Review Article

Epidemiology of metabolic syndrome in Asia

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Metabolic syndrome (MS) is a rising disease entity characterized by a clustering of metabolic conditions. Although prevalence of obesity as defined by the World Health Organization (WHO) is relatively low in Asia compared to western countries, metabolic syndrome is growing into a significant public health problem. Comparative studies indicate that metabolic responses to obesity may be greater in South and East Asians than their western counterparts at given Body Mass Indexes (BMIs). Higher percentage body fat in Asians at given BMIs and over-responsiveness to obesity may in part explain the phenomenon for which the underlying causes are not clear. Furthermore, aborigines may be at an even greater MS risk. The metabolic syndrome definition itself as well as whether it should be defined are controversial. The National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) gives equal weight to each component disorder, while the International Diabetes Federation (IDF) takes central obesity as a pre-requisite. Both criteria adopt ethnic-specific cut-off points for waist circumference. Asian data favour the new NCEP-ATP III definition, as individuals that were selected through the NCEP criteria but disregarded by the IDF criteria had similar Framingham cardiovascular disease risk scores to those picked by both definitions. Prospective data show that the metabolic syndrome not only increases the risk of coronary artery disease but also cerebrovascular disease in Asians. Macronutrient composition and the quality of the diet are associated with the risk of metabolic syndrome. More research is needed to relate diet and metabolic syndrome in Asians.

Key Words: metabolic syndrome, Asian, definition, diet, epidemiology

INTRODUCTION

The significance of metabolic syndrome has unravelled gradually in recent years. The metabolic syndrome is a condition characterized by a constellation of metabolic disorders including: abdominal obesity, insulin resistance/glucose intolerance, atherogenic dyslipidemia (elevated TG, and lower HDL-C), raised blood pressure, proinflammatory and prothrombotic state. It was referred to as the "X syndrome" by Kylin in the 1920's and described as a phenomenon of the clustering of obesity, hypertension, and gout.[1] The concept of syndrome X was reintroduced by Reaven[2] in the late 1980's for the clustering of cardiovascular risks.

Operational definitions of metabolic syndrome

A unified operational definition of the syndrome was first purposed in "*Diagnosis and classification of diabetes mellitus provisional report of a WHO consultation*" in 1998[3]. According to this definition, a person with type 2 DM, impaired fasting glucose, impaired glucose tolerance, or insulin resistance has the metabolic syndrome if two or more of the following component criteria are satisfied: dyslipidemia (elevated plasma triglyceride or low HDL-C), obesity (high BMI or waist-to-hip ratio), hypertension, and microalbuminuria.

On the other hand, the criteria suggested by the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) in 2001 utilized primarily readily available biochemical parameters: fasting plasma triglyceride, HDL-C, glucose, and blood pressure, whose cut-off points were lowered to the higher end of the normal range.[4] In addition, waist circumference was used to define obesity, focusing on abdominal adiposity. A person is diagnosed as having the metabolic syndrome if three or more of the criteria are satisfied. Furthermore, the International Diabetes Federation (IDF) in 2005[5] proposed yet another criteria which mandates central obesity as the essential condition in addition to two other disorders out of the four stated. Cut-off points similar to the NCEP-ATP III criteria were used except for fasting glucose which was lowered to 100mg/dl and ethnic-specific cut-off points for waist circumference were adopted. In the fall of 2005, the revised NCEP-ATP III criteria also adopted the same glucose and waist cut-offs while maintaining the equality principle for all five component disorders.[6]

Although most experts recognize that obesity-related insulin resistance may be the core cause of metabolic syndrome, each medical society has its emphasis in defining the syndrome. The definition used in the WHO-diabetes report centres on diabetes and insulin resistance, whereas IDF focuses on central obesity. While the NCEP- ATP III

