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Review Article

Metabolic Syndrome and Related Risk Factors in Young Ecuadorians

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Abstract

Metabolic syndrome refers to a combination of hypertension, abdominal obesity, insulin resistance and hyperlipidemia. It is associated with other conditions such as varying degrees of abnormal carbohydrate metabolism, either diabetes mellitus or glucose intolerance, obesity and insulin resistance. Nowadays it is proven that it is a health condition that promotes atherosclerosis and type 2 diabetes mellitus. Metabolic syndrome was considered a few years ago, as a condition of adulthood, however, it has recently been demonstrated a prevalence increasing in children, adolescents and young adults linked to the significant increase of obesity in these age groups and therefore an increment in complications like cardiovascular morbidity and mortality increasingly in younger ages.

The criteria for the diagnosis of metabolic syndrome have been developed based on the adult population and its practical utility allows secondary prevention. In young populations, metabolic syndrome is much less prevalent, so the inclusion of other markers such as body mass index and markers of inflammation, pro inflammatory cytokines, C-reactive protein, is essential to make a diagnosis closer to their reality.

We review the literature on metabolic syndrome and its major components in young adults, an age group that for their living conditions is becoming more vulnerable, the same ones that in case of not been controlled, could make complications such as cardiovascular disease, cerebrovascular disease, type 2 diabetes mellitus being present increasingly in younger ages. We include the results of research conducted in young students in the first semester of the Faculty of Medical Sciences of the Central University of Ecuador.

Keywords: *Metabolic Syndrome; Obesity; Insulin Resistance; Diabetes; High Blood Pressure*

Abbreviations

ATP III: Adult Treatment Panel III; BP: Blood Pressure; CVD: Cardiovascular Diseases; IR: Insulin Resistance; DM2: Mellitus Diabetes Type 2; MS: Metabolic Syndrome; BMI: Body Mass Index; LDL: Low Density Lipoprotein; HDL: High Density Lipoproteins; ENSANUT: ECU National Health and Nutrition Examination Survey; UCE: Central University of Ecuador; WHO: World Health Organization; IDF: International Diabetes Federation; JNC 7: Seventh Report of the Joint National Committee; TC: Total Cholesterol; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; AP: Abdominal Perimeter

Introduction

Metabolic Syndrome (MS), described in 1998, refers to a combination of hypertension, abdominal obesity, insulin resistance (IR) and hyperlipidemia [1]. Nowadays it is well known it is a condition that promotes atherosclerosis and type 2 diabetes mellitus [2].

MS is synonymous of ''X syndrome'' and ''insulin resistance syndrome'' cause it is tightly associated with obesity, although this relation is not exclusive, as it is shown in the fact of no obese people with MS [4].

MS was considered until some years ago, as an own condition from the adulthood, however it has been proved a growing prevalence in children, teenagers and young adults, related to a substantial increment in obesity in these age groups [4-6] and therefore the cardiovascular morbi-mortality increasingly earlier ages.

Since some decades before, some researchers and organizations have proposed several metabolic syndrome definitions. The one from the World Health Organization (WHO), first international accepted definition, consider MS with the following criteria: glucose intolerance, either type 2 DM or insulin resistance, added to two or more from the following issues: high blood pressure, dyslipidemia, abdominal obesity and microalbuminuria [7]. The *National Cholesterol Education Program Adult Treatment Panel* (NCEP ATPIII) [8], propose changes about leave out the IR and grant greater importance to the hypertriglyceridemia and HDL-cholesterol's fraction, defined the risk factors and cut-off points for the diagnosis of MS. According to these criteria, it is necessary the concurrence of at least 3 of the following factors: abdominal obesity, raised triglycerides, low concentrations of HDL-c, elevated blood pressure and raised plasma glucose. Since then, the cut-off point for defining hyperglycemia has been modified, which allows an earlier detection of insulin resistance [9,10].

During childhood and adolescence, obesity has been considered for the World Health Organization (WHO) as a public health issue. Changes in life style that trigger scientist technical evolution have been indicated as a determining factor of this condition [11]. In this age group, obesity seems to be the most important trigger of IR, which turns children and obese teenagers in a risk group for MS development.

