed "florid nephropathy," and predicts ESRD and a 16-fold increase in renal failure deaths, as well as a 2.5-fold increase in

cardiovascular deaths, and a 50% mortality rate within 5 years.[36]

The following information was derived from the medical records: demographic data, formal diagnoses by the health care provider of diabetes and hypertension,[24,37] diagnoses of renal and genitourinary disease, medications, height, serum creatinine levels, diagnosis of, or event compatible with, ischemic cardiac disease (angina, congestive heart failure, myocardial infarction, compatible EKG changes), cerebrovascular disease (transient ischemic attacks, stroke), and peripheral vascular disease (eg, ischemia, claudication, ulcers, amputations). Date of diagnosis of diabetes and presence of retinopathy and neuropathy were recorded for diabetics. Nondiabetics and diabetics were compared in three age-matched categories: 20 to 39 years, 40 to 59 years, and 60+ years.

Data were entered into an EPI-INFO program and analyzed by the Statistical Analysis System. Proportional data were compared using the Mantel-Haenszel weighted odds ratio with Cornfield 95% confidence intervals. Univariate correlations were evaluated using both Pearson and Kendall $\tau$ coefficients.

Full confidentiality was maintained in the execution of this study and analysis of its results. Subjects are identified only in aggregate and no personal descriptors are used.

## RESULTS

**Study Subjects** The female/male ratio was 1.55:1 for nondiabetics, and 1.35:1 for diabetics. Nondiabetics were 20 to 88 years old, mean 42.1 ± 14.0 years, and diabetics were 20 to 98 years old, mean 56.9 ± 12.9 years. The median and mean ages of nondiabetics and diabetics were matched within 2 years for each of the three age groups.

The mean body mass index (BMI) of nondiabetics was 28.0 ± 5.6 kg/m$^2$, the mean percent of "ideal" body weight was 116 ± 24% (percent of NCHS age- and sex-specific median values), and the percent "obese" 40.9% (≥120% of ideal body weight[38]). The mean BMI of diabetics was 29.5 ± 5.1 kg/m$^2$, mean percent of ideal BMI 117 ± 21%, and proportion obese, 38.9%. Diabetic women were heavier than nondiabetic women in the 20 to 39 year age group, 33.9 ± 7.7 *v* 27.9 ± 6.9 kg/m$^2$ ($P$ = .02), and in the 40 to 59 year age group, 31.4 ± 5.5 *v* 28.5 ± 4.1 kg/m$^2$ ($P$ < .05), but there were no differences between diabetic and nondiabetic older women, nor in men in any age group.

The mean age at diagnosis in diabetics was 49.3 ± 12.9 years, and mean time since diagnosis was 8.0 ± 6.3 years. Almost half had diabetes for less than 5 years, and almost two-thirds for less than 10 years.

**Observations** Table 1 shows the blood pressure profiles of study subjects. Women without diabetes had lower systolic (SBP) and diastolic (DBP) blood pressures than men, and lower rates of elevated SBP, DBP, and all forms of "hypertension." These differentials became less marked with increasing age, as SBP and rates of hypertension rose more prominently with age in women than in men. Rates of elevated DBP fell after middle age in both sexes.

Mean SBP and DBP in female diabetics, however, were similar to those of diabetic men, and all definitions of hypertension, except for elevated DBP, occurred with similar frequency in diabetic women and men. Diabetics had higher blood pressures than nondiabetics, and much higher rates of hypertension. Almost 50% of diabetics had elevated SBP or DBP, or both, indicating "suspected" or inadequately treated hypertension.[29,37] Fifty-eight point four percent of diabetics had "confirmed" hypertension by diagnosis or treatment, and 68.4% had confirmed or suspected hypertension. An increased risk of diabetics for hypertension persisted when controlled for BMI.

Antihypertensive drugs were prescribed for 9.8% of nondiabetics and 46.3% of diabetics. Of diabetics receiving antihypertensive drugs, 65.6% were receiving diuretics, 47.9% were receiving β-blockers, 38.5% were receiving angiotensin converting enzyme inhibitors, and 17.7% were receiving other agents. Many subjects were receiving more than one agent: 17.7% were receiving diuretics and β-blockers in combination. The prescriptions for hypertensive nondiabetics were similarly distributed.

