



Light smoking is associated with metabolic syndrome risk factors in Chilean young adults

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Abstract

Aims Metabolic syndrome (MetS) is a cluster of risk factors for cardiometabolic diseases. While cigarette smoking is associated with MetS in adults, young adulthood is an under-studied, susceptible period for developing long-term morbidity from MetS. We examined associations between cigarette smoking and MetS risk factors.

Methods We studied 430 participants in Santiago, Chile who have been followed in a longitudinal cohort since infancy and assessed in adolescence for MetS. Participants were evaluated at 22 years from May 2015 to July 2017. Adiposity, blood pressure, and blood samples were measured. MetS was defined using International Diabetes Federation criteria. A continuous MetS score was calculated using z -scores. Participants self-reported cigarette and alcohol consumption using standardized questionnaires. We used multivariate regressions to examine associations between smoking and MetS risk factors, adjusting for sex, MetS in adolescence, alcohol consumption, and socioeconomic status.

Results Thirteen percent of participants had MetS and 50% were current smokers. Among smokers, mean age of initiation was 14.9 years and consumption was 29 cigarettes weekly. Smokers had larger waist circumferences, higher BMIs, and lower high-density lipoprotein (HDL) cholesterol compared to non-smokers. Being a current smoker was significantly associated with higher waist circumference ($\beta=2.82$; 95% CI 0.63, 5.02), lower HDL ($\beta=-3.62$; 95% CI -6.19 , -1.04), higher BMI ($\beta=1.22$; 95% CI 0.16, 2.28), and higher MetS score ($\beta=0.13$, 95% CI 0.02, 0.24).

Conclusions Cigarette smoking at light levels (mean < 30 cigarettes weekly) was associated with MetS risk factors in a sample of Chilean young adults.

Keywords Metabolic syndrome · Cigarette smoking · Young adult · Obesity · Cholesterol · Waist circumference

Introduction

The increasing prevalence of obesity globally has been a main driver for higher rates of type 2 diabetes and cardiovascular disease [1]. Overweight and obesity are serious health issues and preventable causes of mortality that affect over 1 billion people worldwide [2]. In particular, obesity plays a role in the development of the metabolic syndrome (MetS), a cluster of risk factors that include abdominal obesity, hypertension, hyperglycemia, and dyslipidemia [3]. MetS has been associated with a threefold increase in the risk for cardiovascular disease and a sevenfold increase in the risk for type 2 diabetes [4–6]. Therefore, identifying risk factors for the early onset of MetS is crucial for preventing chronic disease.

A growing body of evidence in adults indicates that cigarette smoking is one such risk factor for MetS [7–9]. Cigarette smoking is associated with insulin resistance,

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abdominal obesity, and dyslipidemia [10–13]. However, few studies have examined the effects of cigarette smoking on cardiovascular risk among young adults (ages 18–25) [14]. Young adulthood is a unique period of transition with high risks for excess weight gain and the initiation of smoking and alcohol consumption [15–17]. Weight gain during adolescence and young adulthood is associated with an increased risk for developing type 2 diabetes and hypertension as an adult, which may persist even with weight loss in adulthood [15]. Therefore, young adults may be especially susceptible to develop long-term morbidity and mortality associated with MetS. As young adults are expected to have lower cumulative smoking exposure than older adults, studying a younger population may also provide an opportunity to better understand how light smoking relates to MetS risk.

This study examined the association between cigarette smoking and MetS risk factors among young adults in a longitudinal cohort study in Santiago, Chile. We hypothesized that being a current smoker would be associated with MetS risk factors in young adults.

Methods

Study sample and setting

The current study sample included 430 young adults of low- to middle-income backgrounds in Santiago, Chile. Participants have been followed in a longitudinal cohort study since infancy, which began as an iron deficiency anemia (IDA) preventive trial conducted between 1991 and 1996, or a neuromaturation study [18]. Details about the inclusion criteria and preventive trial have been previously described, in which infants without IDA were randomized to receive either usual nutrition or iron supplementation [18]. Infants with IDA were enrolled in neuromaturation study along with the next non-anemic control [19]. When the participants were 16-years old, we invited 888 adolescents to participate in an observational study of obesity and cardiovascular risk between 2009 and 2012. These participants represented two of three randomized groups during infancy. Of those adolescents recruited, 679 participants (76%) were assessed [20]. When the participants were 22-years old, we conducted a second wave of assessment for obesity and cardiovascular risk, once again recruiting from those invited to participate at age 16 years ($N=888$).

