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Prevalence of insulin resistance and its relationship with cardiovascular disease risk factors among Thai adults over 35 years old

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Abstract

Aims—To estimate the prevalence of insulin resistance (HOMA-IR) and to study its relationship with selected cardiovascular disease risk factors among Thai adults.

Methods—This cross-sectional study was comprised of 227 men and 990 women undergoing routine health check-up. The prevalence of insulin resistance was estimated using diagnostic criteria previously employed in Asian and other populations. Spearman's rank correlation coefficients were used to evaluate associations of HOMA-IR with selected cardiovascular disease risk factors. Multivariable logistic regression procedures were used to evaluate associations of hypertriglyceridemia, low HDL-Cholesterolemia, and hypertension with varying HOMA-IR values.

Results—Approximately 25.1% of men (HOMA-IR ≥ 1.56) and 21.5% of women (HOMA-IR ≥ 1.64) were classified as having insulin resistance. HOMA-IR values were statistically significantly and positively associated with body mass index, body fat percentage, waist circumference, and serum triglycerides. The values were inversely correlated with HDL-Cholesterol. When compared with those whose HOMA-IR values were within the lowest quartile (<0.45), men with HOMA-IR values in the highest quartile (≥ 1.58) had higher risks of hypertriglyceridemia (adjusted OR=2.83), low HDL-Cholesterolemia (adjusted OR=2.79), and hypertension (adjusted OR=2.76). Similar associations were observed among women.

Conclusion—Insulin resistance, as determined using HOMA-IR, was positively associated with selected cardiovascular disease risk factors among Thai adults.

Keywords

Insulin Resistance; HOMA-IR; Risk Factors; Epidemiology; Thailand

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Introduction

Insulin resistance is a condition in which peripheral tissues become nonresponsive to the effects of insulin. Many longitudinal studies in adults have demonstrated that insulin resistance is a risk factor of the development of type 2 diabetes [1,2]. Moreover, insulin resistance has also been reported as being strongly associated with the development of incident atherosclerotic disorders [3,4]. Given the multitude of serious complications that may arise from diabetes, it is imperative to establish a simple and practical method for identifying individuals at high risk for insulin resistance and to initiate early targeted diabetes prevention strategies. The gold standard test for diagnosing insulin resistance has been euglycemic-hyperinsulinemic glucose clamp [5]. Because of its invasiveness, complexity and expense, the euglycemic glucose clamp method is of limited use for clinical screening exams and population-based epidemiological studies.

The homeostasis model assessment of insulin resistance (HOMA-IR) was developed in response to the need for a simpler and more practical measurement of insulin resistance in large epidemiologic studies [6]. HOMA-IR uses information about fasting glucose and insulin concentrations to derive an estimate for insulin resistance, with higher values corresponding to increasing degrees of insulin resistance. The index has been validated as a proxy measure of insulin resistance in non-diabetic children and adults, with studies reporting correlations ranging from 0.82-0.91 when compared with measures derived from euglycemic glucose clamp assessments [7,8]. Ohnishi et al, in their study of Japanese men and women, reported that the sensitivity and specificity of HOMA-IR were 64.3% and 78.9% respectively when compared with the euglycemic glucose clamp gold standard. Using a threshold of ≥ 1.73 , the prevalence of insulin resistance was found to be 19.6% for men and 20.3% for women [9]. At present, little is known about the prevalence of insulin resistance among Thai adults. In this study, we estimated the prevalence of insulin resistance (HOMA-IR) and studied its relationship with cardiovascular disease risk factors (i.e., hypertriglyceridemia, low HDL-Cholesterolemia, and hypertension) among Thai men and women.

Materials and Methods

Study Population and Data Collection

We conducted a cross-sectional study of 1,265 hospital personnel (246 men and 1,019 women) who participated in annual health examinations at King Chulalongkorn Memorial Hospital in Bangkok, Thailand during the period of August 2008 through October 2008. Given that blood chemistry evaluations are not routinely measured on all participants under the age of 35 years, this research was restricted to those participants who were ≥ 35 years of age at the time of annual health examination. Eligible participants were asked to provide information about their age, marital status, occupation, educational attainment, medical history, use of anti-hypertensive, antidiabetic, or lipid lowering medications, smoking status, alcohol consumption habits, and physical activity. Participants underwent routine clinical physical examinations which included collection of venous blood samples after an overnight fast, and measurement of height, weight, waist circumference and resting blood pressures. Standing height was determined without shoes and measured to the nearest 0.5 centimeter. Weight was determined without shoes and with participants lightly clothed. Weight was measured using an automatic electronic scale (Seca, Inc., Hamburg, Germany) to the nearest 100 grams. Waist circumference was measured with a heavy-duty inelastic plastic fiber tape measure to the nearest 0.5 centimeter while the subject stood balanced on both feet, with the feet touching each other and both arms hanging freely. Measurement was taken midway between the inferior margin of the last rib and the iliac crest at the end of expiration [10]. Percent body fat (%BF) estimates were determined using the Tanita bioelectrical impedance