Nowadays, there is ongoing debate about the underlying cause of MS, but most scientists agree that IR and obesity are the most important factors, without take aside the genetic predisposition that plays a preponderant role, meaning etiopathogenesis of MS is a complex interaction of genetic and environmental factors [12,13].

In general terms, the criteria for the diagnosis of MS have been elaborated based on the adult population and their practical usefulness makes secondary prevention possible [14,15]. In younger populations, MS is a lot less prevalent [16], so that it becomes indispensable for its diagnosis, the inclusion of other markers such as body mass index (BMI) and inflammatory markers (proinflammatory cytokines, ultra-sensitive C-reactive protein (CRP).

Since MS was described and considered a health problem, several studies were initiated to try to establish its prevalence in the population. In the 1980s, appear several research about epidemiological aspects of diabetes mellitus and hypertension association [17], but the epidemiological study that provided evidence for the existence of MS was the San Antonio Herat Study [18], in which it was shown that total prevalence of obesity, diabetes mellitus or glucose intolerance, hypertension, hypertriglyceridemia and hypercholesterolemia, was much higher than each of them isolated.

Prevalence of MS in Young Adults

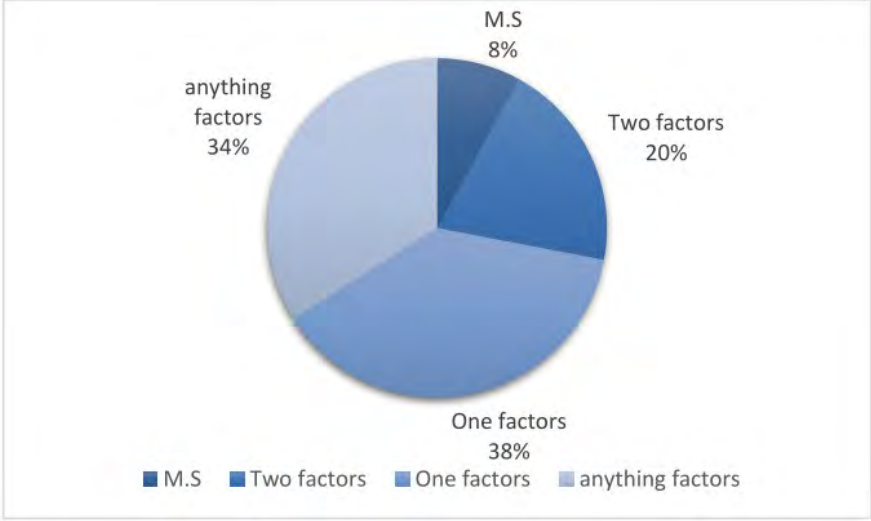
The global prevalence of MS ranges from < 10% to 84%, depending on age, region, urban or rural environment, ethnicity and the definition of the metabolic syndrome used [19-21]. In the United States, between 1994 and 2000, the prevalence of MS in adults increased from 23% to 27% along with an increase in obesity and physical inactivity [22]. Developing regions such as Latin America, due to the change in lifestyle factors that contribute to the development of SM, may show even greater increases in their prevalence in relatively short periods of time [23].

A Mexican study of newly enrolled students at "Universidad de Veracruz" found a prevalence of MS of 2.8%, but the percentage of students at high risk for developing MS was 34%, the highest risk was for women with 43.75% [24]. In Brazil, the prevalence of MS varies

from 1.1% in the adolescents of public schools, 6% in adolescents with a family history of DM2 and 26.1% in obese children and adolescents [25].

In Ecuador, the follow-up given to the diagnosis of MS for predicting the risk of cerebrovascular disease and diabetes mellitus is limited. Despite there are important isolated data to justify the study of MS, there are few publications on this subject, perhaps the most significant is the one reported in a study of a male population sample from the Highland Region of Ecuador between 30 and 60 years, in which was demonstrated a prevalence of MS of 13.4% according to ATPIII criteria and 33.1% according to IDF [26]. There are no studies on MS and their risk factors in the young population.