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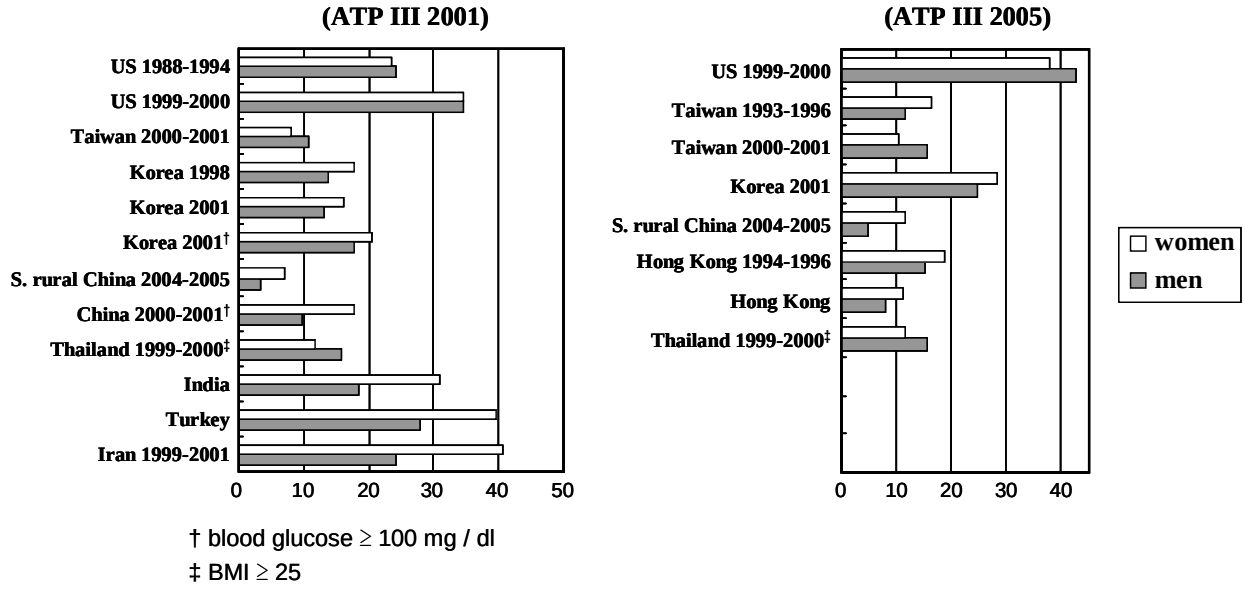

Figure 1. Prevalence rates of metabolic syndrome in Asians

guideline gives equal weights to abdominal adiposity, high blood pressure, hyperglycemia, elevated triglyceridemia and low-HDL cholesterol. Prevalence rate estimated from different definitions would vary inevitably and long-term cardiovascular risks of these definitions may also differ.

Prevalence of metabolic syndrome in Asian countries

Most prevalence data in literature used either the 2001 or the 2005 version of the NCEP-ATP III definition (Figure 1). According to the 2005 version; China,[7] Taiwan,[8, 9] Hong Kong[10], and Thailand[11] had similar prevalence rates ranging between 10-15%. However, it was much lower (around 5%) in southern rural China.[12] On the other hand, rates for Koreans,[13] approximately one quarter, were higher than the Chinese and Thais, even though their average body mass index (BMI) was similar to other East Asian countries. India[14] had strikingly high prevalence rates compared to the rest of Asia, approaching that of US population. Metabolic syndrome prevalence in Turkey[15] and Iran[16] was comparable to that of the US with a large excess in females. Considering the relatively low mean BMI and the low prevalence of obesity (BMI > 30) in east and south Asians, the magnitude of the metabolic syndrome prevalence is unusually high.

Excess metabolic risk in Asians

A series of comparative data pointed out that under fixed BMI or fatness, metabolic risk was much greater in South Asians compared to Caucasians in terms of diabetes mellitus, insulin resistance and hypertriglyceridemia.[17] Our study comparing data from NHANES II and from Nutritional and Health Survey in Taiwan also showed that Taiwanese, a group of East Asians, experienced higher absolute and relative risk of hypertension, hyperglycemia, dyslipidemia, and hyperuricemia than non-hispanic US white and US blacks.[18] An integrated graph of this phenomenon relating BMI and metabolic risks is provided in figure 2. This phenomenon is most likely due to a higher

