Sex Differences in Metabolic Morbidities: Influenced by Diet or Exercise Habits?

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We implemented a nationwide population-based study in Taiwan to compare the physical and biochemical parameters, diet and exercise lifestyles, and prevalences of diabetes, hyperlipidemia, and hypertension between males and females, and to clarify the determinants of diabetes, hyperlipidemia, and hypertension in Taiwan. In this cross-sectional study, 7,578 subjects were selected from the general population by stratified random sampling for the Surveillance of Taiwanese Civil Health in 2002. Blood samples were taken and information on body composition, demographics, exercise and dietary habits, and medical and drug histories were obtained from structured interviews administered by well-trained interviewers. A total of 6,600 subjects (87.1%), aged 15.6–95.0 years old, completed the survey. The overall prevalences of diabetes, hyperlipidemia, and hypertension were 9.9%, 22.8%, and 15.7%, respectively, and hyperlipidemia (27.0%) and hypertension (19.2%) were more prevalent in males. Males were more likely to have high-fat and high-cholesterol diets, compared with females. Although there were differences in the prevalences of hyperlipidemia and hypertension between the sexes, adjusted logistic regression analysis demonstrated little contribution of diet and exercise habits to the risks of diabetes, hyperlipidemia, or hypertension after adjusting for age, sex, waist-to-hip ratio, serum blood sugar levels, cholesterol, triglycerides, apolipoprotein A1, apolipoprotein B, glutamate oxaloacetate transaminase, glutamate pyruvate transaminase, creatinine, uric acid, and blood pressure.

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According to the literature, sex differences exist in many health issues, including metabolic diseases. For example, men have been identified as more likely to suffer from obesity, have diets low in fruit and vegetables, and have unhealthy behaviors, resulting in specific diseases [1–4]. Research in the United States demonstrated that lifestyles and psychosocial factors were related to body weight changes, and that these had marked differential sex effects [5]. Sex differences in disease formation mediated by disparities of lifestyles have also been demonstrated [6]. However, there have been few studies of the relationships among sex, lifestyles and metabolic diseases in Asian populations, and the findings have been equivocal [7,8].

Hypertension, hyperlipidemia and diabetes have been increasing in incidence across the globe and have been the focus of much research interest [9,10]. The

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factors contributing to hypertension, hyperlipidemia and diabetes, such as the relationship between cholesterol (Chol) diet and serum Chol levels, has been debated in the literature [11–14]. Controversy remains over whether or not an unhealthy lifestyle results in the development of diabetes, hyperlipidemia and hypertension [15–18].

Little is known about the relationships among sex, biochemical profile, metabolic disease and lifestyle, especially in normal Asian populations. In this study, we report the results of a nationwide, population-based study in Taiwan, and assess the overall risk factors. The aims of this cross-sectional study in a normal population were: first, to compare the differences in physical and metabolic characteristics between different the sexes; second, to compare the differences in prevalences of diabetes, hyperlipidemia, and hypertension between different sexes; third, to compare the differences in lifestyles between the sexes; and finally to clarify the determinants of diabetes, hyperlipidemia, and hypertension in a Taiwanese population.

Materials and Methods

Data acquisition

Data were obtained from the Project of Surveillance for diabetes, hyperlipidemia, and hypertension in Taiwan. This was a cross-sectional study on health, health behavior, and disease status of stratified selected subjects in Taiwan from March 1, 2002 to October 30, 2002, performed by the Taiwan Bureau of Health Promotion [19]. General population was defined as citizens of Taiwan registered by household. The detailed selection methods are available in the report of Project of Surveillance for diabetes, hyperlipidemia, and hypertension in Taiwan [19]. The selection design was briefly as follows: (1) 68 townships were randomly selected in proportion to the 359 nationwide townships in the seven major areas in Taiwan; (2) 8–44 "lin" (smaller units than towns) were selected from each township, based on population size; and (3) four eligible household respondents were selected from each selected lin by systematic stratified random sampling.

