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Associations of Physical Environment and Lifestyles with Metabolic Syndrome among Ecuadorian Adults

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Abstract

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Introduction: In Ecuador, it has been reported that approximately 3 of 10 adults aged 20 years or older have metabolic syndrome, based on the 2012 Ecuador National Health and Nutrition Survey (ENSANUT-ECU). Metabolic syndrome (MetS) is a multidimensional, progressive, and complex disorder characterized by the sum of elevated fasting glucose, hypertension, elevated serum triglycerides, low serum high-density lipoprotein (HDL) levels, and abdominal obesity. MetS culminates in adverse outcomes, including cardiovascular disease (CVD) and type 2 diabetes mellitus (DM2). Several biological and behavioral factors, including age (i.e. > 40 yr), sex (female), smoking, unhealthy dietary habits, and sedentary behaviors have been recognized to contribute to the development of MetS. Moreover, physical environment, including elevation and humidity have been suggested to potentially influence the development of metabolic diseases through a reduction in peripheral oxygen saturation and heat stress. Some studies have described an inverse association between elevation and lower obesity prevalence and incidence, as well as lower diabetes and hypertension proportions. In the case humidity and its effects on MetS, research is scarce, a single study has reported a positive association between diabetes mellitus, central obesity, higher systolic blood pressure, and lower physical activity in elder residents living in high relative humidity areas.

Similar research situation is observed on dietary intake and cardiovascular risk factors among Ecuadorians, most data in healthy population come from research in high-income countries, where findings on this topic are yet controversial. Therefore, it is necessary to investigate the associations of physical environment, health-related lifestyles with metabolic syndrome in the Ecuadorian population.

Objectives: This study aimed to (1) determine the epidemiologic characteristics of physical environment, health-related lifestyles, and carbohydrate and fat intake among Ecuadorian adults; and (2) examine their interactive associations with MetS and its components. This study was composed of three sub-studies.

The first sub-study aimed to examine the associations among elevation of residence, health-related lifestyles, and prevalence of MetS in the Ecuadorian population aged 20 years or older using national survey data. The objective of the second sub-study was to estimate the climate conditions through national meteorological data and investigate their associations with lifestyles and MetS among Ecuadorian adults. The objective of the third sub-study was to explore the macronutrient profile and determine associations of carbohydrate and fat intake, physical environment, and health-related lifestyles with MetS among Ecuadorian adults using national survey and meteorological data.

Methods: The study included 6,024 Ecuadorians (1,964 men and 4,060 women) aged 20 to 60 years who participated in the 2012 Ecuador National Health and Nutrition Survey (ENSANUT-ECU). Dietary intake was measured using a 24-hour dietary recall; sociodemographic characteristics and health-related lifestyles (i.e. physical activity) were measured via standardized questionnaires. MetS was defined on the basis of the National Cholesterol Education Program Adult Treatment Panel III and the Latin American Diabetes Association criteria.

The first sub-study categorized geographical elevation into two groups, including low elevation (0-2,000 masl) and high elevation (above 2,001 masl). Multiple logistic regression analysis was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for MetS across the elevation groups.

The second sub-study additionally used the mean annual relative humidity (%) for 2012 from the National Institute for Meteorology and Hydrology INAMHI. We classified relative humidity into two groups, low relative humidity (50% - 80%) and high relative humidity (above >80%). ORs and 95% CIs for MetS across the relative humidity groups were estimated using multiple logistic regression analysis.

The third sub-study divided participants by sex and status of dietary intake; low-carbohydrate high-fat (LCHF, energy from carbohydrate <45%), high-carbohydrate low-fat (HCLF, energy from carbohydrate >65%), and medium-carbohydrate -fat (MCF, 45% to 65% of energy from carbohydrate). ORs and 95% CIs for MetS across the different diet intake groups were estimated using multiple logistic regression analysis. Furthermore, interactive associations among carbohydrate and fat intake, physical environment, health-related lifestyle, and MetS were analyzed.

Results: In the first sub-study, it was found that residing at low elevation increased prevalence of MetS in men (OR=1.37; 95% CI: 1.05-1.76) and elevated fasting glucose in both men (OR=1.80; 95% CI: 1.32-2.46) and women (OR=1.55; 95% CI: 1.24-1.93) after adjusting for confounders. Additionally, a lack of physical activity was identified as an important factor that raises the risk of increased waist circumference in both men (OR=2.05; 95% CI: 1.22-3.45) and women (OR=1.38; 95% CI: 1.05-1.83) living at low elevation.

The second study found that living in high relative humidity (>80%) increased ORs of reduced HDL cholesterol (OR=1.25; 95% CI: 1.06-1.56) and MetS (OR=1.20; 95% CI:1.01-1.42) in women. Furthermore, physically active men living in high relative humidity showed lower OR of elevated triglycerides (0.56; 95% CI:0.37-0.85) while menopausal women living in high relative humidity showed increased ORs of MetS (5.42; 95% CI: 1.92-15.27), elevated blood pressure (3.10; 95% CI: 1.15-8.35), and increased waist circumference (OR=1.34; 95% CI: 1.09-1.63).

Lastly, in the third sub-study we found that in women, LCHF intake showed an inverse association with increased blood pressure (OR= 0.34, 95% CI: 0.19–0.59), while MCF intake showed inverse associations with increased blood pressure and elevated fasting glucose (OR=0.50, 95% CI: 0.32-0.79; OR= 0.58, 95% CI: 0.37-0.91, respectively). Moreover, inverse associations were observed in women who were consuming MCF intake and residing in low relative humidity with MetS (OR=0.63; 95% CI: 0.40-0.98) and in women with LCHF diet and residing at high elevation with reduced HDL cholesterol (OR=0.57; 95% CI: 0.35-0.94). Additionally, higher ORs of increased waist circumference were observed in men with LCHF intake who were physically inactive (OR=2.30; 95%CI: 1.17-4.52) and living in high relative humidity (OR=2.44; 95%CI: 1.23-4.83).

Conclusions: Physical environment, health-related lifestyles, and diet pattern showed significant effects on prevalence of MetS and its components in Ecuadorian adults. Residence at low elevation and residence in high relative humidity increased ORs of MetS and its components in both men and women, while physical activity significantly reduced ORs of MetS and its components in men. In addition, women consuming LCHF and/or MCF intakes showed inverse associations with MetS and its components. Further analyses showed interactive associations of carbohydrate and fat intake, physical activity, and physical environment with MetS among Ecuadorian adults. The obtained results suggest that comprehensive health and nutrition programs focusing on not only lifestyles but also physical environment should be conducted. The findings from these studies may constitute the baseline for further investigation on adequate environment conditions, lifestyles, and dietary intake for the prevention of MetS.

Keywords: metabolic syndrome, elevation, humidity, Ecuadorian adults, carbohydrate and fat intake, physical activity

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Table of contents

Tables

Figures

Chapter 1. Introduction

1-1. General characteristics of Ecuador

Ecuador is located in northwestern South America, bordered by Colombia on the north, Peru on the east and south, and the Pacific Ocean on the west. Ecuador also includes the Galápagos Islands in the Pacific. Ecuador has a total area of 283,561 km^{2,} its population of approximately 17 million is >70% urban (1), although the rural and agricultural sectors remain important. Ecuador is geographically diverse and is home to important ethnic and racial minorities, including Afro-Ecuadorians, Montubios (mixed-race rural residents of the coastal region), and members of 14 indigenous groups. The majority of Ecuadorians live in the central provinces, the Andes mountains, or along the Pacific coast. The tropical forest region to the east of the mountains (Amazon) remains sparsely populated and contains approximately 3% of the population (1).

The country is classified as an upper-middle-income country, with a developing economy that is highly dependent on petroleum and agricultural products. Oil accounts for 40% of exports and contributes to maintaining a positive trade balance; while in the agricultural sector, Ecuador is a major exporter of bananas, flowers, and cocoa (2). Positive economic performance has enabled higher levels of investment in social expenditure and contributed to reducing income inequality. Nonetheless, poverty rates remain high and about 35% of the population live in poverty, particularly in rural areas (3).

1-2. Nutritional characteristics of Ecuador

In Ecuador, high rates of undernutrition and overweight or obesity coexist at the individual, family, and national levels. Ecuador, like most developing countries, has experience in treating undernutrition, while increases in rates of overweight and obesity have been observed in the recent years with an inadequate treatment and prevention approach. The increasing double burden of undernutrition and overweight or obesity is expressed within the context of the Social Determination of Health (4). In Latin American countries, stunting among children persists along with overweight or obesity in mothers within the same household, although household members also suffer from micronutrient deficiencies (5). In Ecuador, 13.1% of households, mothers with excess body weight coexist with a stunted child <5 years old. Moreover, among households with overweight or obese mothers, 12.6% have an anemic child and 14% have a zinc-deficient child. In addition, 8.9% and 32.6% of women aged 12–49 y have excess body weight and anemia or zinc deficiency, respectively (6). Malnutrition is related to the epidemiologic transition, globalization, urbanization, occupational structures, and changing patterns of diet and physical activity (7). Dietary intake in Latin American countries still include large proportions of unprocessed foods, traditional diets have been replaced in whole or in part by energy-dense foods, particularly processed foods high in fat, sugar, and salt (8). In addition, traditional lifestyles have changed dramatically, particularly in terms of substantial reductions in physical activity (9).

The current nutritional situation in Ecuador is not significantly different from the transition trends observed worldwide. Although average incomes have increased in the past two decades, the country remains highly unequal, with a Gini coefficient that is still approximately 0.46 (10). Rapid social and economic development in the face of persistent poverty and inequality are factors that provide the context for this malnutrition phenomenon. Although the prevention of undernutrition and overweight or obesity should frame health policy in Ecuador, decision makers have yet to recognize the implications of their high prevalence or to fully understand that the presence of this problem could lead to the onset of Cardiovascular Disease.

1-3. Metabolic syndrome in Ecuador

Metabolic Syndrome in Latin America and the world

For the past decade, some studies have reported the weighted mean prevalence of MetS in the Latin American countries was 24·9 %, higher than that reported in developed countries (11). In fact, studies conducted in Puerto Rico, Chile, Colombia, Venezuela, Mexico and Brazil prevalence rates of MS are different in 1.5–20.0 % compared with those reported in the USA (21.8 %) and some European countries: Spain (24.7 %), Portugal (23.9 %) and Italy (24.1 %) (12). Though, this mean prevalence of MS in Latin America was lower than that reported for some ethnic groups in other parts of the world. MS prevalence among Mexican Americans has been reported at 31.9 % (13) and 32.8% for Afro-American people (12).

The difference in MetS prevalence across countries is likely the result of different governmental and sociocultural factors at the population level, which can affect the type of available foods and access, health care policies, education, employment and the physical environment. This is in addition to individual factors such as biology/genetics and sociocultural aspects, which are also likely relevant to the different prevalence of MetS between countries. These aspects may be referred to as ethnic differences, as many of these characteristics often cluster in specific populations. Even within the same country, in the same local environment, the prevalence of MetS differs along certain ethnic groups. For example, in the United States, the prevalence of MetS is highest in Hispanics and lowest in African-Americans (14).

Morbidity and mortality trends in Latin America have changed in recent decades because of shifts in nutrition and lifestyle habits among the population. As a result of these factors, the region has gone from being one in which malnutrition was the main concern to one in which cardiovascular and chronic degenerative diseases are now the leading cause of death, as has been the case in developed countries (15).

Importance of metabolic syndrome in Ecuador

In Ecuador, Cerebro-Cardiovascular diseases are the leading causes of death; diabetes, hypertension and dyslipidemia are known as their major risk factors (16). According to Ecuador National Statistics, the prevalence of diabetes in 2016 in Ecuadorian adults is 7.3% and it increases up to 10% in people over the 50 years of age to 10% (17). According to results from the Ecuador National Health and Nutrition Survey 2012 (ENSANUT-ECU) the prevalence of hypertension in Ecuadorians over the age of 18 yr. corresponds to 9.3% (18) and substantially increases to 44.4% in people over the age of 60 years (19). Additionally, the prevalence of hypercholesterolemia in 2012 in adults was 24.5% (18).

Metabolic disorders, including abdominal obesity, hypertension, elevated blood glucose and dyslipidemia, often cluster in conjunction, which is metabolic syndrome (20). Metabolic syndrome is considered a public health problem that requires to be studied in order to prevent cardiovascular disease and diabetes (21,22). In Ecuador, the prevalence of metabolic syndrome in the adult population is estimated to be 31.2% nationwide and it varies across regions, the coast and the Galapagos Islands have the highest prevalence of MetS (35.0% and 41.9%) while, the highlands and the Amazon show a prevalence of 29.9% and 26.6%, respectively (23) A comparison among regions is presented in Figure 1-1.

Figure 1-1. Significant metabolic abnormalities on each region of Ecuador. All the metabolic abnormalities highlighted on each region are significant against at least another region ($p < 0.05$) (23)

Risk factors for metabolic syndrome

Several factors have been associated with the onset of metabolic syndrome, biological factors such as: sex (female) and age (> 40yr.), obesity, abdominal obesity and insulin resistance (24). Although insulin resistance mechanisms for MetS onset still unclear, obesity has been fully probed to increase the risk of metabolic syndrome and cardiovascular disease (25). Lifestyle patterns, such as smoking, alcohol consumption, unhealthy dietary habits, and physical inactivity are also known risk factors for metabolic syndrome (26, 24). In addition, physical environments, including elevation and climatic factors have been reported to associate with onset of metabolic diseases (27-34).

1-4. Characteristics of physical environment in Ecuador

Ecuador is located in northwestern South America and cross by the Equator; it covers 283,561 square kilometers of land. Ecuador is the smallest country in south America, however, it is one of the most environmentally diverse countries in the world, and it has contributed notably to the environmental sciences (35). Ecuador is comprised of four distinct geographical regions: the highlands, which correspond to the Andean mountain chain, the coast, the Amazon and the Galapagos Islands, located 973 km west of northern South America.

The geographical regions of Ecuador have different climates due to their difference in elevation and proximity to the Pacific coast (36) and they form five climatic floors: the warm floor (0–1000 m above sea level (masl) at 25 ℃); the temperate floor (1000 to 2000 masl, at temperatures that range from 16 to 23℃); the cold floor (2000 to 3000 masl at 12 ℃); the paramo/moor floor (from 3000 to 4000 masl close to 0 ℃); and the glacial floor (4000 masl < 0 ℃) (37). Climate models predict ambient temperature increases between 2 and 7℃ in tropical South America by the end of the 21st century (38). Both tropical and mountain regions are expected to show emerging environmental conditions, including higher maximum temperatures and drier conditions (39).

1-5. Elevation conditions and metabolic disorders

Elevation and obesity

Studies performed in Peru and the USA have reported that living at high elevations has a lower adult prevalence and risk of overweight and obesity (40,28), especially in men (28). According to nationally representative study of the Peruvian adult population, an inverse association of obesity with elevation was found. Living in high elevation compared with those at lower elevation had lower age-adjusted adult prevalence of overweight (30.6;95% CI, 28.9%-32.3%) vs. (37.2%; 95% CI, 35.4%-39.0%). Similarly, age-adjusted obesity prevalence was lower in high elevation (8.0%; 7.0%-9.1%) vs. (16.4%; 14.7%-18.2%) (40).

Moreover, a quasi-experimental study in service member of the U.S. Army found that members staying at higher elevation duty locations had a lower incidence of obesity, service members stationed at high elevation had a 41% (95% CI, 35%–46%; p 0.001) lower hazard rate of obesity as compared to those stationed at low elevation, after adjusting for confounding variables (28). A summary of the associations between elevation and metabolic disorders in previous studies is presented in Table 1-1.

Elevation and type 2 diabetes mellitus

A cross-sectional study in a US adult population showed that living at high elevation (1,500−3,500 masl) had 12% lower odds of having diabetes compared to low elevation (0−499 masl), after adjusting for risk factors. Additionally, the odds of being obese and having diabetes were lower among men only (41).

Elevation and metabolic syndrome

During the past decade, limited studies have actively examined the association between elevation and metabolic syndrome (Table 1-1). A recent cross-sectional study among Ecuadorian university students found that living at high altitude (2,758–2,787 masl) had lower odds of hypercholesterolemia, hyperglycemia and MetS than living at sea level, after adjusting for potential confounders. Residing at high altitude lower prevalence of hypercholesterolemia (OR = 0.30; $p < 0.05$), hyperglycemia (OR = 0.22; $p < 0.001$) and metabolic syndrome (OR = 0.28; $p < 0.05$). Additionally, lower self-reported energy intake was found in high altitude compared to sea level after adjustment for potential confounders ($p < 0.001$) (42).

A cohort study in Spain among university students followed for a median time of 10 years showed that students living in high elevation (>456 masl) exhibited a significantly lower risk of developing metabolic syndrome during follow-up compared to those living at low elevation (<122 masl) (HR= 0.75; 95% CI: 0.58–0.97; p for trend = 0.029) (43).

In addition, a cross-sectional study based on the Peru National Survey of Chronic Diseases data found that prevalence of metabolic syndrome was significantly higher in lower elevation (1,000 masl) (19.7%) than in higher elevation (>3,000 masl) (10.2%), $p<0.001$. The prevalence of the metabolic syndrome abnormalities was higher in the adult population in low elevation that the ones living at high elevation, increased waist circumference (35.5% vs. 21.1%), elevated blood pressure (20.9% vs. 15.0%), elevated fasting glucose (3.9% vs. 1.7%), hypertriglyceridemia (31.3% vs. 25.7%), and low HDL cholesterol (57.4% vs. 52.5%); $p<0.05$ (44). These findings indicate that living at low elevation might play an important role in contributing to the development of metabolic syndrome.

Table 1-1. Summary of the associations between elevation and metabolic disorders in previous studies

Author, year	**Country, study design**	**Subjects**	**Exposure**	**Outcome**	**Main Results**
Woolcott O et al., 2016 (40)	Peru, cross-sectional study	31,549 adults aged 20 year-old and above	Altitude: group I (0-499 masl) group II (500-1,499 masl), group III (1,500-2,999 masl), group IV (over 3,000 masl)	1) Obesity 2) Overweight	1) High elevation: 30.6% (95% CI, 28.9%-32.3%) vs. low: 37.2% (95% CI, 35.4%-39.0%), 1) Interaction between altitude and sex (↑) (p<0.001). [Men high elevation] 2) adjusted prevalence ratio of overweight (↓)
Voss et al., 2014 (81)	USA, quasi-experimental, retrospective study	98,009 US Army members with 3.2 years of exposure	High altitude (.>1.96 kilometers above sea level) duty assignment with low altitude (<0.98 km)	1) Obesity	[High elevation] 1) HR 0.59 (95% CI:0.54–0.65); p 0.001. (↓)
Woolcott O et al., 2014 (41)	USA, cross-sectional study	285,196 adults aged 20 and over	Altitude: group I (0-499 masl) group II (500-1,499 masl), group III (1,500-3,500 masl)	1) Type 2 diabetes mellitus	[Men high elevation] 1) OR: 0.84 (95% CI: 0.76 - 0.94) (↓) [Women] 1) OR: 1.09 (0.97-1.22) (-)

López-Pascual A et al., 2018 (42)	Ecuador, cross-sectional study	260 Ecuadorian university graduates over 20 years of age	Sea level (4-6 masl) vs high altitude (2,758-2,787)	1) Metabolic syndrome 2) Hypercholesterolemia 3) Elevated fasting glucose 4) Low self-reported intake	[High elevation] 1) OR:0.24; $p < 0.05$ 2) OR: 0.24; $p < 0.001$ 3) OR: 0.25; $p < 0.05$ 4) (↓); $p < 0.001$
López - Pascual et al., 2016 (43)	Spain, cohort study	6,860 university students over 25 years old	Altitude: high (>456 masl) low (<122masl)	1) Metabolic syndrome	[High elevation] HR= 0.75 (95% CI: 0.58–0.97); p for trend = 0.029.
Pajuelo J et al., 2012 (44)	Peru, cross-sectional study	3,384 adults aged 20 year-old and above	Altitude: group I (<1000 masl) vs group II (>3000 masl)	1) Metabolic syndrome 2) Increased waist circumference 3) Increased fasting blood glucose 4) High blood pressure 5) Reduced HDL-cholesterol	1) Low elevation:19.7% High:10.2% ($p<0.001$) 2) (↑) 3) (↑) 4) (↑) 5) (↑)

(↑) positive association; (↓) negative association (-) non-significant association.

HDL, high-density lipoprotein; masl, meters above the sea level.

1-6.Climate conditions and metabolic disorders

Ambient temperature and obesity and type 2 diabetes mellitus

Ambient temperature has been linked to cardiovascular morbidity and mortality and has taken the interest of some researchers. To our knowledge there are only two studies performed in Spain and the USA that analyzed the associations of ambient temperature and metabolic syndrome. A nationally representative study of the Spanish population showed a novel association between ambient temperature and obesity that remained after adjustment for confounders, energy expenditure was potentially described as an explanatory mechanism (33). Interestingly, a cross-sectional study of U.S. adults found no significant differences in temperature categories and obesity. However, extreme temperatures trended to the lowest odds of obesity (28).

Additionally, there is only one study that have explored the associations of ambient temperature and type 2 diabetes mellitus and obesity. It was found that ambient temperature explained 12.4% of the variation in the prevalence of type 2 diabetes, after adjusting for potential confounders. Conversely, ambient temperature didn’t show any effect on obesity prevalence (34). Studies on climate and obesity are still scarce and controversial, findings of previous studies are presented in Table 1-2.

Ambient temperature and hypertension

A cross-sectional study performed in China found an inverse association between ambient temperature and blood pressure. Additionally, mediation analysis demonstrated that the association of ambient temperature and the risk of cardio-cerebrovascular events was potentially mediated by blood pressure (45).

Ambient temperature and metabolic syndrome

The association of ambient temperature and metabolic syndrome and its components is not well described yet and there is only one study that explored these associations (Table 1-2). The study was conducted in the US and revealed that temperature was associated with an increased risk of developing elevated fasting blood glucose only, for metabolic syndrome and other components no significant associations were found (46).

Table 1-2. Summary of the associations between ambient temperature and metabolic disorders in previous studies

Author, year	Country, study design	Subjects	Exposure	Outcome	Main Results
Valdes S et al., 2014 (33)	Spain, cross-sectional study	5,061 subjects in 100 clusters	Mean annual temperature (Q4 vs Q1)	1) Obesity	1) OR 1.38 (1.14-1.67) (p 0.001 for difference, P<0.001 for trend) (↑)
Voss JD et al., 2013 (28)	USA, cross-sectional study	422,603 adults	Mean annual temperature	1) Obesity	1) Parabolic relationship
Speakman J et al., 2016 (34)	USA, cross-sectional study	2,654 counties, 170,430,015 individuals	Monthly ambient temperature for each county	1) Type 2 diabetes mellitus 2) Obesity	1) 12.4% of the variance in prevalence ($F_{2,2648} = 188.5$, $p < 0.0005$) 2) (-)
Yu Bo et al., 2020 (45)	China, cross-sectional study	38,589 participants aged 30-79 yr.	Monthly outdoor temperature	1) High blood pressure 2) Cardio-cerebrovascular disease	1) Increase of 6.7mmHg in SBP and 2.1mmHg in DBP for each 10 ℃ (↓) 2) (↓) 2) Mediated by blood pressure
Wallwork R et al., 2016 (46)	USA, longitudinal study	587 active male participants between 1993 and 2011	Ambient temperature levels at each participant's address	1) Metabolic syndrome 2) Elevated fasting glucose	1) (-) 2) HR 1.33 (95% CI: 1.14, 1.56)

(↑) positive association; (↓) negative association (-) non-significant association.

