Myocardial infarction in young Mexicans associated to metabolic syndrome

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Abstract

Background: *Acute coronary diseases are catastrophic, especially in young patients.* **Objective:** *To determine the risk of metabolic syndrome (MS) for premature acute myocardial infarction (AMI), combined with familial, behavioral, and nutritional factors in the northeast of Mexico.* **Material and methods:** *This is a case control study of patients less than 47 years of age with no personal history of angina, AMI, or cerebrovascular disease. Cases corresponded to patients with AMI (incident and primary cases; n = 55) and controls were blood donors located at the same hospital (n = 55). Behavioral, nutritional, and cardiometabolic risk factors were measured. Multivariate logistic regression was used for estimating odds ratios (OR) and 95% confidence intervals (95% CI).* **Results:** *MS increased the risk for premature AMI (95% CI: 1.73-39.5) eightfold, followed by smoking (OR: 7.76; 95% CI: 1.27-47.3), family history of AMI or sudden death (OR: 11.0; 95% CI: 2.03-60.4), and sedentary lifestyle (OR: 2.26; 95% CI: 2.52-9.80), independent of potential confounders.* **Conclusions:** *The study highlights the magnitude of the risk of MS for AMI in Mexican young adults. The phenomenon of coronary diseases among young adults needs essential attention from the health sector.*

KEY WORDS: *Acute myocardial infarction. Metabolic syndrome. Risk factors.*

Introduction

Lifestyle changes have favored the onset of cardiovascular conditions at increasingly younger ages and, although acute myocardial infarction (AMI) generally occurs in people older than 45 years, young individuals suffer it too. For example, in Spain, 5.6% of AIMs were at a younger ages[1], and in Portugal, 6.7%[2]. In Mexico, the Health Ministry published a frequency of 6.2% over the 2004-2007 period[3].

Premature AMI represents a new public health challenge, and is this field which is responsible to address its main risk factors, with smoking standing out. There are studies that report a prevalence of 69% of this habit in patients with AMI younger than 46 years[4]. The MONICA project, with a 9-year follow-up in 21 countries, revealed that smokers between 35 and 39 years of age had a 5-fold higher risk for AMI in comparison with non-smokers[5]. Another factor is atherosclerosis due to the formation of atheromas that harm the arteries and to its relationship with mean platelet volume elevated values[6]. Obesity, which is common in ages younger than 45 years, also increases the risk for suffering AMI by up to 5-fold[7]. This problem has been found even in individuals younger than 35 years with coronary artery disease. One study carried out in Kuwait reported that obesity occurred in 20%, and overweight in 39% of AMI cases in young subjects[8].

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Central obesity has been described as a cardiovascular risk predictor, even more important than body mass index, since it is associated with cardio-metabolic damage induced by arterial hypertension, dyslipidemia and glucose intolerance[9]. On the other hand, recreational drugs such as cocaine have acquired relevance as a risk factor in young individuals; only in the USA, 450,000 recorded visits to the emergency department were related to its consumption[10], and in the United Kingdom, 45% of young adults admit having used it at least once; many of them were smokers and alcohol consumers as well[11]. AMI risk has been described to increase up to 23-fold within the first 60 minutes after the use of cocaine[12]. Another important factor, associated since decades with premature AMI, is a family history of coronary disease, with a risk up to 4-fold higher for developing the disease[13]. In the Czech Republic, 64% of patients younger than 45 years were found to have a family history of cardiovascular disease[14], and in Austria, in patients younger than 40 years, 32% had a family history of premature infarction and 76% had a family history of hyperlipidemia. The latter study found that the phenotype for familial hypercholesterolemia increased to up to 24-fold the risk of AMI in young subjects[15].

