Link Between Hypertension and Diabetes Mellitus Epidemiological Study of Chinese Adults in Taiwan

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Objective: To elucidate the relationship between hypertension and non-insulin-dependent diabetes. Research Design and Methods: The study consisted of a random sample of adults aged ≥40 yr from the Ta-An district of Taipei City and 5 of 12 villages of Taiwan province, which had established primary health-care centers since 1984. A total of 11,478 subjects were recruited into the survey with a response rate of 65.3 and 72%, respectively. Blood glucose and blood pressure levels were measured, and a structured questionnaire was given to each participant. Those identified as having diabetes received further blood tests for lipids and creatinine and were evaluated for vascular complications. Results: The age- and sex-adjusted prevalence of hypertension among diabetic subjects was twice that of nondiabetic subjects (30.6 vs. 16.4%, $P < 0.0005$). Hypertensive subjects had a higher prevalence of diabetes than normotensive subjects (10.2 vs. 4.9%, $P < 0.0005$). Among hypertensive subjects, the prevalence of diabetes was 12.7% for those taking antihypertensive drugs and 9.1% for those not taking any drug ($P < 0.05$). The prevalence of diabetes significantly increased as mean arterial pressure rose, whether the subjects were stratified by various factors. Multiple regression analysis, including sex, age, body mass index, and other risk factors as independent variables, also showed a significant association between diabetes and hypertension. Conclusions: The univariate and multivariate analyses revealed that there seemed to be a tight link between hypertension and non-insulin-dependent diabetes. Family history of diabetes, diabetes duration, diabetes regimen, control of blood glucose, and the presence of nephropathy, as attested by proteinuria, did not contribute to the risk of hypertension. Further studies are necessary to determine whether these two conditions are causally related. *Diabetes Care* 14:1013–20, 1991

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It is well documented that there is an association between the level of plasma glucose concentration and blood pressure in nondiabetic individuals (1–6). Moreover, it is reported that the prevalence of hypertension is increased in diabetic patients compared with nondiabetic individuals (7–17). Although the association of hypertension and glucose intolerance is expected to increase with obesity and age, this association exists even when these two factors are removed (7,10,13,17), although some investigators failed to substantiate this association (18,19).

Although the association of impaired glucose tolerance with hypertension can be indirectly inferred from several epidemiological studies (8,20,21), the full range of this association has been described in only three large-scale community studies (3,17,22). Aforementioned studies evaluating diabetes and hypertension have typically been completed in white populations. However, there is little information concerning this association among Oriental populations.

In Taiwan, a high prevalence of hypertension has been repeatedly reported (23,24). Meanwhile, the prevalence of diabetes mellitus for those aged ≥40 yr in Taipei City has increased greatly in the last 20 yr (25). Our investigation in Taiwan from 1985 to 1986 for those aged ≥40 yr showed that the prevalence rate of hypertension was 34.8% for diabetic subjects, which was much higher than the 17.4% for subjects without dia-

betes (25). Our data agreed with Sowers et al.'s (26) review of various available data that diabetic subjects had a two- to threefold increase in hypertension compared with nondiabetic subjects. The information obtained from our epidemiological study was analyzed to evaluate the relationship between hypertension and non-insulin-dependent diabetes among Chinese subjects.

RESEARCH DESIGN AND METHODS

The epidemiological survey of diabetes mellitus was conducted between November 1985 and June 1986. Among 78 subdistricts of the Ta-An district in Taipei City, 8 were randomly selected. Among 12 villages of 11 counties of Taiwan province, which had established primary health-care community centers in 1984, 5 villages (Suan-Shi, Bar-Ter, Zu-Tan, Su-Fu, and Chi-Ku villages) were randomly selected. The total number of subjects aged ≥40 yr who were recruited into the diabetes survey in Taipei City was 4272 (2194 men, 2078 women) and that of Suan-Shi, Bar-Ter, Zu-Tan, Su-Fu, and Chi-Ku villages of Taiwan province was 7206 (3582 men, 3624 women), with a response rate of 65.3 and 72% respectively.