For the current analysis, we studied the first 430 young adults evaluated at age 22 years from May 2015 to July 2017. We conducted cross-sectional analyses assessing the relationship between smoking and components of the MetS at age 22 years. For control variables, we used data collected at age 16 years related to obesity or MetS diagnosis and at infancy on socioeconomic status. The participants in our

current study sample had complete data from assessments at both age 16 and 22 years in addition to complete data about their socioeconomic status. This sample was representative of those assessed at age 16 in participant characteristics, with no statistically significant differences in sex (53% male in the original cohort vs. 49.5% male in the final analytical sample), obesity (14% in the original cohort vs. 14.0% in the final analytical sample), MetS (8.9% in the original cohort vs. 8.6% in the final analytical sample), and socioeconomic status on the Graffar index (26.9 in the original cohort vs. 27.02 in the final analytical sample), all P values >0.05 [21]. The study was approved by the institutional review boards of the University of Michigan, Ann Arbor, Institute of Nutrition and Food Technology, University of Chile, and University of California, San Diego. Informed and written consent were provided according to the norms for Human Experimentation, Code of Ethics of the World Medical Association (Declaration of Helsinki, 1995).

Measurements

Participants were assessed in young adulthood at age 22 years. The measurements were conducted in the same manner as previously described at age 16 years [20]. Participant height (cm), weight (kg), waist circumference (WC, cm), and systolic and diastolic blood pressure (SBP and DBP, mm Hg) were measured by a research physician at the Institute of Nutrition and Food Technology using standardized procedures. Weight was measured to the closest 0.1 kg using a SECA scale and height to the closest 0.1 cm using a Holtain stadiometer. Measurements were performed twice, with a third measurement if the first two measurements differed by 0.3 kg for weight or 0.5 cm for height. Body mass index (BMI, kg/m^2) was calculated and obesity status was determined according to World Health Organization classifications [22]. In the prior analysis at age 16 years, obesity was defined as z score cut-off ≥ 2 standard deviations for BMI, as recommended for children and adolescents. In our current analysis at age 22 years, obesity was defined as $\text{BMI} \geq 30.0$. Fasting serum glucose concentration (mg/dL) was measured using an enzymatic-colorimetric test (QCA S.A., Amposta, Spain). Fasting serum triglycerides (mg/dL) and high-density lipoprotein cholesterol (HDL, mg/dL) levels were determined using dry analytical methodology (Vitros®; Ortho Clinical Diagnostics Inc., Raritan, NJ, USA). Using a standardized questionnaire based on the Health Behavior in School-Aged Children studies, participants self-reported smoking and drinking habits including current smoking status (smoker or non-smoker), age at first cigarette, number of cigarettes consumed each week, and frequency of alcohol consumption in the past month [23]. The degree of smoking was assessed based on the total number of cigarettes consumed per week. We assessed socioeconomic status (SES)

using a composite score calculated from the modified Graffar index (range 13 to 78), in which a higher score indicated a lower SES [21]. For the modified Graffar index, parents answered 13 questions including maternal and paternal years of education, parental occupation, and family income, which contributed to their composite score.

Definition of MetS criteria and risk factors

MetS was defined using the 2009 Joint International Diabetes Federation and American Heart Association/National Heart, Lung, and Blood Institute criteria for age ≥ 16 years. MetS was diagnosed if a participant had at least 3 of the 5 following criteria: (i) abdominal obesity (WC ≥ 80 cm in females and ≥ 90 cm in males); (ii) high blood pressure (SBP ≥ 130 mm Hg, DBP ≥ 85 mm Hg); (iii) fasting hyperglycemia (≥ 100 mg/dL); (iv) elevated triglycerides (≥ 150 mg/dL); (v) reduced HDL (≤ 50 mg/dL in females and ≤ 40 mg/dL in males) (3). In our analysis, MetS risk factors refer to waist circumference, blood pressure, fasting blood glucose, triglycerides, and HDL cholesterol levels.