Table 2 shows that urinary albumin excretion (UAE) was higher in diabetics than nondiabetics, with rising risk as the intensity of albuminuria increased, and no differences between men and women. The increased risk of diabetics for elevated UAE persisted after controlling for blood pressure levels. Presumed elevation of serum creatinine (≥1.2 mg/dL in women and ≥1.4 mg/dL in men) was more common in diabetics, and the partial protection evidenced in female nondiabetics was erased. These creatinine levels correspond approximately to creatinine clearances of 53 mL/min for women and 65 mL/min for men, using the Cockcroft Gault formula,[39,40] and are reasonable definitions of suspected renal insufficiency. Rates of albuminuria and renal insufficiency were not substantially altered by exclusion of subjects with "genitourinary" diagnoses, including urinary tract infections.

Cardiovascular disease was less common in female nondiabetics than in males. Rates were much higher in diabetics, and the differential between female and male rates was reduced.

TABLE 1. BLOOD PRESSURE AND RATES OF HYPERTENSION IN NAVAJO ADULTS (INCLUDES SUBJECTS ON ANTIHYPERTENSIVE MEDICATION)

| | Age Group | Nondiabetics | | Diabetics | | Adjusted O.R. Diabetics *v* Nondiabetics (CI) | | |
|---|---|---|---|---|---|---|---|---|
| | | Female | Male | Female | Male | | | |
| SBP (mm Hg) mean ± SD | 20–39 | 118 ± 14 | 129 ± 14 | 131 ± 12* | 135 ± 14** | | | |
| | 40–59 | 124 ± 13 | 125 ± 15 | 134 ± 19* | 137 ± 20* | | | |
| | 60+ | 130 ± 18 | 137 ± 17 | 141 ± 17* | 139 ± 21 | | | |
| | All | 121 ± 15 | 129 ± 15 | 137 ± 18 | 138 ± 20 | | | |
| DBP (mm Hg) mean ± SD | 20–39 | 69 ± 11 | 76 ± 11 | 84 ± 14* | 83 ± 12* | | | |
| | 40–59 | 74 ± 10 | 79 ± 13 | 79 ± 12* | 83 ± 12 | | | |
| | 60+ | 73 ± 9 | 73 ± 9 | 75 ± 10 | 77 ± 10 | | | |
| | All | 71 ± 11 | 77 ± 11 | 78 ± 12 | 81 ± 12 | | | |
| Percentage with SBP ≥ 140 mm Hg | 20–39 | 5.6 | 30.4 | 29.4* | 33.3 | Women | 3.7 | (2.2–6.9) |
| | 40–59 | 1.5 | 14.8 | 34.9* | 44.4* | Men | 2.3 | (1.3–4.0) |
| | 60+ | 25.0 | 35.0 | 53.6* | 43.1 | All | 3.1 | (2.1–4.5) |
| | All | 11.5 | 25.2 | 43.3 | 42.5 | | | |
| Percentage with DBP ≥ 90 mm Hg | 20–39 | 3.7 | 17.4 | 35.3* | 28.6 | Women | 8.2 | (3.2–2.9) |
| | 40–59 | 4.1 | 20.4 | 19.8* | 28.4 | Men | 1.7 | (0.9–3.4) |
| | 60+ | 0 | 5.0 | 4.5 | 11.3 | All | 3.1 | (1.9–5.6) |
| | All | 3.2 | 16.8 | 13.7 | 21.4 | | | |
| Percentage with SBP ≥ 140 and/or DBP ≥ 90 mm Hg | 20–39 | 9.3 | 31.9 | 41.2* | 47.6 | Women | 4.4 | (2.6–7.9) |
| | 40–59 | 13.5 | 27.8 | 40.6* | 48.2** | Men | 2.1 | (1.2–3.6) |
| | 60+ | 25.0 | 35.0 | 55.5* | 45.8 | All | 3.1 | (2.1–4.5) |
| | All | 13.3 | 30.8 | 49.8 | 47.1 | | | |
| Percentage with hypertension by diagnosis and/or treatment | 20–39 | 3.6 | 11.6 | 44.4* | 61.9* | Women | 7.1 | (4.3–14.0) |
| | 40–59 | 12.0 | 29.6 | 47.7* | 65.9* | Men | 6.2 | (3.6–11.7) |
| | 60+ | 21.6 | 20.0 | 61.3* | 63.9* | All | 6.5 | (4.7–10.4) |
| | All | 9.4 | 19.6 | 53.8 | 64.6 | | | |
| Percentage with hypertension by diagnosis, treatment, SBP ≥ 140, or DBP ≥ 90 mm Hg | 20–39 | 10.8 | 34.8 | 50.0* | 61.9** | Women | 6.4 | (3.9–10.7) |
| | 40–59 | 18.7 | 40.7 | 61.7* | 73.2* | Men | 3.2 | (1.9–5.5) |
| | 60+ | 37.8 | 50.0 | 75.7** | 68.1 | All | 4.7 | (3.3–6.7) |
| | All | 17.9 | 39.2 | 67.4 | 69.7 | | | |

