

# Smoking Habits According to Metabolic Traits in an Island Population of the Eastern Adriatic Coast

Sasa Missoni<sup>1</sup>, Zijad Durakovic<sup>1</sup>, Rashmi Sahay<sup>2</sup>, Branka Salzer<sup>3</sup> and Ranjan Deka<sup>2</sup>

<sup>1</sup> Institute for Anthropological Research, Zagreb, Croatia

<sup>2</sup> University of Cincinnati, Center for Genome Information, Department of Environmental Health, Cincinnati, Ohio, USA

<sup>3</sup> Labor Center, Zagreb, Croatia

## ABSTRACT

*The study deals with the connection between metabolic syndrome (MS) and smoking habits of 1602 males and 828 females aged 18–97 years from the island of Hvar, Croatia. The age-adjusted prevalence of MS was higher in males (18.1–31.2%) than females (9.7–24.2%) by all five criteria that were defined, except the one by AHA/NHLBI. The overall prevalence of MS reached 12.9% by WHO using body mass index (BMI), 13.1% by EGIR, 14.5% by WHO using waist to hip ratio (WHR), 18.2% by NCEP/ATP III, 18.9% by AHA/NHLBI, and 26.7% by IDF criteria. The prevalence of smoking habits was similar in males (24.7%) and females (23.8%). The frequency of mild, moderate and heavy smoking was higher in males than females, 35.8:26.6%, 31.0:27.0%, and 35.9:7.7%, respectively. Age and sex had significant influence on BMI and WHR, both being highest in male former smokers (28.15 kg/m<sup>2</sup> and 0.973, respectively) and in female non-smokers (27.18 kg/m<sup>2</sup> and 0.869, respectively). The appearance of arterial hypertension (HTN) differed according to frequency of smoking; males had higher prevalence than females using WHO and EGIR criteria of blood pressure ≥140/90 mmHg, even after age adjustment. In males and females respectively, systolic HTN in non-smokers was 20.7:15.1%, in former smokers 17.9:15.2% and in current smokers 16.9:13.0%; diastolic HTN in non-smokers was 19.8:12.7%, in former smokers 22.4:10.5%, and in current smokers 11.3:9.1%. By NCEP, AHA, IDF criteria of blood pressure ≥130/85 mmHg, arterial HTN was also more prevalent in males than females; systolic HTN in non-smokers being 31.4:19.8%, in former smokers 29.9:12.7%, and in current smokers 25.4:11.1%; and diastolic HTN in non-smokers was 20.5:11.5%, in former smokers 24.8:11.3%, and in current smokers 14.7:9.4%. According to AHA/NHLBI and IDF criteria of high plasma glucose as ≥5.6 mmol/L, both males and females in all the three categories of smokers had glucose levels above the normal range (5.80–6.31 mmol/L in males and 5.80–5.91 mmol/L in females), except female current smokers (5.51 mmol/L). By WHO, EGIR and NCEP/ATP III criteria of high plasma glucose as ≥6.1 mmol/L, only male non-smokers (6.31 mmol/L) and former smokers (6.24 mmol/L) had elevated levels. Considering normal HDL-cholesterol as >1.0 mmol/L in males and >1.2 mmol/L in females, both males and females in all the three smoker's categories had HDL within normal range; females having higher HDL levels (1.52 mmol/L) than males (1.30 mmol/L). Considering normal value for triglycerides as <1.7 mmol/L, male former smokers (1.76 mmol/L) and current smokers (1.81 mmol/L) had higher levels; and as a whole group triglycerides were higher in males than females, 1.66:1.37 mmol/L respectively. The prevalence of MS differed between males and females using various MS criteria. Both males and females had the highest prevalence of MS by IDF criteria; male former smokers 60.5%, female non-smokers 51.4%, male non-smokers 53.8%, female former smokers 38.2%, and lowest in both male and female current smokers 39.8 and 33.0% respectively. In males, the lowest prevalence of MS was observed in non-smokers by AHA criteria (30.5%), in former smokers by WHO criteria (35.7%), and in current smokers using EGIR criteria (18.1%). Females in all the three smoker's categories had the lowest prevalence of MS using EGIR and WHO criteria. MS were less prevalent in current smokers than in non-smokers and former smokers.*

**Key words:** smoking habit, BMI, WHR, glycaemia, cholesterol, triglycerides, blood pressure, metabolic traits

## Introduction

Metabolic syndrome (MS) is a major public health problem and is associated with atherosclerotic cardiovas-

cular diseases (CVD) and Type 2 diabetes mellitus<sup>1–8</sup>. Among various MS risk factors, which includes obesity,

glucose intolerance, low HDL-cholesterol, high triglycerides, presence of arterial hypertension (HTN), hyperuricemia, and hyperfibrinogenemia, smoking habits could be an important predisposing factor for development of atherosclerosis and CVD as its complication because of the presence of high levels of free-oxygen radicals in blood and changes in lipoprotein metabolisms<sup>7–10</sup>. Smoking habit is an important public health problem and known as an propitious factor in aging process because of induction of inflammatory processes by free-oxygen radicals causing oxidative damage and vascular endothelial dysfunction leading to atherosclerosis and its associated complications such as coronary heart disease, cerebrovascular and other vascular diseases, Type 2 diabetes, essential tremor, cancer etc.

The article deals with the prevalence of smoking habits of a population living in the Hvar island at the eastern Adriatic Croatian coast, relating smoking habits to metabolic diseases based on clinical and biochemical parameters. Previous reports had shown high prevalence of obesity and arterial HTN in these island communities<sup>7,8</sup>. The Croatian islands are inhabited by a unique group of populations, predominantly of Slavic origins. These islanders are distinct from the mainland Europeans by practicing an agricultural subsistence in a rural setting and for the most part living on a typical Mediterranean way of life. The aim of the study is to search the connection between metabolic syndrome and smoking habits in an island population of the Adriatic.