Given the low prevalence rate of MetS in adolescents and young adults compared to older adult populations, a continuous MetS score was calculated based on the equations of Brage and colleagues [24, 25]. Compared to the dichotomous definition of MetS stated above, a continuous MetS score derived from the MetS risk factors could be more statistically sensitive to detect an association between exposures and overall MetS risk [26–28]. Briefly, each of the 5 risk factors for MetS were converted to *z*-scores or number of standard deviation units from the sample mean. We then calculated a continuous, normally distributed MetS score by averaging those 5 values.

Statistical analysis

We used SPSS (version 25.0, Chicago, IL, USA) to perform statistical analyses. Independent *t* tests and χ^2 tests were used to compare means and categorical variables, respectively, between smokers and non-smokers. Multivariable linear regression models were used to examine the association between current smoking status (independent variable) and each MetS risk factor as a continuous variable (dependent variable): waist circumference, SBP, DBP, fasting blood glucose, triglycerides, HDL cholesterol as well as BMI and MetS score. The independent variable, current smoking status, was dichotomized to current smoker or non-smoker, with non-smoker labeled as the reference group. In addition, multivariable logistic regression models were used to examine the association between current smoking status (independent variable) and each dichotomous MetS criteria (dependent variable): abdominal obesity, high blood pressure, fasting hyperglycemia,

high triglycerides, and low HDL cholesterol, as well as obesity and the MetS diagnosis. All models were adjusted for sex, MetS at adolescence, frequency of alcohol consumption, and SES based on the Graffar index. A *P* value of < 0.05 denoted statistical significance.

Results

The participants were, on average, 22.5 years old and 49% male. At the 16-year evaluation, 14.0% were in the obese range and 8.6% met criteria for MetS. The prevalence of both obesity and MetS increased at age 22 years to 24.9% and 13.3%, respectively. At age 22 years, 50% of participants reported current smoking and 65.3% reported alcohol consumption at least once in the past month. Among smokers, the mean age of smoking initiation was at age 14.9 years and the mean consumption was 29 cigarettes per week. The background characteristics of participants according to smoking status are shown in Table 1. We found no significant difference in sex, socioeconomic status by Graffar index, and MetS or obesity at age 16 years between smokers and non-smokers at age 22 years. At the 22-year wave, smokers had larger waist circumferences, higher BMIs, and lower HDL cholesterol compared to non-smokers. There was also a significant difference in the frequency of alcohol consumption in the past month between smokers (79.5%) and non-smokers (51.2%).

Table 2 presents linear regression models used to determine associations between smoking (current smoker or non-smoker) and the MetS risk factors, adjusted for sex, MetS at adolescence, frequency of alcohol consumption, and socioeconomic status by Graffar index. Being a current smoker was significantly associated with higher waist circumference ($\beta = 2.82$; 95% CI 0.63, 5.02), lower HDL cholesterol ($\beta = -3.62$; 95% CI -6.19 , -1.04), higher BMI ($\beta = 1.22$, 95% CI 0.16, 2.28), and higher MetS score ($\beta = 0.13$; 95% CI 0.02, 0.24) at 22-years. We did not observe a significant association between being a current smoker and SBP, DBP, fasting blood glucose, or triglyceride level.

Table 3 presents logistic regression models used to determine associations between smoking (current smoker or non-smoker) and each categorical component of the MetS criteria, obesity, and MetS (Yes/No) adjusted for sex, MetS at adolescence, frequency of alcohol consumption, and socioeconomic status by Graffar index. The odds of meeting the criteria for low HDL cholesterol among current smokers were 76% greater than among non-smokers (OR = 1.76; 95% CI 1.15, 2.67). We did not observe a significant association between being a current smoker and the other dichotomized components of the MetS criteria, obesity, or MetS (Yes/No).