The Unit of Metabolic and Infectious Diseases from the Faculty of Medical Sciences of the Central University of Ecuador (UCE) carried out a research work in medical students between 17 and 25 years [27], in which was determined the risk factors associated with the prevalence of metabolic syndrome. In the study done by Ruano C., *et al*. there were included all students enrolled in first, second and third semester from the Medicine Career of the Medicine's Faculty of the UCE, period October 2014 March 2015 (n = 883). The researchers found a prevalence of 8.2% (n = 73) of SM (IDF), which was higher in women (68%). It should be noted that 16.08% of the students had at least two risk factors for development of MS and 50% of them at least one, constituting a population with a high risk of MS, only 34.65% of the population studied did not present any risk factor [28] (Graph 1).



Graph 1: *Risk factors for M.S (n = 883).*

Obesity and MS

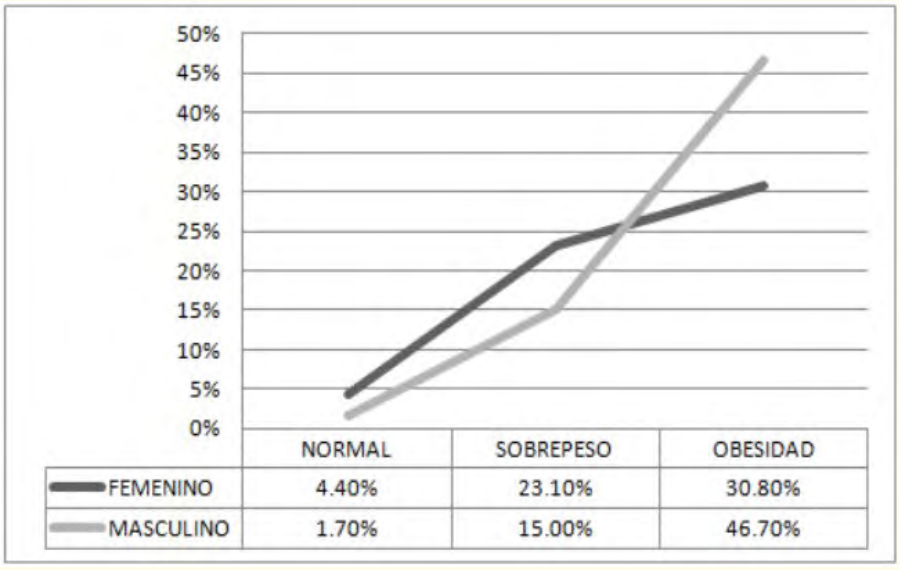
At present, obesity in adolescence is a serious public health problem. In developed countries, there are about 110 million young people diagnosed as overweight or obese [29]. It is known that obesity increases cardiovascular risk and metabolic syndrome in children [30], adolescents and adults [31], and it is true that inflammation plays an important role in the development of these issues [32]. Some authors attribute the high percentages of overweight and obesity to the lack of physical activity that is becoming more frequent at an early age. Physical activity is inversely associated with different metabolic indicators such as lipid profile, IR and peripheral vascular resistance, all of them, components of MS [33]. In sedentary subjects, lipid profile alterations have been found, including high levels of triglycerides,

decrease in HDL cholesterol, and elevation of non-HDL and Apo B cholesterol, all of which are associated with increased cardiovascular risk [34].

Data published in the "Encuesta Nacional de Salud y Nutrición" ENSANUT-ECU 2011 - 2013, indicate that the prevalence of overweight and obesity in Ecuador in adolescents aged 12 to 19 years is 26%, while in those older than 19 years it rises to 62.8% being greater in women (65.5%) than in men (60%) [35]. Other authors found a prevalence of overweight and obesity of 13.7% and 7.5% respectively [36].

In the studies made in Central University, the prevalence of pre-obesity was 22.24% and obesity 3.14% [27], 20,9% of women and 24.7% of men were found pre-obese, 2.3% of women and 4.6% of men had obesity.28 In the diagnosis of pre-obesity and obesity was used the body mass index (BMI) taking into account the recommendations from the WHO.

The prevalence of MS according to BMI by sex was also calculated (Graph 2), finding that 4.40% of women and 1.70% of men with a normal weight had MS; in the students who presented overweight, the prevalence increased to 23.10% in women and 15.00% in men and with obese students rises to 30.80% and 46.70% in women and men respectively [28].