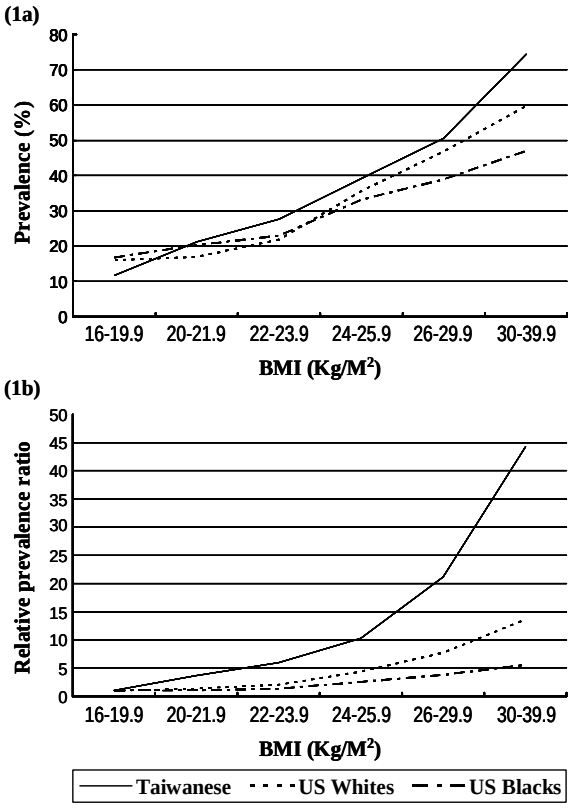

Figure 2. Age-standardized prevalence (1a) and relative prevalence ratio (1b) in the presence of two or more metablic risk factors† by BMI levels in three populations: Taiwanese, non-hispanic US whites, and US blacks. †High blood pressure: SBP>130, DBP>85 or on antihypertensives, hyperglycemia: fasting glucose> 100mg/dl or on lipid-lowering drug Low HDL-C: HDL-C< ♂ 40/ ♀ 50 mg/dl.

percentage of body fat accumulation in Asians than in Caucasians at fixed BMI level as pointed out by a series of studies from Deurenberg et al,[19,20] comparing data among Indonesians and Singaporeans with Caucasians.

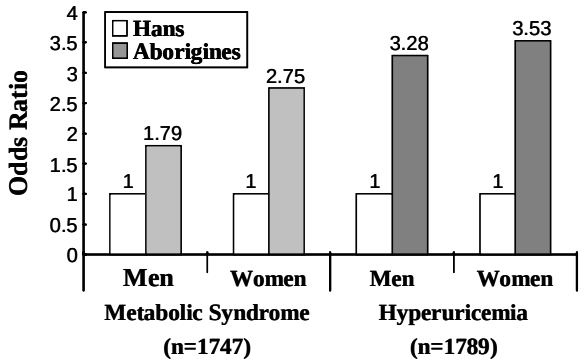

Figure 3. Odds ratio of aboriginal ethnicity on the presence of metabolic syndrome and hyperuricemia, Nutrition Health Survey in Taiwan 1993-1996. Potential confounding factors controlled for both health conditions: age, physical activity, presence of physical disability, education level, and amount of alcohol consumption; additional confounding factors controlled for hyperuricemia: BMI, and waist circumference.

Recent study from Taiwan[21], Korea[22], and Australian aborigines[23] further supported this hypothesis.

Our study[24] (figure 3) found that aborigines residing in Taiwan had a much greater risk of ascertaining metabolic syndrome than Han Chinese, despite controlling for potential intermediate factors such as age, physical activity, education level and alcohol consumption. This indicated the potential effect of genetics or the interaction between genetics and the environment. Studies showed that insulin sensitivity was poorer in Asian Indians than Caucasians at fixed body fat percentages.[25] Increased body fat percentage may affect individuals differently due to differences in genetic make-up, intra-uterine (developmental) environment, and dietary and physical activity patterns.

Applicability of available definitions of metabolic syndrome to Asians

ATP III and IDF definitions are two of the most popular definitions for metabolic syndrome. However, it is controversial as to which one is better in defining metabolic syndrome. We addressed the differences between these two definitions with regard to prevalence estimation and its relations with cardiovascular risks.

Comparing data from the Nutrition and Health Survey in Taiwan[26] and NHANES III (figure 2), prevalence estimates from the two definitions did not differ much in US populations,[27] but with Taiwanese data the IDF estimate for women was 25% lower (12.6% vs 16.5%) and for men it was 50% lower (6.2% vs 11.6%) than that of the ATP III. The discrepancy is likely due to the proportion of men and women with metabolic syndrome defined by the revised ATP III who do not have elevated waist circumferences (figure 4). It is speculated by this author that this phenomenon may be due to either lack of proper indicators for abdominal obesity or a inappropriate waist circumference cut-off point for Asians. Furthermore, we found that there is a greater proportion of Taiwanese that have four or more metabolic disorders clustered or high blood pressure, but only a smaller proportion of people that have high fasting glucose values. Further research is needed to understand the rational and consequences of these different combination patterns.