Some of the above-described risk factors can converge in the so-called metabolic syndrome (MS). In South Africa, a prevalence of 61% of this condition has been reported in individuals younger than 45 years with AMI[16], and MS has been observed to increase the risk of coronary artery disease mortality to the double, and to the triple in the case of AMI and stroke[17]. Furthermore, in the post-infarction follow-up of patients with more than 3 MS criteria, poorer clinical evolution was observed (reinfarction, angina, heart failure or death)[18]. In summary, evidence indicates that there are individual factors that can increase the risk of premature AMI, and it is feasible assuming that in MS with many simultaneously gathered factors, the risk could be considerably increased in young adults. Internationally, there are only few publications looking into the threat MS can represent for suffering an AMI at an early age, and in Latin America and Mexico there are no such publications. For this reason, and in view of the significance of the relationship between MS and coronary disease, we considered relevant, and also necessary, to determine the risk it might represent for AMI, combined with familial, behavioral and nutritional factors, in subjects younger than 47 years from the northeastern region of the country, which was the purpose of this research work.

Methods

A case-control study in subjects younger than 47 years was carried out in the northeastern region of the country between December 2014 and July 2015. The cases were patients diagnosed with AMI (incident and primary cases; n = 55), hospitalized at the IMSS no. 34 Cardiology UMAE, which is a reference center of Mexico's northeast that, in addition to Nuevo León, gives coverage to the states of Coahuila, Tamaulipas, Chihuahua, Durango, San Luis Potosí and Zacatecas. The diagnosis was established according to the American College of Cardiology criteria: a) progressive increase and decrease of troponin or CK-MB (creatine kinase-MB), b) symptoms of ischemia, c) appearance of new necrosis Q-waves in the electrocardiogram (ECG), or d) ECG changes suggestive of ischemia-ST segment elevation or depression[19]. The controls were non-AMI diagnosed subjects, identified as donors at the blood bank of the same hospital (n = 55). Anybody with a previous history of angina, AMI or stroke was excluded. The sample size was sufficient to confer a power higher than 90% with a confidence level of 95%, given the frequency of MS recorded both in cases (83%), and in controls (31%)[20]. The study was conducted with adherence to the General Statute of Health regulations for health-related research. An informed consent letter was provided to all study subjects, and information anonymity and confidentiality were ensured. The protocol was approved by the corresponding Ethics and Research Committee.

Risk factors of behavioral and familial origin

By means of interviews, data on usual tobacco consumption were collected (non-smoker/light smoker with < 6 cigarettes/day; moderate smoker with 6-16 cigarettes/day; heavy smoker with > 16 cigarettes/day) or former smoker; usual alcohol consumption (never/2-4 times per month/2-3 times per week/≥ 4 times per week); usual cocaine consumption (yes/no); usual marihuana consumption (yes/no) and sedentarism (physical exercise yes/no). Information was also gathered on personal history of diabetes and hypertension, family history of a first degree relative with AMI or sudden death (yes/no), and socio-demographic profile (age, gender, marital status, level of education, place of residence and occupation).

Risk factors of nutritional origin

Weight (kg) and height (m) were measured with the patient barefoot and wearing light clothes by using a scale with an integrated stadiometer. Body mass index was calculated as weight/height squared and was categorized as low weight (< 18.5 kg/m^2), normal weight (18.5-24.9 kg/m^2), overweight (25.0-29.9 kg/m^2), obesity (30.0-34.9 kg/m^2) and morbid obesity (≥ 35 kg/m^2). Waist circumference (cm) was measured with a non-flexible measuring tape, with the patient standing up and at the end of a normal expiration, using the border of the last rib and the iliac crest as reference; central obesity was considered from 90 cm on in males and from 80 cm on in females.

Risk factors of cardio-metabolic origin

Systolic and diastolic blood pressure (mmHg) was recorded with the patient at rest, seated or laying down, using a digital sphygmomanometer (Tycos Classic Hand Aneroids, Welch Allyn Inc, Skaneateles Falls, NY, USA). Laboratory analyses were obtained for plasma glucose, triglycerides, total cholesterol, high-density lipoprotein (HDL) cholesterol and low-density lipoprotein (LDL) cholesterol. MS was considered as the presence of three or more of the following of the World Federation of Diabetes criteria[21]: central obesity with waist circumference ≥ 90 cm in males and ≥ 80 cm in females, systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg, triglycerides ≥ 150 mg/dL; HDL cholesterol < 40 mg/dL in males and < 50 mg/dL in females, and fasting plasma glucose ≥ 100 mg/dL. Blood samples were obtained after an 8-hour fasting. It is important mentioning that the laboratory meets the corresponding quality standards. Data collection was in charge of two undergraduate medical students who were making their social service in the field of research, and who were standardized and supervised to verify that stipulated procedures were adhered to.

