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Hyperinsulinemia and Related Atherosclerotic Risk Factors in the Population at Cardiovascular Risk: A Community-based Study

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Background: **A population-based study was conducted in Taiwan to investigate the prevalence of insulin resistance and high serum insulin concentrations and their relationships with potential atherosclerotic risk factors.**
Methods: **We studied 2165 subjects, ages >35, from a community cohort.**
Results: **The distributions of fasting insulin were skewed to the right, with higher concentrations in women than in men. As age increased, insulin increased in women, but decreased in men. As fasting insulin concentrations increased, postloading insulin, glucose, blood pressure, body mass index, waist-to-hip ratio, total cholesterol, triglycerides, LDL-cholesterol, apoprotein B, plasminogen activator inhibitor 1, tissue plasminogen activator, and fibrinogen increased, but lipoprotein(a), HDL-cholesterol, and apoprotein A1 decreased. Multiple logistic regression showed that obesity, high LDL-cholesterol, and low HDL-cholesterol were significant predictors of hyperinsulinemic status.**
Conclusion: **The study subjects with insulin resistance syndrome and related risk factors may be at risk for atherosclerosis, thrombosis, and other coronary heart diseases.**

Hyperinsulinemia has been identified as a risk factor for hypertension and obesity as well as lipid abnormalities in adults *(1–3)*. Prospective studies have also demonstrated that high plasma concentrations of insulin predict the development of coronary heart disease (CHD),[4] independent of other risk factors *(1–3)*. Hyperinsulinemia, which leads to a cluster of cardiovascular risks, is well known as "insulin resistance syndrome" *(4, 5)* and is strongly related to abnormalities of carbohydrate metabolism *(6, 7)*.

Some studies have addressed racial differences in the clustering of insulin resistance syndrome, including hypertension, obesity, dyslipidemia, and hyperinsulinemia *(8)*. Environmental studies showed marked differences in CHD mortality rates among countries and relative impacts on atherosclerosis among populations. Racial discrepancies have also been reported for diabetes mellitus and insulin concentrations *(9)*. Pima Americans, aboriginal Australians, and South Asians have relatively higher prevalences of diabetes than Caucasians *(10–12)*. Common to most of these groups are a recent trend toward urbanization, a decrease in physical activity, and the development of obesity.

Populations with high incidence rates for CHD are also at high risk for diabetes *(11)*, which may be related to insulin resistance. One population-based study has demonstrated that fasting insulin concentrations were lower in the Japanese than in Caucasians *(9)*. The distribution patterns of atherosclerotic risk factors between these two ethnic groups were also different.

For the Chinese population, the distribution of fasting insulin in the general population has not yet been addressed. Moreover, the relationships between insulin concentration, blood pressure, lipid concentrations, and coagulation factors in Chinese remain to be explored. A recent study in Mauritius found that both fasting and 2-h

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[4] Nonstandard abbreviations: CHD, coronary heart disease; CCCC, the Chin-Shan Community Cardiovascular Cohort; BMI, body mass index; WHR, waist-to-hip ratio; LDL-C, LDL-cholesterol; HDL-C, HDL-cholesterol; apo A1, apoprotein A1; apo B, apoprotein B; Lp(a), lipoprotein(a); tPA, tissue plasminogen activator; PAI-1, plasminogen activator inhibitor; and HOMA, homeostasis model assessment.

postload insulin concentrations in Chinese subjects were lower than that in Hindu and Muslim Indian subjects *(13)*.

Community-based studies use many indicators of insulin resistance syndrome. Observations based on quartiles or tertiles of fasting insulin concentrations *(2, 3, 14–25)*, insulin resistance indexed by calculation of fasting and postloading glucose and insulin concentrations *(18, 26)*, or insulin sensitivity index profiles *(18, 26)* have revealed underlying pathophysiological mechanisms and have wide applications in population studies. Associations between these indicators of insulin resistance and atherosclerotic risk factors can be viewed as different aspects of insulin resistance syndrome. The Chin-Shan Community Cardiovascular Cohort (CCCC) study is a prospective community-based investigation of cardiovascular disease risk factors in Chinese adults in Taiwan. Here, we focus on the distribution of fasting insulin concentrations and the linkage between insulin concentration and various atherosclerotic risk factors.