SBP, systolic blood pressure; DBP, diastolic blood pressure.

Relative humidity and metabolic syndrome

The most debated variable of climate is humidity, as there is significant inconsistency in how humidity is incorporated and interpreted in human health studies (47). Humidity is linked with mortality and morbidity levels through its role in affecting heat stress and hydration state related to physiological reactions (48). Humidity variables are rarely incorporated in the research despite their potential direct physiological importance. More often, humidity is treated as a confounding variable that may be related to both the predictor and response variables (49). Studies supporting the association of MetS and humidity are scarce, to our knowledge there is a single research on this field. The study showed a positive association between diabetes mellitus, central obesity and higher systolic blood pressure in elder residents living in high relative humidity areas (50). The main finds are shown in Table 1-3.

Table 1-3. Summary of the associations between relative humidity and metabolic disorders in previous studies

Author, year	**Country, study design**	**Subjects**	**Exposure**	**Outcome**	**Main Results**
Tyrovolas S, et al., 2014 (50)	Mediterranean islands, population-based cohort study	1959 elderly (aged 65 to 100 years)	Air moisture and mean daily temperature	1) Type 2 diabetes mellitus 2) High SBP 3) Central obesity	1) (↑) 2) (↑) 3) (↑)

(↑) positive association. SBP, systolic blood pressure.

1-7. A low-carbohydrate, high-fat diet and metabolic disorders

Definition of a low-carbohydrate diet

Despite de fact that carbohydrates constitute the major source of energy among populations in the globe, popularity of low-carbohydrate high-fat diets has gained the attention of people seeking to lose weight and prevent heart disease, diabetes and obesity (51). According to results from the ENSANUT-ECU 2012, an excessive intake of refined carbohydrates, primarily white rice and white bread, along with a poor intake of fruits and vegetables contribute to overweight and obesity in the Ecuadorian population (18). Although a consensus on the definition of a low-carbohydrate diet has not been established, several studies among Caucasian and European populations have defined a low-carbohydrate diet as the one containing <45% of energy from carbohydrates (52,53). In the case of Ecuador, the Food Dietary Guidelines for the Ecuadorian population (GABA) established the Acceptable Macronutrient Distribution Range (AMDR) as: total carbohydrate intake 55-65%, fat intake 20-30% and protein 10-15% (54).

Effects of a low-carbohydrate diet on metabolic risk

In order to determine the effects of the consumption of low-carbohydrate diet on metabolic risk and obesity, several studies have been conducted in different populations worldwide, as a result of these investigations several meta-analyses have been published and summarized in Table 1-3. A comprehensive meta-analysis of randomized controlled trials (RCTs) showed that low-carbohydrate diets are not significantly different from balanced diets regarding body weight reduction, blood pressure, or lipid profiles (55). In addition, clinical trials have shown that weight loss in the short-term irrespective of whether the diet is low-carbohydrate or balanced in terms of its macronutrient composition. There is probably little or no difference in weight loss and changes in cardiovascular risk factors up to two years of follow-up in overweight and obese adults, with or without DM2 (53).

Conversely, other meta-analyses revealed that the consumption of a low-carbohydrate diet is associated with significant decreases in body weight, waist circumference, systolic and diastolic blood pressure, plasma triglycerides, fasting glucose, an increase in HDL-cholesterol (53). Moreover, they stated that low to moderate carbohydrate diets have greater glucose-lowering effect compared with high-carbohydrate diets. Apart from improvements in HbA1c over the short term, there is no superiority of low-carbohydrate diets in terms of glycemic control, weight, or LDL cholesterol (56).

Most of these RCTs have included populations from the US, Australia, and European and Asian countries and the findings have suggested that the association among low-carbohydrate intake and metabolic diseases might fluctuate according to ethnicity, life conditions and nutritional status.

In addition, to support RCTs, epidemiological studies have found that LCHF diets result in similar weight loss and had similar improvements for a number of metabolic risk markers, and an HCLF diet had more favorable effects on triglycerides and HDL-cholesterol (57). Studies in the Chinese population found that that both high and low percentages of carbohydrate intake were associated with increased risk of new-onset hypertension, with minimal risk observed at 50% to 55% carbohydrate intake (58). Moreover, compared with the participants who had a balanced carbohydrate and fat intake, the individuals who consumed a HCLF diet had a higher risk of developing hypertension, especially the individuals who were young, live in rural areas, and consume alcohol (59).

Other studies have indicated that increased intake of carbohydrate causes significant increases in fasting blood glucose and serum insulin, as well as changes in the lipid profile, particularly triglycerides and very low-density lipoprotein–cholesterol (60). In Korea, a low-carbohydrate diet did not increase the risk of MetS among adults who consumed a HCLF diet, it was only found a decreased risk of reduced HDL-cholesterol levels (61). Investigations related to carbohydrate and fat intake and metabolic diseases in the Latin American populations have been performed in small groups and with several limitations, up to date Ecuador lacks of this type of research. Therefore, further prospective studies are required to examine the effects of carbohydrate and fat intake on metabolic diseases in the Ecuadorian population.

Table 1-4. Summary of the effects of carbohydrate and fat diet intakes on metabolic disorders in previous meta-analyses of randomized controlled trials

Author, year	**Data, subjects**	**Duration**	**Exposure**	**Main Results** **(Pooled mean difference and 95% CI)**
Hu et al., 2014 (52)	– 23 RCTs (US 13, Europe 5, Australia 3, Israel 2) – 2,788 adults aged 27-60 years	6-24 months	Low-carbohydrate diet (<45% of energy from carbohydrates) vs Low-fat diet (<30% of energy from fat)	Low-carbohydrate – Low-fat – Body weight: -1.0 kg (-2.2-0.2) – Waist circumference: -0.1 cm (-0.6-0.4) – Total cholesterol: 2.7 mg/dL (0.8-4.6) – LDL-cholesterol: 3.7 mg/dL (1.0-6.4) – HDL-cholesterol: 3.3 mg/dL (1.9-4.7) – Triglycerides: -14.0 mg/dL (-19.4- -8.7) – SBP: -1.0 mmHg (-3.5-1.5) – Fasting glucose: -0.3 mg/dL (-1.9-1.3)
Santos F.L. et al., 2012 (53)	– 23 reports, 17 correspond to clinical investigations	3-36 months	Low carbohydrate diet defined by the author of the article	Low-carbohydrate – Body weight: -7.4 kg (-7.2-6.9) – Waist circumference: -5.7 cm (-6.7/-5.41) – Total cholesterol: 2.7 mg/dL (0.8-4.6) – LDL-cholesterol: - – HDL-cholesterol: 1.7 mg/dL (1.4-2.1) – Triglycerides: -29.7 mg/dL (-31.9/-27.4) – SBP: -4.8 mmHg (-5.3/-2.7) – DBP: -3.1 mmHg (-3.5/-2.74) – Fasting glucose: -1.05 mg/dL (-1.7/-0.4)

Snorgaard O, et al., 2017 (56)	– 10 RCTs (US 3, Australia 3, Israel 1, Sweden 1, Japan 1, Canada 1) – 1,376 subjects with DM2	3-12 months	Carbohydrate restriction (below 45%) to diet of 45–60% carbohydrate	Low-carbohydrate Within 1 year – BMI: -1.02 (-2.58-0.54) – HbA1C: -0.34% (0.06-0.63 lower) – LDL-cholesterol: -0.04 mmol (-0.06-0.13) At 1 year or later – BMI: -0.43 (-1.38-0.53) – HbA1C: -0.04% (0.04-0.13 lower) – LDL-cholesterol: -0.01 mmol (-0.1-0.07)
Naude et al., 2014 (55)	– 19 RCTs (Australia/New Zeland 8, Europe 6, US, 5 – 3,209 adults aged 18 years and above	12-24 months	Low-carbohydrate diet (40% of energy from carbohydrates) vs Balanced diet for weight loss (45%-65% of energy from carbohydrates, 25-35% from fat, and 10-20% from protein)	Low-carbohydrate – Balanced diet (non-Diabetes) – Body weight (short term): -0.74 kg (-1.49-0.01) – Body weight (long term): -0.48 kg (-1.44-0.49) Low-carbohydrate – Balanced diet (Diabetes) – Body weight (short term): -0.82 kg (-1.25-2.90) – Body weight (long term): -0.91 kg (-2.08-3.89)

RCT, randomized control trial; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL, high density lipoprotein; LDL, low density lipoprotein; BMI, body mass index; HbA1C, glycated hemoglobin.

Table 1-5. Summary of the associations between carbohydrate and fat diet intakes and metabolic disorders in previous studies

Author, year	**Country, study design**	**Subjects**	**Exposure**	**Outcome**	**Main Results**
Tay J, et al., 2008	Australia, parallel study	122 adults aged 18 to 65 yr.	VLCHF diet (4% of total energy as carbohydrate, 35% as protein, 61% as total fat , 20% saturated fat); HCLF diet (46% of total energy as carbohydrate, 24% as protein, 30% as total fat, 8% saturated fat).	1) Weight loss 2) CVD	1) VLCHF: -11.9±6.3 kg, HCLF: -10.1±5.7 kg; p=0.17 (↑) 2) HDL-cholesterol increased VLCHF 18% vs. HCLF 6%, p=0.002-time X diet interaction). 2) LDL-cholesterol decreased VLCHF 0.06±0.58 mmol/l, HCLF -0.46±0.71 mmol/l; p<0.001).
Li Q, et al., 2021	China, prospective cohort study	12,177 adults	Energy intake from carbohydrate (Q5 vs Q1)	1) High blood pressure	1) U-shaped association between the percentage energy consumed from total carbohydrate (mean, 56.7%; SD, 10.7) and new-onset hypertension (P for nonlinearity <0.001)
He D, et al., 2021	China, cohort study	10,459 participants aged over 12 yr.	LCHF (proportion of energy from carbohydrate <45%); HCLF (proportion of energy from carbohydrate >65%); and MPCF (65% ≥proportion	1) High blood pressure	1) HCLF (hazard ratio: 1.295, 95% CI: 1.167–1.436) (↑)

			of energy from carbohydrate ≥45%)		
Mukherjee S, et al., 2009	India, experimental study	320 participants aged 33-55 yr.	Control group consumed <70% carbohydrate as part of their diet vs experimental group carbohydrate consumption was >70%.	1) Type 2 diabetes mellitus	1) Fasting glucose (↑) 2) Triglycerides (↑)
Ha K, et al., 2018	South Korea, cross-sectional study	16,349 participants aged 30 yr. or older	Deciles of percentage of energy from carbohydrate, protein, and fat by sex.	1) Metabolic syndrome 2) HDL-cholesterol	1) Women in the highest decile of the low carbohydrate-diet. (OR=0.70; 95% CI: 0.50-0.97; p for trend= 0.1433). 2) Women in the lowest decile (OR=0.76; 95% CI: 0.59-0.99; p for trend= 0.0005)

(↑) positive association; (↓) negative association (-) non-significant association.

VLCHF, very low-carbohydrate high-fat; HCLF high-carbohydrate low-fat; SBP, HDL, high density lipoprotein; LDL, low density lipoprotein; MPCF, medium proportion of carbohydrate and fat.

1-8. Purpose of research

The present study aimed (a) to determine the epidemiologic characteristics of physical environment, health-related lifestyles, and carbohydrate and fat intake among Ecuadorian adults and (b) to examine their association with MetS and its components.

The objective of the first sub-study was to examine the associations among elevation of residence, health-related lifestyles, and prevalence of MetS in the Ecuadorian population aged 20 years or older using national survey data.

The second sub-study aimed to estimate the climate conditions through national meteorological data and investigate their associations with lifestyles and MetS among Ecuadorian adults.

Finally, the objective of the third sub-study was to examine interactive associations among carbohydrate and fat intake, physical environment (i.e. elevation and humidity), lifestyle, and MetS among Ecuadorian adults.

Title	**Study 1.** Low Elevation and Physical Inactivity are Associated with a Higher Prevalence of Metabolic Syndrome in Ecuadorian Adults: A National Cross-Sectional Study	**Study 2.** Associations of Relative Humidity and Lifestyles with Metabolic Syndrome Among the Ecuadorian Adult Population: Ecuador National Health and Nutrition Survey (ENSANUT-ECU) 2012	**Study 3.** Association of carbohydrate and fat intake with prevalence of metabolic syndrome can be modified by physical activity and environment in Ecuadorian adults: the ENSANUT-ECU study
Objective	To examine the associations among elevation of residence, health-related lifestyles, and prevalence of MetS	To estimate the climate conditions through national meteorological data and investigate their associations with lifestyles and MetS among Ecuadorian adults	To examine interactive associations among carbohydrate and fat intake, physical environment (i.e. elevation and humidity), lifestyle, and MetS
Data	ENSANUT-ECU	ENSANUT-ECU, INAMHI	
Subjects	6,024 Ecuadorian adults (1,964 men and 4,060 women) aged 20 to 60 years		6,023 Ecuadorian adults (1,964 men and 4,059 women) aged 20 to 60 years

Figure 1-2. Construction of the present study

Chapter 2. Low Elevation and Physical Inactivity are Associated with a Higher Prevalence of Metabolic Syndrome in Ecuadorian Adults: A National Cross-Sectional Study[1]

Abstract

Elevation and health-related lifestyles have been associated with the development of MetS. However, such associations have not been investigated extensively in a global context. The present study aimed to determine the associations among elevation of residence, health-related lifestyles, and the risk of MetS in an Ecuadorian adult population. This cross-sectional study was conducted utilizing secondary data from the 2012 Ecuador National Health and Nutrition Survey (ENSANUT-ECU). A total of 6024 adults (1964 men and 4060 women) 20 to 60 years old were included in the study. Elevation was obtained by georeferencing techniques and categorized into low (0–2000 masl) and high (>2001 masl). Dietary intake was measured using a 24-hour recall and health-related lifestyle via risk and physical activity standardized questionnaire. MetS was defined on the basis of the National Cholesterol Education Program Adult Treatment Panel III and the Latin American Diabetes Association criteria. Multiple logistic regression analyses were used to examine whether elevation of residence and health-related lifestyles can increase the risk of MetS. Residing at low elevation increased prevalence of MetS in men (1.37; 95% CI,1.05–1.76) and elevated fasting glucose in both men (1.80; 95% CI, 1.32–2.46) and women (1.55; 95% CI, 1.24–1.93) after adjusting for confounders. Additionally, a lack of physical activity was identified as an important factor that raises the risk of increased waist circumference in both men (2.05; 95% CI, 1.22–3.45) and women (1.38; 95% CI, 1.05–1.83) living at low elevation. Our findings suggest that low elevation of residence and physical inactivity are associated with a higher prevalence of MetS in Ecuadorian adults.

2-1. Introduction

MetS is a multidimensional, progressive, and complex disorder characterized by the sum of elevated fasting glucose, hypertension, elevated serum triglycerides and low serum high-density lipoprotein (HDL) levels, and abdominal obesity (62). The worldwide prevalence of MetS is estimated to be between 10% and 84%

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[1] This study was published in the Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy vol. 13, pages 2217—2226 in June 2020.

depending on the age, gender, and ethnicity of the population (63). Additionally, 20% of adults in the Western world was found to have MetS (64). Latin America exhibits a high prevalence of abdominal obesity and MetS, similar to or even higher than developed countries (65). MetS culminates in adverse outcomes, including cardiovascular disease (CVD) and type 2 diabetes mellitus (DM2) (21). The specific causes that trigger MetS are still unknown, although genetics, lifestyle, and environmental factors have been identified (66,67). In Ecuador, Ecuador National Health and Nutrition Survey (ENSANUT-ECU) presented data on cardiometabolic risk factors nationwide for 2012, reporting a 27% prevalence of MetS nationally, which was higher in women than in men (29.2% and 25.2%, respectively) (68). For 2013, DM2 was the first cause of mortality, corresponding to 4695 deaths (7.44% of the annual total) (69).

Several biological and behavioral factors, including age (ie >40 yr), sex (female), smoking, unhealthy dietary habits, and sedentary behaviors have been recognized to contribute to the development of MetS. Moreover, the environment has been suggested to potentially influence the development of metabolic diseases (27,70). All of these factors have contributed to the design of health policies in urban environments (71). As such, elevation, defined as the distance above sea level, has been proposed to increase pulmonary and cardiovascular functions (72,73). Many studies have reported that populations living at high elevation have lower serum low-density lipoprotein (LDL) cholesterol, higher HDL cholesterol, and lower fasting glucose levels as well as reduced obesity rates (74,70). It is also reported to increase glucose uptake and its tolerance, which reduces blood glucose levels (75-77). Furthermore, living at high elevation is associated with severe hypoxia and a reduction in peripheral oxygen saturation leading to a decrease in insulin sensitivity, whereas mild hypoxia may improve insulin sensitivity (76,78,79). Some studies have described an inverse association between elevation and lower obesity prevalence and incidence (80-82,40,28), as well as lower diabetes (83), and hypertension proportions (84,73). One Spanish study utilizing a university student cohort found that living at a high elevation was associated with a lower risk of MetS than living at a low elevation after a median follow-up period of 10 years (43). Another Ecuadorian study also reported that residence at high elevation (2,758 – 2,787 meters above sea level (masl)) was associated with a lower prevalence of MetS, hypercholesterolemia, and hyperglycemia than residence at sea level (4-6 masl) (42).

However, the association between elevation of residence and MetS development has not been extensively investigated. Furthermore, socioeconomic characteristics, dietary patterns, smoking, alcohol consumption, and physical activity patterns may also explain these associations (63,43). Therefore, effects of elevation of residence and lifestyle on populations living in the highest regions of the world should be further investigated. In this context, we examined the associations among elevation of residence, health-related lifestyles, and prevalence of MetS in the Ecuadorian population using national survey data from the Ecuadorian National Health and Nutrition Survey (ENSANUT-ECU).

2-2. Subjects and Methods

Study design and subjects

This study used data from the 2012 ENSANUT-ECU, which is a cross-sectional study with a complex, multistage, probability sampling design. The survey was conducted by the Ministry of Public Health of Ecuador (MSP). Detailed explanations of the ENSANUT-ECU are available elsewhere (68).

The initial samples were 20 years old or older with complete 24-hour dietary recall, anthropometric data, and biochemical variables related to metabolic syndrome; the initial data consisted of 11,044 participants. Among the eligible participants, we excluded those with missing physical activity information (n = 4,166, rural residents), incomplete risk factor data (n = 493), and participants taking medication for hypertension (n = 361). Therefore, the final sample consisted of 6,024 Ecuadorians (1,964 men and 4,060 women) over 20 years old. The study was approved by the MSP and the Institutional Review Board of Seoul National University (code: SNU 19-04-003). Written informed consent was obtained from all participants.

Measurement and Definition of Metabolic Syndrome

Anthropometric data including height, weight, and waist circumference were measured at people's houses by trained health technicians using calibrated equipment. Body mass index (BMI) was calculated from weight and height data (kg/m^2). Blood pressure was measured at three consecutive times according to standardized procedures of anthropometry and a determination of blood pressure manual (18); the mean of the readings was used in this study. For measurement of levels of fasting blood glucose, serum total cholesterol, HDL cholesterol, and triglycerides, blood samples were collected from participants who fasted for at least 8 hours and stored at -80℃ until analysis. An enzymatic colorimetric method was utilized to measure the concentrations of glucose, total cholesterol, HDL-C, and triglycerides using an automated auto-analyzer (Modular Evo-800, Roche Diagnostics, Mannheim, Germany). Details of laboratory procedures have been described in the ENSANUT-ECU 2012 report (18). LDL-cholesterol was calculated according to Friedewald's formula: [LDL-cholesterol] = [total cholesterol] – [triglycerides/5]. However, this calculation was valid when the triglycerides level was ≤ 400 mg/dL (85). The definition of metabolic syndrome was based on the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) criteria for Latin America and the Metabolic Syndrome Diagnosis Criteria established by the Latin

America Association of Diabetes. MetS was diagnosed when three or more of the following components existed: waist circumference $\geq$ 94 cm for men and $\geq$88 cm for women, systolic blood pressure $\geq$ 130 mmHg or diastolic blood pressure $\geq$ 85 mmHg, HDL cholesterol < 40 mg/dL for men and < 50 mg/dL for women, triglycerides $\geq$ 150 mg/dL, and fasting blood glucose $\geq$ 100 mg/dL.

Measurement of Sociodemographic Variables and Health-Related Lifestyles

General- and socio-demographic variables including age, ethnicity, family economic status, and education level were collected. Data for ethnicity were obtained from the housing information standardized questionnaire; according to ENSANUT-ECU, the five main ethnic groups were categorized as mestizo and the rest of population (indigenous, montubio, afro-descendent and white). For family economic status, the population was divided into quintiles based on the Wealth Index Q1(poor), Q2, Q3 (intermediate), Q4 and Q5 (rich). Education level was categorized into primary school (<=7th grade), secondary school (>8th grade <12th grade), and college or higher (college or associates degree or college graduate or above). Additionally, the questionnaire included the elevation of residence, which was obtained through georeferencing methods; elevation was classified as high elevation if the participant's residence was located over 2,001 masl and low elevation if the participant's residence was under 2,000 masl (86,87).

Health-related lifestyles included current alcohol consumption, current smoking, and physical activity; data were obtained using risks and physical activity standardized questionnaires (88,89). Current alcohol consumption was defined by the number of alcoholic beverages consumed per day in the past 30 days and categorized as "Yes" or "No" according to the United States National Survey on Drug Use and Health (NSDUH). Current smoking status was defined as current tobacco consumption ("Yes" or "No") for those who had smoked in the last 30 days according to the WHO-Ecuador, 2007 and based on the NSDUH (88).

Physical activity was defined according to the U.S Department of Health and Human Services as "Yes" for those who participated in vigorous-intensity activities for at least 75 min, moderate-intensity activity for at least 150 min, or an equivalent combination of moderate and vigorous-intensity activity during the last 7 days and "No" for activities performed in less than 75 min in the past seven days (89).

Assessment of Dietary Intake

Dietary intake was measured by a single 24-hour dietary recall method administered by a trained technician at each participant's residence. The recall data included all kinds of food and beverages consumed by subjects within a 24-hour period. Energy intakes was estimated with dietary intakes and the food composition table in the Ecuadorian Food Dietary Guideline (GABA) (39). To evaluate the adequacy of energy intake, percentage (%) of estimated energy requirements (EER), based on the age-, sex-, and physical activity level-specific equations published in Dietary Reference Intakes, was calculated (90,91).

