Education and the Metabolic Syndrome in Women

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OBJECTIVE — The main objective was to examine the association between the metabolic syndrome and socioeconomic position (as indicated by education) among women.

RESEARCH DESIGN AND METHODS — The study sample comprised healthy women (aged 30–65 years) in Sweden who were representative of the general population in a metropolitan area. Socioeconomic position was measured by educational level (mandatory [≤9 years], high school, or college/university). The metabolic syndrome was defined as the presence of two or more of the following components: *1*) fasting plasma glucose level ≥7.0 mmol/l; *2*) arterial blood pressure ≥160/90 mmHg; *3*) fasting plasma triglycerides ≥1.7 mmol/l and/or HDL cholesterol <1.0 mmol/l; and *4*) central obesity (waist-to-hip ratio >0.85 and/or BMI >30 kg/m^2).

RESULTS — After adjustment for age, the risk ratio for the presence of the metabolic syndrome comparing the lowest (≤9 years) with the highest (college/university) education was 2.7 (95% CI 1.1–6.8). This association persisted after controlling for menopausal status, family history of diabetes, and behavioral risk factors.

CONCLUSIONS — Low education is associated with increased risk for metabolic syndrome in middle-aged women. These findings show that not only are women with low socioeconomic position at increased risk for individual risk factors that are associated with cardiovascular disease and type 2 diabetes, they are also at increased risk for the metabolic clustering of risk factors.

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A number of studies have shown evidence of increased risk for morbidity and mortality in individuals from lower as compared with higher socioeconomic positions (1–5). However, most of this research has focused on men, with the relationship between socioeconomic position and women's health being given little attention. Of the few studies that have focused on socioeconomic inequalities in women's health (3,6,7), some show even stronger associations than those observed in men (6,7). However, there is relatively little information on how these associations are mediated biologically. Biological risk factors such as hypertension, obesity, dyslipidemia, and hyperglycemia are known to be highly interrelated (8–10) and to be strong risk factors for both cardiovascular disease and type 2 diabetes. Thus, in the presence of a combination of these risk factors, even more powerful effects on disease have been suggested (11). This clustering has been given various names, such as syndrome X (8), the insulin resistance syndrome (12), or the metabolic syndrome (12). Although many definitions of this clustering of metabolic risk factors have appeared in the literature, the World Health Organization (WHO) recently proposed a more standardized working definition for the metabolic syndrome that has been adopted here (13).

Although individual components of the metabolic syndrome have been related to socioeconomic factors (14–16), no studies have investigated the relationship between education level and the metabolic syndrome in women. The Whitehall II Study of a selected sample of British civil servants showed relationships between low occupational grade and the metabolic syndrome, with a stronger association in women than in men (17). The Whitehall II Study, however, used a somewhat weaker definition of the metabolic syndrome (if three or more of the following were in the top quintile: postload glucose, systolic blood pressure [sBP], triglycerides, HDL cholesterol, or waist-to-hip ratio) than the one recommended by the WHO (13). Our goal in this study was to investigate the association between socioeconomic position (as measured by education) and the metabolic syndrome (as defined by WHO) in a representative population sample of middle-aged women.

RESEARCH DESIGN AND METHODS

— The study group consisted of 300 healthy women aged between 30 and 65 years, comprising the control group of the Stockholm Female Coronary Risk Study. The subjects were identified using the census register of the greater Stockholm area. Potential study subjects were contacted by a letter inviting them to participate, in which the objectives and the focus of the study were explained. Those who did not call the clinic spontaneously were contacted by phone from the research clinic. When a subject refused to participate, a new subject was selected to obtain a final number of 300 healthy women. The nonresponse rate was 17%. The study was approved by the Karolinska Hospital Ethics Committee (No. 91;119), Stockholm, and

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Abbreviations: CHD, coronary heart disease; dBP, diastolic blood pressure; HRT, hormone replacement therapy; sBP, systolic blood pressure; WHO, World Health Organization.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

the study subjects gave informed consent to participate.