Because it was not practical to perform oral glucose tolerance tests (OGTTs) in all subjects of this large population survey, they were screened first by measuring the capillary glucose levels with Glucometers (Ames, Elkhart, IN), either at the fasting state or 2 h after a meal. Those who met the following criteria were deemed as having diabetes: *1*) capillary whole-blood glucose when fasting >6.7 mM or 2-h postprandial >11.2 mM on the screening test; *2*) subjects who underwent a 75-g OGTT (which was done if capillary whole-blood glucose level at fasting was 5.6–6.7 mM or 2-h postprandial 7.8–11.2 mM on the first screening) and had a 1- and 2-h postloading level >11.2 mM; and *3*) a history of diabetes mellitus treated regularly with insulin or sulfonylureas. Blood pressure was measured with a mercury sphygmomanometer with a 10 × 22-cm cuff after resting for 20 min in the sitting position. The second measurement was conducted 2 min later then the average of two measurements was taken. All sphygmomanometers were calibrated before the conduction of the survey. Systolic pressure was recorded at the first perception of successive sounds, and the diastolic pressure was recorded at the complete disappearance of sounds (Korotkoff phase 5). All readings were taken with 2 mmHg accuracy. Subjects who had systolic blood pressure ≥160 mmHg and/or diastolic pressure ≥95 mmHg or received treatment with antihypertensive agents were deemed to be hypertensive (27). The mean arterial pressure (MAP) was derived from the following formula: (systolic pressure/3) + (diastolic pressure × 2/3). All participating nurses attended a 1-wk training course on operating a glucometer and a sphygmomanometer and practicing interviewing skills based on a structured questionnaire. The content of the questionnaire included living area (urban or rural), age, sex, body mass index (BMI), educational level (6 levels from illiterate to college), physical activity at work (light, moderate, and heavy), family income, family history of diabetes, presence and therapy of hypertension, and frequency of exercise per week (<2, 2–4, and >4 times).

Seven hundred and fifteen subjects were identified to be diabetic. Of these, 608 subjects consented to further blood tests, including cholesterol, high-density lipoprotein cholesterol, and creatinine, and were evaluated for vascular complications (large vessel diseases, retinopathy, and proteinuria) according to the protocol of the World Health Organization Multinational Collaborative Study (28). The duration, regimens, and the status of blood glucose control were also recorded (29). All of the aforementioned items related with diabetic subjects were included in the subsequent multiple regression analysis. All 608 diabetic subjects were classified as having non-insulin-dependent diabetes, although in 4 subjects the possibility of insulin-dependent diabetes could not be ruled out because of the presence of characteristic symptoms of uncontrolled diabetes, e.g., polyuria, polydipsia, weight loss at the time of diagnosis, and having been treated with insulin within 1 yr of diagnosis. Five hundred fourty-five adults who had a normal blood glucose on the first screening were randomly selected as a comparison group that was matched for sex and age with the diabetic group. Among them, 513 subjects were shown to have normal glucose tolerance on OGTT and went through tests similar to those arranged for diabetic subjects.

Statistical analyses. Means ± SD were calculated for continuous measurements, and *t* test or one-way analysis of variance (ANOVA) was used to test the significance of the difference in continuous variables among comparison groups. χ^2 Test was used to examine the differences in prevalence or categorical variables among various groups, and the Mantel-Haenszel χ^2 test was used to test the significance of the differences in age- and sex-adjusted prevalence. Multiple regression analyses were used to examine the association between diabetes and hypertension where other risk factors were adjusted.

RESULTS

Among 545 subjects who first showed a normal blood glucose level on the screening examination, 25 subjects were proved to have impaired glucose tolerance and 5 to be diabetic according to OGTT. From this result, the specificity for the first screening test to correctly identify nondiabetic subjects was >99%. If all 10,763 people who had been initially classified as nondiabetic subjects had undergone OGTT, we would have detected 99 diabetic subjects, and these additional 99 subjects would have increased the prevalence rate of diabetes from 6.23% (715/11,478) to 7.09% (814/11,478) (Table 1).

