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Metabolic syndrome: First prevalence study in primary care, Honduras☆

Síndrome metabólico: primer estudio de prevalencia en atención primaria, Honduras

Metabolic syndrome (MS) is becoming one of the main public health problems of the 21st century.[1] Its pathogenesis is complex, with many uncertainties remaining.

MS is defined as a series of risk factors for type 2 diabetes mellitus (T2DM), cardiovascular disease, non-alcoholic fatty liver disease, and obstructive sleep apnea, characterized by insulin resistance and compensating hyperinsulinism associated with carbohydrate and lipid metabolic disorders, high blood pressure (HBP) and obesity.[2,3]

A cross-sectional, observational, analytical study with probabilistic, stratified, and randomized sampling is reported here. Confidence level: 95% and error: 5%. The study objective was to assess the prevalence of MS in the population over 18 years of age (n = 4836) in the municipality of San Ignacio, Francisco Morazán, Honduras, within the context of a primary care public health strategy initiative involving 16 of its communities, from September to December 2015, with a global population of 8831 inhabitants. The study protocol was evaluated and approved by the bioethics committee of the scientific research unit (registry no. 00003070).

The inclusion criteria were: permanent residents in the municipality over 18 years of age who gave their informed consent to participate in the study. Pregnant women, patients with disabling diseases or cognitive impairment, temporary residents who would therefore be unavailable for assessment and follow-up, and subjects who did not give their written informed consent were excluded from the study.

The study was divided into two phases. A first phase was designed to identify the risk factors using a screening protocol validated by the School of Medical Sciences of the Universidad Nacional Autónoma de Honduras, which evaluated the sociodemographic variables collected in a personal interview: age, sex, race, educational level, occupation, community of residence, and socioeconomic level. The clinical data recorded included prior diagnosis and/or any family history of T2DM and HBP, alcohol and/or tobacco consumption, and the measurement of the abdominal circumference (AC) as an anthropometric variable. A total of 2525 inhabitants meeting the inclusion criteria were interviewed (males: 791, females: 1734). Of these, 1380 (males: 377, females: 1003) met the defined risk criteria (score $\geq$ 5) and were subsequently evaluated in the second phase of the study, consisting of a clinical/anthropometric evaluation:

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Table 1 Prevalence of metabolic syndrome (MS) adjusted to its main risk factors and sociodemographic characteristics in relation to gender; community-based PHC, Honduras, 2015.

Characteristics	n = 342	Gender	
Overall prevalence	65.8%	Male 28.1% ($p = 0.603$)	Female 37.7% ($p = 0.704$)
Age (mean ± SD): 56.9 ± 15.9 (years)			
<40	6.2	1.5	4.7
40–49	11.1	2.9	8.2
50–59	14.9	6.7	8.2
60–69	14.9	5.2	9.7
≥70	18.7	11.7	7.0
Education			
Primary	15.2	8.5	6.7
Secondary	39.6	16.7	22.9
University	6.7	2.1	4.6
None	4.4	1.8	2.6
Marital status			
Single/unmarried couple	43.6	19.3	24.3
Married	17.6	9.1	8.5
Widowed	4.7	0.9	3.8
Smoking			
Yes	3.5	2.9	0.6
No	62.3	25.1	37.2
Alcohol			
Yes	3.8	3.5	0.3
No	62.0	24.6	37.4
Physical activity			
Yes	18.4	11.4	7.0
No	47.5	16.7	30.8
Family history			
HBP	30.2	12.9	17.3
DM2	21.1	8.2	12.9
Both	16.7	6.2	10.5
Previous diagnosis			
HBP	24.3	7.9	16.4
DM2	6.7	1.5	5.2
Both	4.9	0.6	4.3
GD	0.3	–	0.3
BMI (mean ± SD): 27.57 ± 5.48 (kg/m^2)			
≤18.5	0.6	0.3	0.3
18.5–24.9	12.3	8.2	4.1
25–29.9	24.3	11.1	13.2
30–34.9	21.1	6.4	14.7
35–39.9	4.1	1.5	2.6
≥40	3.5	0.6	2.9
Components of MS			
AC (M >90 cm, F >80 cm)	59.5 (CI: 3.24–10.26)	23.1, Se: 91%, Sp: 52%	36.4, Se: 98%, Sp: 15%
Blood glucose >100 mg/dl	51.0 (CI: 6.13–16.86)	20.8	30.2
TG > 150 mg/dl	54.5 (CI: 3.60–09.84)	22.3	32.2
HDL-cholesterol (M: <40 mg/dl, F: <50 mg/dl)	4.4 (CI: 1.61–96.87)	1.2	3.2
Blood pressure >130/85 mmHg	26.0 (CI: 4.57–21.06)	12.9	15.1