Materials and Methods

STUDY DESIGN AND POPULATION

The CCCC cohort consisted of 3602 inhabitants at least 35 years of age when recruited in 1990–1991 from Chin-Shan, a suburban community 36 kilometers from metropolitan Taipei. With the approval of the institutional committee, documents at the community household registration office were reviewed to validate the basic demographic data, including the genders, birth dates, and addresses of residents in the community. The baseline response rate was 82.8% of all 4350 identified eligible individuals. A follow-up program was conducted every other year. This report used data on the coagulation profiles collected in 1992–1993 and data on atherosclerotic risk factors and insulin profiles collected in 1994–1995. The leading causes of deaths, mainly from cardiovascular disease and cancer in this community, reflect the national mortality patterns in Taiwan between 1990 and 1994 *(27)*.

DATA COLLECTION AND CLINIC EXAMS

A clinic was set up at the Chin-Shan Community Health Center by the study team, which consisted of 20 senior medical students, 2 assistant nurses, and 10 cardiologists and local practitioners. Trained medical students canvassed door-to-door with the assistance of community leaders to extend invitations for the baseline survey. Information collected included sociodemographic characteristics, lifestyle, personal and family histories of diseases, and the history of hospitalization. With the consent of participants, a team of physicians and medical students conducted physical examinations and laboratory tests on those participants invited to the clinic. Blood pressures were measured with subjects in the sitting position after resting for 10 min. Body weight was measured using a calibrated balance. Body mass index (BMI) was calculated as weight (kilograms) divided by height (meters) squared. The circumferences of the smallest part of waist and the thickest part of the hip in the standing position were measured, and the waist-to-hip ratio (WHR) was calculated. Electrocardiograms (12-lead) were recorded concurrently. Specimens for blood analysis were also collected in the morning, before 1200.

BLOOD SAMPLING AND ANALYTIC METHODS

All subjects with a minimum fasting period of 12 h underwent an oral glucose tolerance test with 75 g of glucose loading in accordance with the World Health Organization standard. Tests were performed in the morning, before 1000. Immediately before the glucose loading, serum samples for determinations of blood lipids, plasma glucose, and serum insulin were obtained. A second serum sample was taken 2 h later. The serum samples were refrigerated immediately and transported to the National Taiwan University Hospital within 6 h. Serum samples were then stored at −70 °C for batch assays of total cholesterol, triglycerides, LDL-cholesterol (LDL-C), HDL-cholesterol (HDL-C), apoprotein A1 (apo A1), apoprotein B (apo B), and lipoprotein(a) [Lp(a)], as described previously *(28)*. Standard enzymatic methods were used to determine serum cholesterol and triglycerides (methods 14354 and 14366, respectively; Merck). HDL-C was measured in the supernatant after precipitation with magnesium chloride-phosphotungstate reagents (method 14993; Merck). The LDL-C content was measured as "total cholesterol minus cholesterol in the supernatant" by the precipitation method *(29)* because the HDL-C was precipitated by the use of heparin/citrate reagent (method 14992; Merck). apo A1 and apo B concentrations were measured by turbidimetric immunoassay using commercial kits (Sigma). Lp(a) was determined by enzyme-linked immunosorbent assay (Organon) regardless of isoform.

Blood samples for glucose analysis were drawn into glass test tubes, each containing 80 mol/L fluoride/oxalate reagent. After centrifugation at 1500*g* for 10 min at 4 °C, glucose concentrations were measured on supernatants by enzymatic assay (commercial kit 3389; Merck) in a Eppendorf 5060 automated analyzer. The plasma insulin concentration was determined using the ELISA method in which a reagent kit supplied by the Dako was used. The plate antibody binds α chains somewhere near the intrachain disulfide. The conjugate antibody binds very close to the cleavage site in proinsulin, and its epitope is partially composed of a lysine residue at position 30 on the β chain. Thus, the assay will not measure intact proinsulin and provides specificity for insulin *(30)*. The lower limit of detection for insulin was 0.158 pmol/L, with a CV of 5.0%.

The measurements of coagulation profiles were made in the following manner: Tissue plasminogen activator (tPA) was analyzed using an enzyme immunoassay (Asserachrom tPA; Diagnostica Stago), and plasminogen activator inhibitor (PAI-1) and fibrinogen were measured using commercial kits. PAI-1 was measured using an enzyme immunoassay (Asserachrom PAI-1; Diagnostica

Table 1. Basic characteristics of the study population by gender: 1994–1995.