analysis (BIA) system (Tanita Model BC 532, Tokyo, Japan). The BIA system was routinely calibrated, and quality control measures were followed as recommended by manufacturers. Systolic and diastolic blood pressures, measured using an automatic sphygmomanometer (UDEX-II α , UEDA, Corp., Tokyo, Japan), were taken in the sitting position after participants rested for at least 5 minutes. Patients taking anti-diabetic medications, or who had a medical diagnosis of diabetes (n=48) were excluded from further consideration. Hence a total of 1,217 participants (227 men and 990 women) remained for inclusion in the present study.

Clinical Laboratory Analyses

Serum triglyceride (TG) concentrations were determined using standardized enzymatic glycerol phosphate oxidase assay procedures. High density lipoprotein-cholesterol (HDL-C) was measured by a chemical precipitation technique using dextran sulfate. Fasting plasma glucose (FPG) concentrations were determined using the hexokinase method. Fasting serum insulin concentrations were measured using a solid-phase, two-site chemiluminescent immunometric assay (Immulin 1000, Insulin). All assays were completed without knowledge of participants' medical history. Plasma lipids, lipoproteins and glucose concentrations were reported as mg/dl and insulin concentrations were reported as μ IU/ml.

Analytical Variable Specification

We estimated insulin resistance using the HOMA-IR index, which was calculated by dividing the product of fasting glucose (mg/dl) and fasting insulin (μ IU/ml) by 405 [6]. The HOMA-IR values have been shown to correlate well with values obtained using the "gold standard" clamp technique [7]. For the purposes of these analyses we defined hypertriglyceridemia as serum concentrations ≥ 150 mg/dl for men and women. Reduced high-density lipoprotein-cholesterol (HDL-C) was defined as <40 mg/dl in men and <50 mg/dl in women. Hypertension was defined as sustained BP readings of systolic BP ≥ 140 or diastolic BP ≥ 90 mm.

All participants provided informed consent; and all research protocols were reviewed and approved by the Ethics Committee of the Faculty of Medicine, Chulalongkorn University, and the Human Subjects Division, University of Washington.

Statistical Analyses

All statistical analyses were performed separately for men and women. Frequency distributions of socio-demographic, behavioral and clinical characteristics were examined. With regards to estimating the prevalence of insulin resistance among Thai adults, we report prevalence estimates based on the upper 10th percentile of HOMA-IR values for normal-weight male and female subjects with normal fasting plasma glucose in this study. For comparison with other study populations, we also report prevalence estimates according to diagnostic criteria previously used in Asian [9] and non-Asian [11] populations. Finally, insulin resistance prevalence estimates were determined within strata of participants' normal, overweight and obese status and according to the number of cardiovascular disease risk factors (i.e., 0, 1, 2, and 3).

Associations of HOMA-IR with selected cardiovascular disease risk factors were determined using the Spearman's rank correlation coefficients. Univariate and multivariable logistic regression procedures were employed to calculate unadjusted odds ratios (OR) to assess associations of HOMA-IR with selected cardiovascular disease risk factors (i.e., hypertriglyceridemia, hypertension and low HDL-Cholesterolemia). Confounding was empirically assessed by entering covariates into a logistic regression model one at a time, and by comparing the adjusted and unadjusted ORs. Final logistic regression models

included those covariates which altered unadjusted ORs by at least 10% [12]. All statistical analyses were performed using SPSS (version 17.0, SPSS Inc. Chicago, IL, USA) software. All reported P-values are two tailed, and confidence intervals were calculated at the 95% level.

Results

Table 1 summarized the major clinical and socio-demographic characteristics of 1,217 participants. Male and female participants were similar with respect to age, physical activity levels, fasting insulin, fasting glucose concentration and HOMA-IR values. The frequencies of smoking and alcohol consumption were higher among men. Men also had a higher prevalence of hypertension (36.1% vs. 16.6%), hypertriglyceridemia (35.7% vs. 13.6%) and low HDL-cholesterolemia (29.1% vs. 22.0%) than women.