Statistical Analyses

All statistical analyses were performed using SAS version 9.4 software (92). The complex sampling design parameters including strata, cluster, and weight were applied to PROC SURVEY procedures. All p-values were two-sided ($\alpha=0.05$).

All analyses were stratified by sex and geographical elevation. All variables are expressed as means ± standard error for continuous variables and as percentages (%) for categorical variables. For continuous variables, p-values were obtained from t-tests and $\chi 2$-tests for categorical variables to test the difference between sex and elevation; if more than 50% of the cells had expected counts less than 5, the T Fisher Exact Test was used.

Geographical elevation was categorized into two groups, including low elevation (0-2,000 masl) and high elevation (above 2,001 masl). Multiple logistic regression analysis was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for MetS across the elevation groups. In the multiple logistic regression model, the confounders of ethnicity, socio-economic status, education level, BMI (except for the model of waist circumference), physical activity, current alcohol consumption, current smoking, and total energy intake were adjusted when comparing both groups.

2-3. Results

General characteristics of study participants

Six thousand twenty-four participants (4,060 females and 1,964 males) were included in the study. The general characteristics of the study participants by sex and elevation are shown in Table 2-1. The mean age of the Ecuadorian participants was 34.7 ± 0.46 (SE) years old at low elevation and 34.4 ± 0.54 at high elevation for men and 35.1 ± 0.35 years old at low elevation and 35.3 ± 0.35- at high elevation for women. Ethnicity, family economic status, physical activity, and current smoking of study subjects were significantly different between living at high and low elevation in both sexes ($p < 0.05$). However, education level and alcohol consumption were significantly different between high and low elevation in men only (*p*

= 0.0151, *p* = 0.0387, respectively). Additionally, Table 2-2 shows a similar trend of the general characteristics of the initial population (n = 11,044) and the remaining one (n = 6,024).

Table 2-1. Demographic and health-related lifestyle characteristics of study subjects according to their elevation of residence

	Men (%)			**Women (%)**		
	High elevation (n=783)	**Low elevation** (n=1181)	***p*-value [a]**	**High elevation** (n=1469)	**Low elevation** (n=2591)	***p*-value [a]**
Age (years)			0.0946			0.5917
20-29	39.4	38.1		36.1	35.5	
30-39	26.8	31.0		28.7	31.1	
40-49	23.7	18.2		23.7	23.8	
50-59	10.1	12.7		11.5	9.6	
Ethnicity			**0.0011**			**0.0450**
Mestizo	93.0	85.6		92.7	85.8	
Others	7.0	14.4		7.3	14.2	
Family economic status [b]			**<0.0001**			**<0.0001**
Low	16.6	34.1		16.7	33.5	
Middle	42.5	50.8		37.8	48.0	
High	40.9	15.1		45.5	23.5	
Education level			**0.0151**			0.2165
Primary school	24.1	26.9		25.2	29.4	
Secondary school	43.8	52.6		43.4	49.1	
College or higher	32.1	20.5		31.4	21.5	
Current alcohol consumption [c] (yes)	53.0	58.8	**0.0387**	25.5	26.6	0.6248
Current smoking [d] (yes)	40.5	28.5	**<0.0001**	7.5	4.7	**0.0009**
Physical activity [e] (yes)	52.7	37.0	**<0.0001**	20.3	14.6	**<0.0001**

Bold values indicate the statistical significance

[a] All continuous variables were tested using a *t*-test and all categorical variables were tested using χ2-test, when > 50% of the cells had expected counts less than 5, the T Fisher Exact Test was used.

[b] For family economic status, the Wealth Index was used: Low (Q1 and Q2), Middle (Q3 and Q4) and High (Q5).

[c] Alcohol consumption was defined as "yes" when participants drank alcoholic beverages in the past 30 days.

[d] Current smoking was defined as "yes" when participants smoked cigarettes in the past 30 days

[e] Physical activity was defined as "yes" when participants performed vigorous-intensity activities for at least 75 min, or moderate-intensity activities for at least 150 min, or an equivalent combination of moderate- and vigorous-intensity activity during the past seven days

Table 2-2. Comparison of general characteristics of participants of ENSANUT-ECU 2012 according to their elevation of residence

	Initial Population (11,044 participants)						**Remaining Population (6,024 participants)**					
	Men			Women			Men			Women		
	Low elevation	High elevation	p-value [a]	Low elevation	High elevation	p-value [a]	Low elevation	High elevation	p-value [a]	Low elevation	High elevation	p-value [a]
Number of people, N	2188	1338		4653	2865		1181	783		2591	1469	
Age, years, N (%)			0.0645			0.2970			0.0946			0.5917
20-29	729 (34.3)	473 (36.2)		1520 (33.7)	892 (34.2)		410 (38.1)	295 (39.4)		922 (35.5)	499 (36.1)	
30-39	771 (29.0)	415 (26.2)		1540 (29.7)	935 (28.1)		405 (31.0)	254 (26.8)		935 (31.1)	521 (28.7)	
40-49	375 (20.2)	332 (23.3)		1053 (24.2)	685 (22.4)		258 (18.2)	189 (23.7)		616 (23.8)	377 (23.7)	
50-59	313 (16.5)	118 (14.3)		540 (12.9)	181 (15.3)		108 (12.7)	45 (10.1)		118 (9.6)	72 (11.5)	
Ethnicity, N (%)			**<.0001**			**0.0009**			**0.0011**			**0.0450**
Mestizo	1755 (73.3)	1175 (83.2)		3739 (74.4)	2471 (79.9)		1011 (85.6)	728 (93.0)		2222 (85.8)	1362 (92.7)	
Others	433 (26.7)	163 (16.8)		914 (25.6)	394 (20.1)		170 (14.4)	55 (7.0)		369 (14.2)	107 (7.3)	
Family economic status [b], N (%)			**<.0001**			**<.0001**			**<.0001**			**<.0001**
Low	1066 (43.9)	424 (26.1)		2359 (45.4)	1175 (33.7)		403 (34.1)	130 (16.6)		926 (33.5)	309 (16.7)	
Middle	891 (43.2)	516 (36.7)		1803 (41.0)	1014 (34.4)		600 (50.8)	333 (42.5)		1264 (48.0)	617 (37.8)	
High	231 (12.9)	398 (37.2)		491 (13.7)	676 (31.9)		178 (15.1)	320 (40.9)		401 (18.5)	543 (45.5)	
Education level, N (%)			**0.0005**			0.0853			**0.0151**			0.2165
Primary school	733 (33.7)	434 (29.8)		1684 (35.2)	1111 (38.0)		318 (26.9)	189 (24.1)		761 (29.4)	370 (25.2)	
Secondary school	1136 (49.7)	587 (46.0)		2240 (45.4)	1143 (41.3)		621 (52.6)	343 (43.8)		1273 (49.1)	638 (43.4)	
College or higher	319 (16.6)	317 (24.2)		729 (19.4)	611 (20.7)		242 (20.5)	251 (32.1)		557 (21.5)	461 (31.4)	

Bold values indicate the statistical significance

[a] All continuous variables were tested using a *t*-test and all categorical variables were tested using $\chi 2$-test, when > 50% of the cells had expected counts less than 5, the T Fisher Exact Test was used.

[b] For family economic status, the Wealth Index was used: Low (Q1 and Q2), Middle (Q3 and Q4) and High (Q5).

Anthropometric and biochemical measurements according to elevation of residence

Table 2-3 shows the anthropometric and biochemical measurements of the MetS components and energy intake of the study participants. While blood pressure, total cholesterol level, triglyceride level, and energy intake were higher in men than women, BMI and EER (%) were higher in women than in men. A higher BMI was observed in both women and men living at low elevation than that in residents living at high elevation; however, a significant difference was only observed in women living at low elevation (*p* = 0.044). Fasting glucose levels of both men and women living at low elevation were significantly higher than those of residents living at high elevation (*p* = 0.0002 for men, *p* < 0.0001 for women). Both energy intake and EER (%) increased significantly as elevation decreased for both sexes (*p* < 0.0001). Similar results were obtained when analyzing elevation by quartiles as shown in Table 2-4.

Table 2-3. Anthropometric and biochemical measurements of MetS and macronutrient intake among study subjects according to their elevation of residence

	Men (mean ± SE)			Women (mean ± SE)		
	High elevation (n=783)	Low elevation (n=1181)	*p*-value[a]	High elevation (n=1469)	Low elevation (n=2591)	*p*-value[a]
Anthropometric and biochemical variable						
BMI (kg/m^2)	26.3 ± 0.3	26.8 ± 0.2	0.2410	27.1 ± 0.2	27.5 ± 0.2	**0.0440**
Waist circumference (cm)	94.6 ± 3.4	95.2 ± 1.7	0.8690	101.8 ± 5.5	91.9 ± 1.54	0.0840
SBP (mmHg)	125.3 ± 3.2	124.2 ± 1.3	0.7430	116.4 ± 1.4	115.7 ± 1.1	0.7470
DBP (mmHg)	81.3 ± 3.4	78.5 ± 1.3	0.4490	73.4 ± 1.5	72.9 ± 1.1	0.8324
Fasting glucose (mg/dL)	90.3 ± 0.9	96.9 ± 1.5	**0.0002**	89.5 ± 0.7	95.1 ± 1	**<0.0001**
Total cholesterol (mg/dL)	187.6 ± 2.0	185.1 ± 1.7	0.3419	180.5 ± 1.4	180.1 ± 1.3	0.8611
HDL cholesterol (mg/dL)	40.6 ± 0.5	41.5 ± 0.5	0.2205	46.4 ± 0.5	46.4 ± 0.4	0.9958
LDL cholesterol (mg/dL)	112.9 ± 1.6	110.7 ± 1.4	0.2936	108.5 ± 1.2	109.2 ± 1.1	0.6952
Triglyceride (mg/dL)	178.5 ± 6.4	174.1 ± 5.7	0.6061	128.7 ± 3.2	125.8 ± 2.9	0.5111
Macronutrient intake						
Energy (kcal)	2003.3± 20.1	2250.7 ± 20.1	**<0.0001**	1721.7 ± 16,5	1922.7 ± 13.8	**<0.0001**
EER (%)	75.6 ±1.0	88.0 ± 1.0	**<0.0001**	90.4 ± 0.9	103.2 ± 0.9	**<0.0001**

Bold values indicate the statistical significance

[a] All continuous variables were tested using a t-test and all categorical variables were tested using χ2-test.

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; EER, estimated energy requirement.

Table 2-4. Anthropometric and biochemical measurements of MetS and macronutrient intake among study subjects according to quartiles of elevation of residence

	Quartiles of elevation									
	Men					Women				
	Q1 (n=491)	Q2 (n=491)	Q3 (n=492)	Q4 (n=490)	p for trend	Q1 (n=1016)	Q2 (n=1014)	Q3 (n=1016)	Q4 (n=1016)	p for trend
Median (meters above sea level)	16	215	2206.5	2808.3		17.0	230.0	1554.0	2798.0	
Anthropometric and biochemical variable (mean ± SE)										
BMI (kg/m2)	27.1±0.3	26.2±0.3	26.5±0.3	26.3±0.5	0.0971	27.5±0.2	27.5±0.3	27.3±0.2	27.0±0.2	**0.0288**
Waist circumference (cm)	96.1±2.3	93.9±2.5	99.6±9.0	92.2±2.1	0.1195	92.1±2.1	91.9±2.6	98.9±5.7	101.6±6.8	0.1684
SBP (mmHg)	124.4±1.6	124.2±2.4	133.8±9.2	121.1±0.7	0.2994	116.1±1.6	115.8±1.5	114.7±0.8	116.6±1.9	0.8822
DBP (mmHg)	78.4±1.6	78.9±2.5	88.9±9.6	77.2±1.3	0.7389	73.1±1.6	73.2±1.4	71.7±0.6	73.8±1.9	0.8076
Fasting glucose (mg/dl)	96.3±1.6	98.5±3.2	89.5±1.1	90.6±1.3	**0.0007**	96.3±1.4	93.7±1.3	88.7±1.1	90.0±0.8	**<.0001**
Total cholesterol (mg/dl)	186.6±2.4	182.5±2.5	185.6±2.2	188.2±2.6	0.2414	181.8±1.9	178.5±1.8	177.0±1.6	181.1±1.7	0.3934
HDL cholesterol (mg/dl)	41.4±0.6	41.7±0.8	40.7±0.8	40.5±0.6	0.4800	47.3±0.6	45.3±0.7	46.1±0.5	46.3±0.6	0.9042
LDL cholesterol (mg/dl)	111.5±2.0	109.0±2.1	110.8±1.8	114.0±2.1	0.2121	110.3±1.6	107.9±1.6	106.2±1.3	109.2±1.5	0.3204
Triglycerides (mg/dl)	178.5±8.2	166.4±7.6	187.0±11.0	174.0±7.4	0.6783	122.6±3.3	131.4±6.1	123.4±3.4	130.4±4.0	0.8166
Macronutrient intake (mean ± SE)										
Energy (kcal)	2261.5±25.7	2253±34.5	1996.1±25.8	2007.8±25.7	**<.0001**	1960.3±20.2	1888.9±19.1	1715.0±19.0	1728.3±20.2	**<.0001**
EER (%)	87.8±1.2	89.2±1.7	76.1±1.4	75.5±1.3	**<.0001**	104.9±1.3	102.2±1.2	89.9±1.2	90.9±1.1	**<.0001**

Bold values indicate the statistical significance

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; EER, estimated energy requirement.

Prevalence of metabolic syndrome and its association with elevation of residence

The prevalence and ORs for MetS in Ecuadorian adults according to elevation are shown in Table 2-5. Living at low elevation significantly increased ORs of MetS in men (1.37; 95% CI: 1.05-1.76) and elevated fasting glucose levels in both men (1.80; 95% CI: 1.32-2.46) and women (OR=1.55; 95% CI:1.24-1.93) after adjusting for ethnicity, family economic status, education level, BMI, physical activity, current alcohol and smoking status, and total energy intake. We further analyzed the data according to quartiles of residential elevation, and found that ORs of MetS in men and ORs in elevated fasting glucose levels in both sexes were negatively elevation-dependent ($p_{trend} < 0.0001$ for all) and it is shown in Table 2-6.

As shown in Supplementary table 1, health-related lifestyle factors including current alcohol consumption, current smoking status, and physical activity individually increased ORs of MetS and/or elevated fasting glucose levels in residents at lower elevation over that in those living at high elevation; these are concordant to results shown in Table 2.5. However, interestingly, non-smoking or non-alcohol drinking women living at low elevation showed higher ORs of increased waist circumference, and men with low energy intake and living at low elevation had higher ORs of elevated fasting glucose levels. Furthermore, a lack of physical activity was also significantly associated with elevated fasting glucose levels in men (2.05; 95% CI:1.22-3.45) and women (1.38; 95% CI:1.05-1.83) living at low elevation, in addition to MetS and elevated fasting glucose levels (Figure 2.1). The obtained data suggest that low elevation of residence and physical inactivity may play important roles in development of MetS.

Table 2-5. Prevalence and odds ratio for MetS among study subjects according to their elevation of residence

	Men		Women	
	High elevation (n=783)	Low elevation (n=1181)	High elevation (n=1469)	Low elevation (n=2591)
Increased waist circumference				
Prevalence (%)	18.22	34.95	25.50	41.20
OR (95% CI)	1.00 (reference)	1.00 (0.85-1.51)	1.00	1.12 (0.94-1.34)
Elevated blood pressure				
Prevalence (%)	10.66	17.83	5.50	8.70
OR (95% CI)	1.00	0.94 (0.74-1.20)	1.00	0.89 (0.71-1.18)
Reduced HDL cholesterol				
Prevalence (%)	19.80	29.90	24.71	39.60
OR (95% CI)	1.00	1.10 (0.88-1.36)	1.00	1.15 (0.99-1.34)
Elevated triglycerides				
Prevalence (%)	18.50	26.70	10.70	15.70
OR (95% CI)	1.00	1.05 (0.85-1.31)	1.00	0.94 (0.80-1.10)
Elevated fasting glucose				
Prevalence (%)	3.20	13.20	3.80	11.30
OR (95% CI)	1.00	**1.80 (1.32-2.46)**	1.00	**1.55 (1.24-1.93)**
Metabolic syndrome				
Prevalence (%)	12.80	23.73	10.40	19.00
OR (95% CI)	1.00	**1.37 (1.05-1.76)**	1.00	1.10 (0.93-1.30)

Bold values indicate the statistical significance

All values accounted for the complex sampling design effect of the national surveys using PROC SURVEY procedure. A multiple logistic regression analysis was performed after adjusting for ethnicity, family economic status, education level, BMI (except for the model of waist circumference), physical activity, current alcohol consumption, current smoking and total energy intake.

Abbreviations: OR, odd ratio; CI, confidence interval; HDL, high-density lipoprotein.

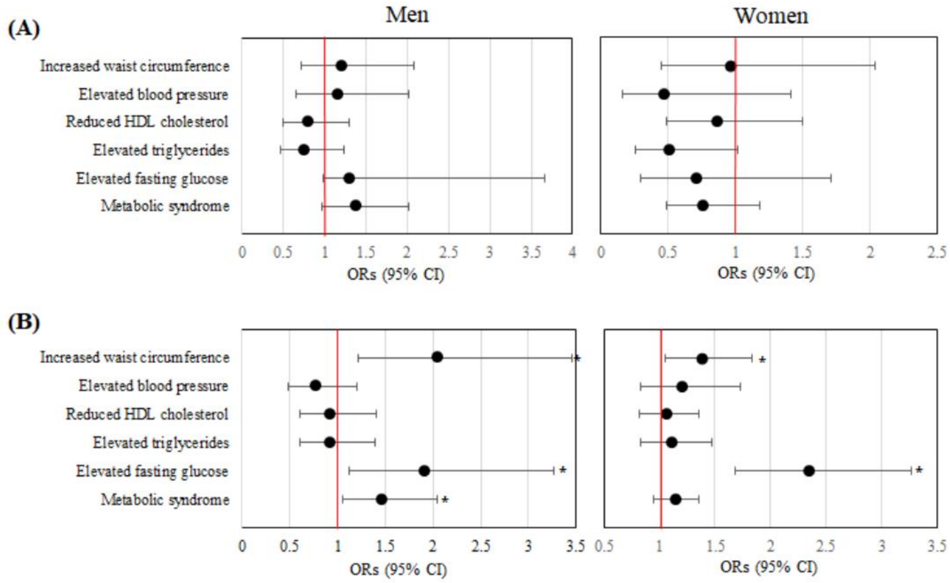

Figure 2.1. Odds ratios for MetS among low elevation residents according to physical activity.

(A) Physically active and (B) physically inactive subjects. ORs were calculated based on high elevation residents (reference). All values were obtained from a multivariable logistic regression model applying appropriate sampling weight after adjusting for ethnicity, family economic status, education level, BMI (except for the model of waist circumference), current alcohol consumption, current smoking and total energy intake.

* $p < 0.05$

Table 2-6. Multivariable adjusted odds ratio (OR) and 95% confidence intervals (CI) for the Metabolic Syndrome components among participants according to their elevation

	Quartiles of temperature									
	Men					Women				
	Q4 (n=490)	Q3 (n=492)	Q2 (n=491)	Q1 (n=491)	p for trend	Q4 (n=1016)	Q3 (n=1016)	Q2 (n=1014)	Q1 (n=1016)	p for trend
Median (meters above sea level)	2808.3	2206.5	215.0	16.0		2798.0	1554.0	230.0	17.0	
Increased waist circumference										
OR (95% CI)	1.00	1.77 (1.29±2.42)	1.10 (0.42±2.93)	1.19 (0.76±1.86)	0.4540	1.00	1.19 (0.83±1.71)	1.20 (0.62±2.33)	1.42 (0.69±2.82)	0.264
Elevated blood pressure										
OR (95% CI)	1.00	1.08 (0.83±1.41)	1.02 (0.79±1.33)	1.43 (0.97±1.97)	0.059	1.00	0.99 (0.74±1.31)	1.09 (0.81±1.46)	1.34 (0.99±1.76)	0.075
Reduced HDL cholesterol										
OR (95% CI)	1.00	1.24 (0.41±3.75)	2.04 (0.68±6.18)	1.01 (0.43±2.35)	0.9101	1.00	1.13 (0.85±1.50)	1.40 (0.98±1.92)	1.39 (0.81±1.31)	0.829
Elevated triglycerides										
OR (95% CI)	1.00	0.88 (0.59±1.29)	0.92 (0.61±1.39)	0.72 (0.49±1.04)	0.139	1.00	0.94 (0.69±1.30)	1.08 (0.77±1.53)	0.88 (0.63±1.21)	0.649
Elevated fasting glucose										
OR (95% CI)	1.00	0.73 (0.41±1.30)	**2.44 (1.40±4.24)**	**2.39 (1.41±4.05)**	**<.0001**	1.00	0.79 (0.51±1.23)	**2.17 (1.42±3.30)**	**2.06 (1.41±3.02)**	**<.0001**
Metabolic syndrome										
OR (95% CI)	1.00	0.90 (0.66±1.22)	**1.58 (1.14±2.18)**	**1.55 (1.12±2.13)**	**<.0001**	1.00	0.88 (0.64±1.21)	1.35 (0.95±1.91)	1.12 (0.81±1.53)	0.2048

Bold values indicate the statistical significance

All values accounted for the complex sampling design effect of the national surveys using PROC SURVEY procedure. A multiple logistic regression analysis was performed after adjusting for ethnicity, family economic status, education level, BMI (except for the model of waist circumference), physical activity, current alcohol consumption, current smoking and total energy intake.

Abbreviations: OR, odd ratio; CI, confidence interval; HDL, high-density lipoprotein

2-4. Discussion

Nationally representative data from the ENSANUT-ECU were utilized to determine whether living at low elevation (0-2,000 masl) is associated with development of MetS in adult men and women. In our study, elevation over 2,000 masl is classified as high elevation since it has shown to be associated with physiological changes at rest and marked changes in exercise. Opposed to it, living at low elevation (1-2,000 masl) has no physiological effects at rest and presents a decreased in physical performance (86,87). Our study showed a higher prevalence of MetS in men and elevated fasting glucose levels in both men and women living at a lower elevation than in those living at a higher elevation. To our knowledge, this is the first study to report an association between residing elevation and prevalence of MetS utilizing a large number of Ecuadorian adults.

Two studies using a university student cohort reported that young adults living at high elevation show a lower prevalence of MetS (42,43). Several studies have also shown an inverse association between high elevation and MetS development. One study including 285,196 adults from the United States showed a lower prevalence of diabetes in men living above 1,500 masl (93). A Peruvian study also reported lower serum triglycerides and blood pressure in people living at higher elevation, while no significant differences in prevalence of MetS were observed between those living at sea level and those living at a higher elevation (94). Another study performed in an Andean population reported a lower waist circumference at a higher elevation; an adjusted inverse association between geographical elevation and obesity that varied by sex was also found (40). Furthermore, lower fasting glucose and better glucose tolerance were associated with a high elevation (95,96,88), and lower prevalence (97,28) and incidence (81,82,98) of overweight or obesity were also found in residents at high elevation.