TABLE 1
Prevalence of hypertension in diabetic and nondiabetic subjects

	Diabetic subjects		Nondiabetic subjects		Total	
Hypertension	*n*	%	*n*	%	*n*	%
Yes	249	34.8 (30.6)*	1873	17.4 (16.4)	2122	18.5 (17.2)
No	466	65.2	8890	82.6	9356	81.5
Total	715	100.0	10763	100.0	11478	100.0

Number in parentheses denotes age- and sex-adjusted prevalence.
*$P < 0.0005$, Mantel-Haenszel χ^2 test for age- and sex-adjusted proportions.

The age- and sex-adjusted prevalence rate of hypertension in diabetic subjects was 30.6%, which was twice that of nondiabetic subjects (Table 1). Compared with normotensive subjects, the hypertensive subjects were older (60.9 ± 9.1 vs. 51.6 ± 10.1, $P < 0.00001$ based on Student's *t* test), heavier (24.5 ± 3.3 vs. 23.1 ± 3.1 kg/m^2, $P < 0.00001$ based on Student's *t* test), and more likely to have diabetes mellitus (age- and sex-adjusted prevalence of 10.2% vs. 4.9% $P < 0.0005$ based on Mantel-Haenszel χ^2 test). Table 2 shows that among hypertensive subjects, the prevalence rate of diabetes was significantly higher in patients who received antihypertensive agents than in those who did not ($P < 0.05$ based on Mantel-Haenszel χ^2 test). The mean ± SD MAP was 91.4 ± 9.9 mmHg for normotensive subjects, 104.8 ± 11.2 mmHg for hypertensive subjects who took antihypertensive agents, and 113.8 ± 11.9 mmHg for hypertensive subjects not taking antihypertensive drugs. The difference among groups was significant ($P < 0.01$ based on 1-way ANOVA followed by the least significant difference procedure).

Because MAP of treated hypertensive subjects was still significantly higher than those without hypertension, the data of treated hypertensive subjects were combined with those of untreated hypertensive subjects in subsequent analyses. The prevalence rate of diabetes was calculated on the basis of quintile of MAP. The ranges of MAP and number of observations (in parentheses) for each quintile were as follows: *1*) <83.34 mmHg (2466), *2*) 83.34–92.00 mmHg (2127), *3*) 92.01–96.67 mmHg (2480), *4*) 96.68–105.33 mmHg (2179), *5*) >105.33 mmHg (2226). Figures 1–4 show the prevalence of diabetes based on the quintiles of MAP stratified by various variables. The prevalence of diabetes increased as MAP rose among study subjects stratified by sex (5776 men or 5702 women as shown in Fig. 1), age (40–51 yr [3793], 52–61 yr [3981], or >61 yr [3704] as shown in Fig. 2), BMI (<21.930 kg/m^2 [3836], 21.930–24.449 kg/m^2 [3839], or >24.449 kg/m^2 [3803] as shown in Fig. 3), and living areas (urban [4272] or rural [7206] as shown in Fig. 4). The similar relationship between diabetes and MAP persisted when the study subjects were stratified by different levels of education, family income, physical activity at work, and frequency of exercise.

Table 3 shows regression coefficients and their standard errors for independent variables significantly associated with diabetes and included in the multiple regression models. In model 1 of Table 3 in which all study subjects were included, MAP was significantly associated with diabetes after adjustment for sex, age,

TABLE 2
Prevalence of diabetes mellitus among hypertensive subjects with or without antihypertensive therapy

			Diabetes prevalence (%)	
Antihypertensive therapy	*n* of cases	*n* with diabetes	Crude	Age and sex adjusted
Yes	674	96	14.2	12.7*
No	1448	153	10.6	9.1

*$P < 0.05$, Mantel-Haenszel χ^2 test for age- and sex-adjusted proportions.