Well-trained interviewers (public health nurses) administered face-to-face structured interviews. Interview appointments were made by phone prior to interviews being conducted. Participating subjects were told not to eat on the morning of the day of the interview. Fasting blood samples (no food intake for at least 8 hours) were taken in the morning and heparinized blood samples were centrifuged at 2,000 rpm for 20 minutes at 4°C, within 4 hours of drawing. Serum was separated and stored in aliquots at –20°C and transported to the laboratory center of the Bureau of Health Promotion in a –20°C to –40°C environment. Demographic information and information on lifestyles, including exercise and dietary habits, and medical and drug histories were collected by questionnaires conducted by the interviewers at the same time. Regular exercise was defined as more than three times a week, for more than 30 minutes each time, and reaching more than 130 heart beats/minute on each occasion. Dietary habit was assessed using a structured questionnaire composed of 14 questions and modified for use in a Chinese context for subjects residing in Taiwan, employing the Nutrition and Health Survey in Taiwan (NAHSIT) [19]. The characteristics of nutritional components were identified and demonstrated in the reports [19]. For instance, a high-Chol diet was defined based on four criteria: (1) eating meat with fat or skin; (2) the frequency of eating egg yolks; (3) the frequency of lard use; and (4) the frequency of gravy use. Blood pressure (BP) (sitting position, rest for at least 10 minutes, repeat measurement), pulse, waist and hip circumferences were also examined following the standard procedures translated from the WHO guidelines [20,21]. BP was measured for a third time if the difference between the first two measurements was > 10 mmHg. The average of the two closer measurements was then used as the final BP measurement.

Blood tests

Blood parameters measured included fasting blood sugar (AC sugar), glycosylated hemoglobin, uric acid (UA), blood urea nitrogen (BUN), creatinine, total Chol, high-density lipoprotein, low-density lipoprotein, triglyceride (TG), apolipoprotein-A1 (ApoA1), apolipoprotein-B (ApoB), glutamate oxaloacetate transaminase (GOT), and glutamate pyruvate transaminase (GPT). AC sugar, Chol, and TG levels were measured by colorimetry, glycosylated hemoglobin was detected using high performance liquid chromatography, high-density lipoprotein was detected by electrophoresis, and ApoA1 and ApoB were detected by immunoturbidimetric tests. We defined abnormal results according to the standards of JNC VI (The Sixth Report of the Joint National Committee on

Prevention, Detection, Evaluation and Treatment of High Blood Pressure), the American Diabetes Association, and NCEP-ATP III (National Cholesterol Education Program, Adult Treatment Panel III Framingham Point Scores). Hypertension was defined as systolic BP > 140 mmHg or diastolic BP > 90 mmHg. Subjects who had been prescribed antihypertensive medication or had taken antihypertensive drugs were also defined as having hypertension. Patients with AC sugar > 126 mg/dL or those who had taken oral antidiabetic agents were defined as having diabetes. Hypercholesterolemia was defined as a blood Chol level of ≥ 240 mg/dL, and hypertriglyceridemia was defined as a blood TG level of ≥ 200 mg/dL. Subjects who had taken cholesterol-lowering or triglyceride-lowering medication for hyperlipidemia were also defined as hyperlipidemic.

Statistical analysis

Data were analyzed by comparing means using descriptive statistics such as *t* tests, χ^2 tests, and logistic regression analysis. SPSS version 14.0 (SPSS Inc., Chicago, IL, USA) was used and two-tailed *p* values of < 0.05 were considered statistically significant.

Results

A total of 7,578 subjects completed the interviews. Blood samples were obtained from 6,602 subjects and blood pressure information was available for 6,941 subjects. Overall, 6,600 subjects (87.1%) fulfilled the study criteria and were included in the final analysis, of which 3,435 (52%) were females. Table 1 shows the characteristics of the study participants. Their ages ranged from 15.6 to 95.0 years, with a mean age of 43.0 ± 16.9 years (male, 43.07 ± 17.31 years; female, 43.01 ± 16.49 years), and a median age of 41.7 years. There were sex differences in systolic BP, with an average of 118.89 ± 16.5 mmHg for males and 112.36 ± 18.95 mmHg for females ($p < 0.001$). Males had a slightly higher mean diastolic BP than females (77.8 *vs.* 72.3 mmHg), though this did not reach statistical significance. There was a significant difference in hip circumferences between males and females (mean, 97.0 ± 7.7 *vs.* 96.0 ± 8.3 cm, $p = 0.001$). With regard to biochemical parameters, sex differences were detected in serum levels of TG, ApoA1, GOT, GPT, creatinine, and UA ($p < 0.001$).