Some causes of mortality were also associated with elevation; specifically, living at high elevation was associated with a lower mortality rate from coronary heart disease and ischemia, whereas a higher mortality from chronic obstructive pulmonary disease was observed (73). People living at high elevation, above 2,500 masl, display a fall in arterial oxygen saturation and present physiological adaptations to this environmental pressure (86,75). These two responses produce an increase in hemoglobin concentrations, enlarged lung volume and increased ventilatory response (88,74). In this case, the highest regions of the world demonstrate the biological human adaptation to low oxygen concentrations (hypoxia), including the Ethiopian Siemen Mountains, the Tibetan Himalayan valleys, and the Andean Altiplano in South America (28). Genetic and physiological adaptations, principally to hypoxia, that affect glucose metabolism and trigger appetite suppression and reduced caloric consumption (99) might explain the inverse association between elevation, diabetes, and cardiovascular diseases.

Furthermore, at sea level, the partial pressure of oxygen is approximately 160 mmHg, which represents 21% oxygen respired compared to 15% O_2 at ~3000 masl at high-elevation. This fact leads to a condition of moderate hypoxia for ten sequential nights, which increases whole-body insulin sensitivity in obese men (100,99). Even though evidence suggests that exposure to lower levels of oxygen may enhance body metabolic homeostasis, intervention studies in humans are needed for further research.

In this study, we analyzed sex and elevation separately and found that men had a higher prevalence of MetS when living at low elevation than at high elevation; currently available data suggest that sex-specific pathophysiological differences in MetS may be associated with different effects of sex hormones on adipose tissue, genetic factors between men and women, or a combination of all (102,103). Diagnostic criteria for MetS vary for the cutoff points and definition of its components in a gender-specific manner. Glucose and lipid metabolism are directly modulated by estrogen and testosterone, with a lack of estrogen or a relative increase in testosterone inducing insulin resistance and an increase in the lipid profile.

Health-related lifestyle factors, physical activity patterns in particular, are inversely associated with development of MetS (66). Our results are also consistent with those from other studies. Moderate exercise has been shown to have a positive impact on lipid profile (cholesterol and triglycerides), while a lack of physical activity has been associated with increased abdominal circumference (104,105). In addition, physical inactivity has been associated with a higher risk of type 2 diabetes, regardless of age, sex, ethnicity, or BMI (106). Evidence shows that the prevalence of MetS, diabetes and dyslipidemias is higher in obese, overweight, and physically inactive individuals, and physical inactivity is independently related to an increased risk of each of these diseases (107). Although an extensive literature exists on physical related health benefits, measuring physical activity at a population level is difficult because of the existence of a variety of measurement methods. In the present study, the participants' oxygen consumption levels were not available, which may have resulted in an over-estimation of physical activity level for some individuals from a physiological perspective; thus, this should be considered when interpreting our result and merits caution.

Other health-related lifestyle factors, including alcohol consumption and current smoking, were related to MetS and/or elevated fasting glucose levels in men living at a low elevation. These findings agree with previous studies where heavy alcohol consumption was associated with increased risk of MetS, while very light alcohol consumption had an inverse association (108). Another study showed that several alcohol-drinking patterns were positively correlated with the prevalence of MetS in men (109). Moreover, our study showed that men in the "No" current alcohol consumption group had a lower risk of elevated fasting glucose levels in comparison to the "Yes" group; these findings agree with some studies where drinking alcohol showed a less favorable alteration on glucose metabolism, blood pressure, hypertriglyceridemia, and central obesity (110,111). In addition, adult smokers have lower levels of plasma apolipoprotein A1, the main protein component of HDL, which is related to an increased risk of MetS and DM2 (112-115). One hypothesis is that nicotine itself may lead to fat accumulation, attributable to its effect on insulin resistance (116,117). A meta-analysis of 13 prospective studies using long-term observation of the development of MetS revealed smoking to be a contributing factor for MetS depending on the amount of nicotine accumulation in the body (118), which may explain our finding of a high risk of MetS in men. Interestingly, our data also showed that non-smoking or non-alcohol drinking women living at low elevation had a higher risk of increased waist circumference. Thus, elevation may influence waist circumference or obesity more than health-related lifestyles in women; however, further investigations are needed to confirm these associations

Self-reported energy intake significantly differed by elevation in men and women ($p < 0.0001$); this inverse-adjusted association suggested a regulatory role for appetite in contracting MetS. However, our results are independent of energy intake, which was used as a confounder in the multiple logistic regression analysis. Previous studies reported that exposure to hypoxia under resting conditions increases energy expenditure and lipid metabolism and reduces appetite and food intake (119). Acute exposure to hypoxia tends to stimulate the neuroendocrine system, triggering a strong endocrine response that improves oxygen delivery via cardiorespiratory and hemopoietic adaptations (88). In this context, leptin and norepinephrine could increase sympathetic nerve activity, causing changes in energy expenditure and food intake at high elevation (120). It is notable that high EER was associated with elevated fasting glucose in women at low elevation; in contrast, men with a low EER showed increased fasting glucose. This result suggests that EER influences insulin sensitivity. Several physiologic mechanisms may help to explain this finding (121,122).

Our study has several limitations. Among initial participants (n = 11,044), physical activity data from a rural population were not collected for the ENSANUT-ECU; thus, we analyzed only 6,024 participants residing in urban areas after excluding rural residents (n =4,166) and others (n = 854). Consequently, we cannot exclude the possibility of residual bias, and our results should be interpreted with caution. One should consider reverse causality, attributable to a cross-sectional study design. Also, energy intake data from a single 24-houe recall method, which were used in this study due to data availability, could not represent individual's usual energy intake. In addition, both the elevation exposure and the outcome are categorized as low or high and presence or absence respectively; however, continuous variables would give a more information regarding dose-response association. Despite these limitations, our study has some strengths. This is the first study on the association of residential elevation with MetS, which includes a large number of Ecuadorians selected from a nationally representative population. The analyses are adjusted for socio-economic and lifestyle factors to avoid any potential bias. Additionally, all data were collected by trained technicians, reducing data inaccuracy and preventing recall and response biases.

2-5. Conclusions

In conclusion, living at low elevation (0–2,000 masl) is associated with a higher prevalence of MetS in men and an elevated fasting glucose level in both sexes. Additionally, a lack of physical activity was identified as an important factor that increases ORs of increased waist circumference in both men and women living at low elevation. Our findings suggest that low elevation of residence and physical inactivity may play important roles in development of MetS in Ecuadorian adults.

Chapter 3. Associations of Relative Humidity and Lifestyles with Metabolic Syndrome Among the Ecuadorian Adult Population: Ecuador National Health and Nutrition Survey (ENSANUT-ECU) 2012[2]

Abstract

The effects of physical environment on MetS are still largely unexplained. This study aimed to analyze the associations of relative humidity of residence, lifestyles, and MetS among Ecuadorian adults. Data from 6,024 people aged 20 to 60 years were obtained from an Ecuador national population-based health and nutrition survey (i.e. ENSANUT-ECU, 2012) and the mean annual relative humidity (%) from the Ecuador National Institute for Meteorology and Hydrology (2012). Odds ratio (OR) with 95% confidence intervals (CI) for MetS according to groups of relative humidity were calculated using multiple logistic regression. Living in high relative humidity (>80%) increased ORs of reduced HDL cholesterol (1.25; 95% CI: 1.06-1.56) and MetS (OR=1.20; 95% CI: 1.01-1.42) in women. Furthermore, physically active men living in high relative humidity showed lower OR of elevated triglycerides (0.56; 95% CI:0.37-0.85) while menopausal women living in high relative humidity showed increased ORs of MetS (5.42; 95% CI: 1.92-15.27), elevated blood pressure (3.10; 95% CI: 1.15-8.35), and increased waist circumference (OR=1.34; 95% CI: 1.09-1.63). Our results show that residence in high relative humidity and menopausal status increase ORs of MetS and its components in Ecuadorian women; however, physical activity significantly reduces OR of elevated triglycerides in men. The obtained findings may help make public health policies regarding environmental humidity management, nutritional education, menopausal care, and physical activity promotion to prevent the onset of MetS among Ecuadorian adults.

3-1. Introduction

MetS is comprised of elevated fasting glucose, hypertension, dyslipidemia, and abdominal obesity (20), and can lead to type 2 diabetes mellitus (DM2), heart disease, and cardiovascular disease (CVD) (21). Over

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[2] This study was published in the International Journal of Environmental Research and Public Health, vol. 17, pages 2217—2226 in December 2020.

a billion of the world population is estimated to have MetS (22); in Latin American countries, a higher prevalence is observed, especially in women (123). Human biology, lifestyle, and the environment have been found to promote the onset of MetS, though the specific causes are still unknown (21). Like other Latin American countries, 31.2% of adults in Ecuador have MetS and approximately 85% of the total population have at least one of the MetS abnormalities (23). Ischemic Heart Disease, DM2, and CVD were the top three causes of mortality in the Ecuadorian adult population in 2019 (3.1%, 6.5% and 6.2% of the annual total mortality) (16). Therefore, it is important to identify potential determinants of MetS development in Ecuador to set up strategies to minimize MetS onset as well as its subsequent diseases.

Biological factors (i.e. sex (female) and age (>40 yr.)) and lifestyle patterns (i.e. smoking, alcohol consumption, unhealthy dietary habits, and physical inactivity) are recognized as risk factors for MetS development. In addition, physical environments, including elevation and climatic factors, have been reported to associate with onset of metabolic diseases (27-34). Among several physical environments, humidity is the most debated due to its inconsistent results in human health studies (48).

Humidity is linked to physiological responses through heat stress and hydration states (49). Despite the importance of humidity on human body metabolism, it is rarely incorporated as an independent variable in many research studies. Rather, humidity is considered as a confounding variable that may be related to the exposure and/or health outcomes (50). Studies supporting the association of metabolic disorders and humidity are limited; however, a few studies showed that mortality in the USA tends to increase in hot and humid areas (124). The less humid mountainous regions on the other hand, showed the lowest prevalence of Obesity (<30%) and MetS (30-35%) compared to the rest of the country (125). Another study showed a positive association between diabetes mellitus, central obesity, higher systolic blood pressure, and lower physical activity in elder residents of the Mediterranean islands living in high relative humidity areas (51). In addition, sociodemographic characteristics, epidemiological transition, globalization, and changes in lifestyle patterns (i.e. reduced physical activity and increased consumption of macronutrients and alcohol, and smoking) may modify these associations (17,21).

We hypothesized that relative humidity is associated with risk of MetS and that lifestyle patterns could modify the risk. To this end, we determined the associations of relative humidity, lifestyles, and dietary patterns with MetS among Ecuadorian adults based on data from the ENSANUT-ECU 2012 and the National Institute for Meteorology and Hydrology (INAMHI).

3-2. Subjects and Methods

Study Design

A cross-sectional study was performed using ENSANUT-ECU, a nation-wide population-based health and nutrition survey conducted by the Ecuadorian Government and its Ministry of Public Health. Detailed explanations of the study design and data source profiles of ENSANUT-ECU are available elsewhere (18). In brief, ENSANUT-ECU collected data, that included sociodemographic characteristics of the population, housing, risk factors, food consumption, anthropometry, blood pressure, and nutritional biomarkers.

Written informed consents were obtained from all participants using consent forms, and a protocol of the study was approved by the Institutional Review Board of Seoul National University (code: SNU 19-04-003).

Subjects

A total of 11, 044 participants over 20 years of age were initially included for ENSANUT-ECU with complete variables related to MetS. Among these individuals, we excluded 4,166 rural residents who did not have physical activity data and other risk factors (n=493), as well as participants who took medication for hypertension (n=361). Thus, 6,024 adult Ecuadorians (1,964 men and 4,060 women) were finally included in this study as illustrated in Figure 3-1.

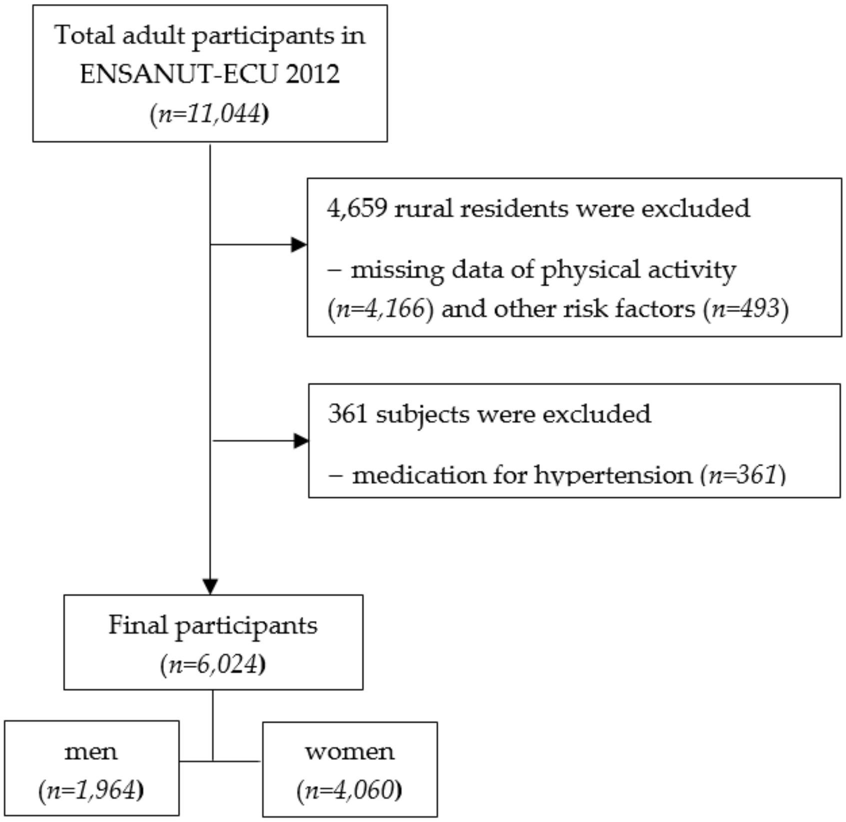

Figure 3-1. Flow diagram for the selection of study participants.

General Characteristics

The general information of participants, including age, sex, ethnicity, education level, and economic status of family were collected from the housing questionnaire of ENSANUT-ECU 2012. Data regarding elevation of residence was also obtained. Ethnicity was classified as mestizo (Indian with European mix) and others (i.e. indigenous, montubio, afro-descendent, and white); education level as primary, secondary, and college or higher; and economic status of family as poor (Q1, Q2), middle (Q3, Q4), and rich (Q5). For menopause status, we subdivided women in two groups: menopausal stage "Yes" for >= 50 years of age and "No" for < 50 years old. This classification was based on the WHO parameters.

Lifestyles

Information regarding lifestyles was included as follows: current alcohol consumption and smoking ("Yes" or "No") were based on the alcohol beverage intake and smoking in the past 30 days according to the United States National Survey on Drug Use and Health and WHO-Ecuador (48). Physical activity was divided in two groups: "Yes" for the performance of vigorous-intensity activity for at least 1 hr. 15 min, moderate-intensity activity for at least 2 hr. 30 min, or both for the past 7 days prior to the collection of data, and "No" for any activity that that took less than 1 hr. 15 min (49).

Anthropometric Measurements

Anthropometric measurements, including body mass index (BMI), height, weight, and waist circumference of participants, were performed at their residence by trained technicians using standardized procedures and portable equipment (126). Blood pressure was measured twice using a sphygmomanometer according to standardized measurement techniques (126); the mean of the readings was used in this study. Blood samples of total cholesterol, HDL cholesterol, triglycerides, and glucose were collected from participants under an 8-hour fasting period and measured using an enzymatic-colorimetric assay Modular Evo-800 (Roche Diagnostics). The Friedewald's formula was used to calculate LDL-cholesterol (85). Detailed explanations of laboratory procedures are reported in the ENSANUT-ECU (18).

Dietary intake

For dietary intakes, trained technicians collected data using the 1-day 24-hour dietary recall method at the participants' houses. The daily energy intake was calculated using the food composition table of the Food Dietary Guidelines for the Ecuadorian population (GABA) (54). Analyses of calorie intake and estimated energy requirements (EER), according to the age-, sex-, weight-, height- and physical activity level-specific equations were included in our study (51,52).

Relative humidity

The mean annual relative humidity (%) of urban area for 2012 was obtained from the National Institute for Meteorology and Hydrology INAMHI (112), and was used as a proxy for relative humidity at the participants' city of residence in order to assess the long-term association of ambient humidity with metabolic dysfunction. Areas above 80% were categorized as high relative humidity and the rest as low humidity areas. This categorization was based on the assumption that relative humidity above 80% is considered as high and causes thermal discomfort and adverse health outcomes in hot-humid tropics (128, 129, 51), as in the case in Ecuador.

Metabolic Syndrome

The diagnosis of MetS was based on the harmonized guidelines of the National Cholesterol Education Program Adult Treatment Panel III and the Latin American Diabetes Association as the presence of three or more of the following components: waist circumference (men ≥94 cm, women ≥88), blood pressure (systolic ≥130 mmHg and/or diastolic ≥85 mmHg), HDL cholesterol (men <40 mg/dL and women <50 mg/dL), elevated triglycerides (≥150 mg/dL), or fasting glucose (≥100 mg/dL).

Statistical Analyses

All analyses were stratified by sex and relative humidity, with data presented as percentages or means with standard errors depending on the type of analysis. Differences in groups were compared using Chi-square and t-tests depending on the variable that was analyzed. Odds ratios (OR) and 95% confidence intervals (CIs) for MetS across the relative humidity groups were estimated using multiple logistic regression analysis. In the regression model, general and sociodemographic variables (age, ethnicity, economic status, and education level), anthropometric measurements (BMI, except for the model of waist circumference), lifestyles (physical activity, current alcohol consumption, current smoking, and total energy intake), elevation of residence, and menopausal status were considered. Statistical significance was defined as p-value < 0.05 in a two-tailed manner. Statistical analyses were performed using the PROC SURVEY procedures of SAS version 9.4 software (92).

3-3. Results

The analyzed characteristics of the participants according to sex and relative humidity are shown in Table 3-1. The mean age of participants was 34.6 ± 0.44 (SE) for men and 35.2 ± 0.35 years of age for women. A significant difference between groups was found in the following variables: ethnicity, economic status, education level, physical activity, elevation, and ambient temperature of residence ($p < 0.05$). However, age and smoking were significantly different in women only ($p = 0.0332$, $p <.0001$, respectively).

Table 3-1. Descriptive characteristics of participants according to relative humidity of residence

	Men			Women		
	Low relative humidity	High relative humidity	p-value	Low relative humidity	High relative humidity	p-value
Number of people, N (%)	869 (44.2)	1095 (55.8)		1525 (37.6)	2535 (62.4)	
Age, years, N (%)			0.744			0.0332
20-29	305 (38.5)	400 (38.7)		498 (33.5)	923 (39.6)	
30-39	292 (29.6)	367 (28.7)		544 (30.3)	913 (30.0)	
40-49	198 (20.9)	249 (19.5)		397 (25.5)	595 (20.5)	
50-59	74 (11.0)	79 (13.1)		86 (10.7)	104 (9.9)	
Ethnicity, N (%)			<.0001			0.0003
Mestizo	802 (88.2)	937 (73.4)		1397 (86.4)	2186 (79.0)	
Others	67 (11.8)	158 (26.6)		128 (13.6)	349 (21.0)	
Family economic status [a], N (%)			<.0001			<.0001
Low	191 (21.3)	342 (32.9)		400 (22.8)	835 (33.6)	
Middle	391 (44.4)	542 (49.6)		637 (40.6)	1245 (49.7)	
High	287 (34.3)	211 (17.5)		488 (36.6)	455 (16.7)	
Education level, N (%)			0.0004			<.0001
Primary school	217 (22.9)	290 (28.9)		415 (24.3)	716 (32.6)	
Secondary school	395 (48.4)	569 (52.5)		694 (47.3)	1218 (45.4)	
College or higher	257 (28.7)	236 (18.6)		416 (28.4)	601 (22.0)	
Current alcohol consumption [b], N (%)			0.2684			0.9006
Yes	478 (56.6)	631 (59.9)		392 (25.7)	672 (25.4)	
No	391 (43.4)	464 (40.1)		1133 (74.3)	1863 (74.6)	
Current smoking [c], N (%)			0.1086			<.0001
Yes	303 (30.9)	350 (26.5)		114 (8.1)	118 (3.5)	
No	566 (69.1)	745 (73.5)		1411 (91.9)	2417 (96.5)	
Physical activity [d], N (%)			0.0432			0.0007
Yes	394 (44.7)	456 (38.6)		276 (20.0)	400 (14.2)	
No	475 (55.3)	639 (61.4)		1249 (80.0)	2135 (85.8)	
Environmental conditions (mean ± SE)						
Elevation (masl)	1345.7 ± 58.6	703.1 ± 45.8	<.0001	1456.8 ± 48.9	650.7 ± 28.7	<.0001
Temperature (°C)	20.4 ± 0.2	22.6 ± 0.2	<.0001	20 ± 0.2	22.7 ± 0.1	<.0001

[a] Low (Q1 and Q2), Middle (Q3 and Q4) and High (Q5) according to the Wealth Index; [b] "Yes" alcoholic beverage consumption in the past 30 days; [c] "Yes" cigarette smoking in the past 30 days; [d] "Yes" vigorous-intensity activities performance for at least 1 hr. 15 min, or moderate-intensity activities for at least 2hr. 30 min, during the past seven days; masl, meters above sea level.

Table 3-2. shows that men had higher levels of blood pressure, total cholesterol, triglycerides, and energy intake whereas women had higher BMI and EER (%). BMI was significantly different in women in the high relative humidity group only (p = 0.0461). Both sexes showed higher HDL cholesterol in high relative humidity (men p = 0.0278; women p = 0.0146). Additionally, in the high relative humidity sex groups, a significant increase of energy intake and EER (%) was observed (p < 0.05).

Table 3-2. Anthropometry, biomarkers of MetS and energy intake by relative humidity of residence

	Men			**Women**		
	Low relative humidity (869)	**High relative humidity (1095)**	**p-value**	**Low relative humidity (1525)**	**High relative humidity (2535)**	**p-value**
Anthropometric and biochemical variable (mean ± SE)						
BMI (kg/m2)	26.5± 0.2	26.8 ±0.2	0.4684	27.2 ±0.2	27.6 ±0.2	0.0461
Waist circumference (cm)	94.7± 2.2	95.6± 2.4	0.7722	98.3 ±3.7	91.5 ±1.3	0.0796
SBP (mmHg)	125.1± 2.1	123.9± 1.7	0.6468	116.3 ±1.3	115.6 ±0.9	0.6341
DBP (mmHg)	79.9± 2.2	79.0± 1.7	0.7634	73.7 ±1.3	72.3 ±0.8	0.3956
Fasting glucose (mg/dL)	93.8± 1.2	95.2± 1.9	0.5249	92.7 ±0.8	93.0 ±1.1	0.8312
Total cholesterol (mg/dL)	186.7± 1.8	184.8± 1.8	0.4416	181.4 ±1.3	178.3±1.3	0.0899
HDL cholesterol (mg/dL)	40.6± 0.5	42.2± 0.6	0.0278	45.5 ±0.5	47.0 ±0.4	0.0146
LDL cholesterol (mg/dL)	112.2± 1.5	110.4± 1.5	0.3928	108.9 ±1.1	108.7±1.0	0.8622
Triglyceride (mg/dL)	179.2± 5.5	169.4± 6.7	0.2589	129.7 ±3.2	122.2 ±2.3	0.0541
Macronutrient intake (mean ± SE)						
Energy (kcal)	2123.8±20.2	2210.5±20.8	0.0028	1826.9±15.1	1868.5±14.3	0.0463
EER (%)	81.6±1.0	86.1±1.0	0.0033	97.1±0.9	99.8±0.9	0.0364

BMI, body mass index; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; EER, estimated energy requirement.

