UNIVERSITI PUTRA MALAYSIA

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By

MOULOUD AGAJANI DELAVAR

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Doctor of Philosophy

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Chairman: **Professor Dr. Lye Munn Sann**

Faculty: **Medicine and Health Sciences**

Metabolic syndrome is a cluster of interconnected cardiovascular risk factors. Existing data suggest that it has reached an alarming rate, and it is found more common in women than in men. Obesity plays a central role in metabolic syndrome and it has become a common factor among Iranian women. Accordingly, it is important to elucidate both lifestyle and dietary factors to the development of metabolic syndrome among middle-aged women so as to prevent and manage the syndrome in a much better way.

The research design of the present thesis was a population-based cross-sectional study, and the criteria by the NCEP ATP III were used to classify subjects with metabolic syndrome. Meanwhile, their physical activities were measured using the original International Physical Activity Questionnaires Long form. Food frequency questionnaire (FFQ) was also used in assessing individual's habitual intake. A total of 984 individuals, aged 30-50 year old from fourteen active urban primary healthcare centres in Babol (Iran), were selected using a systematic random sampling

method and sampling proportionate to size. Thus, lifestyle factors associated with metabolic syndrome were analyzed.

Among the Babolian middle-aged women living in the urban area, the prevalence of metabolic syndrome was found to be 31.0 %. Overweight and abdominal obesity were also observed, and these were found around 38.0 % and 76.6 %, respectively. Older age, higher waist circumference, higher systolic and diastolic blood pressure, low education level, housewife and occupation (technician) were found to be associated with the increased odds of metabolic syndrome. Nevertheless, the adjusted odds ratio (OR) showed no significant associations between metabolic syndrome and smoking or the exposure to cigarette smoking. The moderate intensity of the physical activities was positively associated with systolic blood pressure (rho=0.07, p=0.03), cholesterol (rho=0.07, p=0.04), and triglyceride (rho=0.67, p=0.04). Meanwhile, vigorous physical activity was inversely correlated with waist circumference (rho=-0.07, p=0.04). Their total physical activity was found to be positively correlated with triglyceride (rho=0.09, p= 0.01), but was inversely correlated with HDL-cholesterol (rho=-0.07, p=0.04). The chi-square test did not reveal any statistically significant difference in the levels of the physical activities between these women, either with or without metabolic syndrome. The mean total kilocalories consumed per day were 2965. The study also suggests that a good dietary pattern which is rich in fruit, legumes, vegetables, cereals, and fish (component 1), as well as the high intakes of dairy products and eggs (component 4) decrease the likelihood of metabolic syndrome. The adjusted OR for metabolic syndrome in women with low fat intake was significantly higher than in those women with high and moderate fat intake (OR=2.923; 95% CI=1.36, 6.28). The risk

of metabolic syndrome for women in the first quartile category of calcium was found to be higher than those in the highest quartile (OR=13.200; 95% CI =7.94, 21.93), and in the lowest category of black tea was indicated as lower than those in the highest categories (OR=0.181; 95% CI =0.11, 0.31).

The findings of the present study indicated that a high prevalence of obesity and metabolic syndrome was identified among the middle-aged women, making this syndrome one of the major public health problems in Babol. Therefore, it is necessary to emphasize on the benefits of lifestyle modifications, including weight loss, and the intakes or consumption of more fruit, legumes, vegetables, cereals, fish, dairy products, and the increase in the intakes of food containing calcium in reducing the risk of metabolic syndrome.

Abstrak thesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Kedoktoran

CARA HIDUP SESEORANG MERUPAKAN DAN PEMAKANAN FAKTOR BERKAITAN DENGAN SINDROM METABOLIK DI KALANGAN WANITA BERUMUE 30-50 TAHUN, BANDAR BABOL, DAERAH MAZANDARAN, IRAN

Oleh

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Ogos 2009

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Sindrom metabolik merupakan faktor yang membuktikan kewujudan penyakit kardiovascular. Sindrom ini juga amat ketara di kalangan wanita berbanding lelaki. Obesiti memainkan peranan yang penting di dalam sindrom metabolik kerana ia merupakan faktor yang umumnya berlaku di kalangan wanita Iran. Oleh itu, menerangkan bahawa pemakanan dan cara hidup seseorang adalah faktor yang menyumbang kepada perkembangan sindrom metabolik di kalangan wanita pertengahan tahun adalah sangat penting. Pencegahan terhadap sindrom ini juga adalah lebih penting berbanding mengatasinya.

Dalam thesis ini, kriteria yang dikenali sebagai NCEP ATP III telah digunakan untuk menjelaskan sindrom metabolik. Aktiviti fizikal diukur menggunakan borang asal International Physical Activity Questionnaire Long. Food frequency Questionnaire (FFQ) juga digunakan untuk mengukur tabiat pemakanan seseorang. Untuk tujuan ini, sejumlah 984 individu yang berumur di antara 30-50 tahun dari 14 pusat

perkhidmatan kesihatan bandar di Babol (Iran) telah terlibat di dalam kajian yang menggunakan kaedah sampel serampang yang sistematik dan nisbah sampel yang dibuat mengikut saiz yang diperolehi. Faktor cara hidup seseorang didapati mempunyai hubungan rapat dengan sindrom metabolik.