## Material and Methods

### *Study participants and measurements*

The study was conducted in the Middle Dalmatian island of Hvar on the eastern Adriatic coast of Croatia. According to the 2001 census, the total population of Hvar was 11,103 in 24 settlements consisting of 21 villages and 3 small townships. A total of 1430 individuals participated: 602 males and 828 females, aged 18 to 97 years, from various settlements to enter the study (Table 1). All examinations were done in 2007 and 2008 with part of the survey questionnaire directed to smoking habits. The following anthropometric parameters were used for this analysis: body mass index (BMI = weight in kg/height in m<sup>2</sup>), waist circumference, hip circumference, and waist to hip ratio (WHR = waist circumference/hip circumference)<sup>10</sup>. Blood pressure measurements were recorded three times and all the three measurements were used to calculate the mean systolic (SPB) and diastolic blood pressure (DBP). Blood samples were drawn after a 12-hours of fast and serum was separated and kept frozen until shipped to the biochemical laboratory in Zagreb, where biochemical tests were performed for fasting plasma glucose (FPG), HbA1c (%), insulin, total cholesterol, LDL and HDL cholesterol, triglycerides (TG), uric acid, creatinine, fibrinogen, and calcium concentrations using standard methods previously described<sup>11</sup>.

### *Definitions of smoking habits and metabolic traits*

The examinees were grouped into three categories of smoking habits: non-smokers, former smokers and current smokers. Smoking index was calculated according to the number of cigarettes smoked per day multiplied by years of smoking habits<sup>12</sup>. Current smokers were further divided into three groups: mild smokers with a smoking index between 1–200, moderate smokers with a smoking index between 201–600 and heavy smokers with a smoking index of 601 and more. Former smokers were the individuals who stopped smoking at least 30 days before the examination. They were also further divided into three sub-groups: former mild smokers, former moderate smokers and former heavy smokers as defined above.

As regards to metabolic diseases, according to the World Health Organization (WHO) definition of metabolic syndrome<sup>13,14</sup> an individual with MS should be hyperglycaemic with a fasting plasma glucose  $\geq 6.1$  mmol/L and presence of at least two of the following risk factors: abdominal obesity with WHR  $> 0.90$  in men and  $> 0.85$  in women and/or generalized obesity with BMI  $> 30$  kg/m<sup>2</sup>; serum triglycerides  $\geq 1.69$  mmol/L and/or HDL-cholesterol  $< 0.9$  mmol/L in men and  $< 1.00$  mmol/L in women; and high arterial blood pressure as  $\geq 140$  mmHg systolic and  $\geq 90$  mmHg diastolic and/or therapy.

The definition of the European Group for the study of the Insulin Resistance (EGIR)<sup>15,16</sup> includes presence of insulin resistance along with two of the following risk factors: fasting plasma glucose  $\geq 6.1$  mmol/L; waist circumference  $\geq 94$  cm in males and  $\geq 80$  cm in females; serum triglycerides  $\geq 2.00$  mmol/L and/or HDL-cholesterol  $< 1.00$  mmol/L; and high blood pressure as  $\geq 140$  mmHg systolic and  $\geq 90$  mmHg diastolic and/or therapy.

The definition of the Third Report of the National Cholesterol Education Program (NCEP), Evaluation, and Treatment of High Blood Cholesterol in Adults, Adult Treatment Panel III (ATP III)<sup>17</sup> does not explicitly include insulin resistance as a requirement, rather defines MS as co-occurrence of three or more of the following five risk factors: abdominal obesity with waist circumference  $\geq 102$  cm in men and  $\geq 88$  cm in women; hyperglycaemia with fasting plasma glucose  $\geq 6.1$  mmol/L and/or therapy for Type 2 diabetes; serum triglycerides  $\geq 1.69$  mmol/L and/or therapy; HDL-cholesterol  $< 1.04$  mmol/L in men and  $< 1.29$  mmol/L in women and/or therapy; and high blood pressure as  $\geq 130$  mmHg systolic and  $\geq 85$  mmHg diastolic and/or therapy.

The American Heart Association and The National Heart, Lung and Blood Institute<sup>18</sup> (AHA/NHLBI) includes waist circumference  $\geq 102$  cm in men and  $\geq 88$  cm in women and presence of at least two of the following risk factors: fasting plasma glucose  $\geq 5.6$  mmol/L; serum triglycerides  $\geq 1.69$  mmol/L; serum HDL-cholesterol  $< 1.04$  mmol/L in men and  $< 1.29$  mmol/L in women; and high blood pressure as  $\geq 130$  mmHg systolic and  $\geq 85$  mmHg diastolic and/or therapy.

The International Diabetes Federation definition (IDF)<sup>19–21</sup> includes central obesity as an important criterion with waist circumference in Mediterranean's to be  $\geq 94$  cm in males and  $\geq 80$  cm in females, and presence of at least two of the following risk factors: fasting plasma glucose  $\geq 5.6$  mmol/L and/or therapy; serum triglycerides  $\geq 1.7$  mmol/L and/or therapy; HDL-cholesterol level  $< 1.00$  mmol/L in males and  $< 1.30$  mmol/L in females; and high blood pressure as  $\geq 130$  mmHg systolic and  $\geq 85$  mmHg diastolic and/or therapy.