Table 1 Characteristics of study participants ($N=430$) by current smoking status, Santiago, Chile 2015–2017

Characteristic	Total sample ($N=430$)	Non-smokers ($N=215$)	Current smokers ($N=215$)	P value ^a
Age (years)	22.52 ± 0.40	22.55 ± 0.40	22.50 ± 0.40	0.26
Male	213 (49.5)	102 (47.4)	111 (51.6)	0.39
SES by Graffar index ^b	27.02 ± 6.32	27.13 ± 6.36	26.90 ± 6.30	0.70
Anthropometrics				
BMI	26.72 ± 5.70	26.16 ± 5.18	27.27 ± 6.13	0.04
Obesity ^c	107 (24.9)	47 (21.9)	60 (27.9)	0.15
Obesity at 16 years ^d	60 (14.0)	25 (11.6)	35 (16.3)	0.16
Metabolic syndrome				
Waist circumference (cm)	82.59 ± 12.28	81.15 ± 11.82	84.03 ± 12.59	0.02
Abdominal obesity ^e	128 (29.8)	59 (27.4)	69 (32.1)	0.29
SBP (mm Hg)	112.09 ± 11.42	111.51 ± 11.65	112.68 ± 11.17	0.30
DBP (mm Hg)	69.71 ± 7.77	69.33 ± 7.72	70.09 ± 7.82	0.31
High blood pressure ^e	50 (11.6)	26 (12.1)	24 (11.1)	0.76
Fasting blood glucose (mg/dL)	88.53 ± 8.32	88.34 ± 8.06	88.73 ± 8.58	0.63
Fasting hyperglycemia ^e	9 (2.1)	5 (2.3)	4 (1.9)	0.74
Triglycerides (mg/dL)	102.59 ± 65.28	102.32 ± 62.36	102.86 ± 68.22	0.93
High triglycerides ^e	63 (14.7)	32 (14.9)	31 (14.4)	0.89
HDL cholesterol (mg/dL)	44.18 ± 13.48	45.53 ± 13.79	42.84 ± 13.05	0.04
Low HDL cholesterol ^e	244 (56.7)	112 (52.1)	132 (61.4)	0.05
MetS diagnosis ^e	57 (13.3)	27 (12.6)	30 (14.0)	0.67
MetS at 16 years ^f	37 (8.6)	18 (8.4)	19 (8.8)	0.86
MetS score ^g	0.02 ± 0.61	-0.03 ± 0.62	0.08 ± 0.60	0.05
Smoking				
Age at first cigarette (years)	–	–	14.88 ± 2.37	–
Number of cigarettes weekly	–	–	28.97 ± 29.53	–
Alcohol consumption in past month ^h				
No alcohol consumption	149 (34.7)	105 (48.8)	44 (20.5)	<0.001
Alcohol consumption	281 (65.3)	110 (51.2)	171 (79.5)	

SES socioeconomic status, BMI body mass index, SBP systolic blood pressure, DBP diastolic blood pressure, HDL high-density lipoprotein, MetS metabolic syndrome, – not calculated or no applicable value

Categorical values are n (%) and continuous values are mean (standard deviation)

^a P value for t test for continuous variables and χ^2 test for categorical variables

^bA modified Graffar index was used to assess SES, with a higher Graffar index indicating lower SES [21]

^cObesity defined at 22-year follow-up according to World Health Organization cut-off of BMI ≥ 30.0 [22]. Reference: no obesity at age 22 years

^dObesity at age 16 years defined at 16-year follow-up according to World Health Organization z score cut-off ≥ 2 standard deviations for BMI [22]. Reference: no obesity at age 16 years

^eAbdominal obesity, high blood pressure, fasting hyperglycemia, high triglycerides, low HDL cholesterol, and MetS diagnosis defined according to International Diabetes Federation criteria [3]

^fMetS at age 16 years defined at 16-year follow-up according to International Diabetes Federation criteria [3]. Reference: no metabolic syndrome at age 16 years

^gMetS score calculation adapted from Brage equations [24]