Kadar sindrom metabolik di kalangan wanita pertengahan tahun di kawasan bandar Babol addalah 310 %. Kajian juga mendapati bahawa berat badan yang melampau dan obesiti abdominal adalah 38.0 % dan 76.6 %. Selain itu, golongan tua, ukuran keliling pinggang yang tinggi, tekanan darah systolik dan distolik yang tinggi, tahap pendidikan yang rendah, suri rumahtangga dan pekerjaan seperti juruteknik juga didapati berkait rapat dengan penigkatan peluang berlakunya sindrom metabolik. Pelarasan nishah berkaitan atau odds ratio (OR) menunjukkan sindrom metabolik tidak mempunyai hubungan yang ketara dengan tabiat merokok atau pendedahan seseorang terhadap asap rokok. Intensisasi akiviti fizikal yang sederhana adalah berhubung rapat dengan tekanan darah systolik (rho=0.071, p=0.029), kolesterol (rh=0.064, p=0.037) dan triglyceride (rho=0.67, p=0.042). Sebaliknya, aktiviti fizikal yang keterlaluan tidak berkaitan dengan ukuran pinggang (rho=-0.067, p=0.040). Jumlah aktiviti fizikal adalah berkait rapat dengan triglyceride ((rho=0.09, p=0.006), tetapi tidak berkaitan dengan HDL-cholesterol (rho=0.69, p=0.036). Ujian Chisquare menunjukkan tiada perbezaan yang mendadak didapati dalam statistik antara aktiviti fizikal wanita dengan adanya dan juga tanpa sindrom metabolik. Jumlah pengambilan kilocalories sehari ialah 2965. Dapatan penyelidikan ini mengesyorkan bahawa pemakanan yang kaya dengan buah-buahan, kekacang, sayur-sayuran, bijirin and ikan (komponen 1) dan juga pengambilan makanan tenusu dan telur (komponen 4) yang tinggi berkemungkinan dapat menurun peluang seseorang

untuk mendapat sindrom metabolik. Pelarasan OR dalam sindrom metabolik di kalangan wanita yang mempunyai lemak rendah adalah lebih tinggi berbanding wanita yang mempunyai lemak tinggi dan sederhana (OR=2.923; 95% CI=1.36, 6.28). Sementara itu, risiko sindrom metabolik untuk wanita dalam kategori quartile tahap pertama dengan kalsium adalah lebih tinggi berbanding kategori quartile tertinggi (OR-13200; 95% CI=9.12, 21.43). Dalam kategori quartile pertama, teh hitam adalah kategori yong paling rendah daripada mereka yang berada dalam kategori tertinggi (OR=0.181; 95% CI=0.105, 0.14).

Kajian juga mengesahkan kewujudan obesiti yang tinggi dan sindrom metabolik dikesan di kalangan wanita pertengahan tahun, dan ini menjadikan sindrom ini sebagai masalah kesihatan yang utama di kalangan wanita di Babol. Oleh itu, adalah penting untuk menitikberatkan perubahan cara hidup seseorang seperti mengurangkan berat badan, memakan lebih banyak buah-buahan, kekacang, sayur-sayuran, bijirin, ikan, produk tenusu dan juga menambahkan pengambilan makanan yang mengandungi kalsium untuk mengurangkam risiko menghidapi sindrom metabolik.

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I certify that an Examination Committee has met on 20th August 2009 to conduct the final examination of Mouloud Agajani Delavar on her PhD thesis entitled **"Lifestyle and Dietary Factors Associated with Metabolic Syndrome in Urban Middle Aged Women of Babol, City, Mazandaran Province, Iran"** in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U. (A) 106] 15 March 1998. The Committee recommends that the student be awarded the degree of doctor of philosophy (PhD).

Member of the Thesis Examination Committee were as follows:

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This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfillment of the requirement for degree of doctor of philosophy. The members of Supervisory Committee were as follows:

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Date: 16 November 2009

DECLARATION

I declare that the thesis is my original work except for quotations and citations which have been duly acknowledged. I also declare that it has not been previously, and is not concurrently, submitted for any other degree at Universiti Putra Malaysia or at any other institution.

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MOULOUD AGAJANI DELAVAR

Date: 11 September 2009

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LIST OF ABBREVIATIONS

AACE	Association of Clinical Endocrinologists
AHA	American Heart Association
AHA/NHLBI	American Heart Association/National Heart, Lung, and Blood Institute
ATP III	Adult Treatment Panel III
BMI	Body Mass Index
CHO	Carbohydrate
CVD	Cardiovascular Disease
Diastolic BP	Diastolic Blood Pressure
EDTA	Ethylenediaminetetraacetic Acid
ETS	Environmental Tobacco Smoke
FFQ	Food Frequency Questionnaires
HDL	High Density Lipoprotein
IDF	International Diabetes Federation
IPAQ	International Physical Activity Questionnaires
LDL	Low Density Lipoprotein
METs-min	METs*minutes*week, abbreviated
n–6	Linoleic Acids: Omega-6 Fatty Acids
NCEP	National Cholesterol Education Programmed
NIH	National Institutes of Health
OR	Odds Ratios
PA	Physical Activity
PHC	Primary Healthcare Centers
PSFFQ	Picture-Sort Administration of the Food Frequency Questionnaire