*$P < .01$ for significance of difference from age- and sex-matched nondiabetics.

**$P < .05$ for significance of difference from age- and sex-matched nondiabetics.

*CI, confidence interval; DBP, diastolic blood pressure; SBP, systolic blood pressure.*

**Correlations** Univariate analysis showed the following relationships in nondiabetics:

1) SBP with DBP ($r = 0.6$, $P = .0001$), with age ($r = 0.24$, $P = .0001$), and with BMI, ($r = 0.18$, $P = .068$), Pearson coefficients; and with UAE ($r = 0.14$, $P = .0001$), Kendall $\tau$ coefficient.
2) DBP with SBP as above, with age ($r = 0.17$, $P = .0001$), Pearson coefficients; and with UAE ($r = 0.15$, $P = .0001$), Kendall $\tau$ coefficient.

Univariate analysis showed the following relationships in diabetics:

1) SBP with DBP ($r = 0.6$, $P = .0002$), with BMI ($r = 0.21$, $P = .0001$), with age ($r = 0.35$, $P = .0001$), and with log UAE ($r = 0.24$, $P = .0001$, all Pearson coefficients.
2) DBP with SBP as above, with BMI ($r = 0.24$, $P = .0001$), with log UAE ($r = 0.22$, $P = .0001$), and with age ($r = 0.05$, $P = .03$), Pearson coefficients.

Table 3 shows the associations of "confirmed" hypertension with albuminuria, overt nephropathy, and cardiovascular disease in nondiabetics and diabetics, and with retinopathy and neuropathy in diabetics. In nondiabetics, hypertension was associated with a 3.4-fold increase in albuminuria, a sixfold increase in overt albuminuria, and a threefold increase

TABLE 2. ALBUMINURIA, RENAL DISEASE, AND CARDIOVASCULAR DISEASE IN NAVAJO ADULTS

| | Age Group | Nondiabetics (%) | | Diabetics (%) | | Adjusted O.R. Diabetics *v* Nondiabetics (CI) | | |
|---|---|---|---|---|---|---|---|---|
| | | Women | Men | Women | Men | | | |
| Renal dysfunction | | | | | | | | |
| Albuminuria | 20–39 | 12.3 | 15.3 | 41.4 | 50.0 | Women | 4.4 | (2.7–8.0) |
| ≥20 mg/g | 40–59 | 15.0 | 25.0 | 61.8 | 45.8 | Men | 3.5 | (1.9–6.9) |
| | 60+ | 38.7 | 21.4 | 54.6 | 58.4 | All | 4.1 | (2.8–6.3) |
| | All | 17.6 | 19.8 | 56.7 | 51.1 | | | |
| ≥300 mg/g | All | 2.7 | 1.7 | 12.3 | 13.5 | All | 6.0 | (2.2–15.5) |
| ≥1000 mg/g | All | 0.5 | 0 | 5.6 | 5.5 | All | 9.4 | (1.8–349) |
| High creatinine* | All | 3.2 | 5.6 | 11.3 | 9.8 | All | 2.6 | (0.8–7.9) |
| Cardiovascular disease | | | | | | | | |
| All categories | 20–39 | 0.9 | 2.9 | 5.6 | 4.8 | Women | 7.1 | (2.8–20.2) |
| | 40–59 | 1.3 | 7.4 | 23.4 | 36.6 | Men | 5.8 | (2.5–12.7) |
| | 60+ | 10.8 | 20.0 | 34.2 | 58.3 | All | 6.5 | (3.5–11.6) |
| | All | 2.7 | 7.0 | 27.1 | 41.7 | | | |
| Cardiac | All | 2.7 | 5.6 | 22.0 | 29.7 | All | 5.2 | (2.7–9.9) |
| Peripheral vascular | All | 0 | 0.7 | 3.0 | 5.2 | All | 6.4 | (0.9–143) |
| Cerebrovascular | All | 0 | 0.7 | 2.1 | 6.3 | All | 9.0 | (1.1–172) |