With regard to cardiovascular risk, when comparing people picked up by both guidelines (with central obesity) with those identified by NCEP guideline only (without central obesity),[8] no significant differences were observed for levels of blood pressure, HDL-C, fasting triglyceride and glucose, and Framingham coronary artery disease risk score. And these cardiovascular risks were much stronger in both groups of metabolic syndrome patients than people with no such syndrome. This data indicate that a good proportion of people with metabolic syndrome may be missed by the IDF definition even though it may be sound for IDF to consider central obesity appearing early in the chain of events in the pathogenesis of metabolic syndrome. In addition, our recent work[28] comparing the 2001 and 2005 versions of NECP-ATP III definitions found that the new version corresponded to a sharper dose response curve relating the number of metabolic disorders to the risk of ischemic stroke in the Two-township studies in Taiwan. Taken together, among the

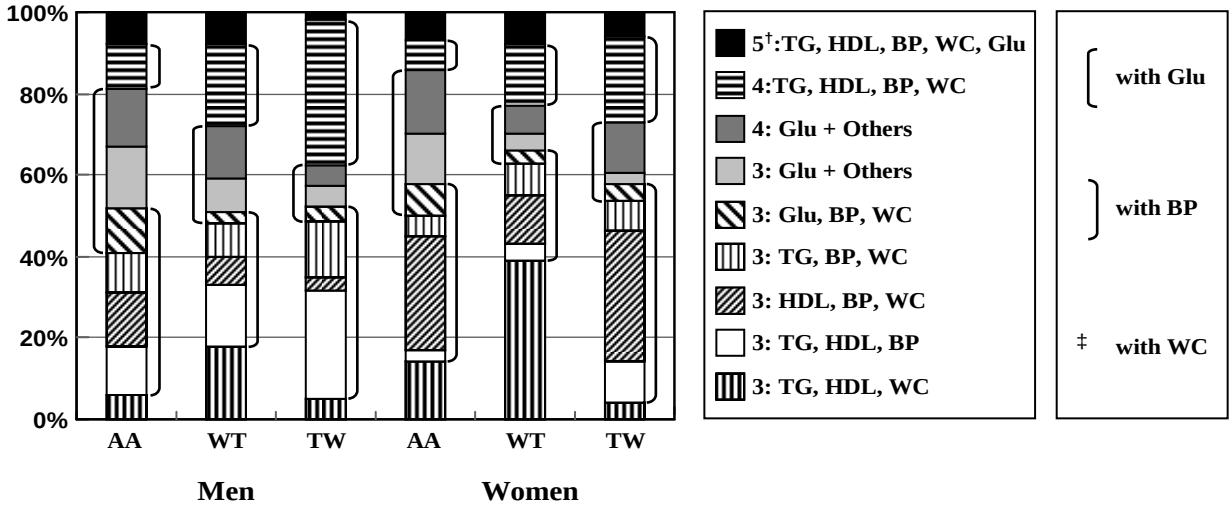

Figure 4. Clustering patterns of metabolic disorders in US non-Hispanic whites (WT), African Americans (AA), and Taiwanese (TW)

available definitions, the new NCEP-ATP III guideline may be more advantageous than others to predict future cardiovascular risks and may be used for screening in Asians.

Metabolic syndrome and cardiovascular events

It is well documented inliterature that metabolic syndrome is associated with increased risk of all cause mortality and cardiovascular events. Ford el al[29] conducted a meta-analysis on 12 prospective studies primarily for Caucasian populations and demonstrated a 74% increase in cardiovascular risk. We have obtained estimates from five prospective studies from Japan,[30,31] Korean,[13] and Taiwan[28,32] that examined the relations between baseline metabolic syndrome status and incidental events on coronary artery disease or cerebrovascular disease, using either the 2001 NCEP-ATP III guideline, 2005 NCEP-ATP III guideline, or the modified criteria using BMI cut-off point to define obesity.

As shown in Table 1, their hazard ratios are in the vicinity of 2 which is very close to the estimate obtained from Asia Pacific Cohort Study Collaboration[33] which gathered individual data from 35 cohorts from mainland China, Hong Kong, Japan, south Korean, Taiwan, Thailand, and Singapore. The APCSC data further showed that the more component disorders one had, the higher the risk in acquiring cardiovascular death.

Diet and metabolic syndrome

A great body of information have accumulated with regard to the relations between diet and each of the component disorder of metabolic syndrome. In general, it is accepted that the Mediterranean diet with fish, vegetable, fruit, red wine, and olive oil may protect against the development of metabolic syndrome.[34-36] But up to this point, only a dozen of cross-sectional studies and a relatively small number of prospective studies have tried to determine the association between diet and the metabolic syndrome and comprised of primarily Caucasian studies (Framingham,[37-39] WHS,[40,41] NHANES,[42] Boston,[43] ATTICA-greece[44]), one Japanese-Brazilian,[45] and a few Iranian study.[46-49] Overall speaking, increased consumption of whole grains, dairy products, vegetables, fruits, calcium, magnesium, fiber from cereals, linoleic acid, and the maintenance of a healthy dietary pattern (high in fruits, tomatoes, poultry, legumes, cruciferous and green leafy vegetables, other vegetables, tea, fruit juices, and whole grains) have shown to be protective. The consumption of refined grains, soft or sweetened drinks, alcoholic beverage and fat as well as keeping to a empty calorie diet, potato and meat diet have been associated with elevated