Statistical analysis

Descriptive statistics was carried out with central tendency and dispersion measures for continuous variables and frequency distribution for categorical variables. The chi-square test was used in the univariate analysis to identify the association between the risk factors under study and premature AMI, and Student's t-test for independent populations was used to identify non-categorical variables mean differences. In the multivariate analysis, binary logistic regression analysis was carried out using the "enter" method, with the OR and 95% CI being estimated. The gender variable was not included in the model given the male predominance in the cases (only two females with premature AMI were identified).

Results

Mean age in cases was 41.6 ± 3.9 years, whereas in the controls it was 31.8 ± 7.6 years (p = 0.001). Male gender, economically active occupation, personal history of diabetes and hypertension, and family history of a first-degree relative with AMI or sudden death were predominant in the cases (Table 1), as well as sedentarism and active smoking, cocaine consumption, morbid obesity and MS. In addition, MS predominance was found in males (62.7% vs. 37.3%; p = 0.033). Furthermore, systolic blood pressure, waist circumference, fasting plasma glucose and triglyceride values were more elevated (Table 2).

The multiple logistic regression model showed that MS increased up to 8-fold the possibilities of premature AMI, followed in risk intensity by smoking, direct family history of AMI or sudden death and sedentarism, regardless of other potential confounders (Table 3). Figure 1 shows MS components distribution according to premature AMI status; the frequency of low HDL cholesterol and elevated blood sugar stands out in the cases. Restricting the analysis only to the population with MS showed a high prevalence of high blood sugar and low HDL cholesterol in the cases (Fig. 2). Figure 3 describes the number of MS components, clearly showing that only patients with premature AMI had 4 and 5 components.

Discussion

The study highlighted the magnitude of the risk for AMI conferred by MS in a Mexican population younger than 47 years. Individual risk factors identification offers the advantage that they can be early addressed, thus avoiding or delaying the establishment of MS strictly speaking and, eventually, the manifestation of AMI. Once MS is present, the risk of premature AMI should be considered, regardless of smoking, sedentarism and family history of AMI or sudden death.

With regard to gender, most studies agree on the high frequency of premature infarctions in males[22].

Table 1. Socio-demographic, personal and familial profile, according to premature AMI condition in northeast Mexico, 2015

Variable	Cases (n = 55)	Controls (n = 55)	p
Male gender (%)	96.4	76.4	0.002
Level of education (%)			
Up to secondary school	49.1	41.8	
High school or more	50.9	50.2	0.444
Marital status with partner (%)	80.0	65.5	0.080
Occupation with income (%)	90.0	76.4	0.039
Place of residence (%)			
Local (Nuevo León)	36.4	70.9	0.001
Foreign (Coahuila, Tamaulipas, San Luis Potosí)	63.6	29.1	
Personal history			
Diabetes (%)	38.0	7.0	0.001
Hypertension (%)	40.0	10.0	0.001
Family history of first-degree relative with AMI or sudden death (%)	49.1	14.5	0.001

Table 2. Behavioral, nutritional and cardio-metabolic risk profile according to premature AMI condition in northeastern Mexico, 2012

Variable	Cases (n = 55)	Controls (n = 55)	p
Alcohol consumption (%)			
Never	34.5	40.0	
1-4 monthly	58.2	53.7	
1-4 weekly	7.3	5.6	0.778
Sedentarism (%)	83.6	52.7	0.001
Active smoking (mild, moderate or heavy) (%)	63.6	40.0	0.046
Cocaine consumption (%)	9.1	0.0	0.020
Marihuana consumption (%)	9.1	1.8	0.200
Systolic blood pressure (mmHg)*	129.4 ± 22.1	116.1 ± 11.9	0.001
Diastolic blood pressure (mmHg)*	78.8 ± 13.6	76.2 ± 7.6	0.230
Waist circumference (cm)*	104.0 ± 12.5	95.8 ± 9.3	0.001
Body mass index (kg/m^2)*	30.2 ± 6.1	27.3 ± 3.7	0.003
Nutritional status (%)			
Normal weight	14.6	30.9	
Overweight	47.3	45.5	
Obesity	25.5	21.8	
Morbid obesity	12.7	1.8	0.048
Fasting plasma glucose (mg/dL)*	167.0 ± 91.0	95.4 ± 19.0	0.001
Total cholesterol (mg/dL)*	174.7 ± 43.5	194.5 ± 38.8	0.020
HDL cholesterol (mg/dL)*	33.1 ± 11.4	47.4 ± 8.8	0.001
LDL cholesterol (mg/dL)*	100.0 ± 38.3	121.0 ± 33.1	0.090
Triglycerides (mg/dL)*	184.3 ± 82.5	141.3 ± 91.9	0.017
Metabolic syndrome (%)	82.9	30.8	0.001