PHC: primary health care; SD: standard deviation; GD: gestational diabetes; T2DM: type 2 diabetes mellitus; Sp: specificity; HBP: high blood pressure; BMI: body mass index; AC: abdominal circumference; Se: sensitivity; MS: metabolic syndrome; TG: triglycerides; % (95% confidence interval).

weight, height, the body mass index (BMI), blood pressure (BP), and the collection of a blood sample for biochemical tests (fasting blood glucose, total cholesterol, HDL cholesterol (HDL-C), and triglycerides).

The sample size was calculated using Netquest® (http://www.netquest.com/es/panel/calidad-iso26362.html), with a confidence level of 95% and an error of 5%. The resulting required sample size was n = 301, and the final sample consisted of 342 individuals. The initially selected subjects were not replaced.

The prevalence of MS was determined based on the criteria of the National Cholesterol Education Program–Adult Treatment Panel III (NCEP-ATPIII),[4] and was found to be 65.8%. The principal study data are summarized in Table 1.

In a cross-sectional, population-based study, Wong-McClure et al. reported a high general prevalence of MS in Central America, with a higher prevalence in Honduras (21.1%; CI: 16.4–25.9) than in all the other countries in the region. These authors also found the prevalence to be notably greater among females than in males in all 5 of the studied countries.[5] This increased prevalence of MS in women has not been observed in studies of MS in developed countries, where the prevalence is reportedly very similar in both sexes or higher among the male population.[6] Nevertheless, previous studies have described a greater prevalence of MS in women in Latin America.[7]

Villamor et al.[8] found the prevalence of MS to be positively correlated to age, regardless of gender. They also described an inverse correlation to female educational level and a positive correlation to household food security and height among males. The metabolic risk factor burden was disproportionally greater in women of a lower socioeconomic status and in males of a higher socioeconomic status.

A significant aspect of both studies is that they were conducted in the main cities of the respective countries, in which the sociodemographic, economic, and nutritional variables are relatively different from those found in our study. In effect, our study was conducted in an area not subject to the constant effects of globalization, and still essentially characterized by agriculture and cattle raising.

Latin American women have experienced one of the greatest annual increases in obesity rates between 1990 and 2010: 11.4% and 6.2% in the rural and urban settings, respectively.[9] These increases are not homogeneous within the region. In this study, 78.9% (males: 37%, females: 41.9%) presented an AC consistent with the respective mean (±standard deviation) (96.86 ± 11.44 cm).

However, when patients with and without MS were compared in relation to sex, there were no significant differences ($p = 0.1657$). Nevertheless, a sedentary lifestyle and obesity in women were positively associated with the risk of MS.

A multivariate analysis revealed an association between MS and AC > 80 cm in women and >90 cm in men (odds ratio [OR]: 5.7; 95% CI: 3.2–10.2), BMI > 25 kg/m^2 (OR: 3.5; 95% CI: 2.2–5.8), fasting blood glucose > 100 mg/dl (OR: 10.4; 95% CI: 6.1–16.8), triglycerides > 150 mg/dl (OR: 5.9; 95% CI: 3.6–9.8), and total cholesterol >200 mg/dl (OR: 2.24; 95% CI: 3.7–1.4).

In conclusion, it can be stated that MS is a genuine public health problem, and that early identification of the affected population is essential, since the syndrome is associated with diseases that lead to a very high mortality rate worldwide. MS is a public health problem that may be fully dealt with in primary care, as the diagnosis poses no major difficulties.

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Conflicts of interest

The authors state that they have no conflicts of interest.