**Serum creatinine ≥ 1.2 mg/dL in women, ≥ 1.4 mg/dL in men.*

*CI, confidence interval.*

in probable renal insufficiency. Nondiabetics without hypertension had little heart disease and no cerebrovascular or peripheral vascular disease; hypertension was associated with a 6.4-fold increase in cardiovascular disease overall, and a greater than fourfold increase in cardiac disease. Hypertension by the other definitions in Table 1 correlated similarly.

Forty percent of diabetics without confirmed hypertension had microalbuminuria. Hypertension was associated with only a minimal increase in rates of microalbuminuria, but rates of overt albuminuria were increased almost threefold, and serum creatinine elevations were increased almost eightfold. Hypertension was also associated with a threefold increase in cardiac disease, while cerebrovascular and peripheral vascular disease were increased more than fivefold. Retinopathy risk was doubled but an apparent increase in neuropathy was not significant.

Table 4 shows that hypertension and elevated UAE were established in more than half the diabetics in the early years of diagnosed disease, and cardiovascular disease in more than one-fifth. Rates rose modestly

TABLE 3. HYPERTENSION AND ITS ASSOCIATIONS IN NAVAJO ADULTS

| | Nondiabetics | | | Diabetics | | |
|---|---|---|---|---|---|---|
| | Nonhypertensive (%) | Hypertensive (%) | OR for Hypertensives *v* Nonhypertensives (CI) | Nonhypertensive (%) | Hypertensive (%) | OR for Hypertensives *v* Nonhypertensives (CL) |
| UAE ≥ 20 mg/g | 14.1 | 35.7 | 3.4 (1.6–7.2) | 46.5 | 60.2 | 1.9 (1.2–3.1) |
| UAE ≥ 300 mg/g | 1.6 | 4.8 | 6.1 (1.3–2.8) | 6.3 | 17.5 | 3.2 (1.4–3.1) |
| Elevated serum creatinine | 2.9 | 8.7 | 3.2 (0.7–13.4) | 2.4 | 16.3 | 8.0 (2.7–26.9) |
| Cardiovascular disease | | | | | | |
| All | 2.5 | 14.0 | 6.4 (2.0–20.1) | 18.7 | 39.4 | 2.8 (1.7–4.6) |
| Cardiac | 2.5 | 10.0 | 4.4 (1.2–15.2) | 16.4 | 32.0 | 2.4 (1.4–4.0) |
| Peripheral | 0 | 2.0 | Undefined | 1.2 | 5.8 | 5.2 (1.1–33.7) |
| Cerebral | 0 | 2.0 | Undefined | 1.2 | 5.4 | 5.2 (1.1–33.7) |
| Retinopathy | N/A | N/A | | 31.0 | 47.3 | 1.9 (1.1–3.4) |
| Neuropathy | N/A | N/A | | 23.8 | 31.5 | 1.6 (0.9–2.8) |

*NA, not applicable; UAE, urinary albumin excretion.*

with increasing duration of diabetes. Rates of retinopathy and neuropathy, however, were low in the early stages of recognized diabetes and rose impressively with increasing disease duration.

## DISCUSSION

Several methodologic issues influence the findings in this study. A cohort effect due to changing health patterns in the Navajo confounds interpretation of age-related trends, and a survivor effect masks the full impact of severe hypertension, overt nephropathy, and cardiovascular disease on the Navajo population. Cardiovascular disease is further underestimated by the insensitive method of ascertainment, and renal disease by exclusion of treated ESRD patients from the study population.

It is probable that blood pressures and morbidities in the nondiabetic clinic patients studied here exceed those in the general Navajo population, but the relationships of variables within that population and comparisons with matched diabetics are instructive. The diabetics are probably more representative of the entire diabetic population in that area.