* $\bar{x} \pm S$

Atherosclerosis progression is said to be delayed with estrogen replacement therapy in the female population[23]. The risk of premature AMI by a family history of first-degree relative was not surprising, since other authors have referred it in the past[24]. Familial combined hyperlipidemia (cholesterol, triglycerides and Apo B) has been confirmed in up to 38% of those who survive an AMI before 40 years of age[25]. Among the behavioral factors, sedentarism, which is regarded by the World Health Organization as the fourth most prevalent coronary risk factor, stood out. In this study, 8 out of every 10 patients with premature AMI were

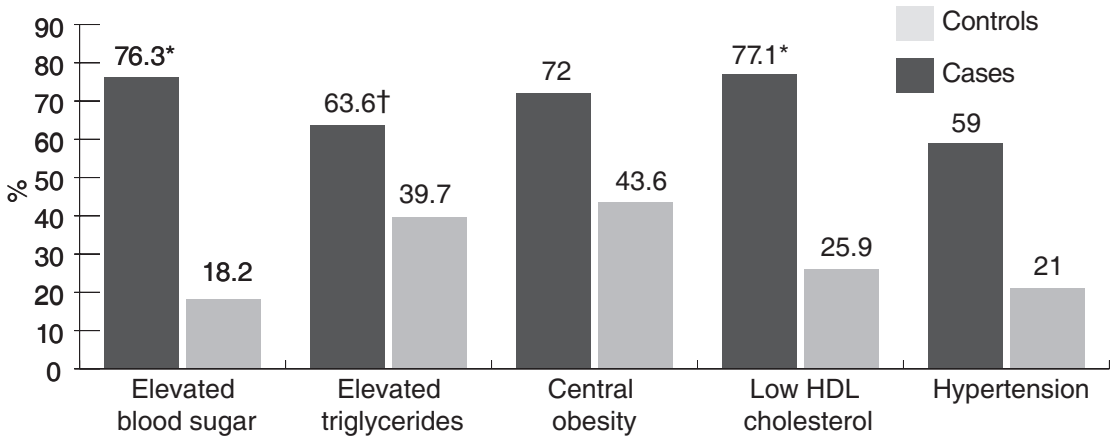

Figure 1. *MS components distribution, according to premature AMI condition in northeastern Mexico, 2015 (n = 110).*
**p = 0.028.*
†p = 0.001.
Elevated blood sugar: ≥ 100 mg/dL: elevated triglycerides: ≥ 150 mg/dL; central obesity: waist circumference ≥ 90 cm in males and ≥ 80 cm in females; low HDL cholesterol: < 40 mg/dL in males and < 50 mg/dL in females; hypertension: systolic blood pressure ≥ 130 mmHg and diastolic blood pressure ≥ 85 mmHg.

Table 3. Binary logistic regression analysis of risk factors for premature AMI in northeastern Mexico, 2015 (n = 110)

	OR (95% CI)	p
Metabolic syndrome	8.27 (1.73-39.5)	0.008
Smoking > 6 cigarettes per day	7.76 (1.27-47.3)	0.026
Direct family history of AMI or sudden death	11.0 (2.03-60.4)	0.005
Sedentarism	2.26 (2.52-9.80)	0.045
Age	1.27 (1.09-1.49)	0.002

Other variables present in the model: nutritional status (p = 0.85), cocaine consumption (p = 0.99) and alcohol consumption (p = 0.38). $R^2 = 0.79$, Hosmer-Lemeshow test with p = 0.270.