	Men (n = 953)		Women (n = 1212)	
	Mean	SD	Mean	SD
Age, years[a]	54.8	11.7	52.8	11.5
BMI, kg/m^2[a]	23.8	3.3	24.6	3.5
WHR[a]	0.92	0.06	0.88	0.07
SBP, mmHg[b,c]	124	18	126	21
DBP, mmHg	77	11	77	11
Cholesterol, mmol/L[a]	5.017	1.138	5.275	1.190
Triglycerides, mmol/L	1.479	1.106	1.400	1.039
HDL-C, mmol/L[a]	1.190	0.310	1.241	0.310
LDL-C, mmol/L[a]	3.517	1.112	3.698	1.164
Lp(a), g/L	0.134	0.148	0.146	0.157
apo A1, g/L[a]	1.25	0.25	1.29	0.23
apo B, g/L	0.93	0.29	0.95	0.31
Fasting glucose, mmol/L	6.328	1.721	6.273	1.887
Fasting insulin, pmol/L[a]	40.18	39.46	55.97	76.77
Postloading glucose, mmol/L[a]	7.549	4.219	8.160	4.052
Postloading insulin, pmol/L	193.0	236.1	279.8	348.7

[a,b] Difference between men and women: [a] $P < 0.001$; [b] $P < 0.01$.
[c] SBP, systolic blood pressure; DBP, diastolic blood pressure.

Stago), whereas fibrinogen was measured using a clotting assay (STA-Fibrinogen; Diagnostica Stago).

DIAGNOSTIC CRITERIA

Subjects were defined as hypertensive according to the Fifth Joint National Committee criteria *(31)*: a systolic blood pressure of 140 mmHg and higher and/or diastolic blood pressure of 90 mmHg and higher, or receiving regular antihypertensive therapy. The presence of CHD was defined on the basis of a finding of abnormal Q or QS patterns on an electrocardiogram or a clinical history of myocardial infarction or angina pectoris with admission documents. A history of stroke was defined on the basis of a history of hemiparesis or hemiplegia, and was confirmed by one neurologist. Subjects were defined as having diabetes mellitus if their fasting plasma glucose concentrations were >7.77 mmol/L or they were receiving oral hypoglycemic agents or insulin injections. A BMI >27 kg/m^2 and a WHR >0.94 were considered abnormal because these were 90th percentile values for the study population. The quartiles for fasting insulin, specified by sex in the study population, were established with the following cutoffs: ≤16.50 pmol/L, 16.50–29.99 pmol/L, 29.99–52.45 pmol/L, and ≥52.45 pmol/L for men; and ≤27.27 pmol/L, 27.27–42.33 pmol/L, 42.33–67.84 pmol/L, and ≥ 67.84 pmol/L for women. The top quartile concentration was defined as hyperinsulinemia. Homeostasis model assessment (HOMA) was used to identify insulin resistance syndrome, using the formula: [fasting insulin (mIU/L) × fasting glucose (mg/dL) × 0.05551]/22.5 *(26)*.

STATISTICAL ANALYSIS

We first compared the distribution of fasting serum insulin by age and sex. The distribution of the insulin concentration appeared highly skewed to the right and justified the use of geometric means. Sex- and age-specific quartiles for fasting insulin were defined. The interaction between fasting insulin and the atherosclerotic risk factor was examined for each hyperinsulinemia quartile. All

Table 2. Geometric means and 95% confidence intervals for variables with right-skewed distributions for the study population: 1994–1995.

	Men (n = 953)	Women (n = 1212)
Triglycerides, mmol/L	1.219 (0.384–3.827)	1.174 (0.384–3.624)
Lp(a), g/L	0.071 (0.005–0.942)	0.079 (0.006–0.973)
PAI-1, μg/L[a]	16.0 (2.5–103.5)	17.9 (2.6–121.8)
tPA, μg/L	8.0 (2.6–24.3)	7.7 (2.8–21.7)
Fibrinogen, μmol/L	8.588 (5.558–13.235)	8.735 (6.117–12.440)
Fasting insulin, pmol/L[b]	27.27 (3.59–190.86)	40.90 (8.61–196.60)
Postloading insulin, pmol/L[b]	109.1 (10.8–1126.5)	182.2 (28.0–1171.7)
Insulin resistance by HOMA[b]	7.319 (0.933–59.481)	11.121 (2.009–62.207)

[a,b] Difference between men and women: [a] $P < 0.05$; [b] $P < 0.001$.