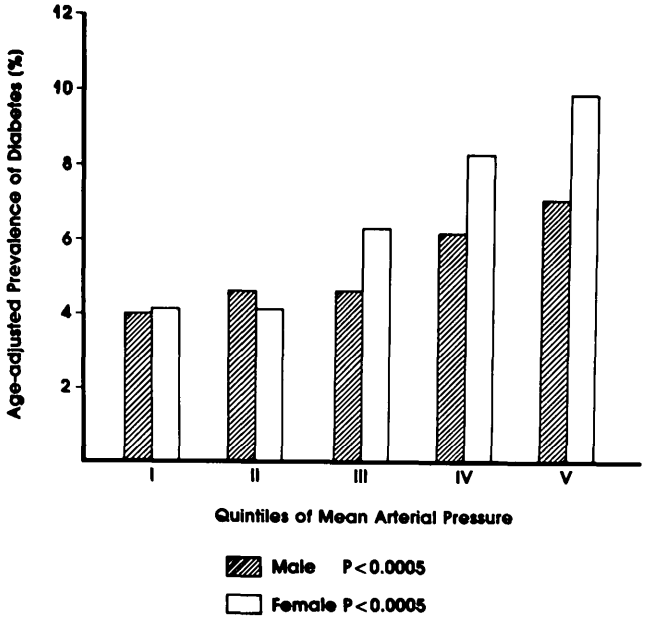

FIG. 1. Age-adjusted prevalence of diabetes mellitus by sex based on quintiles of mean arterial pressure.

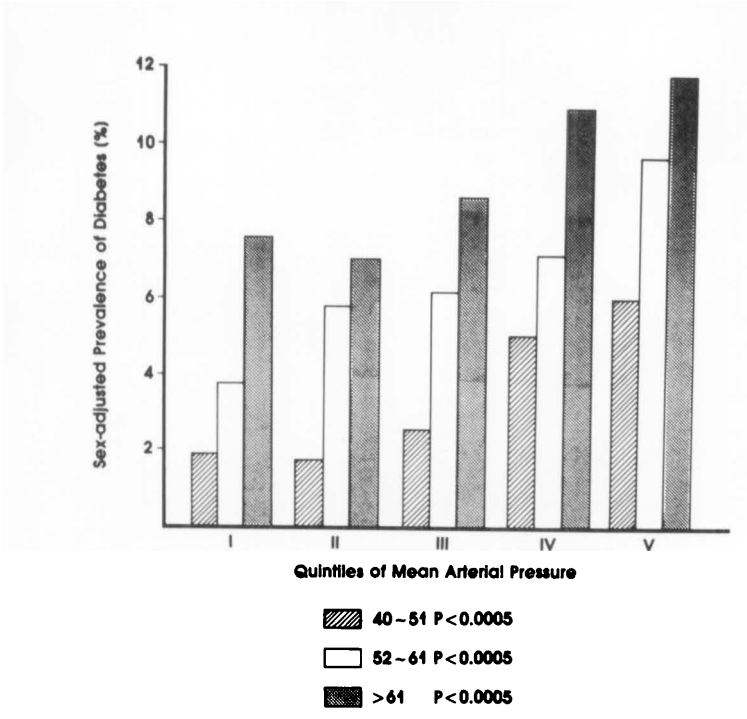

FIG. 2. Sex-adjusted prevalence of diabetes mellitus by age based on quintiles of mean arterial pressure.

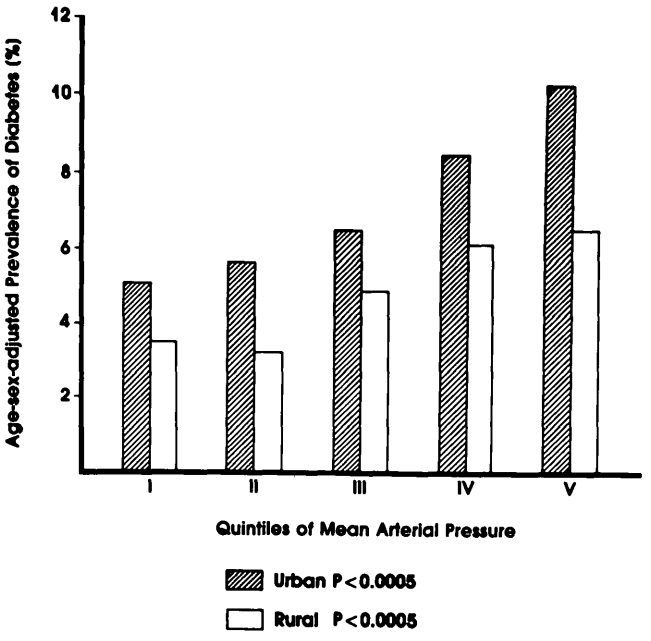

FIG. 4. Age- and sex-adjusted prevalence of diabetes mellitus by living area based on quintiles of mean arterial pressure.