### Statistical analysis

The means and standard errors were computed to determine smoking habits in relation to anthropometric parameters, systolic and diastolic blood pressure, metabolic traits, and metabolic syndrome, using the SPSS software version 17.0. The anthropometric measures were adjusted for age and gender which were standardized using age-structure of the US population, and their components were computed by using cut-offs of all five definitions of metabolic syndrome<sup>22</sup>. We calculated Pearson's correlation coefficient examined the pairwise relationship between the quantitative traits adjusted for age, gender, and their interaction term, as is the Fischer Exact Test (table 2 x 2).  $\chi^2$ -test was applied to examine the prevalence of smoking habits in males and females, adjusted for age (Table 1). Similarly, in males and females former smokers and current smokers smoking indexes (mild, moderate and heavy smoking) were tested (Table 2). Two-way ANOVA examined the relationship between smoking habits and BMI and WHR in males and females, adjusting for age (Table 3). Smoking habits of males and females in relation to arterial HTN, by two criteria (WHO and EGIR, and NCEP/ATP III, AHA/NHLBI and IDF), was tested by  $\chi^2$  test (Table 4). The influence of smoking habits and sex on metabolic traits was tested by two-Way ANOVA (Table 5). Finally, relationships between smoking habits and MS defined by the five criterias were also tested in both sex (Table 6).

## Results

Table 1. presents the gender-wise prevalence of smoking habits. The frequency of non-smokers was 44.7% in females and 36.3% in males ( $p < 0.001$ ); of former smokers was 17.5% in males and 10.1% in females ( $p < 0.001$ ), and current smokers were not significantly different between males (24.7%) and females (23.8%).

In Table 2. frequencies of smoking indexes in males and females, former and current smokers are presented. In former smokers, the frequency of mild smoking was 41.1% in females and 28.1% in males ( $p < 0.001$ ); of moderate smoking was 27.3% in males and 18.6% in females ( $p < 0.001$ ), and of heavy smoking was 9.3% in males and 3.4% in females ( $p < 0.001$ ). In current smoker group, 35.8% males and 26.6% females were mild smokers ( $p < 0.001$ ); 31.0% males and 27.0% females were moderate smokers ( $p < 0.001$ ); and males (35.9%) outnumbered females (7.7%) for heavy smoking ( $p < 0.001$ ).

**TABLE 1**  
AGE-ADJUSTED PREVALENCE (%) OF SMOKING HABITS IN THE POPULATION OF THE ISLAND OF HVAR (N=1,430)

Smoking habits	Sex	
	Males (N=602)	Females (N=828)
	% $\pm$ SE	% $\pm$ SE
Non smokers	36.3 $\pm$ 3.7	44.7 $\pm$ 4.3
Former smokers	17.5 $\pm$ 2.5	10.1 $\pm$ 0.9
Current smokers	24.7 $\pm$ 1.8	23.8 $\pm$ 1.56

$\chi^2=65.182$ ,  $df=2$ ,  $p < 0.001$

**TABLE 2**  
AGE-ADJUSTED PREVALENCE (%) OF SMOKE INDEX BY SMOKING HABITS IN THE POPULATION OF THE ISLAND OF HVAR (N=634)

Smoking habits	Smokers (smoke index)	Sex	
		Males (N=298)	Females (N=336)
		% $\pm$ SE	% $\pm$ SE
Former smokers	Mild (1–200)	28.1 $\pm$ 4.5	41.1 $\pm$ 10.4
	Moderate (201–600)	27.3 $\pm$ 5.9	18.6 $\pm$ 6.2
	Heavy (>600)	9.3 $\pm$ 4.0	3.4 $\pm$ 1.8
Current smokers	Mild (1–200)	35.8 $\pm$ 9.1	26.6 $\pm$ 6.5
	Moderate (201–600)	31.0 $\pm$ 6.4	27.0 $\pm$ 5.6
	Heavy (>600)	35.9 $\pm$ 7.7	7.7 $\pm$ 1.8

former smokers:  $\chi^2=22.697$ ,  $df=2$ ,  $p < 0.001$ ;

smokers:  $\chi^2=20.200$ ,  $df=2$ ,  $p < 0.001$

Table 3. presents the smoking habits in relation to BMI and WHR in males and females. The influence of sex on BMI ( $p=0.001$ ) and WHR ( $p < 0.001$ ), and age ( $p < 0.001$ ) were all significant. In males and females respectively, in nonsmokers BMI was 27.78:27.18 kg/m<sup>2</sup>; in former smokers 28.15:27.03 kg/m<sup>2</sup>; and in current smokers 26.97:25.83 kg/m<sup>2</sup>. BMI was highest in male former smokers and female non-smokers. As regards to WHR, in males and females respectively WHR was 0.961:0.869 in the non-smokers; 0.973:0.851 in former smokers; 0.957:0.854 in current smokers. The WHR was highest in male former smokers and female non-smokers. In total, males had higher BMI than females (27.71:26.83 kg/m<sup>2</sup>,  $p < 0.001$ ), as was WHR (0.964:0.863,  $p < 0.001$ ).

Age-adjusted prevalence of smoking habits in relation to arterial HTN defined by all five criteria are presented in Table 4. By WHO and EGIR criteria, the systolic HTN in both sex and in all the three smoker's categories together showed a trend ( $p=0.088$ ). In males and females respectively, 20.7:15.1% nonsmokers; 17.9: 15.2% former smokers; and 16.9:13.0% current smokers had systolic HTN. Diastolic HTN in all the three smoker's categories together was more frequent in males than females ( $p = 0.001$ ); respectively, 19.8:12.7% non-smokers; 22.4:10.5% former smokers; and 11.3: 9.1% current smokers.