The numbers of each sex with diabetes, hyperlipidemia, and hypertension are shown in Table 2. The

Table 1. Comparison of characteristics of male and female subjects recruited from the normal population*

	Male ($n = 3{,}165$)	Female ($n = 3{,}435$)	$p^{\dagger}$
Physiological characteristics			
Age (yr)	43.07 (17.31)	43.01 (16.49)	0.893
Systolic BP (mmHg)	118.89 (16.46)	112.36 (18.95)	< 0.001
Diastolic BP (mmHg)	77.77 (10.96)	72.30 (10.93)	0.688
Waist circumference (cm)	84.19 (10.62)	75.64 (10.43)	0.272
Hip circumference (cm)	97.01 (7.70)	96.02 (8.28)	0.001
WHR	0.87 (0.08)	0.79 (0.07)	0.251
Biochemical characteristics			
Fasting sugar (mg%)	94.99 (29.11)	93.94 (28.46)	0.168
HbA1C (%)	5.38 (1.05)	5.34 (1.06)	0.428
Cholesterol (mg/dL)	182.30 (37.90)	184.41 (37.95)	0.245
HDL (mg/dL)	51.26 (14.77)	58.86 (14.26)	0.064
LDL (mg/dL)	116.04 (27.09)	114.50 (27.33)	0.346
Triglyceride (mg/dL)	142.31 (95.71)	113.03 (72.69)	< 0.001
ApoA1 (mg/dL)	136.92 (22.98)	150.76 (24.99)	< 0.001
ApoB (mg/dL)	91.63 (25.22)	85.95 (25.17)	0.713
GOT (IU/L)	23.24 (19.49)	18.89 (14.50)	< 0.001
GPT (IU/L)	23.10 (18.43)	17.84 (12.75)	< 0.001
BUN (mg/dL)	14.91 (4.65)	13.45 (4.50)	0.056
Creatinine (mg/dL)	1.04 (0.28)	0.80 (0.32)	< 0.001
Uric Acid (mg/dL)	7.23 (1.68)	5.55 (1.51)	< 0.001

*Data presented as mean (standard deviation); †*t* test. BP = blood pressure; WHR = waist-to-hip ratio; HbA1C = glycosylated hemoglobin; HDL = high-density lipoprotein; LDL = low-density lipoprotein; ApoA1 = apolipoprotein-A1; ApoB = apolipoprotein-B; GOT = glutamate oxaloacetate transaminase; GPT = glutamate pyruvate transaminase; BUN = blood urea nitrogen.

prevalences of diabetes, hyperlipidemia (hypercholesterolemia or hypertriglyceridemia), and hypertension were 9.9%, 22.8%, and 15.7%, respectively. The prevalences of diabetes, mixed hyperlipidemia, and hypertension in males were 10.0%, 27.0%, and 19.2%, respectively; these were slightly higher than in females (9.9%, 19.0%, and 12.4%, respectively).

Differences in lifestyles between the sexes are shown in Table 3. More than one quarter (856/3,165) of males had regular exercise habits. However, only one fifth (725/3,436) of females reported regular exercise habits. However, males were more likely to have bad diets that were fat- and Chol-rich, compared with females ($p < 0.001$).

Adjusted logistic regression models (Table 4) were used to analyze the relationships between potential predictive factors (sex, age, waist-to-hip ratio [WHR], biochemical parameters, and lifestyle) and disease (diabetes, hyperlipidemia, and hypertension) (data not shown). Overall, the results showed that sex, age, waist circumferences and WHR were significantly associated with diabetes, hyperlipidemia, and hypertension, but that dietary habits and regular exercise habits had little effect (data not shown). Models for diabetes, hyperlipidemia, and hypertension separated by sex were further analyzed (Table 4). Age, WHR, AC sugar, Chol, TG, ApoB, and UA were highly associated with diabetes, hyperlipidemia, and hypertension in both sexes to greater or lesser extents, but exercise and diet habits had lesser effects on diabetes, hyperlipidemia, and hypertension.