RSPs	Respirable Suspended Particulates
SD	Standard Deviation
ß	Beta
Systolic BP	Systolic Blood Pressure
TEE	Total Energy Expenditure
VLDL	Very Low Density Lipoprotein
WHO	World Health Organization
WHR	Waist-to-hip ratio

CHAPTER 1

INTRODUCTION

1.1 Background

Metabolic syndrome is a relatively new concept, but the clustering of individual cardiovascular risk factors has been well researched. For example, in the 1920s, investigators reported the event of hypertension, hyperglycemia, and hyperuricema in specific groups of individuals (Nilsson, 2000). In the 1960s, hyperlipidemia and obesity were found to be associated with this cluster (Avogaro *et al*., 1967). In 1988, Gerald Reaven presented for the first time the concept of "syndrome X" for the clustering of cardiovascular risk factors such as hypertension, glucose intolerance, high triglycerides, and low HDL-cholesterol concentrations found in individuals who tend to develop cardiovascular diseases. Thus he suggested that the common characteristic of the syndrome was resistance to the action of insulin (Reaven, 1988),and associating with other metabolic abnormalities including obesity, microalbuminuria, change in fibrinolysis, and coagulation (Björntorp, 1992; Yudkin, 1999). The syndrome has also been called insulin resistance syndrome, cardiovascular syndrome, and recently is known as metabolic syndrome (Winkler *et al*., 2003).

The World Health Organization (WHO) gave the first definition for the metabolic syndrome which is more complex and prescriptive. It defines that for individuals with normal glucose tolerance, evidence of insulin resistance is a required component for a diagnosis of metabolic syndrome (Alberti and Zimmet, 1998). As a

result, the definition given by the WHO tends to focus much more on patients with the potential for diabetes (impaired glucose tolerance, impaired fasting glucose, or insulin resistance) (Isomaa, et al., 2001). Later, the Adult Treatment Panel III (ATP III) criteria provide a practical tool to identify patients with increased risk for cardiovascular disease. Focus of ATP III is less on type 2 diabetes and more on cardiovascular disease, whereas the criteria given by WHO and the American Association of Clinical Endocrinologists (AACE) require further oral glucose testing, impaired fasting glucose and diabetes. Impaired glucose tolerance on oral glucose tolerance test indicates greater risk for diabetes than does the metabolic syndrome without raised high fasting glucose (Alberti and Zimmet, 1998; Executive Summary, 2001; NCEP, 2002).

It is generally agreed that there are two general approaches to treatment of the metabolic syndrome. Therapeutic lifestyle change make up first-line therapy for metabolic syndrome, with increased emphasis on weight reduction, regardless of the diagnostic criteria used (Ahmad *et al*., 1997; Dengel *et al*., 1998). The second approach, drug treatment, directly treats risk factors of the metabolic syndrome such as atherogenic dyslipidemia, hypertension, the prothrombotic state, and underlying insulin resistance (Rubins *et al*., 1999; Arntz *et al*., 2000).

In a recent survey in the US, it was found that the prevalence of metabolic syndrome was around 25% in white Americans but higher in Mexican and black Americans (Ford, Giles and Dietz, 2002). According to the 2000 census data, around 47 million US adults have the metabolic syndrome. The National Cholesterol Education Programmed (NCEP) defined metabolic syndrome indirectly suggests that the risk

for coronary heart disease and diabetes has been poorly studied (NCEP, 2002). The efforts up until now undertaken in understanding this syndrome have confirmed the effect of metabolic imbalances in the development of critical chronic cardiovascular, neurological, immunologic, renal, and endocrine diseases. With pandemic increase in obesity rates, care for individual with the metabolic syndrome is very important in order to reduce the harmful effects caused by unhealthy diet, excessive eating, physical inactivity, smoking, and stress. Current clinical research studies have shown that changes in lifestyles can prevent or alter a biochemical imbalance that goes to clinical complications of the metabolic syndrome in elderly people. Weight loss can highly reduce the insulin resistance and also indirectly mitigate the metabolic syndrome risk factors. Improved long-term outcomes have been attained as a result of physicians' approval of eating and physical activity that could lead to several favorable parameters such as a healthier waist circumference and improved body mass index, lower blood pressure, improved HDL-cholesterol and triglyceride, and lower blood sugars along with a reduced C-reactive protein (Lara-Castro and Garvey, 2004; National Blueprint for Increasing Physical Activity, 2006). While the clinicians await further research into behavioral science, adiposities, hormones, and the mechanistic connection between insulin resistance and other important factors that will help them identify new goal for therapy, they can do much by advancement of improved lifestyles for all individuals.

1.2 Conceptual Framework for the Metabolic Syndrome

There are three major reasons for cardiovascular disease as a disease of societal change leading to altered lifestyle as shown in figure 1.1. The first is a good one; we