**TABLE 3**  
SMOKING HABITS ACCORDING TO BODY MASS INDEX AND WAIST TO HIP RATIO ACCORDING TO SEX

Sex	Smoking habit	Body mass index (kg/m <sup>2</sup> )		Waist to hip ratio	
		Count	Mean	Count	Mean
Males	Non smokers	279	27.78	279	0.961
	Former smokers	185	28.15	185	0.973
	Current smokers	138	26.97	137	0.957
	Total	602	27.71 <sup>a</sup>	601	0.964 <sup>b</sup>
Females	Non smokers	517	27.18	516	0.869
	Former smokers	113	27.03	112	0.851
	Current smokers	198	25.83	198	0.854
	Total	828	26.83 <sup>a</sup>	826	0.863 <sup>b</sup>

<sup>a</sup> p=0.001, <sup>b</sup> p<0.001, p<0.001 for age as covariate

**TABLE 4**  
AGE-ADJUSTED PREVALENCE (%) OF SMOKING HABITS ACCORDING TO ARTERIAL HYPERTENSION (N=1,430)

Criteria of hypertension	Smoking habits	Sex		
		Males	Females	
		%±SE	%±SE	
WHO, EGIR	Systolic ≥140 mmHg	Non smokers	20.7±5.1	15.1±3.9
		Former smokers	17.9±6.9	15.2±4.9
		Current smokers	16.9±4.4	13.0±2.7
	Diastolic ≥90 mmHg	Non smokers	19.8±4.6	12.7±2.8
		Former smokers	22.4±6.2	10.5±4.2
		Current smokers	11.3±2.8	9.1±2.0
NCEP/ATP III, AHA/NHLBI, IDF	Systolic ≥130 mmHg	Non smokers	31.4±7.6	19.8±5.0
		Former smokers	29.9±9.6	12.7±7.7
		Current smokers	25.4±7.0	11.1±3.6
	Diastolic ≥85 mmHg	Non smokers	20.5±5.7	11.5±3.5
		Former smokers	24.8±7.4	11.3±5.9
		Current smokers	14.7±4.7	9.4±2.8

Systolic hypertension WHO: EGIR  $\chi^2=3.003$ , df=1, p=0.088; Diastolic hypertension WHO: EGIR  $\chi^2=11.300$ , df=1, p=0.001  
Systolic hypertension NCEP, AHA/NHLBI, IDF  $\chi^2=19.027$ , df=1, p<0.001; Diastolic NCEP, AHA/NHLBI, IDF  $\chi^2=14.372$ , df=1, p<0.001; According to the Fisher's Exact Test (table 2x2)

By NCEP, AHA, and IDF criteria, systolic HTN was more frequent in males than females (p<0.001); respectively it was 31.4:19.8% in non-smokers, 29.9:12.7% in former smokers, and 25.4:11.1% in current smokers. Similarly, diastolic HTN was more frequent in males than females (p<0.001); non-smokers 20.5:11.5%, former smokers 24.8:11.3%, and current smokers 14.7:9.4%. Arterial hypertension is statistically different among groups according to smoking habits (p<0.001 in all hypotheses).

Table 5. presents smoking habits in relation to metabolic traits in males and females. By AHA and IDF criteria, serum glucose was above the normal range of ≥5.6 mmol/L in all the three smoker's categories and in both sex, except in female current smokers. By WHO, NCEP and EGIR criteria, serum glucose was above the normal range of ≥6.1 mmol/L in male non-smokers and former

smokers. Serum glucose in males was significantly different than females (p<0.01) and age was the significant factor (p<0.001). The highest serum glucose was in males and females non-smokers 6.31 and 5.91 mmol/L, respectively. HbA1c levels were within the normal range of 4.3 to 6.0% in all the categories of smokers; the highest levels were 5.83% in both sex who were non-smokers, and age was the significant factor (p<0.001). Insulin levels were also within the normal range of 2.6 to 24.9 μU/mL, and males were not significantly different from females; the highest levels were in male former smokers (11.60 μU/mL) and female non-smokers (11.30 μU/mL), and age was again the significant factor (p<0.001).

Total cholesterol levels were above the normal cut-off of <5.00 mmol/L in all the three smoker's categories and in both sex; females had significantly higher cholesterol

**TABLE 5**  
SMOKING HABITS ACCORDING TO METABOLIC TRAITS

Metabolic traits (normal range)	Sex	Smoking habits			Total	Significance
		Non smokers	Former smokers	Current smokers		
Glucose (4.2–6.4 mmol/L)	Males	6.31	6.24	5.80	6.17	ad
	Females	5.91	5.80	5.51	5.80	
HbA1c (4.3–6.0%)	Males	5.83	5.71	5.60	5.74	n.s. d
	Females	5.83	5.72	5.59	5.76	
Insulin (2.6–24.9 $\mu$ U/mL)	Males	10.69	11.60	9.73	10.75	n.s. d
	Females	11.30	10.77	9.81	10.87	
Total cholesterol ( $<$ 5.00 mmol/L)	Males	5.66	5.77	5.52	5.66	ad
	Females	5.96	5.90	5.81	5.92	
LDL-Cholesterol ( $<$ 3.00 mmol/L)	Males	3.62	3.66	3.42	3.59	ad
	Females	3.77	3.75	3.74	3.76	
HDL-Cholesterol ( $>$ 1.00 M, $>$ 1.2 F mmol/L)	Males	1.33	1.32	1.24	1.30	c
	Females	1.55	1.53	1.46	1.52	
Triglycerides ( $<$ 1.7 mmol/L)	Males	1.52	1.76	1.81	1.66	cd
	Females	1.38	1.42	1.30	1.37	
Uric acid (182–403 M, 134–337 F $\mu$ mol/L)	Males	357.53	371.23	350.15	360.10	ad
	Females	269.72	272.61	248.77	265.11	
Creatinine (63.0–107.0 $\mu$ mol/L)	Males	96.88	96.37	96.65	96.67	ad
	Females	80.03	79.74	77.31	79.34	
Fibrinogen (1.6–3.5 g/L)	Males	3.57	3.63	3.57	3.59	ad
	Females	4.02	3.80	3.81	3.94	
Calcium (2.14–2.53 mmol/L)	Males	2.38	2.37	2.40	2.38	n.s. d
	Females	2.39	2.38	2.37	2.38	