All subjects were free of symptoms of heart disease and without hospitalization for any illness during the past 5 years. All women were examined for clinical signs or symptoms of chronic diseases and found to be healthy. They were compared on health-related factors to a random sample of 2,500 women of the same age from the general population of Stockholm. No differences in educational level, BMI, or smoking were found (18). The study group can thus be regarded in these respects as representative of healthy women aged 30–65 years in the normal population. A detailed description of the study design is previously published (19).

The metabolic syndrome

The metabolic syndrome was defined as the presence of two or more of the following components, as recommended by the WHO (13): *1*) fasting plasma glucose level ≥7.0 mmol/l; 2) arterial sBP ≥160 and/or dBP (diastolic blood pressure) ≥90 mmHg; *3*) fasting plasma triglycerides ≥1.7 mmol/l and/or HDL cholesterol <1.0 mmol/l; and *4*) central obesity (waist-to-hip ratio >0.85 and/or BMI >30 kg/m^2).

Education

The highest education was reported by subjects in a self-administered questionnaire, which was later reviewed by a research nurse together with the patient. Education was categorized into three levels: *1*) Low education (mandatory or less than high school) corresponding to ≤9 years of schooling, *2*) medium (high school) corresponding to 10–13 years of schooling, and *3*) high (college, university) corresponding to ≥14 years of schooling. This categorization has been found to be strongly associated with coronary heart disease (CHD) risk in women of this sample (3).

Standard risk factors

Age at examination was obtained from the date of birth as recorded in the census register. Marital status, menopausal status, education level, exercise habits, smoking behavior, and medical history, including history of hypertension, diabetes, and medication, were assessed by means of questionnaires and interview procedures.

Family history of diabetes was defined as having at least one parent diagnosed with either type 1 or 2 diabetes. Smoking status was categorized as never smoked, having smoked previously, or smoking currently. Physical exercise was assessed according to the WHO criteria as follows: Grade I for reading, watching TV, or other sedentary leisure activities; Grade II for walking, cycling, or other forms of physical activity; Grade III for exercises to keep fit, heavy gardening, etc., for at least 4 h/week; and Grade IV for hard training or participation in competitive sports several times a week. Grade I was categorized as lack of physical exercise. Information about consumption of five alcoholic beverages (beer 2.8% alcohol, beer 4.5%, wine 10–15%, sherry 20%, and hard liquor 40%) was obtained by open-ended questions about frequency per year, per month, per week, and per day and about the usual number of specified servings (bottles, cans, or glasses) consumed at each occasion (20). The total average amount of alcohol (100% ethanol) consumed was calculated in grams per day taking into account frequency, amount, and content of alcohol in specific beverages (21). Validation of the alcohol consumption measure using fasting serum levels of the alcohol-specific enzyme γ-glutamyltransferase has been reported previously (22).

The research nurse assessed menopausal status in a gynecological interview. Postmenopausal status was defined as having had no menses for at least 6 months. A history of gynecological surgery was obtained. A patient was classified as having had surgical menopause if she had undergone a bilateral oophorectomy. A complete history regarding hormone replacement therapy (HRT) was also obtained. Women who had begun HRT before menopause were considered menopausal if they were >50 years of age.

Weight and height were measured by the same research nurse in the morning upon arrival at the examination laboratory. Height was measured to the nearest 0.5 cm with subjects standing erect without shoes, heels together. Body weight was measured to the nearest 0.1 kg using a calibrated balance scale. Subjects were wearing ordinary light clothes, and 0.5 kg was deducted from each woman's weight to exclude the weight of clothes. Waist and hip circumference were measured using a steel tape measure with the subjects standing. Waist circumference was measured to the nearest 1 mm at the level midway between the lower rib margin and the iliac crest. Hip circumference was measured to the nearest 1 mm at the widest point between hip and buttocks. BMI was computed as weight (kg)/[height (m)]^2, and waist-to-hip circumference ratio was calculated as waist (cm)/hip (cm).

sBP and dBP were measured by the research nurse as subjects were in the supine position after 5 min of rest. Phase one and phase five of the Korotkoff sounds were used.