	NORMAL	SOBREPESO	OBESIDAD
FEMENINO	4.40%	23.10%	30.80%
MASCULINO	1.70%	15.00%	46.70%

Graph 2: *Prevalence of MS according to BMI.*

The risk of developing MS in overweight women was 6.75 (3.66 - 12.45) times more than in women with normal weight (p 0.001), while in overweight or obese men the risk was 14.06 (4.63 - 42.63) times more than in men with normal BMI (p 0.001) [28].

Abdominal Perimeter and SM

Combined studies of anthropometry and computerized axial tomography have shown a strong association between waist circumference or abdominal perimeter (AP) and abdominal fat, which has given AP a superior discriminatory capacity than body max index (BMI) and waist-to-hip ratio, in that order, as a marker of risk for chronic diseases such as hypertension, T2DM and cardiovascular disease [37].

In the study from Universidad Central, we found that waist circumference or abdominal circumference was altered (women > 80 / men > 90) in 52.3% of women and 26.2% of men (p 0.001) [28].

It was also found that in students who perform physical activity 3 or more days a week and more than thirty minutes (non-sedentary), 70.3% have a normal abdominal perimeter compared to those who do not perform any activity (sedentary) where the percentage of students with normal abdominal circumference decreased to 52.27%, this difference is statistically significant, furthermore, for sedentary lifestyle, an elevated risk was found for developing an increased abdominal circumference OR 1.96 (1.30 - 2.97) (p 0.001) (Table 1) [28].

		BMI *				AP >80 female y >90 male**			
		<25		>25		Altered		Normal	
		"n"	%	"n"	%	"n"	%	"n"	%
No physical activity		347	74.95	116	25.05	221	47.73	242	52.27
1 to 2 days	< 30	14	56	11	44	12	48	13	52
	> 30	199	75.67	64	24.33	105	39.92	158	60.08
3 or more	< 30	6	66.67	3	33.33	3	33.33	6	66.67
	> 30	92	74.80	31	25.20	36	29.27	87	70.73

Table 1: *Days per week that students perform physical activity according to BMI and AP.*

p 0.28/p<0.05*

Other Risk Factors for MS

Table 2 shows the prevalence of other risk factors for MS in relation to sex, found in the study from Universidad Central [28]. HDL-c was altered in 39.7% of women compared to 18.2% in men (p 0.001). The blood pressure levels were above normal limits in men more than in women (24.4% vs 9.8%, p 0.001). The values of total cholesterol, LDL, triglycerides and glucose did not present statistically significant differences by gender. Smoking in men is higher than in women (19.8% vs 7.3%, p 0.001). Regarding sedentary lifestyle, the number of women who do not perform physical activity is greater than in men (92.5% vs 75%, p0.001).