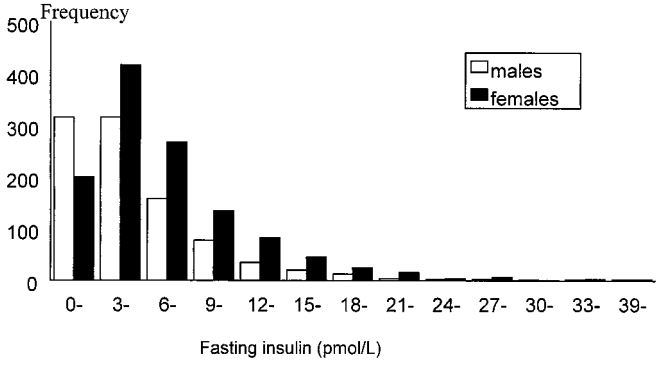

Fig. 1. Histograms of the fasting insulin concentrations in Chinese men and women, the CCCC Study, 1994–1995.

subjects were divided according to the sex-specific quartiles for insulin. Because of the skewed distribution of the insulin index indicators in each gender, a Spearman rank correlation analysis was performed to measure the linear relationship between covariates and three indicators of insulin resistance syndrome. A multiple logistic regression model was constructed to estimate the odds ratios and 95% confidence intervals of covariates to predict the occurrence of hyperinsulinemia. When the glucose and insulin concentrations for fasting subjects were plotted, the localized regression method of Cleveland and Delvin *(32)* was adapted using S-plus 3.3 *(33)*. Data analysis was performed using the SAS release 6.11 software *(34)*.

Results

Excluding 186 deaths and 63 cases of follow-up attrition, there were 2165 individuals (64.6%; 953 men and 1212 women) who had less missing data from both 1992–1993 and 1994–1995 follow-up visits. Table 1 shows the basic characteristics of population by gender. As a group, the men were older and had higher triglyceride concentrations and WHR values, but lower BMI values, than women. Compared with men, women exhibited higher mean systolic blood pressure, serum cholesterol, HDL-C, LDL-C, Lp(a), and apo A1 and B. Under fasting conditions, mean glucose concentrations were similar for both sexes. After glucose loading, the mean glucose concentration was higher in women than in men. Women also had higher mean insulin concentrations during fasting and 2-h postloading conditions.

The geometric means and 95% confidence intervals for variables with right-skewed distributions, displayed by sex, are listed in Table 2. In coagulation profiles, women had higher fibrinogen and PAI-1 concentrations, whereas men had higher tPA concentrations. In the comparisons of indicators of insulin resistance syndrome, women had higher fasting and postloading insulin concentrations, and higher insulin resistance by HOMA.

The distribution of fasting serum insulin was highly skewed to the right and was 0.14–279.83 pmol/L in men and 0.36–866.24 pmol/L in women; women had higher concentrations than men (Fig. 1). In men, serum fasting insulin decreased as age increased, whereas for women, serum fasting insulin increased as age increased (Fig. 2).

The the relationship between serum insulin and fasting glucose is presented using scatter plots in Fig. 3. In the fasting state, insulin concentrations increased progressively as glucose concentrations increased in both genders, and then plateaued for women, but increased slightly for men.

The mean values of clinical and metabolic variables, according to quartile concentrations of fasting insulin for the study population, are shown in Table 3. As fasting insulin concentrations increased, fasting glucose, postloading glucose, insulin, systolic and diastolic blood pressure, BMI, WHR, cholesterol, triglycerides, LDL-C, and apo B increased significantly ($P < 0.001$). The coagulation factors, including fibrinogen, PAI-1, and tPA, also increased significantly ($P < 0.001$) as fasting insulin concentrations increased. Serum Lp(a), HDL-C, and apo A1 decreased significantly as fasting insulin increased.