The prevalence and ORs for MetS according to relative humidity are presented in Table 3-3. Living in high relative humidity had effects on women only; they showed significant ORs of having reduced HDL cholesterol (1.25; 95% CI: 1.06-1.56) and MetS (OR=1.20; 95% CI: 1.01-1.42) after adjusting for confounders.

Table 3-3. Prevalence and adjusted odds ratio (95% confidence intervals) for MetS by relative humidity of residence

	Men		Women	
	Low relative humidity (n=869)	**High relative humidity (n=1095)**	**Low relative humidity (n=1525)**	**High relative humidity (n=2535)**
Increased waist circumference				
Prevalence (%)	34.00	19.17	41.14	25.62
OR (95% CI)	1.00 (ref)	1.13 (0.85-1.48)	1.00 (ref)	1.21 (0.95-1.53)
Elevated blood pressure				
Prevalence (%)	18.50	9.99	8.85	5.35
OR (95% CI)	1.00 (ref)	0.96(0.71-1.28)	1.00 (ref)	1.02 (0.75-1.38)
Reduced HDL cholesterol				
Prevalence (%)	33.34	16.33	25.55	38.69
OR (95% CI)	1.00 (ref)	0.87 (0.66-1.13)	1.00 (ref)	1.25 (1.06-1.56)
Elevated triglycerides				
Prevalence (%)	30.98	14.22	16.96	9.30
OR (95% CI)	1.00 (ref)	0.80 (0.61-1.06)	1.00 (ref)	0.87 (0.68-1.11)
Elevated fasting glucose				
Prevalence (%)	9.24	7.13	9.31	5.73
OR (95% CI)	1.00 (ref)	1.20 (084-1.70)	1.00 (ref)	0.83 (0.61-1.12)
Metabolic syndrome				
Prevalence (%)	24.13	12.41	11.53	17.73
OR (95% CI)	1.00 (ref)	0.84 (0.61-1.14)	1.00 (ref)	1.20 (1.01-1.42)

All values accounted for the complex sampling design effect using PROC SURVEY procedure. OR, odd ratio; CI, confidence interval; HDL, high-density lipoprotein. The multiple logistic regression analysis was adjusted for age, ethnicity, family economic status, education level, BMI (except for the model of waist circumference), physical activity, alcohol consumption, smoking, energy intake and resident elevation.

Table 3-4 shows that current alcohol consumption and smoking enhanced increase of ORs of reduced HDL cholesterol and elevated triglycerides in women residing in high humidity (compared to Table 3). Interestingly, physically active men living in high relative humidity showed significant lower OR of elevated triglycerides (0.59; 95% CI: 0.37-0.85).

Table 3-4. Odds ratios for MetS among residents living in high relative humidity according to lifestyle factors

	Men				**Women**			
	Yes (95% CI)	**p-value**	**No (95% CI)**	**p-value**	**Yes (95% CI)**	**p-value**	**No (95% CI)**	**p-value**
Current alcohol consumption								
Increased waist circumference	1.18 (0.81±1.73)	0.3817	0.99 (0.65±1.51)	0.9757	1.58 (0.99±2.51)	0.0552	0.93 (0.70±1.25)	0.6386
Elevated blood pressure	1.09 (0.78±1.53)	0.6478	1.03 (0.69±1.54)	0.9025	0.83 (0.50±1.37)	0.1115	1.02 (0.78±1.34)	0.8161
Reduced HDL cholesterol	0.86 (0.58±1.27)	0.4400	0.77 (0.48±1.23)	0.2400	1.31 (1.01±1.69)	0.0350	0.99 (0.65±1.53)	0.9746
Elevated triglycerides	0.76 (0.52±1.10)	0.1464	0.78 (051±1.19)	0.2487	0.88 (0.49±1.56)	0.4711	1.03 (0.80±1.34)	0.8119
Elevated fasting glucose	1.09 (0.70±1.73)	0.6922	1.60 (0.94±2.70)	0.0785	0.54 (0.27±1.06)	0.0735	0.95 (0.68±1.33)	0.7663
Metabolic syndrome	0.87 (0.60±1.32)	0.4988	0.88 (0.54±1.41)	0.7616	0.79 (0.47±1.33)	0.3849	1.16 (0.87±1.54)	0.3078
Current smoking								
Increased waist circumference	1.24 (0.78±1.96)	0.3684	1.19 (0.86±1.64)	0.3030	1.43 (0.90±2.28)	0.1290	0.56 (0.21±1.50)	0.2464
Elevated blood pressure	0.56 (0.36±0.87)	0.0101	0.87 (0.61±1.25)	0.4605	0.89 (0.27±2.95)	0.8537	0.91 (0.69±1.19)	0.4910
Reduced HDL cholesterol	0.89 (0.57±1.38)	0.5916	0.99 (0.73±1.36)	0.9612	1.95 (1.30±2.93)	0.0013	1.08 (0.83±1.39)	0.5484
Elevated triglycerides	1.00 (0.63±1.59)	0.9877	0.78 (0.56±1.16)	0.1177	0.41 (0.15±1.07)	0.0681	1.07 (0.86±1.33)	0.5359
Elevated fasting glucose	1.21 (0.62±2.36)	0.5720	0.88 (0.60±1.29)	0.5017	0.66 (0.12±3.60)	0.6278	0.81 (0.61±1.08)	0.1480
Metabolic syndrome	1.03 (0.64±1.65)	0.9118	1.05 (0.67±1.66)	0.7658	0.35 (0.11±1.05)	0.0623	1.09 (0.82±1.47)	0.4500
Physical activity								
Increased waist circumference	0.98 (0.60±1.61)	0.9300	1.37 (0.85±2.20)	0.1937	0.83 (0.44±1.58)	0.5655	1.15 (0.88±1.47)	0.2747
Elevated blood pressure	1.04 (0.70±1.55)	0.7428	1.13 (0.80±1.60)	0.4095	0.69 (1.05±1.13)	0.3457	1.06 (0.78±1.43)	0.7264
Reduced HDL cholesterol	0.94 (0.64±1.38)	0.7484	0.86 (0.58±1.26)	0.4387	1.28 (0.77±2.12)	0.3349	1.20 (0.97±1.48)	0.0975
Elevated triglycerides	0.59 (0.37±0.85)	0.0067	0.94 (0.64±1.38)	0.7556	0.88 (0.49±1.59)	0.6650	1.01 (0.80±1.28)	0.9145
Elevated fasting glucose	1.16 (0.65±2.08)	0.6210	0.84 (0.55±1.27)	0.4022	0.96 (0.42±2.24)	0.9325	0.79 (0.59±1.06)	0.1125
Metabolic syndrome	0.87 (0.54±1.45)	0.5708	0.79 (0.52±1.22)	0.2860	1.03 (0.55±1.91)	0.9368	1.23 (1.02±1.48)	0.0301
	High ^{a} (95% CI)	p-value	Low (95% CI)	p-value	High ^{a} (95% CI)	p-value	Low (95% CI)	p-value
% EER								
Increased waist circumference	0.91 (0.45±1.87)	0.8163	1.24 (0.85±1.80)	0.2672	1.35 (0.98±1.86)	0.0645	0.85 (0.60±1.18)	0.3307
Elevated blood pressure	1.06 (0.52±2.15)	0.6800	1.11 (0.81±1.52)	0.5308	1.18 (0.78±1.78)	0.5875	0.96 (0.71±1.32)	0.3117
Reduced HDL cholesterol	0.96 (0.46±1.99)	0.4993	0.77 (0.53±1.13)	0.2813	1.06 (0.77±1.63)	0.6920	1.32 (0.99±1.79)	0.0578
Elevated triglycerides	0.86 (0.39±1.87)	0.8164	0.82 (0.50±1.06)	0.1985	0.88 (0.66±1.64)	0.4841	1.05 (0.80±1.41)	0.7065
Elevated fasting glucose	0.88 (0.43±1.80)	0.7201	1.01 (0.68±1.56)	0.9564	0.85 (0.55±1.30)	0.4597	0.77 (0.53±1.11)	0.1605
Metabolic syndrome	0.81 (0.33±1.92)	0.6444	0.91 (0.65±1.28)	0.5948	0.91 (0.64±1.29)	0.6005	1.22 (0.91±1.65)	0.1808

ORs were calculated based on low relative humidity residents (reference). ^{a} high (>100%) or low (≤100%) for EER; CI, confidence interval; HDL high-density lipoprotein; EER, estimated energy requirement.

Additionally, OR for MetS in women according to their menopausal status and relative humidity of residence are presented in Table 3-5. Menopausal women living in high relative humidity showed increased ORs of MetS (5.42; 95% CI: 1.92-15.27), elevated blood pressure (3.10; 95% CI: 1.15-8.35), and increased waist circumference (OR=1.34; 95% CI: 1.09-1.63) compared to women without menopause.

Table 3-5. Odds ratios for MetS among women living in high relative humidity according to menopausal stage.

	Women (n=4060)			
	Yes (95% CI)	**p-value**	**No (95% CI)**	**p-value**
Menopausal stage				
Increased waist circumference	1.34 (1.09±1.63)	0.0045	0.22 (0.02±3.04)	0.2550
Elevated blood pressure	3.10 (1.15±8.35)	0.0253	0.80 (0.60±1.07)	0.1382
Reduced HDL cholesterol	1.48 (0.59±3.74)	0.4064	1.13 (0.93±1.37)	0.2243
Elevated triglycerides	2.37 (0.96±5.90)	0.0627	0.87 (0.70±1.08)	0.2130
Elevated fasting glucose	0.90 (0.31±2.64)	0.8510	0.81 (0.61±1.08)	0.1442
Metabolic syndrome	5.42 (1.92±15.27)	0.0015	0.89 (0.71±1.12)	0.3177

ORs were calculated based on low relative humidity residents (reference). CI, confidence interval; HDL high-density lipoprotein.

3-4. Discussion

This study showed a positive association between relative humidity and MetS as well as reduced HDL cholesterol in women. Menopausal women living in high relative humidity showed higher ORs of MetS, elevated blood pressure, and increased waist circumference. Moreover, physically active men living in high relative humidity had lower OR of elevated triglycerides compared to physically inactive men living in the same humidity. To our knowledge, this is the first study to suggest that relative humidity is associated with MetS in an adult population, using nationally representative data.

The prevalence of MetS in adult Ecuadorians shows similar trends with other Latin American countries and the USA (123,51). However, higher OR of MetS in populations living in high relative humidity has never been reported before. An approximation to this finding could be observed in a study in the USA, where high relative humidity states presented a higher prevalence of MetS, obesity, and DM2 (51).

To further explore our findings, we performed additional analyses of MetS abnormalities, lifestyle patterns and relative humidity. In Women who reside in high relative humidity, consume alcohol, and smoke, higher OR of reduced HDL cholesterol and physical inactivity increased the OR of MetS. These lifestyle factors could play moderating roles in MetS. Apart from the lack of previous studies on relative humidity and MetS, complementary research has investigated the effect of physical environment (i.e., humidity, temperature, elevation, radiation, etc.) on people’s health (130-133,124). It was found that disparities in ambient temperature and relative humidity are associated with CVD (131), myocardial infarction morbidity and mortality (134,135), acute coronary syndrome (136,137), and DM2 (50).

Ecuador has four different geographical regions. The coast and the Galapagos Islands have the highest prevalence of MetS (35.0% and 41.9%) while the highlands and the Amazon have a prevalence of 29.9% and 26.6%, respectively (23). Each region has different environmental conditions and climatological patterns. According to Köppen’s climate classification, Ecuador has 11 different types of microclimates ranging from Tropical to Oceanic. Ecuador is situated on the equatorial line, and thus produces little seasonality throughout the year: a warm rainy season lasts from January to April, with a cool and dry season from May through December (138). The mean annual humidity in the coastal region is around 65% while in the Amazon it is around 85% (127). The effects of high air humidity on human health are still controversial (139), and whether these climatological patterns may trigger MetS is difficult to answer here.

In order to identify a difference between sex, we analyzed sex and relative humidity individually. It was found that women living in high relative humidity had higher ORs of MetS and low HDL cholesterol. These pathophysiological differences may be explained by the effects of sexual hormones on the human body physiology (140,141). The metabolism of lipids is modulated by endogenous sex hormones that might cause insulin resistance and abnormalities in the lipid profile (142). Additionally, menopausal stage increased ORs of MetS, elevated blood pressure, and increased waist circumference in women living in high relative humidity compared to non-menopausal women living at the same humidity levels, indicating sex hormones may explain these differences. Several studies also revealed that menopause is associated with an increased risk of MetS and its components, which support our outcomes (143-145).

Energy intake differed by sex and relative humidity ($p < 0.05$). This association suggested a regulatory role of hormones on appetite regulation and the onset of metabolic abnormalities. In contrast with our findings, other studies reported that exposure to high ambient temperatures and humidity under resting conditions caused poor appetite and reduced energy intake (146,147), which may be explained by some physiological factors such as reduced digestive enzyme activity and metabolic rate decrease (148).

Moreover, it has been proposed that an increase in relative humidity is associated with physical activity impairment (149,150). Our findings indicate that physical activity is inversely associated with MetS and elevated triglycerides, similar to other studies that have shown a positive impact with exercise on cholesterol and triglyceride profile, abdominal obesity, and DM2 (151,66). Several studies have described the benefits of physical activity on MetS and its components. However, the measurement of physical activity becomes difficult due to the use of different methods; thus, this should be considered when interpreting our results.

Alcohol consumption and current smoking were also associated with reduced HDL cholesterol in women living in high relative humidity areas. Some studies have shown that alcohol consumption has negative effects on the metabolism of glucose, cholesterol and triglycerides (152,153). In addition, smoking has been shown to alter the lipids and lipoprotein metabolism. Smokers have also shown lower adjusted levels of HDL cholesterol than nonsmokers (154,155).

This study must be interpreted considering the following limitations. First, among initial participants (n = 11,044), physical activity data was collected only for the urban population; thus, we excluded the rural residents (n =4,166) and others (n = 854), resulting in a total of 6,024 urban participants included for this study. Therefore, we cannot exclude the possibility of residual bias, and our results should be interpreted with caution. Second, casual inferences were excluded due to its cross-sectional design. Third, we could not infer the individual's usual energy intake using a 1-day 24-hour dietary recall. Forth, missing data on leptin and/or irisin concentration, which may help to better elucidate the association between humidity and MetS, is another limitation of the study. Therefore, further studies in the fields of human biology and environment are needed to determine the influence of relative humidity on MetS in the adult population. Despite of these limitations, we utilized data from the ENSANUT-ECU 2012 which was conducted in a nation-wide scale across the entire country, using standardized protocols and instruments and is the only survey collecting all the required biomarkers for the diagnosis of MetS. Moreover, to our knowledge this is the first study determining the association of relative humidity with MetS in a nationally representative population sample.

3-5. Conclusions

Our study suggests that living in high relative humidity (> 80%) increases ORs of MetS and reduced HDL cholesterol in women. Furthermore, menopausal status enhances increase in OR of MetS and augments ORs of elevated blood pressure and increased waist circumference, while performing physical activity decreases OR of elevated triglycerides in men. These findings come from nation-wide data and highlight the importance of management of relative humidity and lifestyles in Ecuadorians. Intersectoral programs aimed at controlling relative humidity in homes and work environments, providing nutritional education and menopause care, and increasing physical activity are needed to promote healthy life conditions and prevent metabolic disorders.

Chapter 4. Association of carbohydrate and fat intake with prevalence of metabolic syndrome can be modified by physical activity and physical environment in Ecuadorian adults: the ENSANUT-ECU study[3]

Abstract

The associations of lifestyle and environment with metabolic syndrome (MetS) and cardiovascular disease have recently resulted in increased attention in research. This study aimed to ex-amine interactive associations among carbohydrate and fat intake, physical environment (i.e. elevation and humidity), lifestyle, and MetS among Ecuadorian adults. We utilized data from the Ecuador National Health and Nutrition Survey 2012 (ENSANUT-ECU), with a total of 6,023 participants aged 20 to 60 years included in this study. Logistic regression was used to determine the association of status of carbohydrate and fat intake, low-carbohydrate high-fat diet (LCHF) and medium -carbohydrate and -fat (MCF) diet with MetS, where the high-carbohydrate low-fat (HCLF) diet was used as a reference. Women with LCHF and MCF diets showed lower prevalence of increased blood pressure (OR=0.34, 95% CI:0.19–0.59; OR=0.50, 95% CI: 0.32-0.79, respectively). Women with MCF diet also showed lower prevalence of elevated fasting glucose (OR=0.58, 95% CI: 0.37-0.91). Moreover, there were negative associations between MetS and reduced HDL cholesterol in women with MCF diet residing in low relative humidity (OR=0.66, 95% CI: 0.45-0.98) and in women with LCHF diet residing at a high elevation (OR=0.37, 95% CI: 0.16-0.86). Additionally, higher prevalence of increased waist circumference was observed in men with both MFC and LCHF diets who were physically inactive (OR=1.89, 95% CI: 1.12-3.20; OR=2.34, 95% CI: 1.19-4.60, respectively) and residing in high relative humidity (OR=1.90, 95% CI: 1.08-2.89; OR=2.63, 95% CI: 1.32-5.28, respectively). Our findings suggest that LCHF intake is associated with lower blood pressure, while MCF intake is associated with lower blood pressure and fasting glucose in Ecuadorian women. Furthermore, the associations of carbohydrate and fat intake with prevalence of MetS can be modified by physical activity, relative humidity, and elevation. The obtained outcomes may provide useful information for health programs focusing on dietary intake and lifestyle according to physical environment of the population to promote health and prevent metabolic diseases.

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[3] This study was published in Nutrients vol. 13, 1834 in May 2021.

4.1 Introduction

Metabolic syndrome (MetS), characterized by the presence of hyperglycemia, hypertension, hypertriglyceridemia, low high-density lipoprotein cholesterol (HDL), and abdominal obesity, is a major public health problem (62). Over a billion people worldwide is estimated to have MetS (22); and in most developing countries, MetS represents one of the largest contributors to the global burden of type 2 diabetes mellitus (DM2) and cardiovascular disease (CVD) (156,21). Like to other Latin American countries, Ecuador reports a 31.2% prevalence of MetS and 85% of the total population has at least one of its abnormalities (23). In 2019, DM2 and CVD constituted the first causes of mortality in Ecuadorian adults (6.5% and 6.2%, respectively) (16). Thus, it is urgent to identify potential determinants of MetS development in Ecuador for better strategies to prevent MetS onset, as well as its subsequent diseases.

Complex interactions between genetics, physical environment (i.e. elevation and humidity), and health-related lifestyles have been identified to lead to onset of MetS, though exact causes remain unknown (157,158,66,29). In reference to environmental and lifestyle factors, low elevation (<2000 masl), high relative humidity (>80%), inadequate food intake, alcohol consumption, tobacco smoking, and physical inactivity have been reported as risk factors for MetS development (159,158 28, 71,29). However, an extensive investigation between dietary intake and cardiovascular disease has not yet been assessed among Ecuadorians, most data in healthy population come from research in high-income countries, where findings on this topic are yet controversial (160-162, 61).

Recent scientific evidence on health benefits of low-carbohydrate high-fat (LCHF) diets focusing on weight loss and decrease of risk of CVD, make many people intentionally change their carbohydrate and fat intake patterns. Several meta-analyses of randomized con-trolled clinical trials (RCTs) revealed that low-carbohydrate diet resulted in reduction of body weight and positive changes in triglycerides and high-density lipoprotein (HDL) levels, although a low-carbohydrate diet increased low-density lipoprotein (LDL) levels (162,163). However, another meta-analysis of RCTs showed that weight loss, blood pressure, or lipid profile were not significantly different in populations with low-carbohydrate and energy balanced diets (55); which suggest the effect of low-carbohydrate diet on MetS and/or CVD is still controversial. Furthermore, most of these investigations focusing on dietary patterns and MetS involved adults from the US and European countries; and a few studies have been conducted in Latin American populations (164,165). One study on the Brazilian population found that lower protein and higher carbohydrate intakes were related to lower HDL levels and higher risk of hypertriglyceridemia in women (166).

These worldwide findings indicate that the associations between LCHF diet and metabolic disorders may fluctuate in terms of sociodemographic characteristics, lifestyles, and environmental conditions of the populations; thus, there is a need to investigate interactive associations among various dietary factors and environmental conditions in various populations. In this context, we aimed to examine the associations between carbohydrate and fat intake and MetS according to health-related lifestyles and physical environment among Ecuadorian adults.

4-2. Subjects and Methods

Study Design

The present study used data from the Ecuador National Health and Nutrition Survey (ENSANUT-ECU) 2012, a nation-wide cross-sectional survey conducted by Ecuador's Ministry of Public Health. The ENSANUT-ECU collected information on sociodemographic status, health-risk and food consumption, and anthropometry, blood pressure, and blood biomarkers. Detailed explanations of ENSANUT-ECU are available elsewhere (18).

Subjects

Participants in this study were Ecuadorian adults from ages 20 to 60 years who completed a dietary recall survey as well as anthropometric and biochemical measurements which related to MetS (11,044 participants). Participants with missing information on physical activity (n=4,166) and lifestyles (n=494), or participants who took medication for hyper-tension and other diseases (n=361) were excluded. Thus, the final 6,023 Ecuadorian adults (1,964 men and 4,059 women) were selected for this study.

General characteristics

The sociodemographic data of participants including sex, age, ethnicity, education, and family economic status were obtained by using the standardized questionnaire for housing information. Ethnicity was classified as mestizo (Amerindian with European mix) and others (i.e. Amerindian, montubio, Afro-Ecuadorian, and white); education as primary (<= 7th grade), secondary (7th grade < -- <=12 the grade), and college or higher; and family economic status was categorized as low (first and second quintile), middle (third and fourth quintiles), or high (fifth quintile).

Physical Environmental Conditions

Information on elevation of residence was collected in the housing questionnaire of EN-SANUT. It was obtained through georeferencing; elevation was divided in two groups, high elevation for residence over 2000 masl and low elevation for residence under 2000 masl (86,87). The data on relative humidity (%) in

2012 of the participant's residence was obtained from the National Institute for Meteorology and Hydrology (127). According to previous studies, high relative humidity was established if residence was above 80% and low relative humidity below 80% (50,129).