a – significant difference only by sex ( $p < 0.01$ ), b – significant difference only by smoking habits ( $p < 0.01$ ), c – significant difference by sex and smoking habits ( $p < 0.01$ ), d – age is significant covariate ( $p < 0.001$ )

than males ( $p < 0.01$ ), and age was the significant factor ( $p < 0.001$ ). The highest cholesterol levels were in female non-smokers (5.96 mmol/L) and male former smokers (5.77 mmol/L). LDL-cholesterol was above the normal cut-off of  $< 3.00$  mmol/L in all the three categories of smokers and in both sex; females had higher LDL-cholesterol than males ( $p < 0.01$ ), and age was the significant factor ( $p < 0.001$ ). The highest LDL levels were in female non-smokers (3.77 mmol/L) and in male former smokers (3.66 mmol/L). The HDL-cholesterol levels were normal in all the categories of smokers; females being significantly different than males ( $p < 0.01$ ); and the highest levels were in non-smoking females (1.55 mmol/L) as well as males (1.33 mmol/L). Triglycerides were higher than normal in male current smokers (1.81 mmol/L) and male former smokers (1.76 mmol/L); males having significantly higher levels than females ( $p < 0.01$ ), and age being a significant factor ( $p < 0.001$ ).

Uric acid levels were below the normal range in all the three smoker's categories in both sex; males had higher uric acid levels than females ( $p < 0.01$ ) and age was the significant factor ( $p < 0.001$ ). The highest values were in male (371.23  $\mu$ mol/L) as well as female (272.61  $\mu$ mol/L)

former smokers. Serum creatinine was in the normal range in all the three categories in both sex, males in general had higher values than females ( $p < 0.01$ ) and age was significant ( $p < 0.001$ ). The highest creatinine levels were in males (96.88  $\mu$ mol/L) and females (80.03  $\mu$ mol/L) nonsmokers. Plasma fibrinogen was above the normal range in all the categories of smokers and in both sex; being higher in females than males ( $p < 0.01$ ) and age being significant ( $p < 0.001$ ). The highest fibrinogen levels were in female non-smokers (4.02 g/L) and male former smokers (3.63 g/L). Calcium levels were in the normal range in all the three smoker's categories and in both sex, and age was the significant factor ( $p < 0.001$ ). The levels were highest in male current smokers (2.40 mmol/L) and female non-smokers (2.39 mmol/L).

Table 6. presents the prevalence of smoking habits in relation to MS defined by five criterias. According to all these criterias, prevalence of MS was quite different between males and females and therefore gender-specific results were presented. In males, highest prevalence of MS was in all the three smokers' categories using IDF criteria; 53.8% in non-smokers, 60.5% in former smokers, and 39.8% in current smokers. Lowest prevalence

**TABLE 6**  
THE PREVALENCE OF SMOKING HABITS ACCORDING TO METABOLIC SYNDROME

Metabolic syndrome	Males			Females		
	Smoking habits			Smoking habits		
	Non smokers	Former smokers	Current smokers	Non smokers	Former smokers	Current smokers
WHO with BMI	36.6%	35.7%	20.3%	24.7%	19.1%	12.2%
WHO with WHR	41.6%	40.5%	24.1%	25.4%	19.6%	13.6%
EGIR	38.7%	38.4%	18.1%	24.8%	18.6%	11.6%
NCEP	33.7%	42.2%	27.1%	36.8%	27.3%	21.8%
AHA/NHLBI	30.5%	38.4%	21.1%	43.4%	27.3%	27.9%
IDF	53.8%	60.5%	39.8%	51.4%	38.2%	33.0%

(18.1%) was in male current smokers by EGIR criteria and prevalence ranged between 20.3% by WHO-BMI criteria in current smokers to 42.2% in former smokers using NCEP criteria. In females also using IDF criteria the prevalence of MS was the highest; 51.4% in non-smokers, 38.2% in former smokers, and 33.0% in current smokers; the lowest prevalence (11.6%) was in current smokers using EGIR criteria.

## Discussion

The prevalence of smoking in an island population of the Hvar in Croatia, adjusted for age according to the standard US population, was studied. There are different ways to define a person as smoker and former smoker. We defined former smokers as individuals who stopped smoking at least thirty days before the examination, and used the number of cigarettes smoked per day multiplied by the years of smoking to characterize smokers as current smokers, former smokers and non-smokers. Smoking-index was developed to further classify current and former smokers into mild, moderate and heavy smoking groups. Accordingly, mild current and mild former smokers were those who had an index between 1–200, moderate current and moderate former smokers had an index between 201–600, and heavy current and heavy former smokers has an index of 601 and more<sup>12</sup>. In other studies, frequency of smoking was based on the average number of cigarettes smoked per day during the month<sup>9</sup>, or on the number of cigarettes smoked per day<sup>6</sup>, or depending on those who smoke 20 or more pack per year<sup>4</sup>; and former smokers were those who stopped smoking for more than 3 months<sup>9</sup>.

We observed a high prevalence of smokers, with differences in the frequency of smoking between males and females. The number of male former smokers was higher than female former smokers, but not much difference was noticed between males and females who were current smokers. The frequency of male former smokers in this study is although higher than 15.2% reported earlier in male industrial workers aged 40 to 59 years in Croatia, lesser number of current smokers was observed in com-

parison to 61.7% reported in the same study<sup>12</sup>; which could be due to differences in age, sex and profession of the sampled population.