Laboratory analyses

Venous blood samples were drawn from the right arm of each subject in the resting position by antecubital vein puncture with a 1.4-mm Wasserman needle. The blood sampling was performed between 8:00 and 9:00 A.M. after 12 h of fasting. After drawing the first 2 ml, blood was allowed to run freely into the tubes.

For the analyses of lipid and lipoproteins, venous blood was drawn into a 10 ml precooled sterile tube containing 0.12 ml of 0.34 mol/l tripotassium EDTA and kept on ice until it was centrifuged at 3,000*g*. Plasma (4 ml) was obtained and immediately frozen to −70°C and sent in batches to the processing laboratory once per month for further analyses. Triglyceride level was determined with enzymatic methods with reagents from Boehringer Mannheim (Mannheim, Germany). HDL was determined based on the isolation of LDL and VLDL from serum by precipitation. The cholesterol content of the supernatant (i.e., HDL cholesterol) was measured enzymatically. Fasting serum glucose was analyzed by the glucose oxidase para-amino-phenazone method (23).

All measurements were carried out in the same laboratory (CALAB) with an automated multichannel analyzer (Technicon DAGS; Bayer Diagnostics, Toshiba, Japan) (24).

Statistical analyses

Analyses of covariance estimating least squares means were performed to evaluate the age-adjusted associations between education and the individual components of the metabolic syndrome. Variables that were not normally distributed were log transformed in all analyses. Geometric means are reported and their standard errors (SEM) were estimated using the delta method. Risk ratios and the 95% confidence intervals (CI) for presence of the metabolic syndrome were computed using generalized linear regression models with a logarithmic function and a binomial error structure (25). By using this technique, the model directly estimates the prevalence or risk ratios of the metabolic syndrome in relation to various levels of

Table 1—*Definition of the metabolic syndrome according to WHO*

Component	Factor	Cutoff point	*n* (%) for each component
Hyperglycemia	Fasting plasma glucose level	≥7.0 mmol/l	2 (1)
Elevated arterial blood pressure	sBP	≥160 mmHg	6 (2)
	and/or		
	dBP	≥90 mmHg	37 (12)
Dyslipidemia	Fasting plasma triglycerides	≥1.7 mmol/l	36 (12)
	and/or		
	HDL cholesterol	<1.0 mmol/l	11 (4)
Central obesity	Waist-to-hip ratio	>0.85	62 (21)
	and/or		
	BMI	>30 kg/m²	39 (13)

Subjects are defined as having the metabolic syndrome if two or more of the components listed are present (n = 37).

education. STATA 3.1 (26) and JMP 3.2 (27) were used to run statistical analyses.

RESULTS — The mean age at entry to the study was 56 ± 7 years. Of the women, 30% were premenopausal and 70% were postmenopausal. Cigarette smoking and lack of physical exercise were prevalent in 30 and 19% of the study subjects, respectively. None of the women were on lipid-lowering drugs. Four women were on antihypertensive medication and were excluded from all analyses on the metabolic syndrome. None of the women had previously been diagnosed with type 2 diabetes. Thirty-two women (11%) had a family history of diabetes. Only two women had a fasting plasma glucose level ≥7.0 mmol/l; 13% had elevated arterial blood pressure; 13% also had dyslipidemia; and 28% of the study subjects had central obesity (Table 1). Twelve percent (n = 37) of the study subjects met the criteria of metabolic syndrome as defined in Table 1.

Table 2 shows the age-adjusted associations between education and the factors that comprise the metabolic syndrome. Statistically significant associations were found with all components with the exception of fasting glucose. Other statistically significant associations were found between low education and smoking (P = 0.003) and low alcohol consumption (P = 0.004). The associations with lack of exercise and family history of diabetes were at borderline statistical significance. No statistically significant associations were found between education and menopausal status (P = 0.25, after adjusting for age) or marital status (P = 0.79).