Health-related Lifestyles

According to the United States National Survey on Drug Use and Health [29] and the ENSANUT-ECU, current alcohol consumption and smoking were determined as "yes" if the participant had drunk alcoholic beverages and smoked in the past 30 days of data collection. Physical activity was defined as "yes" if the participant had performed vigorous-intensity activity for at least 75 min, moderate-intensity activity for at least 150 min, or both for the past 7 days prior to the collection of data, and "no" for any activity that that took less than 75 min (89).

Dietary Assessment

Participants' intake of macronutrients (such as carbohydrate, protein, and fat) were esti-mated from the information on all foods and beverages they consumed a day collected by 24-hour recall method. Macronutrient intake was calculated using the food composition table of the Food Dietary Guidelines for the Ecuadorian population (GABA) (54). Participants were divided into three groups based on their macronutrient intake data: LCHF (energy from carbohydrate <45% and >30% from fat), HCLF (energy from carbohydrate >65% and <20% from fat), and MCF (45% to 65% of energy from carbohydrate and 20% to 30% from fat)) [163]. The adequacy of energy intake was evaluated through percentages of estimated energy requirements (EER), in accordance with the age-, sex-, weight-, height- and physical activity level-specific equations (90,91).

Metabolic Syndrome

Participants' height, weight, waist circumference, and blood pressure were measured twice at their residences by trained technicians utilizing standardized procedures (167). The mean of the readings was used for this study. Body mass index (BMI) was calculated from weight and height data (kg/m2). Fasting glucose, total cholesterol, HDL cholesterol, and triglyceride levels were measured from blood samples of participants who fasted for at least 8h before examination. Blood samples were measured using an enzymatic-colorimetric assay Modular Evo-800 (Roche Diagnostics) and Friedewald's formula was used to calculate LDL-cholesterol (85) The detailed laboratory procedures of ENSANUT-ECU are available elsewhere (18).

The subjects with MetS were identified when they had three or more of the following components: (1) waist circumference (men ≥94 cm, women ≥88), (2) blood pressure (systolic ≥130 mmHg and/or diastolic

≥85 mmHg), (3) HDL cholesterol (men <40 mg/dL and women <50 mg/dL), (4) elevated triglycerides (≥150 mg/dL), and (5) elevated fasting glucose (≥100 mg/dL). The diagnosis criteria were based on the National Cholesterol Education Program Adult Treatment Panel III and the Latin American Diabetes Association (168,169).

Statistical Analyses

All analyses were stratified by sex and status of carbohydrate and fat intake (LCHF, HCLF, MCF). All continuous variables were presented as means with standard errors (SE), and categorical variables were presented as percentages. Differences in groups were compared using chi-square and ANOVA depending on the variable analyzed. The adjusted means and SE of the anthropometric and biochemical variables according to the diet type were estimated using a generalized linear model after adjusting for ethnicity, family economic status, education level, elevation, BMI (except for the model of waist circumference), and total energy intake. Odds ratio (ORs) and 95% confidence intervals (CIs) for MetS accord-ing to diet type were estimated using multiple logistic regression analysis after adjusting for confounding variables, including ethnicity, family economic status, education level, elevation, relative humidity, BMI (except for the model of waist circumference), and total energy intake. Statistical analyses were performed using Statistical Analysis Systems (SAS) software version 9.4 (92) applying the PROC SURVEY procedure. All *p*-values were two-tailed and a p-value of < 0.05 was considered statistically significant.

4-3. Results

Table 4-1 shows the general characteristics of the study participants by sex and carbohydrate and fat intake according to carbohydrate and fat content. The mean age for men was 34.6 ± 0.44 (SE) and 35.2 ± 0.35 years for women. Ethnicity, household income, education level, and elevation of residence were significantly different between both groups ($p < 0.05$). However, relative humidity was significantly different in women only ($p = 0.0004$).

Table 4-1. Demographic and health-related lifestyle characteristics of study participants by carbohydrate and fat dietary intake

	Men				Women			
Variables	LCHF	MCF	HCLF	p-value[a]	LCHF	MCF	HCLF	p-value
Number of people, N (%)	330(16.8)	1410 (71.8)	224 (11.4)		797 (19.7)	2907 (71.6)	355 (8.7)	
Age, years, N (%)				0.7632				0.1004
20-29	121 (39.7)	514 (39.2)	70 (33.9)		255 (32.4)	1051 (37.1)	115 (33.7)	
30-39	106 (27.6)	468 (28.5)	85 (36.0)		293 (32.9)	1024 (28.9)	139 (33.0)	
40-49	80 (21.4)	317 (20.6)	50 (17.8)		222 (27.3)	691 (23.2)	79 (19.3)	
50-59	23 (11.3)	111 (11.7)	19 (12.3)		27 (7.4)	141 (10.8)	22 (14.0)	
Ethnicity, N (%)				0.0917				**0.0486**
Mestizo	304 (88.9)	1247 (82.3)	188 (79.4)		723 (87.2)	2562 (83.4)	298 (77.5)	
Others	26 (11.1)	163 (17.7)	36 (20.6)		74 (12.8)	345 (16.6)	57 (22.5)	
Family economic status [b], N (%)				**<.0001**				**<.0001**
Low	55 (11.7)	388 (26.7)	90 (35.7)		174 (18.1)	897 (26.8)	164 (45.9)	
Middle	133 (37.7)	695 (47.4)	105 (51.0)		350 (39.5)	1390 (45.5)	151 (42.9)	
High	142 (50.6)	327 (25.9)	29 (13.3)		273 (42.4)	630 (27.7)	40 (11.2)	
Education level, N (%)				**<.0001**				**<.0001**
Primary school	59 (18.9)	354 (23.4)	94 (43.0)		173 (21.8)	828 (27.2)	130 (41.4)	
Secondary school	147 (39.1)	714 (53.2)	103 (44.5)		369 (44.7)	1368 (47.2)	174 46.1)	
College or higher	124 (42.0)	342 (23.4)	27 (12.5)		255 (33.5)	711 (25.6)	51 (12.5)	
Current alcohol consumption [c], N (%)				0.8775				0.4129
Yes	190 (58.7)	784 (57.8)	135 (55.7)		235 (27.2)	753 (25.6)	76 (21.7)	
No	140 (41.3)	626 (42.2)	89 (44.3)		562 (72.8)	2154 (74.4)	279 (78.3)	
Current smoking [d], N (%)				0.1374				0.1013
Yes	125 (33.3)	467 (29.6)	61 (22.6)		56 (7.1)	165 (6.7)	11 (2.4)	
No	205 (66.7)	943 (70.4)	163 (77.4)		741 (92.9)	2742 (93.3)	344 (97.6)	
Physical activity [e], N (%)				0.8032				0.5826
Yes	147 (44.0)	608 (42.0)	95 (44.6)		138 (19.2)	478 (17.7)	59 (15.5)	

No	183 (66.0)	802 (58.0)	129 (55.4)		659 (80.8)	2429 (82.3)	296 (84.5)	
Elevation [f], N (%)				**<.0001**				**<.0001**
High	167 (52.8)	557 (38.3)	59 (25.4)		367 (51.3)	1014 (38.0)	88 (26.5)	
Low	163 (47.2)	853 (61.7)	165 (74.6)		430 (48.7)	1893 (62.0)	267 (73.5)	
Humidity [g], N (%)				0.1431				**0.0004**
High	173 (30.5)	783 (34.5)	139 (59.0)		443 (30.6)	1843 (38.4)	249 (47.7)	
Low	157 (69.5)	627 (65.5)	85 (41.0)		354 (69.4)	1064 (61.6)	106 (52.6)	

Abbreviations: Low-Carbohydrate High-Fat (LCHF); Medium Carbohydrate and Fat (MCF); High-Carbohydrate Low-Fat (HCLF)

[a] Based on χ^2 test for categorical variables and ANOVA for continuous variables.

[b] Household income was categorized as low (first and second quintiles), middle (third and fourth quintiles), or high (fifth quintile).

[c] Alcohol consumption was defined as "yes" for the consumption of alcoholic beverages over the past 30 days.

[d] Current smoking was defined as "yes" for cigarette smoking over the past month.

[e] Physical activity was defined as "yes" when performing vigorous activities for at least 75 min or moderate activities for at least 150 min over the past 7 days.

[f] Elevation was defined as "high" residence was ≥ 2001 masl.

[g] Humidity > 80% was classified as "high".

Table 4-2 shows anthropometric and biochemical measurements for MetS components and macronutrient intakes. Blood pressure, total cholesterol, triglycerides, and energy intake were higher in men, but BMI and EER (%) were higher in women. Significant differences between diet groups were observed in BMI, systolic blood pressure, diastolic blood pressure, and HDL cholesterol in both sexes ($p<0.05$), while in men, waist circumference was significantly different ($p<0.0001$) and in women, fasting glucose, total cholesterol, LDL cholesterol and triglycerides ($p=0.0126$, $p=0.0002$, $p<0.0001$, $p=0.0008$, respectively). Moreover, men and women with HCLF diets showed a higher energy intake and EER (%) ($p<0.001$, both). Mean contribution rate to energy of carbohydrate, protein, and fat comprised 42.2%, 15.6%, 38.3% in men with LCHF, and 40.7%, 15.9%, 39.3% in women with LCHF.

Table 4-2. Anthropometric and biochemical measurements of MetS and macronutrient intake of participants according to carbohydrate and fat intake

	Men				Women			
Variables	LCHF	MCF	HCLF	p-value	LCHF	MCF	HCLF	p-value
	(330)	(1410)	(224)		(797)	(2907)	(355)	
Anthropometric and biochemical variables (mean ± SE)								
BMI (kg/m2)	26.3± 0.4	26.8±0.2	26.1 ±0.4	**0.0433**	27.1 ±0.3	27.3 ±0.1	28.1±0.5	**<.0001**
Waist circumference (cm)	101.9± 7.7	93.6 ±1.2	93.7± 4.7	**<.0001**	98.4 ±5.1	94.9± 2.9	95.9 ±3.9	0.1364
SBP (mmHg)	132.5± 7.9	122.3 ±0.5	127.9± 1.7	**<.0001**	116.3 ±2.6	115.3± 0.9	120.1 ±2.9	**0.0007**
DBP (mmHg)	88.8± 8.3	77.1 ±0.6	81.9± 4.7	**<.0001**	73.73±2.7	72.6± 0.9	76.6 ±2.9	**0.0047**
Fasting glucose (mg/dL)	94.4± 2.0	94.3±1.3	94.0± 1.3	0.5412	93.0 ±1.4	92.5± 0.8	95.3±2.0	**0.0126**
Total cholesterol (mg/dL)	190.8± 3.5	184.8±1.5	187.0± 3.8	0.5957	183.4 ±2.0	179.7± 1.2	177.1±2.8	**0.0002**
HDL cholesterol (mg/dL)	41.5± 1.1	40.8±0.4	42.5± 0.9	0.0012	47.4±0.7	46.3± 0.4	45.4±0.9	**<.0001**
LDL cholesterol (mg/dL)	113.2± 2.6	111.4±1.3	110.4± 2.7	0.3310	112.2 ±1.8	108.1± 0.9	106.6±2.4	**<.0001**
Triglyceride (mg/dL)	194.1± 15.1	171.7±4.5	174.6±11.1	0.5907	119.8±3.7	129.1±2.8	126.6±6.1	**0.0008**
Macronutrient intake (mean ± SE)								
Energy (kcal)	2024±34.6	2160.6±16.3	2142.6±46.7	**<.0001**	1846.7±26.8	1832.7±11.5	1928.4±36.4	**<.0001**
Carbohydrate(g)	214.4±7.9	322.7±2.6	373.3±8.0	**<.0001**	188.8±7.3	271.1±1.8	338.7±6.6	**<.0001**
Protein (g)	78.3±2.8	71.3±0.6	64.9±1.5	**<.0001**	71.9±2.4	59.9±0.4	57.3±1.1	**<.0001**
Fat (g)	86.4±3.4	65.0±0.6	41.6±1.0	**<.0001**	81.1±3.1	56.7±0.4	37.7±0.7	**<.0001**
% Energy from								
Carbohydrate	42.2±0.6	59.8±0.2	69.8±0.3	**<.0001**	40.7±0.6	59.8±0.1	70.3±0.2	**<.0001**
Protein	15.6±0.4	13.3±0.1	12.2±0.1	**<.0001**	15.9±0.4	13.2±0.1	12.0±0.1	**<.0001**
Fat	38.3±0.6	27.0±0.1	17.5±0.2	**<.0001**	39.3±0.5	27.8±0.2	17.6±0.1	**<.0001**
EER%	72.0±3.6	83.3±0.8	84.9±2.3	**<.0001**	95.1±3.6	97.6±0.7	103.9±2.1	**<.0001**

[a] Based on χ^2 test for categorical variables and ANOVA for continuous variables.

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; EER, estimated energy requirement.

The prevalence and ORs for MetS adults according to carbohydrate and fat intake are summarized in Table 4-3. Women in the LCHF and MCF groups showed a protective factor for high blood pressure (OR=0.34; 95% CI: 0.19-0.59; OR=0.50; 95% CI: 0.32-0.79, respectively). Additionally, women on MCF diet intake showed a protective factor for elevated fasting glucose (OR=0.58; 95% CI: 0.37-0.91) after adjusting for confounding variables.

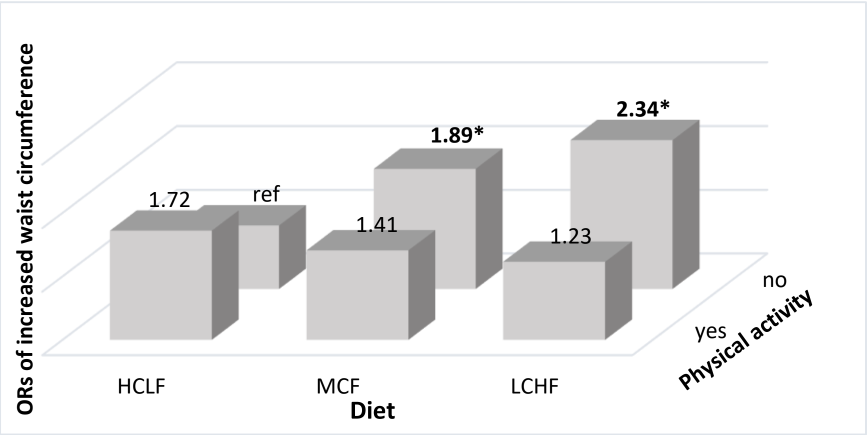
Table 4-3. Prevalence and multivariable-adjusted odds ratio and 95% confidence intervals for MetS among participants according to carbohydrate and fat intake

	Men			Women		
	LCHF (n=330)	MCF (n=1410)	HCLF (n=224)	LCHF (n=797)	MCF (n=2907)	HCLF (n=355)
Increased waist circumference						
Prevalence (%)	55.8	47.28	53.55	63.86	67.13	70.38
OR (95% CI)	1.67 (0.95-2.97)	1.38 (0.93-2.04)	1.00	0.85 (0.54-1.34)	0.75 (0.50-1.13)	1.00
Elevated blood pressure						
Prevalence (%)	25.01	28.99	30.31	10.70	13.72	24.97
OR (95% CI)	0.87 (0.50-1.55)	0.94 (0.61-1.44)	1.00	**0.34 (0.19-0.59)**	**0.50 (0.32-0.79)**	1.00
Reduced HDL cholesterol						
Prevalence (%)	50.44	42.25	50.73	59.73	65.34	66.13
OR (95% CI)	1.39 (0.88-2.44)	1.23 (0.79-1.91)	1.00	0.87 (0.57-1.33)	1.00 (0.70-1.43)	1.00
Elevated triglycerides						
Prevalence (%)	48.18	44.63	44.53	24.17	26.87	26.45
OR (95% CI)	1.10 (0.61-1.85)	0.81 (0.52-1.26)	1.00	0.97 (0.61-1.56)	1.12 (0.75-1.67)	1.00
Elevated fasting glucose						
Prevalence (%)	14.66	15.50	23.96	14.23	13.95	24.39
OR (95% CI)	0.82 (0.43-1.55)	0.69 (0.40-1.17)	1.00	0.68 (0.40-1.16)	**0.58 (0.37-0.91)**	1.00
Metabolic syndrome						
Prevalence (%)	37.03	36.80	34.26	27.00	28.63	38.50
OR (95% CI)	1.17 (0.62-2.18)	0.94 (0.57-1.54)	1.00	0.77 (0.46-1.29)	0.71 (0.47-1.07)	1.00

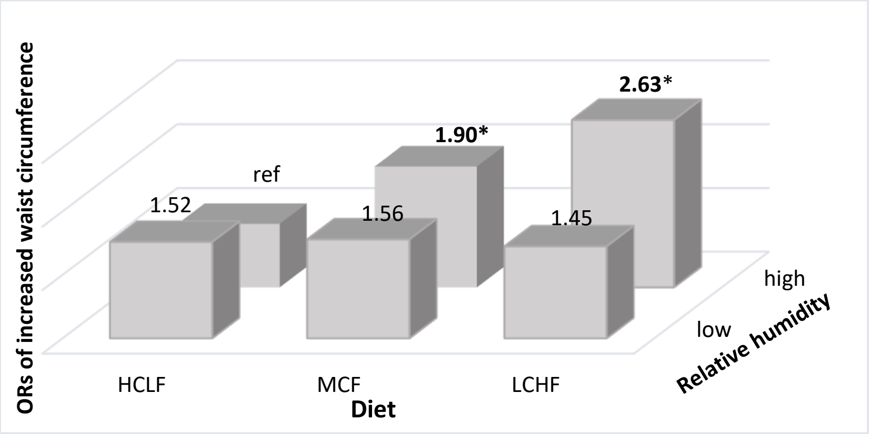
[a] Carbohydrates (55-65%); Fat (20-30%).
All values accounted for the complex sampling design effect of the national surveys using PROC SURVEY procedure. Ethnicity, family economic status, education level, elevation, relative humidity, BMI (except for the model of waist circumference), and total energy intake were adjusted for the multiple logistic regression.
Abbreviations: OR, odd ratio; CI, confidence interval; HDL, high-density lipoprotein.

Further analyses of associations between diet and MetS in addition to health-related lifestyles and physical environment (i.e. elevation and humidity) were performed to explore potential interactions among the variables. When compared to the participants with HCLF diet, higher ORs of increased waist circumference were observed in men with LCHF and MFC diet intakes who were physically inactive (OR=2.34, 95% CI: 1.19-4.60; OR=1.89, 95% CI: 1.12-3.20; respectively) (Figure 4.1A) and living in high relative humidity (OR=2.63, 95%CI:1.32-5.28; OR=1.90, 95%CI: 1.08-2.89; respectively) (Figure 4.1B), whereas men with MCF intake and performing exercise showed a significantly decreased OR of elevated triglycerides (OR=0.45, 95% CI: 0.21-0.98) as shown in Figure 4.1C.

(A)



(B)



(C)

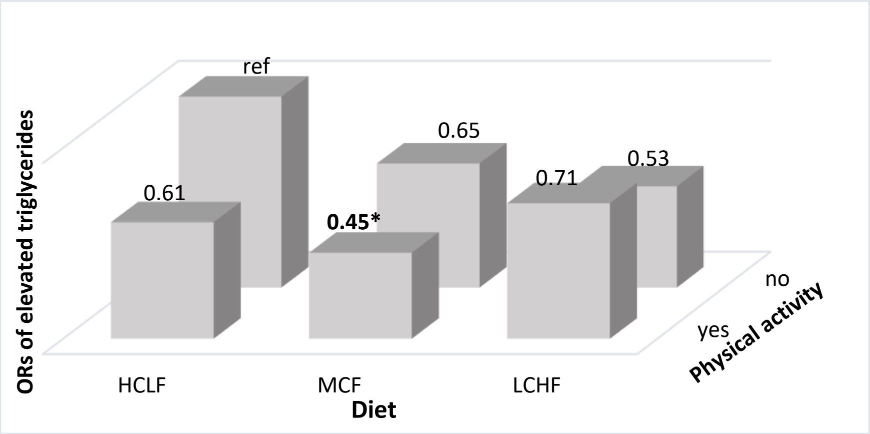
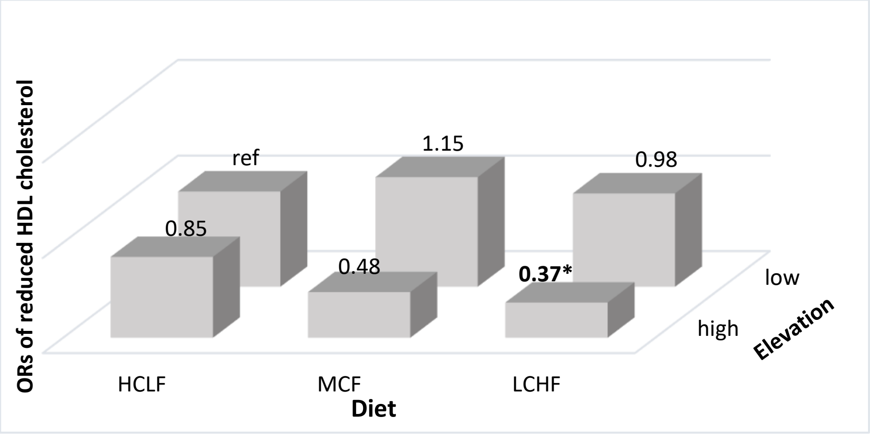


Figure 4-1. Adjusted odds ratios of MetS in Ecuadorian men according to diet, physical activity, and environment (A) Odd ratios for increased waist circumference by the status of carbohydrate and fat intake and physical activity; (B) odd ratios for increased waist circumference by the status of carbohydrate and fat intake and relative humidity; and (C) odd ratios for elevated triglycerides by the status of carbohydrate and fat intake and physical activity. All values accounted for the complex sampling design effect of the national surveys using PROC SURVEY procedure. Ethnicity, family economic status, education level, elevation, relative humidity, BMI (except for the model of waist circumference), and total energy intake were adjusted for the multiple logistic regression. Yes, or No for physical activity, and high (>80%) or low (50-80%) for relative humidity. * indicates statistical significance (p<0.05).

In addition, women with LCHF diet and living at high elevation showed a significantly decreased OR of reduced HDL cholesterol (OR=0.37, 95% CI: 0.16-0.86) (Figure 2A), while women with MCF intake and living in low relative humidity showed a decreased OR for MetS (OR=0.66, 95% CI: 0.45-0.98) (Figure 2B).