According to the frequency of smoking, higher number of female former smokers were mild smokers, and higher number of males were former moderate smokers and also former heavy smokers; this was higher than that reported for industrial workers<sup>12</sup>. In comparison to 7.8% male industrial workers reported as mild smokers<sup>12</sup>, more males than females were observed as mild smokers in this study; however, the frequency of moderate smoking was lower in both males and females when compared to 36.2% male industrial workers as moderate smokers<sup>12</sup>. Nevertheless, in our study the frequency of heavy smoking was much higher in males as compared to 18.2% reported for male industrial workers<sup>12</sup>.

Majority of males and females studied were overweight rather than obese, and males in general had higher BMI and WHR than females. The highest BMI and WHR was observed in male former smokers, which could be due to refraining from smoking; however, in females the non-smokers had the highest BMI and WHR. Furthermore, current smokers in both sex were observed to have the lowest BMI and WHR. It is known that non-smoking habit can delay the disease appearance and ageing process, thus helping in attaining longevity<sup>23,24</sup>. However, this relationship is probably more complex as can be seen by our findings that instead of current smokers, former smokers and non-smokers weighed more. The risk of acute coronary syndrome had been shown to be much higher in obese smokers than non-smokers<sup>25</sup>. The prevalence of MS is considerably high in the population of Hvar, higher than 7.8% reported in the Japanese population<sup>26</sup>. In our study, using BMI as an indicator of obesity, the overall average BMI reached 27.20 kg/m<sup>2</sup>, and WHR 0.91. By all defined criteria, except the one by AHA/NHLBI, the prevalence of MS was much higher in males than females when comparing former smokers with current smokers; the highest prevalence being observed by the IDF criteria.

Using all the five criteria for MS, systolic and diastolic HTN were more prevalent in males than females in all the three categories of smokers. However, depending on

each criteria, differences in systolic and diastolic HTN were noticed between males and females in each of the three categories of smokers. In all tested hypotheses, by two criteria and by sex, appearing of arterial hypertension is statistically different among groups according to smoking habits. For the most part, in both sex, the non-smokers had highest prevalence of systolic and diastolic HTN (except male former smokers for diastolic HTN), and current smokers had the lowest. By some studies mean SBP in smokers was higher than non-smokers<sup>25</sup>, and our results are not in agreement with their results. On the other hand, in the Korean National Health and Nutrition Examination Survey on 9,771 men, no association between smoking habits and high blood pressure had been demonstrated<sup>9</sup>.

Insulin resistance is an important element of MS. Type 2 diabetes is a known risk factor for hyper-lipoproteinemia, atherosclerosis and its associated complications; males with Type 2 diabetes having 1.8 times and females having 2.6 times higher mortality risk than those without Type 2 diabetes<sup>27</sup>. Smoking is also an independent risk factor for MS, insulin resistance and Type 2 diabetes<sup>28</sup>, but its pathophysiological mechanism is still an open area of research. In persons with Type 2 diabetes, smoking could lead to worsening of the disease process and shortening of life-span. In this study, the average serum glucose by AHA/NHLBI and IDF were above the normal range in all group of smokers except female current smokers; and by WHO, NCEP and EGIR criteria these values were also above the normal range in male non-smokers and former smokers; in general higher in males than females, and highest in male and female non-smokers. HbA1c was in the normal range in all three smoker's group and the highest level was 5.83% in both males and females non-smokers, with age as a significant factor. Insulin levels were in the normal range; with no difference between males and females; male former smokers and female non-smokers having the highest levels; and age having a significant influence. Insulin resistance was tightly linked with obesity and hyper-triglyceridemia when studying 511 healthy Taiwanese<sup>29</sup>. Likewise, obesity and insulin-resistance were the important factors for Type 2 diabetes when comparing 305 diabetics with 934 non-diabetics in a study conducted in Beijing<sup>30</sup>.

HDL-cholesterol was within the normal range in all three group of smokers, and females were observed to have higher levels than males; the highest levels being in female and male non-smokers. On the other hand, triglycerides were higher than normal in male current smokers as well as male former smokers, significantly higher in males than females, and age having a significant influence. Smoking habit is known as an propitious factor in aging process<sup>31,32</sup> because of induction of inflammatory processes by free-oxygen radicals causing oxidative damage and vascular endothelial dysfunction leading to atherosclerosis and its associated complications such as coronary heart disease, cerebrovascular disease, other vascular diseases, Type 2 diabetes, cancer etc. Studies have shown an association between smoking habits and metabolic syndrome, supporting that smoking in-

creases the risk of developing insulin resistance<sup>4</sup>. In their study, a dose dependent connection was demonstrated between current smokers and metabolic syndrome, and not with the former smokers. In addition, heavy smoking increased the risk for developing metabolic syndrome, high triglycerides and low HDL levels, while the risk for high triglycerides and low HDL was not significant in former smokers<sup>4</sup>.

Uric acid levels were below the normal range in current and former smokers, in both sex, but the levels were higher in males than females, and age was one of the factors. The levels were highest in male and female former smokers. Elevated uric acid level is an important independent risk factor for atherosclerosis. In addition, higher plasma fibrinogens are known for their proinflammatory response in atherosclerosis. In this study, fibrinogen levels were above the normal range in all three group of smokers, both males and females, females having higher levels than males, and age being a significant factor. The highest levels were noticed in female non-smokers and male former smokers, which probably indicates that it is essential to assess serum hyper-uricemia and plasma fibrinogen as one of the determinants of MS.

Examining smoking habits of our population in relation to MS using all five criteria namely WHO, EGIR, NCEP/ATP III, AHA/NHLBI and IDF, the highest prevalence was observed in both males and females using IDF criteria. Male former smokers and female non-smokers had the highest prevalence; in male non-smokers and female former smokers the prevalence was lower, and in male and female current smokers lowest prevalence was observed. In males, the lowest prevalence of MS was noticed in non-smokers using AHA criteria, in former smokers using WHO criteria, and in current smokers using EGIR criteria. In females, in general lower prevalence was observed; lowest being in current and former smokers using EGIR criteria. Our findings of lower prevalence of MS in smokers, rather than non-smokers, is in contrast to those reported by an earlier study in which 2,412 non-diabetic men aged 35–65 were studied and higher frequency of MS was demonstrated in smokers than non-smokers<sup>29</sup>.