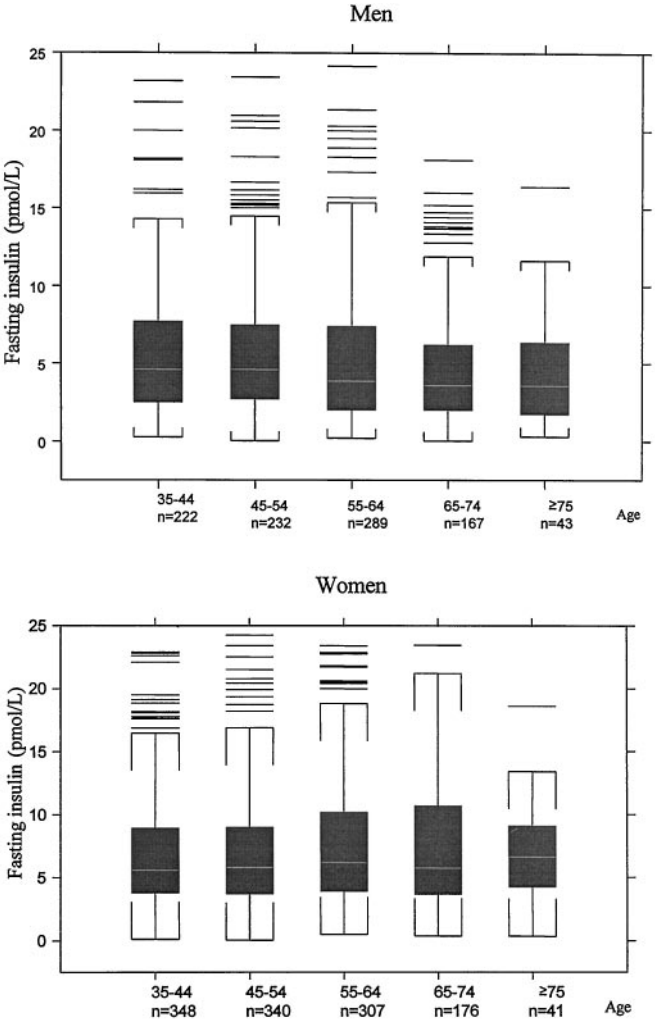

Fig. 2. Box plots of fasting serum insulin in the studied population by gender and age: 1994–1995.