(A)



(B)

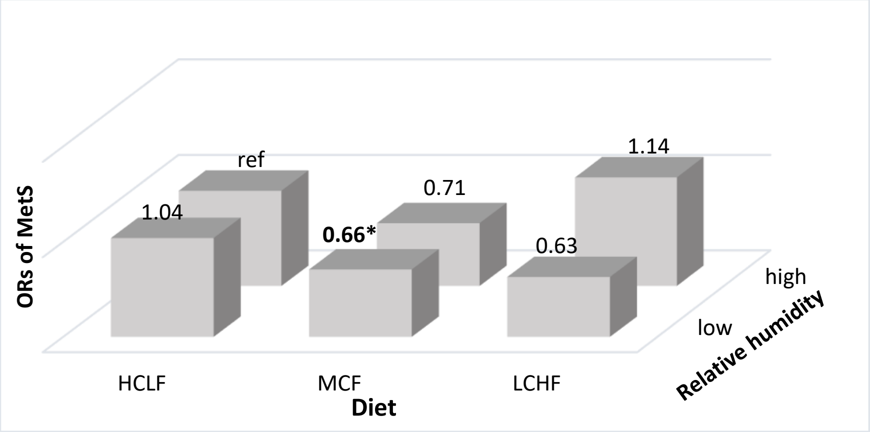


Figure 4-2. Multivariable-adjusted odds ratios for MetS in Ecuadorian women according to diet and physical environment ((A) Odd ratios for reduced HDL cholesterol by the status of carbohydrate and fat intake and elevation; and (B) odd ratios for MetS by the status of carbohydrate and relative humidity. All values accounted for the complex sampling design effect of the national surveys using PROC SURVEY procedure. Ethnicity, family economic status, education level, elevation, relative humidity, BMI (except for the model of waist circumference), and total energy intake were adjusted for the multiple logistic regression. High (>2001 masl) or low (≤2000) for elevation and high (>80%) or low (50-80%) for relative humidity. * indicates statistical significance ($p<0.05$).

4-4. Discussion

In this study, we investigated the associations of carbohydrate and fat intake with MetS according to health-related lifestyles and physical environment (i.e. elevation and humidity) in the Ecuadorian adult population, and found that LCHF and MCF diets were inversely associated with elevated blood pressure in women, while women with MCF diet showed lower prevalence of elevated fasting glucose. Moreover, there were negative associations between MetS and reduced HDL cholesterol in women with MCF diet residing in low relative humidity and in women with LCHF diet residing at a high elevation, whereas higher prevalence of increased waist circumference was observed in men with both MFC and LCHF diets who were physically inactive and residing in high relative humidity. To the best of our knowledge, this is the first study utilizing a large population in Ecuador to explore the interactive associations of carbohydrate and fat intakes, lifestyles, and physical environment with MetS.

The Ecuadorian diet is generally high in carbohydrate and fat (18). Although there is no a universal definition of low-carbohydrate and high-fat diet, several studies agree that in Western populations a low-carbohydrate high-fat diet consists of less than 45% of carbohydrates (170,171), and more than 30% of fats (172) as sources of energy. The intake of LCHF and MCF diets has been found to attenuate blood pressure (173,57); consequently, these facts could be explained by the reduction HDL cholesterol and triglycerides levels, known as a major risk factor for cardiovascular events and hypertension (174). Moreover, LCHF diet may induce hypoglycemia and decrease oxidative stress, which could cause endothelial vasoconstriction and therefore decrease blood pressure (58). Conversely, other studies did not find significant associations among proportions of carbohydrate and fat intake and hypertension (59). In addition, several RCTs have reported that the greater the carbohydrate restriction, the greater the glucose-lowering effect (56), which is in accordance with our findings. The association of carbohydrate and fat intake with glucose levels may be explained by the hyperinsulinemia and postprandial hyperglycemia caused by a decrease in carbohydrate intake (60). On the contrary, HCLF diet has been associated with a higher prevalence of MetS (175) and reduced HDL cholesterol (176). The associations between LCHF, MCF and HCLF are still unclear. Thus, further studies are needed to clarify the optimal types and proportions of carbohydrate and fat and the mechanisms underlying their associations.

In addition, protein content exhibited significant differences among diet groups in this study; an increased intake of protein has been reported to have a greater satiety effect than intake of carbohydrates, helping control hunger between meals and regulate the processes of energy expenditure, thermogenesis and glucose metabolism, which intervene in the pathophysiology of MetS (177-178). The association between protein intake and MetS is still unclear, as some studies have not found associations (179-181) while others have found that low protein intake could be a risk factor for MetS components (182).

To further explore our findings, we analyzed the interactive associations of MetS with carbohydrate and fat intake, physical environment, and health-related lifestyles. Ecuador is a megadiverse country composed by four different geographical regions (the Coast, the Galapagos Islands, the Amazon, and the Andean region); its population resides in a wide elevation range of 0 masl to 3900 masl. In addition, Ecuador has 11 different types of microclimates ranging from Tropical to Oceanic and is located on the equatorial line, thus producing little seasonality. An adequate macronutrient intake was inversely associated with MetS in women living in low humidity and decreased OR of reduced HDL cholesterol was found in women residing at high elevation. Several studies have investigated the effects of physical environment on human's health and it was found that imbalances in relative humidity are associated with coronary diseases (131,137), DM2 (50), and MetS (158). Moreover, epidemiological studies that described that susceptibility to extreme humidity and temperature varies by gender (183), which supports our findings. While the associations of high relative humidity with health outcomes are still controversial, our results showed that high relative humidity combined with LCHF and/or MCF diets may trigger MetS. In the case of elevation, some studies have reported an inverse association between high elevation and MetS and its components, which may be explained by physiological adaptations to hypoxia that increase hemoglobin concentrations and accelerate glucose tolerance and the metabolism of lipids (184,78,77,43,43). Moreover, exposure to high elevation has been found to decrease the levels of HDL, LDL, and associated proteins due to maturation of lipoprotein particles (185).

In addition, we found that physically inactive men and men living in high relative humidity showed a higher prevalence of abdominal obesity, whereas physically active men with a MCF intake and residing in low relative humidity showed a lower prevalence of elevated triglycerides. These findings may be explained by the associations of high relative humidity with heat stress and fatigue, which cause reduction in exercise capacity (149-150). Additionally, some studies have shown a positive impact of exercise on blood cholesterol and triglyceride profiles, abdominal obesity, and DM2, likely due to insulin resistance, adipose and protein metabolism, and epigenetic factors (104,151). Thus, our findings should be interpreted with caution.

This study has several limitations. First, the cross-sectional design of the ENSANUT-ECU data made it difficult to identify the causal relationship between carbohydrate and fat in-take with MetS. Further prospective studies are required to examine the effect of these diets on MetS in Ecuadorian adults. Second, data on dietary intake from the 24 h dietary recall might not represent the usual food intake of participants. However, this study included a nation-wide representative sample of participants. Third, we could not estimate the differences in carbohydrate quality and fatty acid composition in diet groups due to the lack of information. Therefore, more studies are needed to clarify their associations with MetS and its components. Despite these limitations, to the best of our knowledge, this is the first study based on a nationally representative sample of Ecuadorian adults that examined the interactive associations among carbohydrate and fat intake, health-related lifestyle, and physical environment with MetS and its abnormalities.

4-5. Conclusions

The obtained results suggest that LCHF and MFC compared to HCLF intakes may play protective roles in the onset of MetS, and their associations can be modified by physical activity and physical environment such as relative humidity and elevation in Ecuadorian adults. Thus, health programs focusing on dietary intake to promote health and prevent metabolic diseases should consider other factors, including health-related lifestyles and physical environment conditions of the population.

Chapter 5. Overall Discussion and Conclusion

5-1. Overall discussion

Main findings of the study

The present study was conducted to identify the epidemiologic characteristics of the physical environment, health-related lifestyles, and carbohydrate and fat intake among Ecuadorian adults and to examine their association with MetS and its components. The main findings of the study are presented in Table 5-1. First, residence at low elevation increased prevalence of MetS in men and elevated fasting glucose in both sexes. Moreover, a lack of physical activity was identified to raise the risk of increased waist circumference in both sexes. Second, residence in high relative humidity and menopausal status were associated with increased risk of MetS and its components in Ecuadorian women; however, physical activity was inversely associated with the risk of elevated triglycerides in men. Third, consumption of LCHF and MCF diets in women is inversely associated with high blood pressure, while MCF diet may reduce their fasting glucose. Lastly, MCF intake and residence in low humidity enhances decrease in OR of MetS and LCHF diet and residence in high elevation reduces HDL cholesterol in women and for men, LCHF intake, physical inactivity, and high humidity increase OR of increased waist circumference.

Table 5-1. Summary of the main findings of each sub-study

Sub-study	Study design, data	Subjects	Main exposure	Outcome	Association	
					Men	Women
1	Cross-sectional study, ENSANUT-ECU	6,024 adult Ecuadorians (1,964 men and 4,060 women)	Elevation: low (≤2,000 masl) vs high (>2,001 masl)	1) MetS	(↑)	(-)
				2) Increased WC	(-)	(-)
				3) Elevated BP	(-)	(-)
				4) Reduced HDL-C	(-)	(-)
				5) Elevated TG	(-)	(-)
				6) Elevated FG	(↑)	(↑)
			Physical activity at low elevation “no” vs “yes”	1) Increased WC	(↑)	(↑)
2	Cross-sectional study, ENSANUT-ECU and mean annual relative humidity (%) and temperature from INAMHI	6,024 adult Ecuadorians (1,964 men and 4,060 women)	Relative humidity: high (>80%) vs low (≤80%)	1) MetS	(-)	(↑)
				2) Increased WC	(-)	(-)
				3) Elevated BP	(-)	(-)
				4) Reduced HDL-C	(-)	(↑)
				5) Elevated TG	(-)	(-)
				6) Elevated FG	(-)	(-)
			Physical activity in high relative humidity “yes” vs “no”	1) Elevated TG	(↓)	(-)
			Menopause stage “yes” vs “no”	1) MetS		(↑)
				2) Increased WC		(↑)
				3) Elevated BP		(↑)

3	Cross-sectional study, ENSANUT-ECU, INAMHI	6,023 adult Ecuadorians (1,964 men and 4,059 women)	Carbohydrate and fat intake: LCHF (energy from CHO <45%) vs HCLF (energy from CHO>65%)	1) MetS 2) Increased WC 3) Elevated BP 4) Reduced HDL-C 5) Elevated TG 6) Elevated FG	(-) (-) (-) (-) (-) (-)	(-) (-) (↓) (-) (-) (-)
			MCF (45% to 65% of energy from CHO) vs HCLF (energy from CHO>65%)	1) MetS 2) Increased WC 3) Elevated BP 4) Reduced HDL-C 5) Elevated TG 6) Elevated FG	(-) (-) (-) (-) (-) (-)	(-) (-) (↓) (-) (-) (↓)
			MCF in low relative humidity in women	1) MetS	(-)	(↓)
			LCHF at high elevation in men	1) Reduced HDL-C	(-)	(↓)
			LCHF and MCF in high relative humidity in men	1) Increased WC	(-)	(↑)
			LCHF and physical inactivity men	1) Increased WC	(-)	(↑)

(↑) positive association; (↓) negative association (-) non-significant association.

masl, meters above sea level; WC, waist circumference; BP, blood pressure; TG; triglycerides; HCLF high-carbohydrate low-fat; SBP, HDL, high density lipoprotein; LDL, low density lipoprotein, CHO; carbohydrate; MPCF, medium proportion of carbohydrate and fat.

Elevation, health-related lifestyles and metabolic disorders

This study determined that residing at low elevation and physical inactivity contribute to increase the risk of metabolic diseases. Low elevation was positively associated with the prevalence of MetS in Ecuadorian men and elevated fasting glucose in both sexes. Moreover, lack of physical activity augmented the risk of increased waist circumference in men and women living at low elevation.

Regarding the risk of metabolic disorders, not only biological factors but also elevation and lifestyles are important. Previous studies have reported that young adults living at high elevation show a lower prevalence of MetS (42,43). Additionally, an inverse association between high elevation, diabetes, lower triglycerides and blood pressure has been reported (44,84). Furthermore, lower fasting glucose and better glucose tolerance were associated at high elevation (40-44), these findings may be partially explained human adaptation to low oxygen concentrations and the increase in glucose metabolism (76-79). The present study could not estimate people's oxygen levels due to lack of information; however, elevation was classified according to previous studies that have demonstrated physiological changes above that elevation (86,87). Our first sub-study showed that residence below 2,000 masl had a positive association with MetS in men and increased fasting glucose for men and women. Moreover, the lack of physical activity at low elevation increase the risk of increased waist circumference. Previous investigations have suggested a synergistic effect of physical activity and hypoxic exposure on body weight that may enhance the benefits of living at high elevation (186). It has been shown that the combination of hypoxic exposure and exercise compared with exercise alone produces more favorable improvements in fasting insulin, insulin sensitivity, triglycerides, and body fat content (187,188). Moreover, hypoxia contributes to better cardiovascular health and positive clinical implications (189,190), which may facilitate physical activity performance.

Norepinephrine has also been suggested as a potential mechanism affecting the association between elevation and body weight (191). Research has found that plasma norepinephrine concentrations significantly increase with increasing elevation (192) which increases blood flow to the intestines and, subsequently, reduces appetite (193).

Although these mechanisms help explain the associations of elevation and MetS after adjustment for physical inactivity and other variables, it is imperative to consider the influence of other environmental variables, for example, elevation. It has been described that physical inactivity decreases with higher elevation, most likely as a function of precipitation, air temperature, radiation and other factors (194). Further research involving longitudinal data is required to establish temporality of events before statements about mediation can be conclusive.

Relative humidity, health-related lifestyles and metabolic disorders

This study ascertained that living in high relative humidity contributes to increase the risk of metabolic disorders. Living in more than 80% of relative humidity was positively associated with MetS and reduced HDL-cholesterol in adult women. However, physically active men and living in high relative humidity has an inverse association with elevated triglyceride levels.

Investigations on this field are still scarce. Previous studies have found CVD is most sensitive to weather across various climates throughout the world (195). High humidity may lead to increased thrombotic risk (196), aggravating the effects on people with existing cardiac health problems. It has also been found a positive relationship between relative humidity and CVD death, and a positive relationship between temperature and CVD (197). However, others reported no association between humidity and heart disease, including CVD (198). In general, these contrasting conclusions indicate confounders may potentially influence meteorological variables and disease processes. Our study found that only women in the high humidity group had risk for MetS, these results concord with epidemiological studies that described that susceptibility to extreme weather varies by gender and age (177).

One study revealed that specific locations were associated with cold-related and humid-related deaths. In coastal areas, high temperature and high humidity were associated with higher and more significant risks (199). A possible explanation is the air in coastal areas often contain more moisture than inland areas. Although the mechanism on how humidity affects health remains unclear, humidity is linked with anomalous mortality and morbidity, because it affects cold or heat stress and hydration state (131). During extreme temperature and humidity, the body is under considerable constraint from a range of stress-related physiological reactions (200). The potential impacts on metabolic disorders from high body-core temperatures and low hydration levels can be related to atmospheric moisture state, increased metabolism. The underlying mechanisms are unclear and require further investigation (201).

Carbohydrate and fat intake, lifestyles and metabolic disorders

The current findings revealed that the consumption of LCHF and MCF diets is inversely associated with high blood pressure, while MCF diet may reduce their fasting glucose. These findings might be explained by the effects of LC diet on vascular endothelial function by improving no contribution to vasodilation. Furthermore, LCHF diet decreased cardiovascular risks by decreases in body weight, BMI, % body fat, diastolic blood pressure, and blood triglyceride after RCTs interventions (202). Additionally, systematic review and meta-analysis have revealed that adopting healthful dietary modifications may be an effective method for controlling high blood pressure and DM2 in comparison to consuming a high carbohydrate diet (203). However, some studies found low- to moderate-certainty evidence that dietary carbohydrate restriction to a maximum of 40% yields slightly better metabolic control in people (204).

Furthermore, for women MFC intake and residence in low humidity enhances decrease in OR of MetS and LCHF intake and residence in high elevation reduces their HDL cholesterol. For men, LCHF intake, physical inactivity and high humidity increases OR of increased waist circumference. In agreement with our findings, a RCT demonstrated that with a low-carbohydrate diet combined with exercise training resulted in greater reductions in cardiometabolic indices, such as percent of body fat, triglycerides, blood glucose and inflammation and a greater increase in cardiorespiratory fitness compared to similar exercise and standard dietary intake (205). The need for large multicenter randomized controlled trials with metabolic disorders and other endpoints seem warranted and worthy of prioritization. In particular, it should be noted that, as with any other dietary interventions, the evidence for long-term compliance with, and sustainability of, carbohydrate restriction is currently not strong.

Considerations for interpreting the study results

To the best of our knowledge, this is the first study that explores the associations of physical environment, health-related lifestyles, carbohydrate and fat intake with MetS and its components among Ecuadorian adults using a nationally representative population sample. In addition, for the first time, this study provides evidence that high relative humidity might be associated with increased risk of MetS in Ecuadorian adult women. However, there are some points to consider when interpreting the findings of this study in terms of the study design, environment data collection and dietary assessment methods.

This study was based on sociodemographic, elevation, health-related lifestyles data, which are found in the ENSANUT-ECU and climate annual records from INAMHI. The ENSANUT-ECU used a complex, multistage, probability sample design and collected information about sociodemographic and housing characteristics, alcohol and tobacco consumption, dietary intake and physical activity. Therefore, these data are appropriate for examining the health and nutritional status of the Ecuadorian population, although casual relationships between dietary intake, lifestyles and metabolic disorders cannot be identified due to the cross-sectional design of the study.

In the case of relative humidity, the mean annual percentage (%) for 2012 was obtained from the INAMHI and this mean was used as a proxy for relative humidity at the participants' cities of residence in order to assess the long-term association of ambient humidity with metabolic dysfunction. Additionally, in order to control for confounding variables, the statistical model was adjusted for elevation, while adjusting temperature in the model led to an over adjustment because of its correlation with elevation, thus this variable was excluded. Future studies should include other weather conditions beyond temperature and humidity like wind speed, precipitation, rainfall rate, and radiation that might influence physical activity and other lifestyles.

Finally, the differences in carbohydrate quality and fatty acid composition in diet groups could not be estimated due to the lack of information. Therefore, more studies are needed to clarify their associations with MetS and its components.

Public health implications of the study findings

The present study provides several key points for public health nutrition. First of all, it is necessary to enhance physical activity and to maintain a balanced carbohydrate and fat dietary intake, these two strategies need to concord with environment factors, such as elevation and relative humidity. To prevent and manage metabolic disorders in Ecuador, it is necessary to increase physical activity at low elevation and in high relative humidity. In addition, it is imperative to reduce high carbohydrate intake to a moderate or low level. Thus, intersectoral health programs aimed at controlling relative humidity in homes and work environments, providing nutritional education, and increasing physical activity in elevated and humid places are needed to promote healthy life conditions and to prevent metabolic disorders. These programs should consider not only sociodemographic characteristics of the population, but also the lifestyles in the environment conditions of their place of residence.

Several strategies for the prevention of metabolic disorders have been implemented worldwide. In the case of Latin America, all countries signed the Plan of Action for the Prevention of Obesity in Children and Adolescents in 2014, the Plan combats high consumption of nutrient-poor foods that contain large amounts of carbohydrates, fat, and salt; the usual consumption of sugar-sweetened beverages; and the lack physical activity (206). In order to fulfill the Plan, Ecuador has used a front-labeling system referred to as “Traffic Light” for the past seven years. The label indicates levels of total fats, saturated fats, sugars, and sodium found in processed foods through the colors of a traffic light: red indicates an excess level of the specific nutrient; yellow indicates a moderate amount; and green indicates adequate or the recommended amount, according to the WHO nutritional recommendations (207). Additionally, Ecuador implemented a program called “Cycle paths” to contribute to a collective consciousness of healthy physical environments through the use of bicycles and green spaces. Although there are several complex benefits of cycle paths, physical activity represents the greatest benefit in terms of public health. The way that cycle paths have been designed in Latin American cities has been different according to urban design, environment, and political considerations (206).

The present study identified that low elevation, high relative humidity and low-carbohydrate high fat diet and moderate carbohydrate and fat intake were different associated with MetS and its components. These findings are consistent with the few studies that have been performed to date. Therefore, the findings of the present study determined that nutritional recommendations should be personalized based on each person's lifestyle, elevation and humidity in the place of residence. The findings of this study may constitute the baseline for further investigation on adequate environment conditions, lifestyles and dietary intake for the prevention of MetS.

Future studies are needed in the Latin American population and they should comprise sociodemographic characteristics, environment conditions, lifestyles and dietary intake as a whole in order to understand the interactions of these variables on people's health status. This study was limited to deriving optimal environment conditions, lifestyles, and carbohydrate and fat intake due to several limitations of the study design, environment information, and dietary assessment. However, additional well-designed large-scale cohort studies are necessary, with consideration for these limitations.

5-2. Conclusions

In conclusion, this study found that residing at low elevation and in high relative humidity areas, added to physical inactivity increased the risk of MetS in Ecuadorian adult men and women. For women, it was also found that menopausal status increased the risk of MetS, elevated blood pressure and increased waist circumference. In addition, it was found that moderate and low carbohydrate intake were negatively associated with high blood pressure and elevated fasting glucose. Therefore, it is important to consider biological factors, geographical elevation, relative humidity, carbohydrate and fat intake, physical activity and other health-related lifestyles to prevent and manage metabolic disorders among Ecuadorian adults. In addition, these study results may be considered as the baseline for further investigations on adequate environmental and lifestyle conditions that benefit health and prevent metabolic diseases.