^hAlcohol consumption in the past month was self-reported using a standardized questionnaire and included: no consumption, as well as, alcohol consumption on 1–2 occasions, 3–5 occasions, 6–9 occasions, 10 or more occasions [23]

Discussion

This study demonstrated that being a current smoker was associated with a higher MetS score in Chilean young adults independent of sex, adolescent MetS status, and frequency of alcohol consumption ($\beta = 0.13$). Further,

being a current smoker was associated with higher waist circumference ($\beta = 2.82$), lower HDL cholesterol level ($\beta = -3.62$), and higher BMI ($\beta = 1.22$), in addition to meeting criteria for low HDL cholesterol based on the MetS definition (OR = 1.76). These results support our initial hypothesis that cigarette smoking, even at low levels

Table 2 Linear regression models to determine adjusted associations of current smoking status (independent variable) with each MetS risk factor, BMI, and MetS score (dependent variable) at 22-years ($N=430$), Santiago, Chile 2015–2017

Dependent variable ^a	Full models, smoking as independent variable	
	β (95% CI)	<i>P</i> value
Waist circumference (cm)	2.82 (0.63, 5.02)	0.01
SBP (mm Hg)	0.89 (−1.26, 3.03)	0.42
DBP (mm Hg)	0.84 (−0.63, 2.31)	0.27
Fasting blood glucose (mg/dL)	−0.14 (−1.77, 1.49)	0.86
Triglycerides (mg/dL)	4.17 (−8.84, 17.17)	0.53
HDL cholesterol (mg/dL)	−3.62 (−6.19, −1.04)	0.006
BMI	1.22 (0.16, 2.28)	0.02
MetS score ^b	0.13 (0.02, 0.24)	0.02

SBP systolic blood pressure, *DBP* diastolic blood pressure, *HDL* high-density lipoprotein, *BMI* body mass index, *MetS* metabolic syndrome

Linear regression modeling, presenting β estimate and 95% confidence interval

^aEach row is a separate linear regression model with current smoking status as the dichotomized independent variable (reference: non-smoker), adjusted for sex, MetS at 16 years (reference: no MetS at 16 years), alcohol consumption in the past month (reference: no consumption), and Graffar index of socioeconomic status [21]

^bMetS score calculation adapted from Brage equations [24]

Table 3 Logistic regression models to determine adjusted associations of current smoking status (independent variable) with each dichotomous component of the MetS criteria, obesity, and MetS (dependent variable) at 22-years ($N=430$), Santiago, Chile 2015–2017

Dependent variable ^a	Full models, smoking as independent variable OR (95% CI)
Abdominal obesity	1.40 (0.86, 2.25)
High blood pressure	0.92 (0.47, 1.79)
Fasting hyperglycemia	0.63 (0.14, 2.82)
High triglycerides	1.26 (0.71, 2.25)
Low HDL cholesterol	1.76 (1.15, 2.67)
Obesity	1.56 (0.94, 2.59)
MetS	1.46 (0.76, 2.80)

MetS metabolic syndrome, *HDL* high-density lipoprotein

Logistic regression modeling, presenting OR estimate and 95% confidence interval

^aEach row is a separate logistic regression model with current smoking status as the dichotomized independent variable (reference: non-smoker), adjusted for sex, MetS at 16 years (reference: no MetS at 16 years), alcohol consumption in the past month (reference: no consumption), and Graffar index of socioeconomic status [21]

(mean < 30 cigarettes per week in our sample), would be associated with MetS risk factors.