Discussion

The overall prevalence of diabetes in our study was 9.9%. The prevalences of diabetes were 6.6% in an adult population in France in 1985 [22], 6.5% in Argentina in 1998 [23], 6.9% in Vietnam in 2001 [24], 6.8% in Japan in 2002 [25], 6–10% in different states in the US in 2001 [26], and 9.5% in Nepal before 2007 [27]. The prevalences in different countries therefore vary, but Taiwan seems to have a higher prevalence than other Asian countries, approaching that of the US. This could be due to the high-calorie, Western diet that has become popular in Taiwan in recent decades. This suggests a need for public screening for diabetes in Taiwan. No difference in prevalence of diabetes between males and females was found in our subjects.

The overall prevalence of hyperlipidemia in our study was 22.8%, which is lower than in other countries, including 24–36% in Argentina in 1998 [23] and 31–35% in China in 2004 [28]. This would be expected to result in a lower prevalence of cerebral and cardiovascular diseases in Taiwan. However, a difference in

Table 2. Prevalences of diabetes, hyperlipidemia, and hypertension in males and females*

	Total (n = 6,600)	Male (n = 3,165)	Female (n = 3,435)	$p^†$
Diabetes	656 (9.9)	317 (10.0)	339 (9.9)	0.869
Hyperlipidemia	1,506 (22.8)	855 (27.0)	651 (19.0)	< 0.001
Hypertension	1,035 (15.7)	608 (19.2)	427 (12.4)	< 0.001

*Data presented as n (%); $^†\chi^2$ test (comparisons between males and females).

Table 3. Comparisons of exercise and dietary habits between males and females*

	Male (n = 3,165)	Female (n = 3,435)	$p^†$
Exercise			
Regular exercise habit	856 (27.0)	725 (21.1)	< 0.001
Heavy exerciser	650 (20.5)	452 (13.2)	< 0.001
Diet			
Fat-rich diet (ate meat with skin frequently)	1,790 (56.6)	1,204 (35.1)	< 0.001
Cholesterol-rich diet	513 (16.2)	203 (5.9)	< 0.001
Ate greens every day	788 (24.9)	963 (28.0)	0.004
Ate organic vegetables frequently	22 (0.7)	30 (0.9)	0.486

*Data presented as n (%); $^†\chi^2$ test (comparisons between males and females).

Table 4. Relationships among risk factors, diabetes, hyperlipidemia, and hypertension adjusted by sex*