BMI, family history of diabetes, and physical activity at work. For every 1-mmHg increase in MAP, the prevalence of diabetes increased by 0.08%. In another analysis in which MAP was replaced with antihypertensive therapy, it was observed that those who were treated by antihypertensive agents had a prevalence rate 5.8% ($P < 0.001$) higher than those without treatment. Further analysis replacing antihypertensive therapy with hypertension as a dichotomous variable showed that the diabetes prevalence of hypertensive patients was 4.1% ($P < 0.001$) greater than those without hypertension. In model 2 in which 674 subjects under antihypertensive treatment were excluded, diabetes remained significantly associated with hypertension. There was a significant increase in diabetes prevalence with the increase in MAP, whereas other risk factors were multivariate adjusted (Table 3). For every 1-mmHg increase in MAP, the diabetes prevalence rate increased by 0.07%. In another analysis replacing MAP with hypertension as a dichotomous variable, diabetes prevalence was significantly higher among hypertensive than nonhypertensive subjects with a difference of 3.1% ($P < 0.001$).

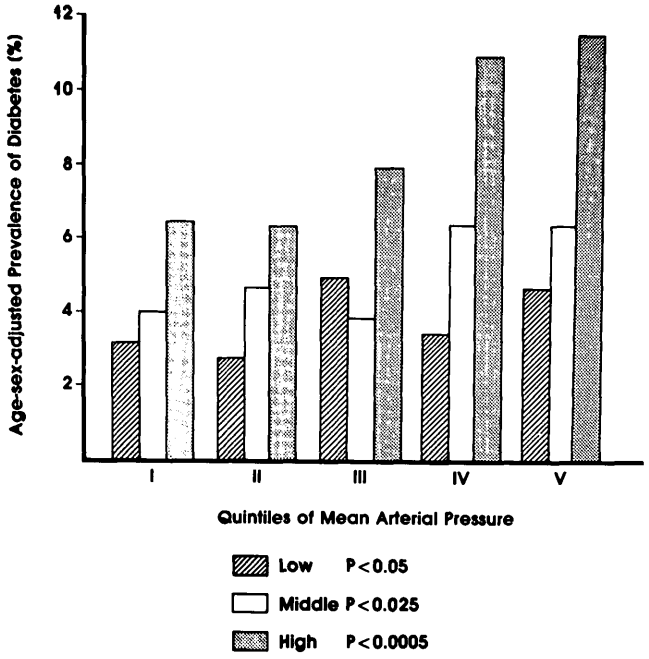

FIG. 3. Age- and sex-adjusted prevalence of diabetes mellitus by body mass index based on quintiles of mean arterial pressure.

Among 608 diabetic subjects, the prevalence of hypertension was 42.2% (27 of 64) and 31.1% (169 of 544), respectively, for those with and without a family history of diabetes ($P = 0.10$). For ≤1 yr duration of diabetes ($n = 308$), 2–5 yr ($n = 156$), and >5 yr ($n = 144$), the prevalence of hypertension was 28.6, 36.5, and 31.9% ($P = 0.14$), respectively, and MAP (mean ± SD) was 99.2 ± 12.9, 101.2 ± 12.7, and 99.3 ± 11.4 mmHg ($P = 0.23$), respectively. No significant difference was observed. The MAP of diabetic subjects who received no hypoglycemic agent ($n = 198$), took oral hypoglycemic agents ($n = 365$), and injected with insulin ($n = 45$) were 101.5 ± 13.3, 99.1 ± 12.0, and 97.8 = 12.2 mmHg, respectively. Those treated with insulin had the lowest MAP ($P <$