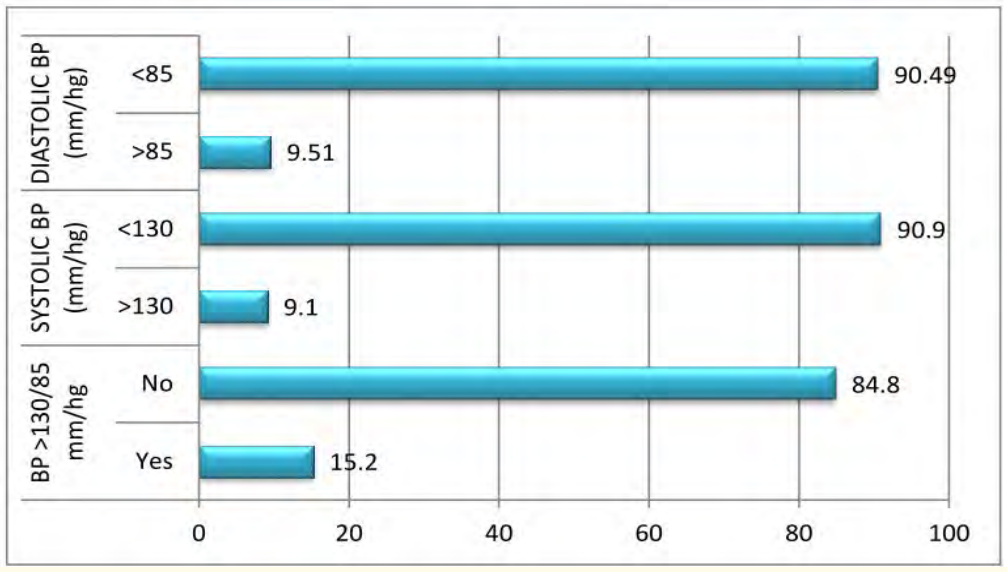
	%Female (n= 559)	%Male (n = 324)	p
Overweight/Obesity	23.3	29.3	0.46
Overweight (25 - 29.9 kg/m^2)	20.9	24.7	
Obesity (> 30 kg/m^2)	2.3	4.6	
Waist circumference (AP) (Men > 90/Women > 80)	52.3	26.2	0.001
Total Cholesterol (> 200 mg/dl)	7.9	5.2	0.12
Borderline High (200 - 239 mg/dl)	7.2	4	
High (> 240 mg/dl)	0.7	1.2	
c HDL < 40 mg/dl Men, <50 mg/dl Women	39.7	18.2	0.001
c LDL > 100 mg/dl	24.9	26.9	0.71
Above optimal (100 - 129 mg/dl)	19.9	22	
Borderline high (130 - 159 mg/dl)	4.3	3.7	
High (> 160 mg/dl)	0.7	1.2	
Triglycerides >150 mg/dl	10.6	12.3	0.63
Borderline high (150 - 199 mg/dl)	6.6	8.3	
High (200 - 400 mg/dl)	3.9	4	
Blood Pressure (> 130/85 mg/dl)	9.8	24.4	0.001
Glucose (> 90 mg/dl)	6.4	11.1	0.01
Smoking	7.3	19.8	0.001
Sedentary lifestyle	92.5	75	0.001

Table 2: *Prevalence of risk factors assessed according to sex.*

In relation to total cholesterol, LDL and glucose, the values were not out of normal range in most of the sample. It is noteworthy that the alterations of the HDL values found in the Ecuadorian study, predominantly occur in women 39.7%, compared to a 18.2% in men. Regarding triglyceride values, it was found that 12.3% in men and 10.6% in women were greater than 150 mg/dl [28].

High Blood Pressure

In the study carried out on university students from Universidad Central, the 15.2% (n = 134) of the sampling had a BP > 130/85, 9.51% (n = 84) presented an increase in systolic BP, whereas diastolic BP was elevated in 9.1% (n = 81) (Graph 3) [38].



Graph 3: *Prevalence of increased BP (> 130/85 mmHg) in general population.*

In the same study, if the JNC 7 cutoff points were taken as a reference, the prevalence of hypertension (> 140/90) was 3.7% and pre-hypertension (120 - 139/80 - 89) was 33.9%. Students with normal BP (< 120/80) were 62.4%.

Comparing the averages of the female and male groups, there were statistically significant differences in both systolic and diastolic BP ($p < 0.05$), with a significantly higher mean in males. The BP levels were above the normal borderline in males more than in females (24.4% vs 9.8%). The authors also found a probable association between the risk of developing hypertension at an early age and some altered risk factors such as triglycerides, BMI, and abdominal perimeter [38].

Inflammatory Markers and SM

Until a few years ago, adipose tissue was considered just an energy-saving energy reservoir, but now, is known to be an active metabolic tissue that releases a significant number of bioactive mediators called adipokines. Some of these mediators (TNF-alpha, IL-6, IL-1) induce a low-grade systemic inflammation in people with excess body fat [39].

Recent studies suggest a possible relationship between the development of cardiovascular disorders and a low-grade chronic inflammation [32], which is mediated by disorders in adipose tissue secretion by cytokines such as ceruloplasmin, leptin, adiponectin, and IL-6

[40-42], that linked to increased blood lipid levels constitutes risk factors for the early development of cardiovascular disease [43], which means that the determination of serum levels in the adolescent population constitutes an effective tool to predict and prevent the risk of cardiovascular disorders [44-46].

Several studies have demonstrated the sensitivity of IL-6 to increases in body weight, and it is therefore considered an excellent marker of metabolic syndrome [43].

In the other hand, this avidity shown by IL-6 has made possible its consideration as a potent inducer of the inflammatory phase in young obese subjects [47].