Sex (male/female)	Diabetes		Hyperlipidemia		Hypertension	
	Male model	Female model	Male model	Female model	Male model	Female model
Age (yr)	1.038† (1.027–1.048)	1.012‡ (1.001–1.022)	0.994 (0.987–1.002)	1.016† (1.007–1.026)	1.035† (1.028–1.041)	1.061† (1.051–1.070)
WHR (%)	1.042† (1.022–1.063)	1.067† (1.046–1.088)	1.053† (1.037–1.070)	1.002 (0.983-1.021)	1.052† (1.036–1.070)	1.034† (1.014–1.054)
Sugar (mg%)	–	–	1.006† (1.003–1.009)	1.004‡ (1.001–1.008)	1.004† (1.002–1.007)	1.001 (0.998–1.005)
Cholesterol (mg/dL)	0.991† (0.984–0.997)	0.992† (0.987–0.998)	–	–	0.998 (0.993–1.003)	0.991† (0.986–0.997)
Triglyceride (mg/dL)	1.003† (1.002–1.005)	1.003† (1.001–1.004)	–	–	1.002† (1.001–1.003)	1.002† (1.001–1.004)
ApoA1 (mg/dL)	1.004 (0.999–1.010)	1.011† (1.006–1.016)	1.000 (0.996–1.004)	1.001 (0.996–1.005)	1.006† (1.002–1.011)	1.004 (0.999–1.009)
ApoB (mg/dL)	1.021† (1.012–1.031)	1.023† (1.015–1.032)	1.042† (1.037–1.046)	1.060† (1.054–1.066)	1.009‡ (1.002–1.016)	1.018† (1.009–1.026)
Creatinine (mg/dL)	0.824 (0.506–1.342)	0.918 (0.685–1.231)	1.806† (1.158–2.815)	0.989 (0.742–1.317)	1.201 (0.854–1.687)	1.351 (0.985–1.852)
Uric acid (mg/dL)	0.882† (0.815–0.955)	1.010 (0.936–1.091)	1.150† (1.086–1.218)	1.180† (1.101–1.265)	1.104† (1.041–1.171)	1.127 (1.049–1.210)
Regular exercise habit (yes/no)	0.901 (0.673–1.206)	0.943 (0.700–1.269)	1.040 (0.844–1.282)	1.068 (0.828–1.378)	1.121 (0.902–1.393)	1.099 (0.839–1.439)
High-cholesterol diet (yes/no)	0.963 (0.687–1.350)	1.330 (0.840–2.105)	1.016 (0.793–1.302)	0.753 (0.477–1.187)	0.961 (0.742–1.244)	1.259 (0.811–1.956)
Organic vegetables (yes/no)	4.281‡ (1.402–13.075)	0.903 (0.206–3.955)	3.610‡ (1.347–9.679)	2.432 (0.873–6.772)	1.233 (0.380–3.994)	1.165 (0.330–4.109)
Vegetarian (yes/no)	1.142 (0.780–1.673)	1.138 (0.858–1.510)	1.095 (0.799–1.502)	0.999 (0.761–1.311)	0.731 (0.503–1.063)	0.960 (0.727–1.268)
Systolic BP (mmHg)	1.006 (0.995–1.016)	1.012‡ (1.003–1.022)	0.995 (0.987–1.004)	0.999 (0.990–1.008)	–	–
Diastolic BP (mmHg)	1.006 (0.990–1.022)	0.992 (0.976–1.008)	1.025† (1.012–1.038)	1.011 (0.996–1.026)	–	–

*Logistic regression analysis, represented as odds ratio (95% confidence interval); †$p < 0.01$; ‡$p < 0.05$. WHR = waist-to-hip ratio; ApoA1 = apolipoprotein-A1; ApoB = apolipoprotein-B; BP = blood pressure.

prevalence of hyperlipidemia was found between sexes (27.0% in males and 19.0% in females). Fat- and Chol-rich diets were also recorded more often in males, suggesting that dietary habits might contribute to the high prevalence of hyperlipidemia in males. Health education, including information on healthy diets, should be provided for the general population in Taiwan.

The prevalence of hypertension in our study was 15.7%, including 19.2% of males and 12.4% of females. This was slightly lower than in other countries, with reported prevalences of 15.5% in Spain in 2005 (adults aged over 15 years) [29], 37.8% in Liaoning Province in China between 2005 and 2007 (adults aged over 35 years, rural population) [30], 39.1% in the Czech population in 2000 (general population, aged 25–64 years) [31], and 28–44% in Argentina in 1998 (aged 20 years and over) [23]. The prevalence in males in our study was significantly higher than that in females (19.2% > 12.4%, $p < 0.001$). Males in the current study also had higher systolic BP than females (118.89 mmHg > 112.36 mmHg). Age-adjusted multiple linear regression (data not shown) also revealed that the average male systolic BP was 6.50 mmHg, which was higher than in females [95% confidence interval (CI): 5.76–7.24]. Although previous studies have reported equivocal results regarding sex differences in BP [32,33], the results of our study demonstrated higher average systolic BP and higher prevalence of hypertension in males than females. These factors are associated with increased risks of cerebral and cardiovascular diseases and should thus be taken into consideration by public health practitioners.

Sex differences in ApoA1 were also found in our study (males 136.9 < females 150.8 mg/dL, $p < 0.001$). ApoA1 is the primary protein component of high-density lipoprotein particles and has been hypothesized to play a key role in reducing the cholesterol content of lipid-rich lesions [34]. Growing evidence supports apolipoprotein levels, rather than standard lipid and lipoprotein levels, as a better marker for predicting vascular diseases. Our results indicating higher ApoA1 level in females may partially explain the lower prevalences of hyperlipidemia and hypertension in females.