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Ectopic Cushing's syndrome: Paradoxical effect of somatostatin analogs

Secreción ectópica de ACTH y respuesta paradójica a análogos de somatostatina

Ectopic ACTH secretion (EAS) is an uncommon cause of ACTH-dependent Cushing's syndrome. Previous large studies[1–3] concluded that two thirds of EAS tumors are located in the thorax and 8%–15% are located in the abdominal cavity. EAS tumors at other sites are less common; of note, up to 15% of tumors remain undetected. The adrenal glands are thus an extremely rare location.

Localization of these tumors can occasionally be difficult and may require extensive diagnostics test, therefore hypercortisolism normalization during this period is crucial. Adrenal steroidogenesis inhibitors as ketoconazole or metyrapone are preferred for their efficacy and safety. Somatostatin analogs (SSAs), have also been used to treat EAS with different results,[4–6] and in some cases a paradoxical increase in ACTH and cortisol after SSAs treatment has been reported.[7] In the present report, we describe a patient with adrenal EAS, who experienced a life-threatening worsening after conventional SSAs administration. We highlight the need to be aware of this rare presentation of EAS, and we remark the difficulties of EAS diagnosis and treatment.

A 48-year-old woman with newly diagnosed hypertension complained of amenorrhea, intense fatigue, muscular weakness and easy bruising, which had increased rapidly over the previous 3 months. Her past history was unremarkable except for recent treatment with enalapril. On examination the patient had normal body mass index, tanned skin with intense thinning with bruising, marked proximal limb muscle atrophy, and a mild moon face. She did not display buffalo hump, purple striae, or supraclavicular fat pads.

Laboratory findings revealed: 3-fold normal rate urinary free cortisol (UFC), (250 μg/day per two times; reference range 12.8–82.5 μg/day) and mild hypokalemia (3.3 mmol/l; reference range 3.50–5.10 mmol/l); lack of cortisol suppression after low-dose (1 mg) dexamethasone (19.67 μg/dl, reference value <1.8 μg/dl). Basal plasma cortisol was 29.56 μg/dl (reference range, 5.27–22.45 μg/dl), and ACTH was 47.83 pg/ml (reference range, 4.7–48.8 pg/ml). Therefore, ACTH-dependent Cushing Syndrome diagnosis was established. Pituitary-centered magnetic resonance imaging (MRI) showed no evidence of pituitary adenoma, and cortisol levels were virtually unchanged after 8-mg dexamethasone suppression test (from 18 to 20 μg/dl). The bilateral inferior petrosal sinus sampling (BIPSS) showed no significant central-to-periphery ACTH gradient, thus ruling out a pituitary origin of ACTH excess.

The results of neck, thorax, and abdomen 3-mm-sliced computed tomography (CT) scan and MRI were unremarkable. The somatostatin receptor scintigraphy (SSRS) and (PET)/CT localized only a slightly higher concentration of somatostatin receptors and glucose uptake in the left adrenal gland, compared with the right. As an ectopic source of ACTH located in the adrenal could be associated with pheochromocytoma and the patient had recent hypertensive state, we also performed urinary catecholamine determination, which was normal, and metaiodobenzylguanidine (^{123}I-MIBG) scintigraphy, which showed increased uptake in the left adrenal.

As SSRS imaging was positive, a high-dose extended-release SSAs was initiated (lanreotide 120 mg) while waiting for ketoconazole provision; however, the patient's condition worsened and become life-threatening one week later, while UFC and ACTH raised up to 800 μg/day and 102 pg/ml respectively. Ketoconazole was started immediately (200 mg three times daily) in a ''block and replace'' regimen. The patient underwent surgery; her left adrenal gland and a contiguous lesion, not detected previously, were removed. Immunohistochemical study revealed heterogeneous but unequivocal ACTH positivity in the medullary area of the adrenal, but not in other areas. This was interpreted as pathological, based on ACTH negative staining in three additional adrenal glands analyzed as controls (Fig. 1A). The other resected lesion turned out to be an extra-adrenal, 2 × 1.5 cm ganglioneuroma; surprisingly, it had negative ACTH immunostaining (Fig. 1B). The patient's clinical condition has improved over the follow-up period and she was able to give up her hypertension pills. Her ACTH and urinary free cortisol levels remained normal at her latest control at ten

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