C-reactive protein (CRP) is an acute phase protein produced by the liver in response to factors released by adipocytes. It increases in a direct proportional way with IL-6 in acute and chronic inflammatory diseases and is an independent predictor of myocardial infarction, arterial disease, sudden cardiac death, even in healthy population [48]. CRP concentrations reflect the inflammation related with lifestyle, including obesity, dietary factors and physical activity, it has also been associated with insulin resistance and pre-clinical atherosclerosis in adults [49].

CRP is considered a powerful indicator of future heart disease [50], elevations in serum concentrations found in adolescent obese subjects reflects the high risk of cardiovascular events that these young people have [51]. Several studies have also shown that, in parallel with the elevation of serum levels of these cytokines, an increase in resistance to the action of insulin occurs in a parallel mode in these patients [46,52].

In the study conducted in the Faculty of Medical Sciences of the UC of Ecuador, in relation to the inflammatory markers, it was found that 19.4% of the general population presented CRP values between 1 and 3 mg/dl, and a 7.4% from 3 to 9 mg / dl. A 7,48% presented alteration of IL6 levels (> 3.1 mg/dl). The average values found in IL6 according to BMI < 25 kg/m^2 and > 25 kg/m^2 showed a slight increase in the overweight and obesity group (p 0.0001) and in the group with MS (p 0.0001) (Table 3) [28].

		CRP	p	IL6	p
Perimeter Abdominal	Increased	0.431 ± 0.533	p > 0.05	2.609 ± 1.14	p >0.05
	Normal	1.01 ± 0.955		2.522 ± 1.818	
Population	Healthy	1.018 ± 0.959	p < 0.05	2.513 ± 1.823	p > 0.05
	MS	0.434 ± 0.505		2.641 ± 1.135	
BMI	Normal	1.022 ± 0.946	p < 0.05	2.245 ± 0.729	p < 0.05
	Overweight and Obese	0.344 ± 0.514		3.231 ± 2.778	

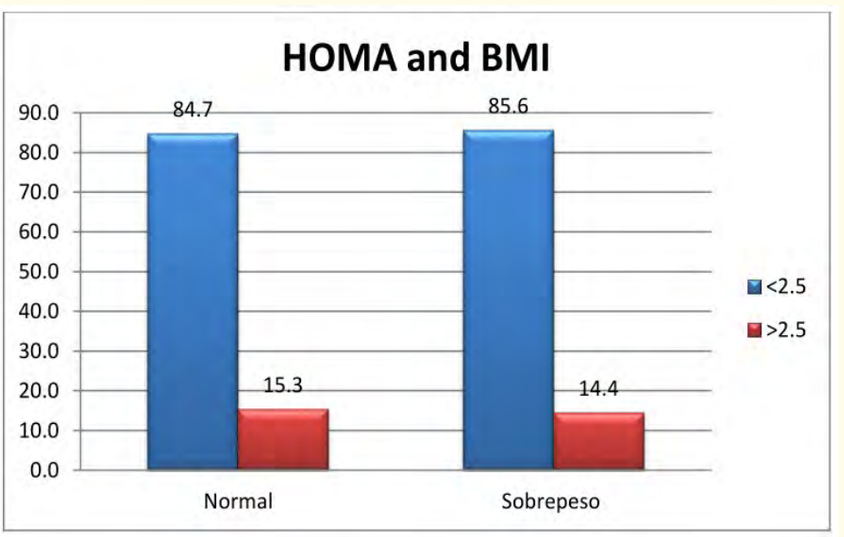
Table 3: *Averages of inflammatory markers in relation to the presence of MS, AP and BMI.*

There are few studies evaluating the association between markers of inflammation and metabolic risk (IR, hypertension, dyslipidemia), which seems to be attenuated when adjusted for obesity. Some authors have reported higher CRP levels in adolescents with MS [52]. In the study carried out in students of the UCE Medicine Career, the levels of us-CRP present a different behavior, it was found that the average us-CRP according to abdominal perimeter, is higher in normal subjects, this does not persist in IL6, where the value is slightly higher in those with increased abdominal perimeter [28].