The causal relationships were clarified by cross-sectional study. It was possible that the occurrence of disease (e.g. hyperlipidemia or hypertension) forced the subjects to modify their dietary habits. For instance, we identified significant associations between male diabetes and male hyperlipidemia, and the consumption of organic vegetables. An overt difference in the consumption of organic vegetables between females and males was identified and could be attributed to different coping methods used by males and females for dealing with diabetes or hyperlipidemia. Thus, the occurrence of diabetes or hyperlipidemia was the cause, and eating organic vegetables was a resultant outcome in the male, but not in the female population.

We further analyzed the contributions of various independent factors to diabetes, hyperlipidemia, and hypertension. In diabetes, WHR [odds ratio (OR): 1.07; 95% CI: 1.05–1.09] in females contributed more than in males, whereas age (OR: 1.04; 95% CI: 1.03–1.05) contributed more in males than in females. With regard to hyperlipidemia, age (OR: 1.02; 95% CI: 1.01–1.03), ApoB (OR: 1.06; 95% CI: 1.05–1.07), and UA (OR: 1.18; 95% CI: 1.10–1.27) contributed more in females than in males, whereas WHR (OR: 1.05; 95% CI: 1.04–1.07) and creatinine level (OR: 1.02; 95% CI: 1.16–2.82) contributed more in the male population.

The prevalences of hyperlipidemia and hypertension were significantly higher in males than in females. A previous study illustrated that there was a sex difference in the overall prevalence of metabolic syndrome in Taiwan (20.4% of men and 15.3% of women), the age at appearance of the first isolated component (mean age, 43.3 years in women *vs.* 45.6 years in men), the mean age for development of metabolic syndrome (mean age, 51.3 years in men *vs.* 56.2 years in women), and the period from the appearance of any isolated component to the development of metabolic syndrome (12.8 years in men *vs.* 5.7 years in women) [35]. Another study from the US also demonstrated that the prevalence and extent of coronary artery calcification were higher in men compared with women in the same age group [36]. The results of our study were consistent with this conclusion that women may develop cardiovascular diseases later in life than men.

In conclusion, differences between the sexes exist in physical characteristics, biochemical parameters, lifestyles, and metabolic diseases in Taiwan. Sex could influence the occurrence of hypertension, hyperlipidemia, and diabetes. We suggest that medical practitioners be aware of the fact that the sexes show variations in morbidities due to metabolic diseases, and they should thus provide suitable interventions for the high-risk patients.

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三高盛行率之性別差異：飲食及運動是否影響三高盛行率？

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我們進行一個台灣全國人口為基礎的抽樣研究以了解不同性別間生理及生化指標、飲食及運動習慣、以及糖尿病、高血脂症、及高血壓盛行率的差異性，並進一步釐清影響三高的因素。2002 年由全國人口中分層隨機抽樣 7,578 位個案進入台灣居民健康普查研究。嚴格受訓的訪員進行包括身體組成、抽血、人口學資料、飲食及運動習慣、及疾病和藥物史的調查和測量。6,600 個案 (87.1%) 完成完整的調查和測量，年齡分布為 15.6 to 95.0 歲。糖尿病、高血脂症、及高血壓盛行率為 9.9%，22.8%，和 15.7%，而男性高血脂症 (27.0%) 及高血壓 (19.2%) 盛行率高於女性。男性之高脂肪飲食習慣及高膽固醇飲食習慣盛行率較高於女性。雖然高血脂症及高血壓盛行率男性高於女性，然而標準化 logistic regression 分析在標準化年齡、性別、腰臀比、血糖、血液膽固醇、三酸甘油脂、脂蛋白 A1、脂蛋白 B、肝功能、肌肝酸、尿酸、及血壓之後，顯示飲食和運動習慣對於三高的影響程度不大。

關鍵詞：糖尿病，高血脂症，高血壓，性別差異

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