The association of diabetes with hypertension by any of several definitions was dramatic; most diabetics were hypertensive, even in the earliest years of diagnosed disease. Rates of hypertension in diabetics were much higher than the 31.2% estimated from a 1986 to 1987 review of Ambulatory Patient Care Codings,[41] but compatible with a 1989 study of diabetic Navajos by record review (54.9% in males and 47.5% in females).[20] Elevated blood pressures in almost half the diabetics, in spite of widespread antihypertensive treatment, indicate opportunities for intensified surveillance and therapy, according to guidelines for minimizing cardiovascular and renal disease risk.[29,37]

The high rates of overt albuminuria and renal insufficiency in Navajo diabetics, although understated, are compatible with Navajo ESRD data. The high rates and marked segregation of cardiovascular disease within the diabetic population are consistent with other observations; most amputations and probably more than half the fatal heart attacks in Navajos now occur in the diabetic minority.[9,12] Pima Indians show a similar phenomenon with nearly all fatal ischemic heart disease and amputations confined to the diabetic population.[11,42]

Blood pressures in nondiabetic women suggest a protective effect that declines with age; therein probably lies their relative protection against cardiovascular disease and their partial protection against most common forms of chronic renal failure.[13] This protective effect is reduced in women with diabetes, a phenomenon that probably contributes to "masculinization" of their cardiovascular risk.[11,43,44] The same phenomenon might also determine the equal susceptibility of female and male Indian diabetics to diabetic nephropathy, which is reflected in our data, confirmed in Pima diabetics,[45,46] and inferred by the female dominance in the Indian diabetic ESRD population nationwide.[13] Long-standing insulin resistance that antedates and accompanies the diabetic state might underlie this masculinizing effect.[7]

The strong association of hypertension with nephropathy in diabetics and nondiabetics probably has primary and secondary components. A major causal role, however, is supported in Pima diabetics by the strong predictive value of blood pressure levels for the progression of albuminuria and of hypertension for the development of ESRD,[31,45,46] and, in the broader population, by the adverse influence of hypertension and the salutary effects of effective blood pressure control on the progression of nondiabetic and diabetic nephropathies.[47,48] An even greater impact of hypertension on the population as a whole is probably mediated through its dramatic association with the more prevalent cardiovascular disease, in both nondiabetics and diabetics.

While "confirmed" hypertension demarcates high-risk status for peripheral and cerebrovascular disease and for renal insufficiency in nondiabetics and diabetics, cardiac disease and microalbuminuria occur with significant frequency in "nonhypertensive" subjects. This implies that these morbidities are generated by blood pressures below this arbitrary level and by other factors as well. Likewise, retinopathy in diabetics is often associated with blood pressures below this arbitrary limit.

The presence of hypertension, microalbuminuria, and cardiovascular disease in a proportion of nondiabetic Navajos (unrecognized diabetics and glucose-intolerant subjects notwithstanding), and their prevalence during the earliest years of recognized diabetes (acknowledging the underestimate), suggest that these conditions are generated in the prediabetic, insulin-resistant state, as others have proposed.[6,49–51] Parallels with Syndrome X in the broader population are striking.[51–53] The proposed inclusion of microalbuminuria in the constellation is novel, but worth further evaluation, in view of the relationship of mi-

TABLE 4. TIME SINCE DIABETES DIAGNOSIS AND MORBIDITY RATES

| | Time Since Diagnosis of Diabetes (%) | | | |
|---|---|---|---|---|
| | <5 yr | 5–9 yr | 10+ | P |
| Hypertension, confirmed | 50.9 | 57.0 | 65.7 | .01 |
| Hypertension, confirmed and suspected | 62.0 | 66.7 | 74.8 | .06 |
| Albuminuria ≥ 20 mg/g | 50.4 | 45.8 | 64.8 | .02 |
| Cardiovascular disease | 21.5 | 31.2 | 38.2 | <.001 |
| Retinopathy | 15.1 | 37.3 | 71.8 | <.001 |
| Neuropathy | 17.7 | 25.0 | 42.5 | <.001 |

croalbuminuria to hypertension and cardiovascular risk in the general population.[34,35,54,55] Retinopathy and neuropathy are probably more specific complications of the hyperglycemic state.

Reversal or prevention of hypertension should reduce future burdens of nephropathy and ESRD as well as cardiovascular disease in diabetics and nondiabetics. Our data predict more striking effects on stroke and peripheral vascular disease than on heart disease, compatible with results in other trials.[56] The prevention of heart disease, and prevention or reversal of albuminuria, probably require the modulation of "subhypertensive" blood pressures and metabolic profiles in the broader community, with population-based health promotion strategies.

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