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## REFERENCES

- PETO R, BMJ, 309 (1994) 937. — 2. HOZAWA A, OKAMURA T, MURAKAMI Y, KADOWAKI T, NAKAMURA K, HAYAHAWA T, KITA Y, NAKAMURA Y, ABBOTT RD, OKAYAMA A, UESHIMA H, Hypertension Res, 30 (2007) 1169. — 3. DELL JL, WHITMAN S, SHAH AM, SILVA A, ANSELL D, Am J Public Health, 95 (2005) 1036. — 4. CHEN CC, LI TC, CHANG PC, LIU CS, LIN WY, WU MT, LI CI, LAI MM, LIN CC, Metabolism: Clinical and Experimental, 57 (2008) 544. — 5. WADA T, URASHIMA M, FUKUMOTO T, Intern med, 46 (2007) 1079. — 6. NAKANISHI N, TAKATORIGE T, SUZUKI K, Industrial Health, 43 (2005) 295. — 7. DEKA R, SMOLEJ NARANCIC N, HUIFENG X, TUREK S, CUBRILLO TUREK M, VRHOVSKI HEBRANG D, JANICIJEVIC B, TOMLJENOVIC A, SZIROVICZA L, LI J, CHAKRABORTY R, RUDAN P, Coll Antropol, 32 (2008) 85. — 8. TUCAK ZORIC S, BILIC CURCIC I, MIHALJ H, DUMANCIC I, ZELIC Z, MAJETIC CETINA N, SMOLIC R, VOLAREVIC M, MISSONI S, TOMLJENOVIC A, SZIROVICZA L, DURAKOVIC Z, CHAKRABORTY R, DEKA R, TUCAK A, RUDAN P, Coll Antropol, 32 (2008) 659. — 9. OH SW, YOON YS, LEE ES, KIM WK, PARK C, LEE S, JEONG E-K, YOO T, The Korean National Health and Nutrition examination survey. Available from: URL: <http://bare.diabetes-journals.org/content/28/8/2064.full>. — 10. WEINER JS, LOURIE JA, Practical Human Biology. Academic Press, London, 1981. — 11. TUREK S, RUDAN I, SMOLEJ NARANCIC N, SZIROVICZA L, CUBRILLO TUREK M, ZERJAVIC HRABAK V, KAIC RAK A, VRHOVSKI HEBRANG D, PREBEG Z, LJUBICIC M, JANICIJEVIC B, RUDAN P, Coll Antropol, 25 (2001) 77. — 12. DURAKOVIC Z, SARIC M, Arhiv hig rada toksikol, 22 (1971) 309. — 13. WORLD HEALTH ORGANIZATION: definition, diagnosis and classification of diabetes mellitus and its complications: report of a WHO consultation. Part 1: diagnosis and classification of diabetes mellitus, Geneva: WHO, 1999. — 14. ALBERTI KG, ZIMMET PZ, Diabet Med 15 (1998) 539. — 15. BALKAU B, CHARLES MA, Diabet Med, 16 (1999) 442. — 16. HILLS SA, BALKAU B, COPPACK SW, DEKKER JM, MARI A, NATALI A, WALKER M, FERRANNINI E, THE RISC INVESTIGATORS, Diabetologia, 47 (2004) 566. — 17. NATIONAL INSTITUTE OF HEALTH. Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). National Institutes of Health, NIH Publication No 01-3670, Bethesda, Md, 2001. — 18. GRUNDY SM, CLEEMAN JI, DANIELS SR, DONATO KA, ECKEL RH, FRANKLIN BA, GORDON DJ, KRAUSS RM, SAVAGE PJ, SMITH SC JR, SPERTUS JA, COSTA F, Circulation, 112 (2005) 2735. — 19. FORD ES, Diabetes Care, 28 (2005) 2745. — 20. ALBERTI KG, ZIMMET P, SHAW J, Lancet, 366 (2005) 1059. — 21. CHEW G, GAN SK, WATTS GF, Med J Austral, 185 (2006) 445. — 22. FORD ES, GILES WH, DIETZ WH, JAMA, 287 (2002) 356. — 23. NICITA-MAURO V, LO BALBO C, MENTO A, NICITA-MAURO C, MALTESE G, BASILE G, Exp Gerontol, 43 (2008) 95. — 24. DOLL R, PETO R, BOREHAM J, SUTHERLAND I, Br Med J, 328 (2004) 1519. — 25. JENSEN MK, CHIUVE SF, RIMM EB, DETHLEFSEN C, TJONNELAND A, LOENSEN AM, OVERVAD K, Circulation, 117 (2008) 3062. — 26. ARAI H, YAMAMOTO A, MATSUZAWA Y, SAITO Y, YAMADA N, OIKAWA S, MABUCHI H, TERAMOTO T, SASAKI J, NAKAYA N, ITAKURA H, ISHIKAWA Y, OUCHI Y, HORIBE H, SHIRAKASHI N, KITA T, J Atheroscler Thromb, 13 (2006) 202. — 27. WENGER NK, Progr Cardiovasc Dis, 46 (2003) 199. — 28. MASULLI M, RICCARDI G, GALASSO R, VACARO ONutrition, Metabolism and Cardiovascular Diseases, 16 (2009) 364. — 29. HSIEH C-H, PEI D, HUNG Y-J, KUO S-W, HE C-T, LEE C-H, WU C-Z, J Korean Med Sci, 23 (2008) 465. — 30. WANG J-J, QUIO Q, MIETTINEN ME, LAPPALAINEN J, HO G, TOUMILEHTO J, Diabetes Care, 27 (2004) 2429. — 31. MISIGOJ DURAKOVIC M, BOK D, SORIC M, DIZDAR D, DURAKOVIC Z, JUKIC I, J Addict Dis, 31 (2012) 389. — 32. NICITA-MAURO V, BASILE G, MALTESE G, NICITA-MAURO C, GANGEMI S, CARUSO C, Immunity & Ageing, 5 (2008) 10. Available from: URL: <http://www.immunityageing.com/>.