Prevalence estimates of insulin resistance for men and women are summarized in Figures 1. Estimates are provided for normal weight, overweight and obese subjects according to several thresholds previously used to defined insulin resistance in Asian and non-Asian populations. As expected, the prevalence of insulin resistance varied widely according to the diagnostic criteria used. Approximately 25.1% of men ($\text{HOMA-IR} \geq 1.56$) and 21.5% of women ($\text{HOMA-IR} \geq 1.64$) were classified as having insulin resistance. Prevalence estimates were slightly attenuated when HOMA-IR values, promoted by Ohnishi et al [9] were used. Using the threshold of 1.73, we noted that 20.7% and 19.1% of Thai men and women, respectively, were classified as having insulin resistance. Regardless of threshold used, the prevalence of insulin resistance was substantially higher in obese adults compared with normal-weight adults (Figure 1). Prevalence of insulin resistance was also determined according to number of cardiovascular disease risk factors (Table 2). Prevalence estimates of insulin resistance were increased across successive number of cardiovascular disease risk factors. These patterns were evident for both men (10.0%, 23.1%, 38.5%, 65.0%) and women (11.7%, 25.9%, 60.2%, 70.4%).

Spearman's rank correlation coefficients for the relationship between HOMA-IR and several risk factors for cardiovascular disease are summarized in Table 3. Among men, statistically significant positive correlations were observed between HOMA-IR values and body mass index, body fat percentage, waist circumference, triglycerides, systolic and diastolic blood pressure. HOMA-IR values were inversely and statistically significantly correlated with HDL-Cholesterol concentrations ($r = -0.227$). Among women, HOMA-IR values were most strongly correlated with body fat percentage ($r = 0.483$), body mass index values ($r = 0.476$), waist circumference ($r = 0.458$), and triglyceride ($r = 0.425$). HOMA-IR values were statistically significantly inversely correlated to HDL-Cholesterol concentration ($r = -0.343$).

The associations between HOMA-IR and selected cardiovascular disease risk factors are described in Table 4. After adjusting for confounding factors, men with HOMA-IR falling within the highest quartile (≥ 1.58), as compared with those with HOMA-IR within the lowest quartile (<0.45) had 2.83-fold increased risk of hypertriglyceridemia (adjusted OR=2.83, 95% CI: 1.15-6.97). Those with HOMA-IR values in the highest quartile had a 2.79-fold increased risk of low HDL-Cholesterol concentrations (adjusted OR=2.79, 95% CI: 1.07-7.23). Similarly, high HOMA-IR values (upper quartile) were associated with a 2.76-fold increased risk for hypertension (adjusted OR=2.76, 95% CI 1.03-7.38).

Among women, association between HOMA-IR values and HDL-Cholesterolemia appeared to have a strong linear component in trend (P-value for trend <0.001). Adjusted odds ratios for successive HOMA-IR quartiles were 1.00, 1.83, 2.53, and 5.63 (with the lowest quartile as the reference group). Adjusted odds ratios for hypertriglyceridemia increased with each

successive HOMA-IR quartile (1.00, 2.64, 2.49, and 8.31, P-value for trend <0.001). After adjusting for the confounding factors, women with HOMA-IR values in the upper quartile had a 2.21-fold increase risk of having hypertension (adjusted OR=2.21, 95% CI 1.21-4.03) as compared with those who had values in the lowest quartile.

Discussion

When HOMA-IR threshold of 1.56 and 1.64 were used for men and women, respectively, the prevalence of insulin resistance was found to be 25.1% for men and 21.5% for women. This prevalence proportion is quite similar to the values that have been reported from studies of Japanese adults. Ohnishi et al. suggested using the HOMA-IR value of 1.73 and reported an insulin resistance prevalence of 19.6% for men and 20.3% for women [9]. In another study of Japanese adults, Yamada et al. reported that post-glucose tolerance insulin concentrations were correlated with hypertriglyceridemia, low HDL-Cholesterol concentration, and hypertension [13]. Chailurkit et al. found that body mass index and waist circumference were positively correlated with HOMA-IR values [14]. Consistent with these previously published reports, we found that HOMA-IR values were statistically significantly and positively associated with body mass index, body fat percentage, waist circumference, and triglycerides. We also noted that HOMA-IR values were inversely correlated with serum HDL-Cholesterol concentrations. Moreover, we noted that participants with HOMA-IR values in the highest quartile had the highest risks of hypertriglyceridemia, low HDL-Cholesterol and hypertension.