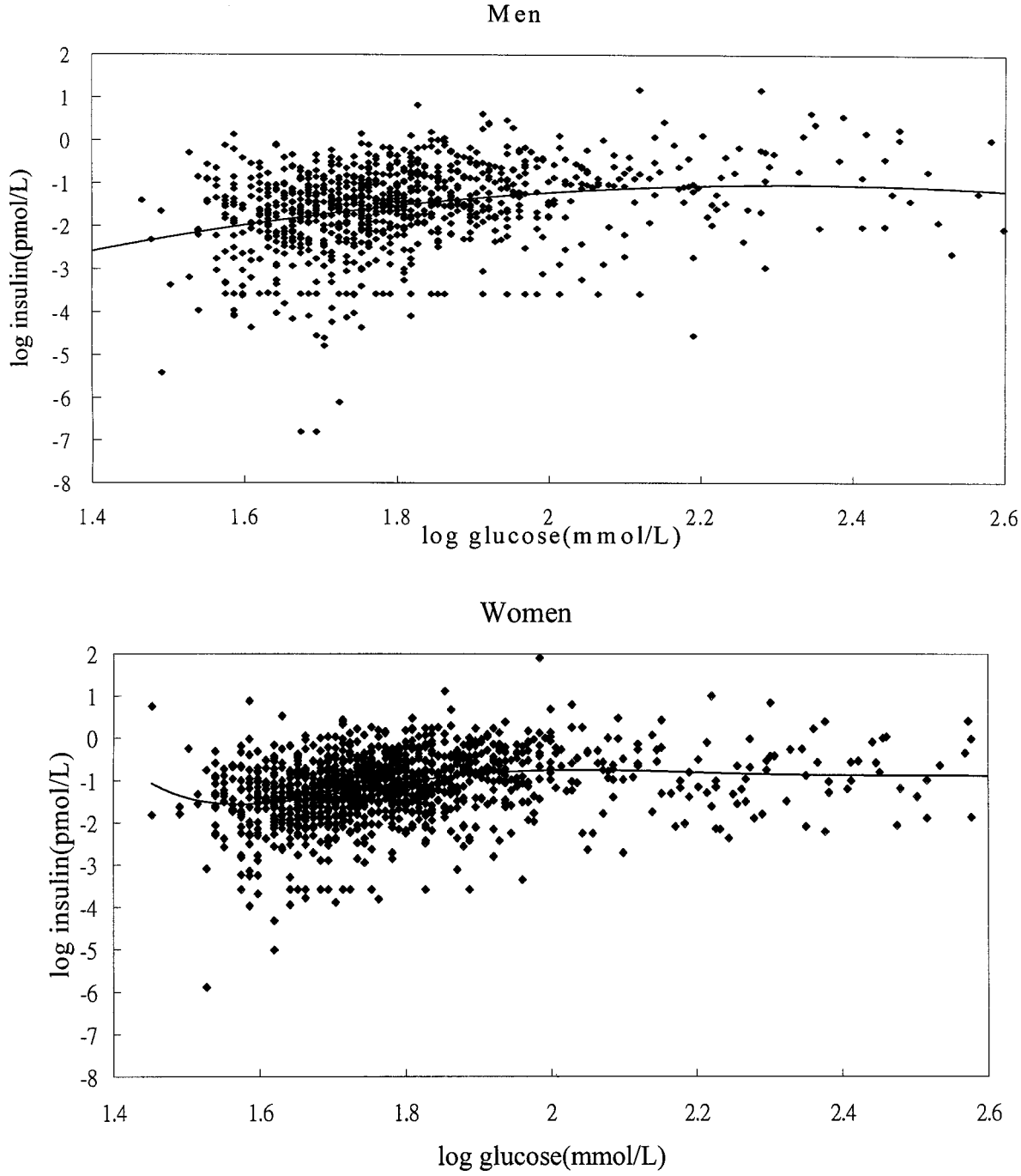

Fig. 3. Scatter plot relationship between fasting serum insulin and fasting plasma glucose in the CCCC Study, 1994–1995.
Local regression models are superimposed.

Fasting insulin concentrations were significantly positively correlated with insulin resistance by HOMA method ($\gamma = 0.97$; $P < 0.0001$). The relationships between these two indicators of insulin resistance syndrome and various atherosclerotic profiles, according to Spearman correlation coefficients, are shown in Table 4. The correlation coefficients were consistent within the two groups for fasting insulin concentrations and insulin resistance index by HOMA. When fasting insulin concentrations were considered, significant positive correlations were found for BMI, WHR, blood pressures, cholesterol, triglycerides, LDL-C, apo B, PAI-1, and tPA in both sexes, and significant negative correlations were found for HDL-C and apo A1 in both sexes. Fasting insulin concentrations also exhibited a significant negative association with age and Lp(a) concentration for men, but not for

Table 3. Mean values of clinical and metabolic variables, according to quartile of fasting insulin concentration in the study population: 1994–1995.

	Quartile of fasting insulin concentration			
	1st	2nd	3rd	4th
Postloading insulin, pmol/L[a]	115.5	169.3	233.2	452.0
Fasting glucose, mmol/L[a]	5.940	6.051	6.217	6.883
Postloading glucose, mmol/L[a]	6.939	7.216	7.383	8.771
SBP, mmHg[a,b]	122	124	125	129
DBP, mmHg[a]	75	77	77	80
BMI, kg/m^2[a]	22.5	23.4	24.5	26.5
WHR	0.88	0.89	0.9	0.92
Cholesterol, mmol/L[a]	4.991	5.120	5.198	5.353
Triglycerides, mmol/L[a]	1.152	1.310	1.479	1.818
HDL-C, mmol/L[a]	1.319	1.241	1.190	1.086
LDL-C, mmol/L[a]	3.336	3.569	3.698	3.905
Lp(a), g/L	0.150	0.146	0.145	0.127
Lp(a), g/L[a,c]	0.092	0.080	0.078	0.066
apo A1, g/L[a]	1.31	1.28	1.26	1.23
apo B, g/L[a]	0.86	0.91	0.97	1.04
PAI-1, μg/L[a,c]	10.8	15.4	18.7	27.9
tPA, μg/L[a,c]	6.1	7.4	8.3	10.3
Fibrinogen, μmol/L[c,d]	8.617	8.529	8.705	8.823

[a] $P < 0.001$, ANOVA *F*-test.
[b] SBP, systolic blood pressure; DBP, diastolic blood pressure.
[c] Geometric mean.
[d] $P < 0.05$, ANOVA *F*-test.

women. Fibrinogen concentration was not associated with fasting insulin concentrations for both sexes.