S. Missoni

Institute for Anthropological Research, Lj. Gaja 32, 10000 Zagreb, Croatia  
e-mail: [sasa.missoni@inantro.hr](mailto:sasa.missoni@inantro.hr)

## ODNOS NAVIKE PUŠENJA PREMA METABOLIČKIM PARAMETRIMA U OTOČNOJ POPULACIJI ISTOČNOG JADRANA

### SAŽETAK

Istražena je povezanost između parametara metaboličkog sindroma (MS) i navike pušenja u 1602 muškarca i 828 žena dobi 18–97 godina sa otoka Hvara. Prevalencija MS korigirana s dobi bila je viša u muškaraca (18,1–31,2%) nego u žena (9,7–24,2%) prema svim kriterijima, osim prema AHA/NHLBI. Ukupna prevalencija MS iznosila je 12,9% prema kriterijima SZO koristeći indeks tjelesne mase (BMI), 13,1% prema EGIR kriterijima, 14,5% prema SZO prema kriterijima SZO omjera opsega struka i kukova (WHR), 18,2% prema NCEP/ATP III, 18,9% prema AHA/NHLBI i 26,7% prema IDF kriterijima. Prevalencija navike pušenja bila je slične učestalosti u muškaraca (24,7%) i žena (23,8%). Učestalost lake, umjerene i teške navike pušenja bila je viša u muškaraca nego u žena (35,8:26,6%, 31,0:27,0%, and 35,9:7,7). Dob i spol bili su značajno povezani s BMI and WHR, najviše učestalosti u muškaraca bivših pušača (28,15 kg/m<sup>2</sup> and 0,973) i u žena nepušačica (27,18 kg/m<sup>2</sup> and 0,869). Učestalost povišenog arterijskog krvnog tlaka (HTN) razlikovala se u skupinama prema navici pušenja: u muškaraca bila je viša nego u žena prema kriterijima SZO i EGIR, visine krvnog tlaka  $\geq 140/90$  mmHg, čak i po korekcijama prema dobi. U muškaraca i žena nepušača učestalost sistoličke HTN iznosila je 20,7:15,1%, u bivših pušača 17,9:15,2%, a u pušača 16,9:13,0%; dijastolička HTN u nepušača bila je učestalosti 19,8:12,7%, u bivših pušača 22,4:10,5%, a u pušača 11,3:9,1%. Prema kriterijima NCEP, AHA i IDF visine krvnog tlaka  $\geq 130/85$  mmHg, HTN bila je više učestalosti u muškaraca nego u žena; sistolička HTN u nepušača bila je učestalosti 31,4:19,8%, u bivših pušača 29,9:12,7%, a u pušača 25,4:11,1%, dok je dijastolička HTN u nepušača bila učestalosti 20,5:11,5%, u bivših pušača 24,8:11,3%, a u pušača 14,7:9,4%. Prema kriterijima AHA/NHLBI i IDF povišene koncentracije glukoze u plazmi  $\geq 5,6$  mmol/L, u muškaraca kao i u žena u sve tri skupine prema navici pušenja ustanovljena je koncentracija iznad razine normale (5,80–6,31 mmol/L u muškaraca i 5,80–5,91 mmol/L u žena), osim u žena pušačica

(5,51 mmol/L). Prema kriterijima SZO, EGIR kao i NCEP/ATP III, koncentracija glukoze u krvi  $\geq 6.1$  mmol/L ustanovljena je u samo u muškaraca nepušača (6,31 mmol/L) i muškaraca bivših pušača (6,24 mmol/L). Muškarci i žene svih triju skupina prema navici pušenja, imali su koncentraciju ukupnog kolesterola u serumu unutar normalnih koncentracija ( $> 1,0$  mmol/L,  $> 1,2$  mmol/L): u žena ustanovljena je viša koncentracija LDL-kolesterola (1,52 mmol/L) nego u muškaraca (1,30 mmol/L). Glede normalne koncentracije serumskih triglicerida  $< 1,7$  mmol/L, muškarci bivši pušači (1,76 mmol/L) i pušači (1,81 mmol/L) imali su višu koncentraciju; u cijeloj skupini glede navike pušenja, koncentracija triglicerida bila je viša u muškaraca nego u žena: 1,66:1,37 mmol/L. Prevalencija MS prema različitim kriterijima, razlikovala se u muškaraca i žena. I muškarci i žena imali su najvišu učestalost MS prema IDF kriterijima; muškarci bivši pušači 60,5%, žene nepušačice 51,4%, muškarci nepušači 53,8%, žene bivše pušačice 38,2%, a najniža učestalost ustanovljena je u muškaraca pušača i žena pušačica: 39,8 and 33,0%. U muškaraca najniža učestalost MS ustanovljena je u nepušača prema AHA kriterijima: 30,5%, u bivših pušača prema SZO kriterijima: 35,7%, i u pušača prema EGIR kriterijima: 18,1%. U žena u sve tri skupine prema navici pušenja, najniža je učestalost MS ustanovljena prema EGIR i SZO kriterijima. Niža učestalost MS ustanovljena je u pušača, u odnosu prema nepušačima i bivšim pušačima.