The prevalence (risk) ratios of the metabolic syndrome in relation to education level and other risk factors are presented in Table 3 in a hierarchical order. Statistically significant associations of increased risk of the metabolic syndrome were observed with education, lack of physical exercise, and no/low alcohol consumption. Crude analyses showed a 2.7-fold (95% CI 1.1–6.8) increased risk of the metabolic syndrome in women with the lowest as compared with women with the highest level of education. These associations persisted even after controlling for age, menopausal status, family history of diabetes, smoking, and lack of physical exercise and no/low alcohol consumption (Table 3).

The crude risk ratios for the metabolic syndrome associated with lack of physical exercise, no/low alcohol consumption, and family history of diabetes were 3.3 (95% CI 1.8–6.0), 2.0 (1.0–4.0), and 2.0 (0.9–4.1), respectively. Other risk factors were not associated with the metabolic syndrome (Table 3).

CONCLUSIONS — Receiving lower levels of education is strongly associated with the metabolic syndrome in a healthy population-based sample of women aged ≤65 years. After adjustment for age, menopausal status, family history of diabetes, cigarette smoking, lack of physical exercise, and alcohol consumption, women with the least education had a 2.3-fold increased risk of exhibiting the metabolic syndrome. Although physical exercise, smoking, and alcohol consumption were associated with both low education and the metabolic syndrome, these factors did not statistically explain the increased risk for the metabolic syndrome in women with low education. To the best of our knowledge, this is the first study to show strong effects of low levels of education on the metabolic syndrome in women free of CHD or diabetes.

The definition of the metabolic syndrome used in the present study (based on the WHO criteria) is also supported by the definition of the insulin resistance syndrome based on the results from the Framingham Offspring Study (10). Coagulation disorders and raised PAI-1, which are not included in the current working definition of the metabolic syndrome by the WHO, have also been reported previously to be associated with both the metabolic syndrome (28–31) and with socioeconomic position (14,28).

The increased risk for the metabolic syndrome in women with the lowest as compared with the highest levels of education was not statistically explained by adjustment for behavioral risk factors, such as cigarette smoking, alcohol consumption,

Table 2—*Distributions of the components of the metabolic syndrome in relation to educational attainment (after adjusting for age)*

	Educational attainment			
	Mandatory	High school	University/college	P value
n	158	61	81	—
BMI (kg/m²)	25.8 ± 0.4	24.5 ± 0.5	23.2 ± 0.4	0.01
Waist-to-hip ratio	0.82 ± 0.01	0.79 ± 0.01	0.76 ± 0.01	0.01
sBP	124 ± 1.3	119 ± 2.0	115 ± 1.8	0.005
dBP	80 ± 0.8	75 ± 1.3	73 ± 1.0	0.001
HDL cholesterol (mmol/l)	1.64 ± 0.03	1.69 ± 0.04	1.82 ± 0.03	0.004
Triglycerides (mmol/l)	1.01 ± 0.04	0.96 ± 0.04	0.84 ± 0.04	0.03
Fasting glucose (mmol/l)	5.01 ± 0.01	4.84 ± 0.04	4.68 ± 0.02	0.47

Data are least squares means ± SEM.

Table 3—*Metabolic syndrome in relation to educational attainment and other risk factors*

		Risk ratios (95% CI)		
Risk factor	*n*	Unadjusted	Age-adjusted	Multivariable-adjusted
Educational attainment				
Mandatory	158	2.73 (1.09–6.83)	2.63 (1.04–6.62)	2.34 (0.98–5.84)
High school	61	1.31 (0.40–4.39)	1.33 (0.40–4.39)	1.27 (0.39–4.14)
College/university (reference category)	81	1	1	1
Lack of physical exercise	55	3.32 (1.81–6.03)	3.29 (1.80–5.98)	2.82 (1.46–5.44)
Low alcohol consumption (no alcohol or ≤1.9 g/day)	67	2.0 (1.02–3.95)	1.96 (1.0–3.87)	1.64 (0.73–3.64)
Family history of diabetes	32	1.95 (0.94–4.08)	1.97 (0.95–4.11)	1.80 (0.87–3.71)
Older age (>60 years)	106	1.39 (0.76–2.56)		1.19 (0.65–2.16)
Postmenopausal women not on HRT	154	1.26 (0.53–2.99)	1.24 (0.53–2.93)	1.10 (0.47–2.61)
Marital status (not cohabiting)	95	1.19 (0.63–2.26)	1.16 (0.61–2.21)	0.99 (0.53–1.86)
Cigarette smoking (current)	89	1.18 (0.57–1.85)	1.13 (0.47–1.85)	0.77 (0.39–1.54)