The abilities of the odds ratios and 95% confidence intervals of various covariates to predict the occurrence of hyperinsulinemia are shown in Table 5. We found that obesity, high LDL-C, and low HDL-C were independent factors. Sex and hypertension were not significant covariates for hyperinsulinemia. As age increased, the odds

Table 4. Spearman correlation between atherosclerotic risk factors and fasting insulin concentration and insulin resistance by HOMA in the studied population by gender: 1994–1995.

	Correlation coefficient			
	Men (n = 953)		Women (n = 1212)	
	Fasting insulin	IR (HOMA)[a]	Fasting insulin	IR (HOMA)
Age	−0.11[b]	−0.12[b]	0.04	0.07[c]
BMI	0.49[b]	0.49[b]	0.42[b]	0.41[b]
WHR	0.26[b]	0.27[b]	0.21[b]	0.23[b]
SBP	0.09[d]	0.11[b]	0.19[b]	0.22[b]
DBP	0.17[b]	0.18[b]	0.19[b]	0.21[b]
Cholesterol	0.08[c]	0.08[c]	0.13[b]	0.14[b]
Triglycerides	0.25[b]	0.27[b]	0.30[b]	0.35[b]
HDL-C	−0.33[b]	−0.33[b]	−0.27[b]	−0.32[b]
LDL-C	0.17[b]	0.17[b]	0.20[b]	0.21[b]
Lp(a)	−0.14[b]	−0.15[b]	−0.04	−0.04
apo A1	−0.18[b]	−0.16[b]	−0.08[d]	−0.09[d]
apo B	0.23[b]	0.24[b]	0.27[b]	0.30[b]
PAI-1	0.34[b]	0.37[b]	0.42[b]	0.45[b]
tPA	0.35[b]	0.37[b]	0.39[b]	0.42[b]
Fibrinogen	0.04	0.05	0.06	0.07[c]

[a] IR, insulin resistance.
[b] $P < 0.001$.
[c] $P < 0.05$.
[d] $P < 0.01$.

Table 5. Multiple logistic regression model to predict the occurrence hyperinsulinemia with various covariates in the study population: 1994–1995.[a]

Variable	Odds ratio	95% Confidence interval	*P*
Sex	0.89	0.70–1.12	0.305
Hypertension, yes/no	1.12	0.84–1.50	0.433
Diabetes, yes/no	1.98	1.43–2.76	0.0001
Age, years			
45–54/35–44	0.95	0.69–1.29	0.723
55–64/35–44	0.99	0.73–1.35	0.942
65–74/35–44	0.91	0.63–1.31	0.601
≥75/35–44	0.63	0.32–1.25	0.186
Obesity	5.51	4.28–7.09	0.0001
BMI ≥27/BMI <27			
Hypertriglyceridemia	1.29	0.93–1.77	0.127
TG ≥2.258/TG <2.258 mmol/L[b]			
High LDL-C	1.36	1.06–1.74	0.014
LDL-C ≥4.138/LDL-C <4.138 mmol/L			
Low HDL-C	2.19	1.67–2.87	0.0001
HDL-C ≤0.905/HDL-C ≥0.905 mmol/L			

[a] The goodness-of-fit test of the final model by Hosmer and Lemeshow method *(34)* was 8.21 with $df = 8$, $P = 0.4129$.
[b] TG, triglyceride.

ratios for the occurrence of hyperinsulinemia decreased, although not significantly.

Discussion

Insulin resistance can be measured quantitatively using the glucose clamp technique, which is laborious and not applicable to clinical practice and population studies *(35)*. Numerous studies have used the top quartiles or tertiles of fasting or postloading insulin concentrations as indicators of insulin resistance syndrome *(9, 14, 35–37)*. Other studies have adjusted from the physiological viewpoint to using several indicators based on fasting and postloading glucose concentrations, such as HOMA, to monitor insulin resistance syndrome *(18, 26)*. In this study, fasting insulin was used as an indicator of insulin resistance syndrome, and hyperinsulinemic was defined as the gender-specific top quartile of insulin concentrations. We found that the fasting insulin concentration was significantly associated with HOMA and postloading insulin concentrations and was an appropriate indicator for insulin resistance syndrome. HOMA and postloading insulin concentrations were higher in women than in men and were also related to various atherosclerotic risk factors in the study population.