TABLE 3
Multiple regression analysis of diabetes prevalence among 11,478 diabetic subjects surveyed in Taiwan

Variables	Comparison	Model 1 (n = 11,478) β	Model 1 (n = 11,478) SE	Model 2 (n = 10,804) β	Model 2 (n = 10,804) SE
Age	Every 1-yr increase	0.0020	0.0002*	0.0018	0.0002*
Body mass index	Every 1-kg/m² increase	0.0067	0.0007*	0.0065	0.0007*
Family history of diabetes mellitus	Yes vs. no	0.0062	0.0010*	0.0061	0.0009*
Physical activity at work	Sedentary vs. laborious	−0.0193	0.0031*	−0.0201	0.0028*
Mean arterial pressure	Every 1-mmHg increase	0.0008	0.0002*	0.0007	0.0002*

All study subjects were included in model 1, and 674 subjects taking antihypertensive agents were excluded in model 2. Only independent variables significantly ($P < 0.05$) associated with diabetes in either model were included in the regression equation.
*$P < 0.01$, based on Z test of regression coefficients.

0.05 by 1-way ANOVA). In diabetic subjects with normal (n = 64), acceptable (n = 112), fair (n = 178), and poor (n = 254) blood glucose control, the mean MAPs were 98.4 ± 13.9, 101.5 ± 13.1, 99.3 ± 12.0, and 99.6 ± 12.2 mmHg, respectively. The difference was not statistically significant (P = 0.34 based on 1-way ANOVA). Among 524 diabetic subjects who had had urinalysis, proteinuria was found in 9.3% of the normotensive subjects (33 of 354) and in 11.2% of the hypertensive subjects (19 of 170), but the difference was not significant (P = 0.61). Fasting serum creatinine levels were measured in 538 diabetic subjects and were 94.6 ± 30.9 μM for normotensive subjects (n = 384) and 100.8 ± 37.2 μM for hypertensive subjects (n = 154).The difference was borderline significant (P = 0.05). MAP was 99.5 ± 12.0 and 101.3 ± 11.7 mmHg, respectively, for diabetic subjects with (n = 473) and without (n = 51) proteinuria. If diabetic subjects who received antihypertensive agents were excluded, the corresponding MAPS were 97.7 ± 11.4 mmHg (n = 347) and 97.9 ± 9.0 mmHg (n = 38). The difference between them was not significant. In the multiple regression analysis of MAP among the 608 diabetic subjects, those with higher BMI, receiving no antihypertensive agents, and living in an urban area had a higher MAP (Table 4). However, family history of diabetes, diabetes duration, diabetes regimen, blood glucose control, or proteinuria was not associated with MAP.

TABLE 4
Multiple regression analysis of mean arterial pressure among 608 diabetic subjects surveyed in Taiwan

Variables	Comparison	β	SE
Body mass index	Every 1-kg/m² increase	0.73	0.14*
Antihypertensive therapy	Yes vs. no	−6.78	1.17*
Living area	Urban vs. rural	3.50	1.05*

Only independent variables significantly associated with mean arterial pressure were shown.
*$P < 0.001$, based on Z test of regression coefficients.

CONCLUSIONS

The univariate studies disclosed a tight link between diabetes and MAP. This link existed when 11,478 diabetic subjects were observed in depth by segregating sex, age, BMI, living area, educational levels, family income, physical activity at work, and frequency of exercise (Figs. 1–4). The strong association between hypertension and diabetes persisted even when diabetic subjects who received antihypertensive agents were excluded from the analysis.

Our analysis was in accordance with the findings of various investigators that the prevalence of diabetes (Table 3) and hypertension were positively associated with BMI (30–33). Although the diabetic subjects in the lowest BMI group (all of whose weights fell within normal limits) showed a weak but statistically significant association between the prevalence of diabetes and hypertension, such an association was much more pronounced in the higher BMI groups (Fig. 3).