Accumulating evidence indicates that both insulin resistance and hyperinsulinemia may be causally related to hypertension [15], type 2 diabetes mellitus [1,16] and cardiovascular disease [15]. Further evidence also indicates that calorie restriction, weight loss, and physical exercise improve insulin sensitivity [17-19]. An increase in prevalence of insulin resistance is observed throughout the world. The prevalence of type 2 diabetes among Thais was reported to be 6.7% (6.0% in men and 7.4% in women) in the Third National Health Examination Survey in 2004 [20]. Insulin resistance could contribute to the development of type 2 diabetes. Given the considerable individual and public health implications with respect to associated morbidity and mortality rates, it is critical to identify these at risk individuals so that preventative and therapeutic protocols can be effectively directed to lower their cardiovascular risk and to delay (and/or prevent) the onset of type 2 diabetes mellitus.

Strength of our study include the extensive amount of fasting insulin and glucose (HOMA-IR) data available for over 1,000 study participants, and the unique opportunity to assess insulin resistance in association with selected CVD risk factors in an occupational cohort of adults in Bangkok, Thailand. Several important limitations, however, must be considered when interpreting the results of our study. First, as the study population was comprised of hospital personnel, results may not be generalizable to the general Thai population. Second, we used self-reported information to assess some characteristic of study participants (e.g., physical activity). Therefore, we cannot exclude the possibility that some misclassification may have occurred. Further, because of this cross-sectional data collection design, we cannot be certain of the temporal relation between HOMA-IR values and risk of dyslipidemias or hypertension. Inferences concerning the risk for incident dyslipidemia, hypertension and other CVD disorders, however, will be enhanced with data forthcoming from on-going prospective studies among Thai adults.

In summary, the present study indicates that the prevalence of insulin resistance was substantially higher in obese adults compared with normal-weight adults. Insulin resistance,

as determined using HOMA-IR, was positively associated with selected cardiovascular disease risk factors among Thai adults.

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Figure 1.

Prevalence of insulin resistance according to various HOMA-IR thresholds among men and women. ^aThreshold was defined by the upper 10th percentile of HOMA-IR values for normal-weight men or women with normal fasting plasma glucose in this study. ^bThreshold was defined by the upper quartile of HOMA-IR among men or women. ^cThresholds were based on Japanese adult studies [9]. ^dThresholds were based on Italian adult studies [11].

Table 1

Socio-demographic and clinical characteristics of study 1217 participants, Bangkok, Thailand, 2008

Characteristic	Men (n=227)		Women (n=990)	
	n	%	n	%
Age (years)				
35-39	48	21.1	254	25.7
40-44	63	27.8	219	22.1
45-49	52	22.9	233	23.5
50-54	33	14.5	152	15.4
≥55	31	13.7	132	13.3
Education				
≤Primary education	60	26.5	104	10.6
<Bachelor degree	127	56.2	425	43.4
≥Bachelor degree	39	17.3	451	46.0
Body mass index (kg/m ²)				
<18.5	4	1.8	35	3.5
18.5-22.9	59	26.0	411	41.5
23.0-24.9	47	20.7	182	18.4
25.0-27.4	65	28.6	172	17.4
27.5-29.9	30	13.2	104	10.5
≥30.0	22	9.7	86	8.7
Smoking status				
Never smoker	125	55.1	949	95.9
Previous smoker	59	26.0	13	1.3
Current smoker	43	18.9	28	2.8
Alcohol consumption				
No	86	37.9	754	76.2
Yes	141	62.1	236	23.8
Physical activity levels				
No	86	37.9	404	40.8
Yes, <150 minutes/week	86	37.9	325	32.8
Yes, ≥150 minutes/week	55	24.2	261	26.4
	Mean (SD)		Mean (SD)	
Body fat percentage (%)	22.6 (5.6)		33.3 (6.3)	
Waist circumference (cm)	86.1 (9.0)		76.1 (9.5)	
Weight (kg)	70.1 (12.0)		59.1 (10.2)	
Height (cm)	166.2 (6.5)		156.1 (4.9)	
Body mass index (kg/m ²)	25.4 (4.1)		24.2 (4.0)	
Systolic blood pressure (mmHg)	121.7 (13.9)		113.8 (14.2)	
Diastolic blood pressure (mmHg)	77.4 (10.5)		72.4 (9.8)	
HDL-Cholesterol (mg/dl)	47.0 (12.1)		60.9 (14.7)	