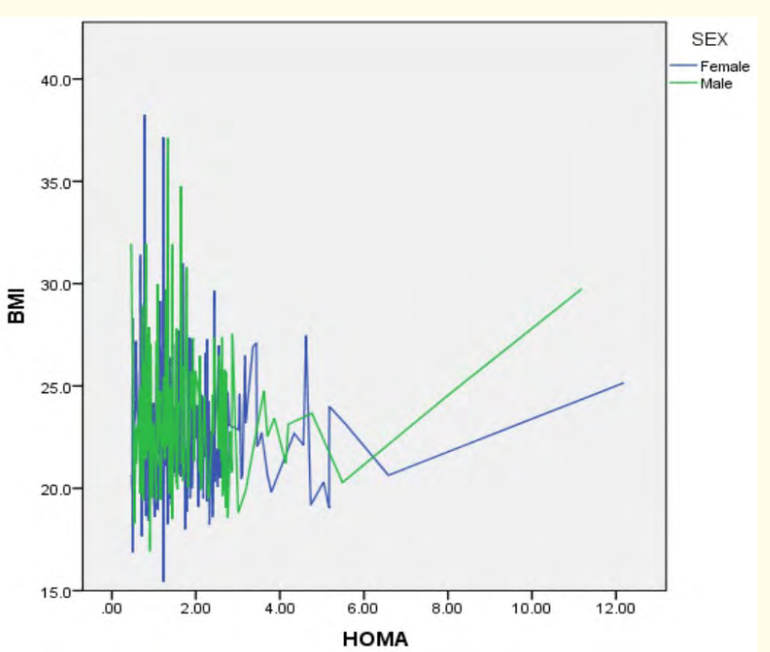
Disorders in Glucose Homeostasis (Insulin Resistance)

IR is defined as a condition characterized by a lower biological activity of the hormone that is expressed in its different metabolic actions, being the most evident in the metabolism of glucose. This takes place in organs and tissues such as the liver, adipose and muscular tissue and in the vascular endothelium too. A certain degree of insulin resistance is physiological during puberty, in pregnancy and with aging, and is usually compensated for an increased secretion of insulin by the beta cells of the pancreas [53].

In the Ecuadorian study [28], the percentage of subjects with insulin resistance who do not present alteration in weight is slightly higher than in students who are overweight and obese, data that do not agree with the literature, can be attributed to genetic variables or to the high indexes of familial pathological antecedents reported by the students, since at least 1 of each 2 has a first degree relative with DM, finding that the overweight and obesity is not a determining factor as it is in an older population (Graph 4 and 5).



Graph 4: *Percentages of insulin resistance assessed by BMI.*



Graph 5: *Insulin resistance versus BMI (stratified by sex).*

Conclusions and Recommendations

Nutritional recommendations in MS aim to improve insulin sensitivity and prevent or treat metabolic disorders. Although some dietary nutrients may have some influence on insulin sensitivity, the main benefits are obtained from weight loss [54]. Several studies recommend decreasing intake of saturated fatty acids and trans fatty acids and increasing the intake of monounsaturated fatty acids (MUFA) and polyunsaturated fatty acids (PUFAs) [29]. The consumption of MUFA and PUFA favors the control of blood pressure, coagulation, endothelial function and insulin resistance, having beneficial effects in the prevention and treatment of MS [24].

Students entering the university have tendency to adopt poor feeding habits and a sedentary lifestyle, which is aggravated by a other issues like stress and heavy workload, that result in the intake of fast foods with poor nutrient supply, a disrupted meal schedule and lack of time to perform physical exercise, and this way developing overweight, obesity and the components of the Metabolic Syndrome [24,25].

In the sample studied in our study it was found that 1 in 13 had MS, 1 in 10 presented two risk factors and 1 in 2 at least one risk factor for MS. 1 out of 4 students had some degree of overweight or obesity and significant percentage changes in plasma lipid levels and blood pressure. Although most of students are still in the low risk categories, it is advisable to continue doing this type of studies that will allow us to increase knowledge about the presence of risk for chronic non-communicable diseases and to diagnose and treat adequately the patients with MS. Considering the large number of people with at least one risk factor, it is essential to promote healthy lifestyles that include non-pharmacological measures such as diet and exercise.

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Conflict of Interest

Declare if any financial interest or any conflict of interest exists.

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