For multivariable-adjusted risk ratios, all risk factors were simultaneously included in the model. The risk ratios of the metabolic syndrome in relation to lack of physical exercise, no/low alcohol consumption, family history of diabetes, older age, postmenopausal status, marital status, and cigarette smoking are relative to the protective category of each risk factor.

and lack of physical exercise. We have previously shown that these behavioral risk factors could not fully explain the increased risk of CHD incidence in women with low education (3). Similarly, data from both Finland and the U.S. showed that behavioral risk factors could not statistically account for the increased risk of incident acute myocardial infarction and all-cause and cardiovascular mortality associated with lower income level (7,32). Although cigarette smoking, alcohol consumption, and lack of physical exercise are clearly important mediators in the link between socioeconomic position and health, these behavioral risk factors do not offer any simple answers for how women who occupy lower socioeconomic positions are at increased risk for the metabolic syndrome.

Further insights in our understanding of how lower socioeconomic position is linked to poor cardiovascular health in women may be advanced by examining the clustering of certain risk factors. In the present study, we looked at the clustering of particular biological risk factors, but in principle there is no reason to believe that other risk factors do not also cluster in women with lower socioeconomic position. This could also be true for behavioral risk factors, such as smoking, and psychosocial factors, including work- or family-related stress. Perhaps it is time to begin examining the joint occurrence of such risk factors rather than searching for their independent effect (33). Björntorp (34,35) argues that unfavorable socioeconomic circumstances coupled with psychosocial stress may lead to a physiological defeat reaction, thereby activating the hypothalamus-pituitary-adrenocortical (HPA) axis as indicated by elevation of the major components of the metabolic syndrome, such as the waist-to-hip ratio. We have previously demonstrated a strong association between low socioeconomic position and obesity, as indicated by BMI >29 kg/m^2 (15), which is consistent with other studies (17). It is worth noting that many of the elements of the metabolic syndrome have also been proposed as markers of "allostatic load" (36–38). McEwen (37,38) has argued that allostatic load is the accumulated burden of lifelong stress resulting from the bodily responses to chronic over- or underload, and that these adaptations leave their mark on human biological and physical functioning (36–38). Both low socioeconomic position and work stress in this sample were associated with atherogenic lipid profile (16) and hemostatic dysfunction (28). Human biological functioning is sensitive to a wide array of socially patterned forces from the earliest moments of human life. A cascading sequence of insults, injuries, and positive achievements accumulating over the course of life may show how different lifelong encounters with socially structured exposures leave an indelible and complex imprint on human biology. Levins and Lopez's (39) concept of a "socialized biology" may be a useful conceptual model with which to interpret the results of the present study. Women with less education have experienced a set of conditions and experiences over their course of life that in combination with any background predisposing factors have left a biological imprint in adulthood—in this case, an increased risk for exhibiting the clustering of biological risk factors known as the metabolic syndrome.

Although conclusions about the direction of causation may be limited by the cross-sectional design of the current study, it seems unlikely that the presence of the metabolic syndrome in adult women could have influenced their educational experiences >30 years earlier. This is only plausible if some background factor present early in life increased both the risk of receiving a low education and the risk of metabolic syndrome in adulthood. Although we cannot directly address that question in the present study, adjustment for family history of diabetes did not substantially alter the effect of low education on the metabolic syndrome.

In conclusion, socioeconomic position (as measured by education) is associated with the metabolic syndrome in middle-aged women. These findings show that not only are women with low socioeconomic position at increased risk for individual risk factors for cardiovascular disease and type 2 diabetes, they are also at increased risk for the clustering of these risk factors. This suggests that the co-occurrence of risk factors may be important in understanding how low socioeconomic position is associated with increased risk for chronic diseases.

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