Characteristic	Men (n=227)		Women (n=990)	
	n	%	n	%
	Median (IQR)		Median (IQR)	
Triglyceride (mg/dl)	124.0 (103.0)		83.0 (54.0)	
Fasting plasma glucose (mg/dl)	87.0 (11.0)		86.0 (9.0)	
Fasting insulin (μ IU/ml)	3.9 (5.1)		4.2 (4.6)	
HOMA-IR	0.9 (1.1)		0.9 (1.0)	

Prevalence of insulin resistance in relation to number of cardiovascular disease risk factors, Bangkok, Thailand, 2008

Table 2

Number of cardiovascular disease risk factors	Insulin resistance ^I				P-value
	No		Yes		
	n	%	n	%	
Among men					<0.001
0	81	90.0	9	10.0	
1	50	76.9	15	23.1	
2	32	61.5	20	38.5	
3	7	35.0	13	65.0	
Among women					<0.001
0	546	88.3	72	11.7	
1	183	74.1	64	25.9	
2	37	39.8	56	60.2	
3	8	29.6	19	70.4	

^I Threshold was defined by the upper 10th percentile of HOMA-IR values for normal-weight men and women with normal fasting plasma glucose in this study.

Table 3

Spearman's rank correlation coefficients for HOMA-IR and selected cardiovascular disease risk factors, Bangkok, Thailand, 2008

Cardiovascular disease risk factors	Among men (n=227)		Among women (n=990)	
	r	P-value	r	P-value
Age (years)	0.104	0.118	0.118	<0.001
Body mass index (kg/m ²)	0.519	<0.001	0.476	<0.001
Body fat percentage (%)	0.541	<0.001	0.483	<0.001
Waist circumference (cm)	0.489	<0.001	0.458	<0.001
Systolic blood pressure (mmHg)	0.360	<0.001	0.253	<0.001
Diastolic blood pressure (mmHg)	0.276	<0.001	0.210	<0.001
Triglyceride (mg/dl)	0.337	<0.001	0.425	<0.001
HDL-Cholesterol (mg/dl)	-0.227	0.001	-0.343	<0.001

Odds ratios (ORs) and 95% confidence intervals (95% CIs) of hypertriglyceridemia, low HDL cholesterolemia and hypertension according to quartiles of HOMA-IR, Bangkok, Thailand, 2008.

Table 4

HOMA-IR	Hypertriglyceridemia	Low HDL cholesterolemia	Hypertension
	OR ^a	OR ^b	OR ^c
Among men	95% CI	95% CI	95% CI
<0.45	Referent	Referent	Referent
0.45-0.86	0.46 (0.18, 1.22)	1.01 (0.37, 2.73)	1.28 (0.49, 3.38)
0.87-1.57	1.76 (0.74, 4.21)	2.24 (0.88, 5.69)	1.34 (0.50, 3.61)
≥1.58	2.83 (1.15, 6.97)	2.79 (1.07, 7.23)	2.76 (1.03, 7.38)
	<i>P for trend = 0.003</i>	<i>P for trend = 0.014</i>	<i>P for trend = 0.045</i>
Among women	OR ^d	OR ^d	OR ^d
	95% CI	95% CI	95% CI
<0.47	Referent	Referent	Referent
0.47-0.89	2.64 (1.15, 6.04)	1.83 (1.01, 3.32)	1.03 (0.54, 1.96)
0.90-1.50	2.49 (1.09, 5.69)	2.53 (1.43, 4.47)	1.50 (0.82, 2.74)
≥1.51	8.31 (3.79, 18.22)	5.63 (3.21, 9.86)	2.21 (1.21, 4.03)
	<i>P for trend <0.001</i>	<i>P for trend <0.001</i>	<i>P for trend = 0.003</i>

^a Adjusted for age (continuous), body mass index (continuous) and smoking status (never, previous, current)

^b Adjusted for age (35-39, 40-44, 45-49, 50-54, ≥55), body mass index (continuous), and exercise (no, <150 minutes/week, ≥150 minutes/week)

^c Adjusted for age (continuous), educational attainment (≤primary education, <bachelor degree, ≥bachelor degree), body mass index (continuous), and smoking status (never, previous, current)

^d Adjusted for age (continuous), and body mass index (<18.5, 18.5-24.9, 25.0-29.9, ≥30.0)