sedentary, with this figure being higher than that in those with no AMI. Other statistics, such as ENSANUT 2012[26], in Mexico, showed that 81.2% of adults were sedentary, similar to reports by the National Health Survey in Colombia, which indicates prevalences ranging from 70% to 85%[27]. One of the works with the highest impact was a study by Cambridge University investigators in a 12-year cohort (1990-2000), which reports that sedentarism was responsible for more than double the deaths in comparison with obesity[28]. Added to this is smoking, which is a habit that is generally acquired at an early age in life due to strong social influence, which, as in other studies, increased the risk to suffer a premature AMI. Hbejan[29] found that risk is increased by up to 5-fold in smokers younger than 50 years; in our study, the highest risk was from the consumption of six cigarettes a day on. Another addiction, cocaine, a drug that has been more strongly implied in the occurrence of AMI in young people, was documented in 1 out of every 10 cases, with frequency being significantly higher than in controls. In Chile, Méndez et al.[30] reported in 2013 a prevalence higher than 40% in patients younger than 40 years with AMI. In Mexico, this subject has been poorly explored and should be more deeply investigated, since the consumption of this type of drugs has increased over the past few years in the young population[31].

As for cardio-metabolic-origin factors, morbid obesity stood out in the cases. Overweight and obesity are concerning in Mexico, where they are at second place in the world, with a prevalence of 71.3% in adults, 35% in adolescents and 34.4% in children[32]. This leads to a reflection on childhood obesity continuity into adulthood, together with a higher possibility to develop cardiovascular diseases and diabetes at earlier ages. Unlike bodily distributed fat, abdominal obesity refers to fat located between abdominal cavity organs, which makes it a better predictor of coronary risk. Here, a significant difference was found in lipid profile components between cases and controls; especially, HDL cholesterol was low in patients with premature AMI. This leads to questioning about the origin of this disorder since early ages. Large investigations, such as the nation-wide research carried out in the USA, have revealed that 23.3% of young subjects aged from 12 to 19 years already exhibit dyslipidemias, with an overweight and obesity prevalence of 32%[33]. It is vitally important mentioning the dangerous association between dyslipidemia and diabetes, since both produce serious alterations, including

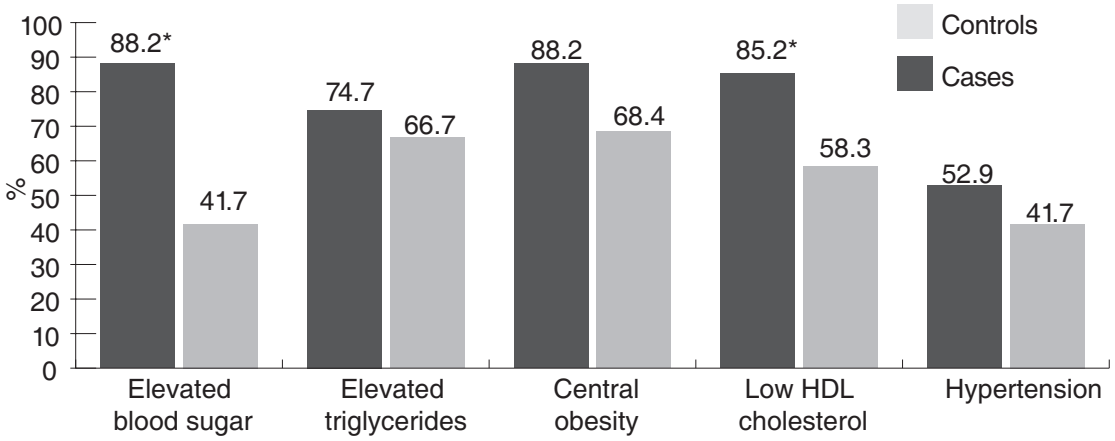

Figure 2. *MS components distribution only in individuals with this syndrome, according to premature AMI condition in northeastern Mexico, 2015 (n = 256).*
**p = 0.001.*
Elevated blood sugar: ≥ 100 mg/dL: elevated triglycerides: ≥ 150 mg/dL; central obesity: waist circumference ≥ 90 cm in males and ≥ 80 cm in females; low HDL cholesterol: < 40 mg/dL in males and < 50 mg/dL in females; hypertension: systolic blood pressure ≥ 130 mmHg and diastolic blood pressure ≥ 85 mmHg.