The fasting and postloading insulin measurements for the 2165 native Taiwanese men and women from the community-based CCCC study provided a unique opportunity to observe how atherosclerotic risk factors are associated with insulin resistance syndrome in the Chinese population. The fasting insulin concentrations in this population had a right-skewed distribution, a pattern similar to that found for other ethnic groups *(3, 9)*. The median concentrations and intervals for fasting insulin for this study population seemed similar to those for Caucasians, higher on average than those for the Japanese *(9)*, but lower than those values for African Americans *(9, 13, 18, 26)*. Although fasting insulin concentrations were likely lower in females than in males for Caucasians, the concentrations were higher in females than in males for both the Japanese and the Chinese. However, triglycerides were fairly high for women in our study, compared with Caucasian women. The relationship was similar for the men in our study compared with Caucasian men. This study also demonstrated the different patterns in the age distribution of fasting insulin between genders: the concentration decreased as age increased in men, but increased gradually in women, peaking for the ages 65–74 years. This was a sex- and age-interactive phenomenon not reported previously.

The patterns of the relationships between fasting insulin and fasting glucose were similar for both genders. In men, there was a persistent positive relationship between glucose and insulin, whereas in women, a small hump was noted for insulin when the fasting glucose was ~8.22 mmol/L, and then the concentration for insulin became flat. The hump of the curve in women may indicate when pancreatic β-cell decompensation occurs *(13, 38)*.

Hypertension shares an important role in insulin resistance syndrome *(1, 2, 23)*. In this study, hyperinsulinemia was associated with higher systolic and diastolic blood pressure in both genders, similar to patterns for Chinese, Japanese, and Caucasians in other studies *(9, 8, 39)*. In the study by Saad et al. *(8)*, insulin concentrations and resistance were related to blood pressure in Caucasians, but not in Pima Indians or African Americans.

Obesity is strongly related to insulin resistance. In particular, individuals with a preponderance of abdominal fat deposition tend to be more insulin-resistant and

have several metabolic abnormalities that place them at risk for an abnormal blood lipid profile *(40)*. Compared with adipocytes located in the gluteo-femoral regions, abdominal adipocytes are more sensitive to lipolytic hormones *(41)*. In this study, BMI and WHR increased as the insulin quartile increased, which is consistent with previous reports *(19, 37, 42, 43)*.

The relationship between hyperinsulinemia and dyslipidemia, especially in subjects with low HDL-C concentrations and hypertriglyceridemia, is well-recognized in clinical practice and population studies *(3, 17, 44, 45)*. In the present study, the concentrations of cholesterol, triglycerides, LDL-C, and apo B increased significantly as insulin concentrations increased for both genders. The concentrations of HDL-C and apo A1 decreased significantly as insulin concentrations increased. Different patterns between genders may exist in different countries. In a Western study, cholesterol concentrations were positively correlated with insulin concentrations only in men *(46)*. It is noteworthy that in our study, Lp(a) concentrations decreased as insulin increased, similar to findings in a Japanese study *(9)*. However, the correlation was significant only for men, not for women ($\gamma = -0.14$ vs -0.04 in men and women, respectively). This suggests that different mechanisms of hyperinsulinemia and dyslipidemia may exist between genders.

The association of coagulation factors and insulin resistance syndrome varied. Several studies have demonstrated increased plasma PAI-1 concentrations for patients with hyperinsulinemia *(26, 47, 48)*, suggesting that insulin resistance syndrome is susceptible to atherothrombosis events. The fibrinogen concentration was also associated with hyperinsulinemia, but with a weaker correlation. The positive correlation between tPA and insulin in this study was different from that reported in the Northern Sweden MONICA study *(36)*, which showed low tPA activity in hyperinsulinemic status. The diversity in population structure may be explained by racial differences. Other factors, such as dietary habits and physical activity, may be taken into consideration to explain the differences in the association.

Lifestyle influences of insulin resistance, including dietary intake and physical activity, are important to the pathogenesis of insulin resistance syndrome *(22, 40)*. In this community-based study, inquiries concerning dietary habit and physical activity will be undertaken later. Controlling obesity and increased exercise are effective means of preventing diabetes and CHD. Further intervention treatments on the populations at risk for CHD are advised.

In conclusion, the present study demonstrated that various atherosclerotic and coagulation risk factors were strongly associated with fasting insulin concentrations. Insulin resistance syndrome may put these participants at risk for CHD.

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