Table 1. Hazard ratios relating metabolic syndrome to cardiovascular events in Asian prospective studies

Study	Subjects	Age	Outcomes	MS definition†	Hazard ratio
KNHANES [13]	Korean (N=4452)	20+	CHD/Stroke	ATPIII.8090.110	♂ 0.8 (0.4-1.7) ♀ 2.4 (1.1-5.1) RR
Hisayama study [30]	Japanese (N=2452)	40+	CHD/Stroke	ATPIII.8090.110	♂ 1.86(1.32-2.62) ♀ 1.70(1.22-2.36)
			CHD		♂ 1.94 (1.19-3.17) ♀ 2.86 (1.56-5.24)
			Stroke		♂ 1.92 (1.23-2.98) ♀ 1.50 (1.03-2.19)
			IS stroke		♂ 1.68 (0.98-2.89) ♀ 1.78 (1.13-2.79)
Cardiovascular Risk Survey [31]	Japanese (N=9087)	40-69	CHD/ IS	ATPIII.BMI25.110	♂ 2.4 (1.4-4.0) ♀ 2.3 (1.2-4.3)
			IS Stroke		♂ 2.0 (1.3-3.1) ♀ 1.5 (1.0-2.3)
CVDFACTS [28]	Taiwanese (N=3453)	20+	IS stroke	ATPIII.8090.110	♂ 2.12 (1.32-3.4) ♀ 1.61 (0.95-2.75)
				ATPIII.8090.100	♂ 2.34 (1.46-3.73) ♀ 1.41 (0.83-2.39)
Kin-Shan study [32]	Taiwanese (N=3602)	35+	CHD	ATPIII.BMI27.100	1.83 (1.16-2.9)
			Stroke		2.05 (1.45-2.91)
APCSC [33]	Asians (N=329,166)	30-75	CHD(fatal)	ATPIII.BMI28.110	2.29 (1.28-4.10)
					2.05 (1.13-3.72) -more adjustment

† ATPIII.8090.110: obesity: waist circumference≥80 cm for women, ≥90 cm for men; blood glucose≥ 110 mg/dl; ATPIII.BMI25.110: obesity: BMI≥25; blood glucose≥ 110 mg/dl; ATPIII.8090.100: obesity: waist circumference≥80 cm for women, ≥90 cm for men; blood glucose≥ 100 mg/dl; ATPIII.BMI27.110: obesity: BMI≥27; blood glucose≥ 110 mg/dl; ATPIII.BMI28.110: obesity: BMI≥28; blood glucose≥ 110 mg/dl

risk. In addition, our yet unpublished meta-analysis consisting of 21 dietary intervention studies showed that a low carbohydrate diet may be associated with a reduced risk of hypertriglyceridemia, low-HDL-C, but an elevated risk of hypercholesterolemia compared to the American Heart Diet.[50] To the best of our knowledge, there has yet to be any dietary studies of this kind from South and East Asians in western literature.

CONCLUSIONS

When obesity becomes a pandemic in the world, the significance of the metabolic syndrome is unravelled, in particular in South and East Asians who seem to react to a greater degree to metabolic risk at a given level of obesity. This may be due to higher body fat composition and an over-responsiveness to obesity in Asians. More research is needed to understand the gene-environment interaction in this observed discrepancy between Asians and Caucasians.

The magnitude of the cardiovascular risk associated with the metabolic syndrome in Asians is similar to, if not larger than, that of Caucasians. In addition, among the several available definitions, the 2005 NCEP-ATP III criteria is most suitable for Asians in terms of the dose-response relationship with ischemic stroke. The IDF definition will miss a sizable number of Asians if used in screening probably due to the inadequacy of current methods to identify central obesity.

Very little has been done to relate dietary characteristics and metabolic syndrome in Asians. More prospective investigations and dietary intervention studies are required to understand the relations between diet and the metabolic syndrome.

Overall speaking, the metabolic syndrome has caught the attention of health professionals in Asian. One of the challenges is to understand its pathogenesis and to identify effective measures to prevent it either at the population level or at the individual level.

AUTHOR DISCLOSURES

Wen-Harn Pan, Wen-Ting Yeh and Lu-Chen Weng, no conflicts of interest.

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