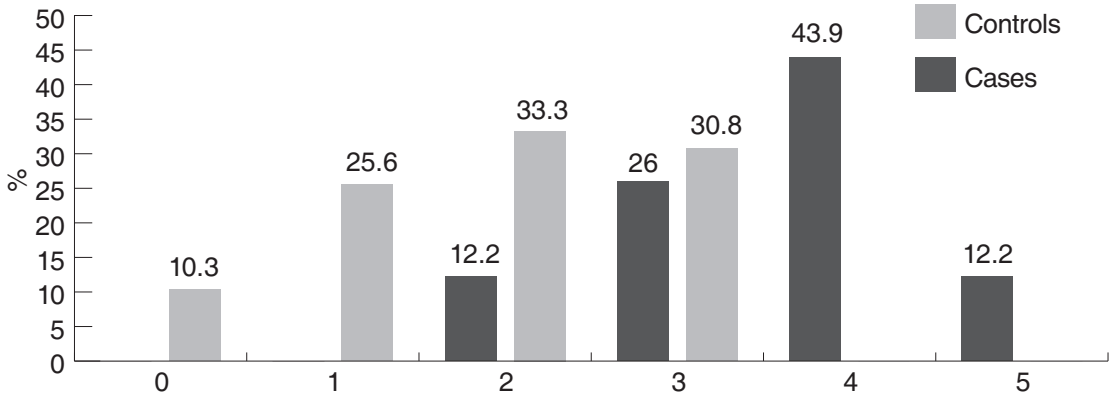

Figure 3. *Number of MS components according to premature AMI condition in northeastern Mexico, 2015 (n = 110).*

insulin resistance. There are evidences that the risk for suffering an AMI in young people with early-onset type 2 diabetes (< 45 years) is 4-fold higher than in those with late onset, and 14-fold higher in comparison with those without diabetes, especially when associated with obesity and sedentarism[34].

A large part of the above analyzed factors are comprised by MS. In fact, this study is one of the first ones in Mexico addressing the subject of AMI associated with this condition. MS predominance was found in males, which is in agreement with observations documented by Chung et al.[35], who identified a prevalence of 87% in the male gender. In Mexico City, a 13.9% prevalence of this syndrome was reported in 17 to 24-year-old students[36] and, in the north of the country, 38.1% in young adults[37], which gives an idea of the future of these young individuals if preventive measures are not taken into account. The fact that this phenomenon has spread globally and that it has been associated with AMI at early ages stands out. Here, a frequency higher than 80% was observed in the cases and it intensely increased the risk for AMI. In Egypt, 66.4% of MS has been reported in patients with AMI younger than 45 years[38], and in Turkey, 37%[39]. On the other hand, Iribarren et al.[40] documented an OR of up to 10.5 between MS and infarction.

In summary, smoking and sedentarism in particular, and MS with factors of obesogenic and cardio-metabolic origin simultaneously brought together, increase the risk for AMI in individuals younger than 47 years from the northeast of the country, regardless of a history of a direct relative with AMI or sudden death. The phenomenon of coronary diseases in young people requires comprehensive attention by the health sector with more involvement of primary care medicine, not only with training of the personnel for opportune

detection of conditions such as obesity and MS, but also to foster self-care and avoidance of habits that are deleterious for health in patients at risk. Elements such as the State, health institutions, the food industry and the family should get involved in this task.

Limitations of the study

The results obtained in this study come from patients that belong to the northeastern region of Mexico, where the prevalence of conditions such as diabetes, dyslipidemia and obesity is higher than in the rest of Mexico. Therefore, this line of investigation requires to be continued in other geographic zones of the country. However, a family history of a first-degree relative with AMI or sudden death, which is indicative of strong genetic makeup, was measured as some sort of approach. Future investigations are necessary in order to delve into the contribution of the genetic profile to the association between MS and AMI in young adults.

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Conflict of interests

The authors declare that no conflict of interests was generated in the performance of this study.

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