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Appendices

Supplementary Table 1. Odds ratio for MetS among low elevation residents according to health-related lifestyle factors

	Men		**Women**	
	Yes[a] (95% CI)	No (95% CI)	Yes[a] (95% CI)	No (95% CI)
Current alcohol consumption				
Increased waist circumference	**2.10 (1.38-3.19)**	**1.59 (1.01-2.76)**	1.01 (0.61-1.66)	**1.37 (1.01-1.84)**
Elevated blood pressure	0.86 (0.52-1.42)	1.11 (0.63-1.96)	0.54 (0.29-1.01)	1.22 (0.80-1.86)
Reduced HDL cholesterol	0.87 (0.58-1.31)	0.81(0.49-1.33)	1.45 (0.92-2.26)	0.98 (0.74-1.30)
Elevated triglycerides	0.94 (0.62-1.42)	0.61 (0.36-1.02)	0.93 (0.54-1.58)	0.95 (0.69-1.30)
Elevated fasting glucose	**3.15 (1.77-5.59)**	1.84 (0.94-3.59)	**2.62 (1.35-5.09)**	**1.84 (1.26-2.70)**
Metabolic syndrome	**1.56 (1.13-2.21)**	1.05 (0.81-1.81)	1.19 (0.71-1.99)	1.13 (0.82-1.57)
Current smoking				
Increased waist circumference	**1.86 (1.12-3.08)**	**1.72 (1.18-2.52)**	1.56 (0.48-5.09)	**1.44 (1.12-1.85)**
Elevated blood pressure	0.90 (0.50-1.62)	1.09 (0.71-1.65)	0.85 (0.15-4.98)	1.20 (0.85-1.67)
Reduced HDL cholesterol	1.36 (0.81-2.29)	0.86 (0.59-1.25)	1.46 (0.42-5.12)	1.06 (0.84-1.34)
Elevated triglycerides	0.86 (0.52-1.41)	0.95 (0.66-1.38)	0.46 (0.18-1.17)	1.11 (0.86-1.44)
Elevated fasting glucose	2.17 (0.93-5.04)	0.56 (0.43-1.31)	**3.26 (1.09-9.69)**	**1.93 (1.39-2.66)**
Metabolic syndrome	**1.65 (1.11-2.47)**	1.27 (0.93-1.75)	0.92 (0.46-1.84)	1.08 (0.91-1.29)
Physical activity				
Increased waist circumference	1.21 (0.71-2.08)	**2.05 (1.22-3.45)**	0.96 (0.45-2.04)	**1.38 (1.05-1.83)**
Elevated blood pressure	1.16 (0.66-2.02)	0.77 (0.49-1.20)	0.47 (0.16-1.41)	1.20 (0.83-1.73)
Reduced HDL cholesterol	0.81 (0.50-1.29)	0.93 (0.61-1.41)	0.86 (0.49-1.50)	1.06 (0.82-1.36)
Elevated triglycerides	0.76 (0.47-1.23)	0.92 (0.61-1.39)	0.51 (0.26-1.02)	1.11 (0.83-1.47)
Elevated fasting glucose	1.30 (0.99-3.66)	**1.91 (1.12-3.27)**	0.71 (0.30-1.71)	**2.34 (1.68-3.27)**
Metabolic syndrome	1.39 (0.96-2.01)	**1.47 (1.05-2.05)**	0.76 (0.49-1.18)	1.14 (0.95-1.36)
	High [a] (95% CI)	Low (95% CI)	High [a] (95% CI)	Low (95% CI)
% EER				
Increased waist circumference	2.00 (0.82-4.88)	1.46 (0.99-2.15)	1.46 (0.99-2.17)	1.19 (0.83-1.70)
Elevated blood pressure	0.82 (0.33-2.03)	1.31 (0.74-2.34)	1.31 (0.74-2.34)	0.93 (0.60-1.44)
Reduced HDL cholesterol	1.07 (0.52-2.22)	1.00 (0.70-1.43)	1.01 (0.71-1.44)	1.05 (0.77-1.43)
Elevated triglycerides	1.03 (0.47-2.24)	1.05 (0.68-1.62)	1.05 (0.68-1.62)	0.96 (0.70-1.33)
Elevated fasting glucose	0.94 (0.36-2.46)	**2.82 (1.78-4.45)**	**3.86 (2.10-6.92)**	**1.52 (1.01-2.27)**
Metabolic syndrome	1.34 (0.71-2.90)	1.10 (0.76-1.60)	1.21 (0.91-1.61)	1.03 (0.84-1.26)

Bold values indicate the statistical significance.

ORs were calculated based on high elevation residents (reference).

[a] Yes or No for current alcohol consumption, current smoking, and physical activity; high (>100%) or low (≤100%) for EER

All values accounted for the complex sampling design effect of the national surveys using PROC SURVEY procedure. A multiple logistic regression analysis was performed after adjusting for ethnicity, family economic status, education level, BMI (except for the model of waist circumference), physical activity, current alcohol consumption, current smoking and total energy intake.

Abbreviations: CI, confidence interval; HDL high-density lipoprotein

Supplementary Table 2. Odds ratio for MetS among LCHF diet residents according to health-related lifestyle and environmental factors

	Men		Women	
	Yes[a] (95% CI)	No (95% CI)	Yes[a] (95% CI)	No (95% CI)
Current alcohol consumption				
Increased waist circumference	1.55 (0.80-3.04)	1.49 (0.66-3.39)	0.54 (0.23-1.23)	0.81 (0.50-1.30)
Elevated blood pressure	0.65 (0.31-1.35)	1.08 (0.45-2.60)	0.54 (0.23-1.23)	**0.41 (0.21-0.79)**
Reduced HDL cholesterol	0.97 (0.49-1.93)	1.55 (0.65-3.68)	1.06 (0.46-2.44)	0.75 (0.47-1.19)
Elevated triglycerides	0.86 (0.42-1.74)	0.83 (0.35-2.01)	1.07 (0.41-2.79)	0.96 (0.56-1.65)
Elevated fasting glucose	0.56 (0.23-1.36)	1.38 (0.36-2.06)	0.56 (0.18-1.73)	0.72 (0.40-1.28)
Metabolic syndrome	0.86 (0.39-1.91)	1.23 (0.47-3.221)	0.54 (0.21-1.41)	0.79 (0.47-1.35)
Current smoking				
Increased waist circumference	1.77 (0.71-4.39)	1.39 (0.75-2.60)	0.01 (-0.01-0.31)	0.76 (0.50-1.15)
Elevated blood pressure	0.87 (0.30-2.55)	0.72 (0.37-1.39)	1.23 (0.09-15.33)	**0.38 (0.22-0.68)**
Reduced HDL cholesterol	1.38 (0.46-4.10)	1.16 (0.63-2.13)	0.39 (0.05-3.02)	0.84 (0.55-1.26)
Elevated triglycerides	1.17 (0.39-3.46)	0.71 (0.37-1.36)	0.79 (0.04-2.71)	0.95 (0.59-1.54)
Elevated fasting glucose	0.72 (0.93-5.04)	0.72 (0.22-2.37)	3.26 (0.96-7.69)	0.62 (0.37-1.05)
Metabolic syndrome	1.10 (0.33-3.66)	0.88 (0.42-1.83)	3.41 (0.32-9.06)	0.69 (0.43-1.11)
Physical activity				
Increased waist circumference	0.70 (0.32-1.53)	**2.30 (1.17-4.52)**	1.38 (0.45-4.24)	0.69 (0.43-1.08)
Elevated blood pressure	1.07 (0.42-2.74)	0.69 (0.34-1.39)	**0.20 (0.05-0.72)**	**0.41 (0.22-0.75)**
Reduced HDL cholesterol	0.81 (0.35-1.86)	1.30 (0.66-2.58)	0.39 (0.15-1.02)	0.93 (0.60-1.46)
Elevated triglycerides	1.28 (0.53-3.06)	0.52 (0.25-1.07)	0.48 (0.16-1.44)	1.15 (0.67-1.85)
Elevated fasting glucose	0.57 (0.17-1.88)	1.19 (0.53-2.70)	1.63 (0.40-6.60)	0.61 (0.35-1.08)
Metabolic syndrome	0.95 (0.34-2.60)	0.82 (0.37-1.83)	0.49 (0.14-1.68)	0.79 (0.48-1.31)
	High[a] (95% CI)	Low (95% CI)	High[a] (95% CI)	Low (95% CI)
Elevation				
Increased waist circumference	1.18 (0.49-2.83)	1.45(0.73-2.87)	0.51 (0.25-1.05)	0.92 (0.54-1.57)
Elevated blood pressure	0.99 (0.40-2.41)	0.72 (0.34-1.57)	0.39 (0.15-1.02)	**0.39 (0.19-0.77)**
Reduced HDL cholesterol	1.14 (0.44-2.79)	1.26 (0.63-2.50)	**0.48 (0.25-0.96)**	1.02 (0.61-1.71)
Elevated triglycerides	1.43 (0.57-3.58)	0.86 (0.43-1.75)	1.33 (0.58-3.02)	0.94 (0.52-1.71)
Elevated fasting glucose	3.19(0.79-12.89)	0.62 (0.28-1.39)	0.51 (0.18-1.49)	0.73 (0.39-1.33)
Metabolic syndrome	1.51 (0.55-4.16)	0.98 (0.44-2.20)	0.61 (0.28-1.32)	0.83 (0.47-1.48)
Relative humidity				
Increased waist circumference	**2.44 (1.23-4.83)**	0.92 (0.44-1.92)	1.47 (0.87-2.47)	0.46 (0.25-1.00)
Elevated blood pressure	0.71 (0.33-1.55)	0.68 (0.32-1.45)	0.62 (0.32-1.19)	0.32 (0.13-0.73)
Reduced HDL cholesterol	0.68 (0.34-1.37)	1.57 (0.75-3.29)	1.44 (0.83-2.51)	0.57 (0.32-1.02)
Elevated triglycerides	0.91 (0.43-1.94)	0.83 (0.39-1.77)	0.82 (0.47-1.44)	1.19 (0.56-2.52)
Elevated fasting glucose	0.83 (0.33-2.13)	0.85 (0.35-2.07)	1.29 (0.65-2.59)	**0.46 (0.22-0.99)**
Metabolic syndrome	1.04 (0.44-2.47)	0.85 (0.37-1.97)	1.05 (0.61-1.82)	0.62 (0.30-1.27)

ORs were calculated based on HCLF diet (reference)

Supplementary Table 3. Odds ratio for MetS among residents with MCF according to health-related lifestyle and environmental factors

	Men		**Women**	
	Yes[a] (95% CI)	No (95% CI)	Yes[a] (95% CI)	No (95% CI)
Current alcohol consumption				
Increased waist circumference	1.44 (0.83-2.48)	1.26 (0.67-2.39)	0.62 (0.29-1.32)	0.95 (0.64-1.43)
Elevated blood pressure	0.64 (0.36-1.13)	1.52 (0.75-3.09)	0.25 (0.08-1.02)	0.62 (0.37-1.04)
Reduced HDL cholesterol	1.10 (0.62-1.96)	1.50 (0.73-3.09)	1.99 (0.94-4.27)	0.82 (0.55-1.23)
Elevated triglycerides	0.72 (0.39-1.34)	0.94 (0.50-1.78)	1.10 (0.45-2.66)	1.14 (0.73-1.79)
Elevated fasting glucose	0.62 (0.31-1.23)	0.86 (0.36-2.06)	0.59 (0.21-1.64)	**0.55 (0.33-0.89)**
Metabolic syndrome	0.79 (0.40-1.53)	1.35 (0.65-2.82)	0.45 (0.18-1.11)	0.81 (0.52-1.27)
Current smoking				
Increased waist circumference	1.77 (0.71-4.39)	1.40 (0.75-2.60)	0.02 (0.01-0.35)	0.87 (0.61-1.24)
Elevated blood pressure	0.74 (0.30-1.83)	0.94 (0.57-1.53)	0.61 (0.06-6.38)	**0.50 (0.32-0.80)**
Reduced HDL cholesterol	1.48 (0.54-4.10)	1.18 (0.72-1.94)	0.77 (0.10-5.92)	0.99 (069-1.43)
Elevated triglycerides	0.61 (0.22-1.69)	0.92 (0.55-1.52)	0.47 (0.03-6.98)	1.11 (0.74-1.66)
Elevated fasting glucose	0.52 (0.18-1.54)	0.66 (0.35-1.25)	2.45 (0.95-9.69)	**0.55 (0.35-0.86)**
Metabolic syndrome	0.98 (0.32-2.94)	1.27 (0.93-1.75)	1.11 (0.12-10.37)	0.69 (0.46-1.04)
Physical activity				
Increased waist circumference	0.81 (0.43-1.54)	1.85 (0.92-3.12)	1.29 (0.47-3.52)	0.85 (0.58-1.25)
Elevated blood pressure	1.32 (0.62-2.80)	0.76 (0.44-1.32)	**0.22 (0.09-0.56)**	**0.56 (0.34-0.94)**
Reduced HDL cholesterol	1.05 (0.52-2.14)	1.20 (0.70-2.07)	0.66 (0.29-1.47)	1.10 (0.74-1.63)
Elevated triglycerides	**0.41 (0.24-0.72)**	1.63 (0.78-3.38)	0.84 (0.34-2.12)	1.23 (0.79-1.90)
Elevated fasting glucose	0.43 (0.17-1.11)	0.91 (0.47-1.76)	**0.56 (0.35-0.92)**	0.71 (0.22-2.36)
Metabolic syndrome	1.48 (0.64-3.42)	0.60 (0.33-1.09)	0.55 (0.20-1.59)	0.77 (0.50-1.19)
	High[a] (95% CI)	Low (95% CI)	High[a] (95% CI)	Low (95% CI)
Elevation				
Increased waist circumference	1.08 (0.49-2.39)	1.37 (0.84-2.23)	0.78 (0.40-1.54)	0.86 (0.60-1.31)
Elevated blood pressure	1.05 (0.47-2.31)	0.85 (0.49-1.49)	0.43 (0.18-1.02)	0.53 (0.31-0.89)
Reduced HDL cholesterol	1.32 (0.52-2.89)	1.20 (0.71-2.04)	0.63 (0.33-1.17)	1.20 (0.79-1.84)
Elevated triglycerides	1.67 (0.74-3.73)	0.65 (0.38-1.12)	1.79 (0.83-3.84)	0.96 (0.60-1.53)
Elevated fasting glucose	1.79 (0.50-6.47)	0.61 (0.34-1.11)	**0.57 (0.35-0.94)**	0.49 (1.18-1.33)
Metabolic syndrome	1.78 (0.73-4.37)	0.79 (0.43-1.44)	0.76 (0.37-1.57)	0.67 (0.42-1.09)
Relative humidity				
Increased waist circumference	**1.78 (1.02-3.10)**	1.03 (0.56-1.92)	1.05 (0.69-1.61)	0.68 (0.39-1.21)
Elevated blood pressure	1.08 (0.60-1.95)	0.76 (0.41-1.41)	**0.54 (0.32-0.93)**	**0.47 (0.23-0.93)**
Reduced HDL cholesterol	1.15 (0.65-2.03)	1.29 (0.68-2.46)	1.20 (0.76-1.89)	0.84 (0.49-1.43)
Elevated triglycerides	0.79 (0.42-1.49)	0.83 (0.45-1.54)	0.79 (0.51-1.21)	1.52 (0.77-2.98)
Elevated fasting glucose	0.74 (0.37-1.50)	0.67 (0.31-1.43)	0.63 (0.36-1.10)	0.54 (0.27-1.06)
Metabolic syndrome	1.33 (0.68-2.62)	0.77 (0.39-1.55)	0.77 (0.41-1.48)	**0.63 (0.40-0.98)**

ORs were calculated based on HCLF diet (reference)

Abstract (in Korean)

에콰도르 성인의 자연환경 및 생활행태 요인과 대사증후군 간의 연관성

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서론: 2012 년 에콰도르 국민건강영양조사에 따르면 20 세 이상 성인 10 명 중 3 명이 대사증후군을 앓고 있다고 보고되었다. 대사증후군은 높은 공복혈당, 고혈압, 고중성지방혈증, 저 HDL 콜레스테롤혈증, 복부비만이 군집되어 나타나는, 다차원적 복합질환을 의미한다. 대사증후군은 심혈관계 질환이나 제 2 형 당뇨병과 같은 만성질환을 유발할 수 있다. 연령 (40 세 이상), 성 (여성), 흡연, 부적절한 식습관, 운동 부족 등과 같은 여러 생물학적, 행태학적 요인들이 대사증후군의 위험요인으로 알려져 있다. 또한, 고도와 습도 등의 자연환경은 말초 산소포화도와 열 스트레스 수준을 변화시켜 대사질환의 발병에 잠재적으로 영향을 줄 수 있다고 제안된 바 있다. 일부 연구를 통해 비만 유병률 및 발생률, 당뇨병 유병률, 고혈압 유병률과 높은 고도 간에 역연관성이 있는 것으로 관찰되었다. 습도와 대사증후군 간의 연관성에 관한 연구는 매우 드문 실정으로, 상대습도가 높은 지역에 거주하는 노인을 대상으로 수행된 한 연구에서 당뇨병, 중심성 비만, 높은 수축기 혈압과 낮은 신체활동 수준 간의 양의 연관성이 보고되었다. 에콰도르 국민의 식생활과 심혈관계 질환 위험요인에 관한 연구 현황도 비슷한 실정인데, 건강한 인구집단을 기반으로 하는 자료는 소득수준이 높은 지역에서 이루어진 연구들이 대부분으로, 이러한 연구결과를 해석하기에는 아직 논쟁의 여지가 있다. 따라서 에콰도르 국민의 자연환경, 건강 관련 생활행태 요인과 대사증후군 간의 연관성을 연구할 필요가 있다.

목적: 본 연구는 (1) 에콰도르 성인의 자연환경, 건강 관련 생활행태 요인, 탄수화물 및 지방 섭취수준의 역학적 특성을 확인하고, (2) 이러한 요인들과 대사증후군 및 그 위험요인 간의 상호작용에 의한 연관성을 분석하기 위해 수행되었다. 본 연구는 다음과 같이 세 가지의 하위 연구로 구성되었다.

첫 번째 연구에서는 에콰도르의 국가 단위 조사자료를 이용하여 20 세 이상의 에콰도르 성인에게서 나타나는 거주지역의 고도, 건강 관련 생활행태 요인, 대사증후군 유병률 간의 연관성을 분석하고자 했다. 두 번째 연구에서는 국가 기상 데이터를 통해 에콰도르의 기후 조건을 추정하고 에콰도르 성인의 생활행태와 대사증후군 간의 연관성을 확인하고자 했다. 세 번째 연구에서는 에콰도르 성인의 다량영양소 섭취현황을 파악하고, 탄수화물 및 지방 섭취수준, 자연환경, 건강 관련 생활행태 요인과 대사증후군 간의 연관성을 규명하고자 했다.

방법: 본 연구는 2012 년 에콰도르 국민건강영양조사에 참여한 20 세 이상의 성인 6,024 명 (남성 1,964 명, 여성 4,060 명)의 자료를 대상으로 수행되었다. 식사조사는 24 시간 회상법을 사용하여 이루어졌고, 인구사회학적 특성과 건강 관련 생활행태 요인 (예: 신체활동)은 표준화된 설문지를 기반으로 측정되었다. 대사증후군은 National Cholesterol Education Program Adult Treatment Panel III 및 Latin American Diabetes Association 기준에 따라 정의되었다. 첫 번째 연구에서는 지리적 고도를 낮은 고도 (해발 0-2,000m)와 높은 고도 (해발 2,001m 이상)의 두 그룹으로 범주화했다. 다중로지스틱회귀분석을 사용하여 고도에 따른 대사증후군의 오즈비 (odds ratio, OR)와 95% 신뢰구간 (95% confidence intervals, 95% CI)을 산출하였다.

두 번째 연구에서는 National Institute for Meteorology and Hydrology (INAMHI)에서 제공한 2012 년 연평균 상대습도 (%) 정보를 추가로 사용하였다. 상대습도는 낮은 상대습도 (50%-80%)와 높은 상대습도 (> 80%)의 두 그룹으로 구분하였으며, 상대습도 그룹에 따른 대사증후군의 OR 및 95% 신뢰구간을 다중로지스틱회귀분석으로 산출하였다.

세 번째 연구에서는 대상자를 성과 다량영양소 섭취 유형 (low-carbohydrate high-fat [LCHF], 탄수화물의 에너지 기여율 45% 미만; high-carbohydrate low-fat [HCLF], 탄수화물의 에너지 기여율 65% 이상; medium-carbohydrate-fat [MCF], 탄수화물의 에너지 기여율 45-65%)에 따라 구분하였다. 다량영양소 섭취 유형에 따른 대사증후군의 OR 및 95% 신뢰구간을 다중로지스틱회귀분석을 사용하여 산출하였다. 또한, 탄수화물과 지방 섭취수준, 자연환경, 건강 관련 생활행태 요인과 대사증후군 간에 상호작용에 의한 연관성이 있는지 분석하였다.

결과: 첫 번째 연구에서는 교란변수를 보정했을 때 낮은 고도에 거주하는 남성의 대사증후군 유병률 (OR=1.37, 95% CI: 1.05-1.76)과 남녀 모두의 높은 공복혈당 유병률 (남성, OR=1.80, 95% CI: 1.32-2.46; 여성, OR=1.55, 95% CI: 1.24-1.93)이 높은 것으로 나타났다. 또한 신체활동 부족은 낮은 고도에 거주하는 남성 (OR=2.05, 95% CI: 1.22-3.45)과 여성 (OR=1.38, 95% CI: 1.05-1.83) 모두에게서 복부비만과 양의 연관성을 갖는 것으로 확인되었다.

두 번째 연구에서는 상대습도가 높은 지역 (> 80 %)에 거주하는 여성의 저 HDL 콜레스테롤혈증 (OR=1.25, 95% CI: 1.06-1.56)과 대사증후군 (OR=1.20, 95% CI: 1.01-1.42) 유병률이 높은 것으로 나타났다. 또한, 상대습도가 높은 지역에 거주하며 신체활동 수준이 높은 남성은 고중성지방혈증의 OR 이 낮았다 (OR=0.56, 95% CI: 0.37-0.85). 상대 습도가 높은 폐경기 여성은 대사 증후군 (5.42, 95 % CI : 1.92-15.27), 혈압 상승 (3.10, 95 % CI : 1.15-8.35), 허리 둘레 증가 (OR = 1.34; 95 % CI : 1.09-1.63).

세 번째 연구에서는 여성에서 LCHF 식사가 고혈압과 역의 연관성을 갖는 반면 (OR=0.34, 95% CI: 0.19–0.59) MCF 식사는 고혈압 (OR=0.50, 95% CI: 0.32-0.79) 및 높은 공복혈당 (OR=0.58, 95% CI: 0.37-0.91)과 역의 연관성을 갖는 것으로 나타났다. MCF 식사를 하며 상대습도가 낮은 지역에 거주하는 여성은 대사증후군과 (OR=0.63, 95% CI: 0.40-0.98), LCHF 식사를 하며 높은 고도에 거주하는 여성은 저 HDL 콜레스테롤혈증과 (OR=0.57, 95% CI: 0.35-0.94) 역의 연관성을 갖는 것으로 확인되었다. 또한, LCHF 식사를 하는 남성 중 신체활동 수준이 낮거나 (OR=2.30, 95% CI: 1.17-4.52) 상대습도가 높은 지역에 거주하는 경우 (OR=2.44, 95% CI: 1.23-4.83) 복부비만의 OR 이 높은 것으로 드러났다.

결론: 에콰도르 성인의 자연환경, 건강 관련 생활행태 요인, 식사패턴은 대사증후군 및 그 위험요인의 유병률과 유의한 관련성을 보였다. 고도가 낮거나 상대습도가 높은 지역에 거주할 때 남녀 모두에게서 대사증후군 및 그 위험요인의 OR 이 높았던 반면, 신체활동 수준이 높은 남성에서 대사증후군 및 그 위험요인의 OR 은 낮게 나타났다. 또한, 여성에서 LCHF 나 MCF 식사는 대사증후군 및 그 위험요인과 역의 연관성을 보였고, 추가분석을 통해 에콰도르 성인에서 탄수화물과 지방 섭취수준, 신체활동, 자연환경과 대사증후군 간에 상호작용에 의한 연관성이 있는 것을 확인하였다. 이러한 연구결과는 생활행태 요인뿐만 아니라 자연환경도 고려한 포괄적인 보건 및 영양사업 수행의 중요성을 시사하며, 대사증후군 예방을 위한 적절한 환경 조건, 생활행태 및 식사 섭취에 관한 후속연구의 기반을 조성할 수 있을 것으로 사료된다.

주요어 : 대사증후군, 고도, 습도, 에콰도르 성인, 탄수화물 및 지방 섭취수준, 신체활동
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