The most recent Chilean National Health Survey ($N=6233$) demonstrated that 41% of Chilean young adults ages 20 to 29 years were actively smoking in 2016 to 2017, which represented one of the highest smoking levels among the sampled age groups [29]. Our sample population had a higher prevalence of current smoking at 50.0%. Both cigarette smoking and MetS are known risk factors for the development of type 2 diabetes and cardiovascular disease [4–6]. Prior studies of middle-aged or older adult populations have found that cigarette smoking is positively associated with MetS [7–9]. In addition, other studies, conducted in older samples (mean ages 42–53), have reported significant dose-dependent relationships between the quantity of cigarettes smoked per day and lower HDL cholesterol, higher triglyceride levels, and abdominal obesity [12, 30]. However, while Clair et al. found a positive dose-dependent trend between smoking and abdominal obesity, the significant association was only observed in those who smoked > 20 cigarettes per day, which represents a heavier level of smoking than observed in our sample population [30]. While our findings are consistent with these previous studies, our study focuses on examining this association in young adults, which is an under-studied yet susceptible population for the long-term morbidity of MetS. A previous study of young adults by Ferreira et al. did not find an association between smoking and metabolic syndrome in a cohort of 364 Dutch individuals followed from ages 16–36 years. However, their cohort had a lower prevalence of smoking during this period (< 30% in adolescence) compared to the prevalence of smoking in our sample [14]. Further, our results are intriguing given our sample's mean smoking consumption of 29 cigarettes per week. Although light smoking is not consistently defined in the literature, this represents a low level of smoking compared to other studies that classify light smokers as those who consume less than 70–140 cigarettes per week [12, 31].

Although the mechanism is not fully understood, there are plausible biological explanations for the role of cigarette smoking in developing MetS risk factors. Slagter et al. also reported that cigarette smoking was associated with lower HDL cholesterol levels [12]. They found that adult smokers had lower levels of plasma apolipoprotein (apo) A1, the main protein component of HDL particles, and smaller HDL particle size. These are unfavorable changes in HDL which are associated with an increased risk of cardiovascular disease [32, 33]. Additional studies have also concluded that smoking is associated with abdominal obesity and weight gain in adult populations [11, 30]. One hypothesis is that nicotine itself may lead to fat accumulation due to its effect on insulin resistance [10, 34] and stress hormone levels [35].

Due to the cross-sectional design of this study, we are unable to prove causality or infer the direction of effects

of the observed association between cigarette smoking and the MetS risk factors. However, we adjusted for the prior diagnosis of MetS during adolescence as that measurement occurred early in exposure to cigarette smoking or before initiation. Another limitation is that our study may not be generalizable to individuals from other cultural or ethnic settings, including poverty or high-income groups, or those with other risk factors such as prematurity. In particular, Herrera and colleagues found a higher prevalence of low HDL cholesterol in a large multi-country Latin American population compared to a large United States population, and our sample had a similarly high prevalence of low HDL cholesterol [36]. Further study is needed to understand the factors that account for this difference. In addition, we did not account for health behaviors such as lower levels of physical activity or unhealthy diet, which might be confounded with cigarette smoking. We did adjust for other possible confounders including socioeconomic status and the frequency of alcohol consumption [17]. There is also the potential for misclassification of cigarette smoking or alcohol consumption since this outcome was self-reported. We attempted to minimize this limitation using standardized questionnaires and having responses verified by a highly-trained research interviewer who was with the participant.

Our study also had several strengths such as a relatively large group of young adults followed successfully since infancy and evaluation by highly trained study personnel. Another strength is the use of a continuous MetS score, as few young, healthy adults meet criteria for the full MetS or its individual categorical components. The use of continuous measures for the MetS risk factors can be more statistically sensitive to detect associations, while dichotomizing a continuous outcome variable may reduce statistical power [26]. Further, linear regression analyses can be more informative about the magnitude of the association for each measurement. Overall, these results may be useful to Latin American or other middle-income countries such as Chile, which underwent a rapid nutritional transition that led to high prevalence of obesity and cardiometabolic diseases [37].

In conclusion, we demonstrated that light cigarette smoking was associated with increased waist circumference, MetS risk score, and BMI in addition to lower odds of low HDL cholesterol based on MetS criteria in a sample of Chilean young adults. The transition from adolescence to adulthood is a critical risk period for excess weight gain, initiation of smoking and alcohol consumption, and the development of MetS, which can lead to long-term chronic diseases [15, 16]. Given that our sample of young adults had relatively low levels of smoking consumption (mean < 30 cigarettes per week), our findings emphasize the need for increased public health interventions to promote the knowledge that even light smoking is associated with adverse health effects including MetS risk factors. This may be an important public

health strategy to curb the growing prevalence of cardio-metabolic diseases.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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