Neither of the two studies on insulin-dependent diabetes showed a consistent relationship between hypertension and duration of diabetes (34,35), although the prevalence and severity of hypertension in the diabetic population was reported to be related to the duration of diabetes (26,36). The prevalence of diabetic nephropathy is known to increase with the duration of diabetes, and it is expected that if diabetic nephropathy is the main cause of hypertension in diabetes, there should be an association between hypertension and the duration of diabetes. Because our study failed to show such an association, we must assume that other factors such as atherosclerosis, weight gain, and essential hypertension may contribute greatly to hypertension in non-insulin-dependent diabetes (37,38).

There were reports that indicated that diabetes regimens and control may contribute to the risk of hypertension (3,39). However, we found no correlation between MAP and diabetes regimens, or between MAP and blood glucose control of the diabetic subjects.

In diabetic subjects, renal disease may be the cause/trigger of hypertension and renal lesion can be the con-

sequence of hypertension, e.g., in diabetic subjects with essential hypertension. Hypertension in diabetic individuals markedly increases the risk and accelerates the course of development of nephropathy (40,41). Correction of hypertension is associated with a reduction in the rate of decline of the glomerular filtration rate in overt diabetic nephropathy (42). Several studies have shown that hypertension is closely related to nephropathy in younger diabetic subjects with insulin-dependent diabetes (43–47), and hypertension is unlikely to be the cause of diabetic nephropathy in this type of diabetes (48). Conversely, essential hypertension usually complicates diabetes of late onset (37). In diabetic subjects with non-insulin-dependent diabetes, blood pressure was similar in all groups stratified by the initial urinary concentration of albumin and no correlation was found between urinary albumin concentration and blood pressure at follow-up (46). However, a higher incidence of hypertension was observed in non-insulin-dependent diabetics with macroproteinuria (49). Our cross-sectional study in non-insulin-dependent diabetes was consistent with the finding of Mogensen and Christensen (46) that nephropathy was not closely associated with either MAP or hypertension. This is explained by the fact that increased albumin excretion in these subjects may have been caused by several other abnormalities in these patients, and the blood pressure elevation may have been due to the weight gain, atherosclerosis, or essential hypertension. These abnormalities are probably more common in non-insulin-dependent diabetes (37,38).

Therefore, the association of non-insulin-dependent diabetes with hypertension cannot be explained by sex, age, BMI, living locality, family history of diabetes, duration of diabetes, renal disease, physical activity, family income, educational levels, blood glucose control, antidiabetic, or antihypertensive medications (10,15,17). It might be related to insulin resistance and hyperinsulinemia, which can occur in both hypertension and diabetes (10,50–52). This concept has been given the name Syndrome X (53).

The multivariate studies substantiated that diabetic subjects with heavier body build and of older age were more susceptible to both diabetes mellitus and hypertension. Some antihypertensive agents are known to suppress insulin release and raise blood glucose levels, and we found a close correlation of diabetes mellitus and antihypertensive agents and a higher prevalence of diabetes for diabetic subjects taking antihypertensive drugs than those not taking drugs (12.7 vs. 9.1%; Table 2). However, it is premature to conclude that antihypertensive drugs are causally related to the development of diabetes mellitus due to the cross-sectional nature of our study design. In contrast to other reports (10,15,17), the diabetic subjects taking antihypertensive medication had significantly lower MAPs than those not taking any medication. This indicates that the antihypertensive campaign was successful. In the last 20 yr, accompanied by a rapid rise in socioeconomic status, there has been a rapid increase in noncommunicable disease, e.g., hypertension and diabetes, in Taiwan. In 1987, heart disease and diabetes ranked third and fifth, respectively, as the causes of death in this area (54). The high prevalence of hypertension and popular use of antihypertensive drugs, which may exert an adverse effect on carbohydrate metabolism, e.g., diuretics (55,56) and nonselective β-blockers (57–60) in Taiwan, remind us to be more cautious in selecting antihypertensive agents.

Although the relationship between hypertension and diabetes has been well studied in white populations, this cross-sectional study first substantiated a close link between diabetes and hypertension among Chinese adults. It should be clear that by its own nature, this cross-sectional study does not allow us to draw any conclusion on the causal relationship between blood pressure and diabetes. To determine whether a causal relationship exists between them, we are undertaking a longitudinal study of a cohort living in Taipei City.

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