EPIDEMIOLOGICAL AND HEALTH SCIENCES
ORIGINAL ARTICLE

Risk factors associated with Arterial hypertension in patients with Systemic lupus erythematosus. Holguín, Cuba

Factores de riesgo asociados a Hipertensión arterial en pacientes con Lupus eritematoso sistémico. Holguín, Cuba

Raisa Rodríguez Hernández[I], Alberto Alberteris Rodríguez[II], Jackeline López Báster[I], Mariela Diéguez Martínez[I], Pedro Enrique Miguel-Soca[I], Yudelkis Cutié Anido[I]

[I]Universidad de Ciencias Médicas de Holguín. Holguín, Cuba.
[II]Hospital Clínico Quirúrgico "Lucía Íñiguez Landín". Holguín, Cuba.

How to cite this paper:
Rodríguez Hernández R., Alberteris Rodríguez A., López Báster J., Diéguez Martínez M., Miguel-Soca PE., Cutié Anido Y. Risk factors associated with arterial hypertension in patients with systemic lupus erythematosus. Holguín, Cuba. Rev haban cienc méd [Internet]. [Cited];16(7):[1085-1099] Available from: http://www.revhabanera.sld.cu/index.php/rhab/article/view/2335

Received: March 14, 2017.
Approved: November 10, 2017.

This paper is a translation to English of its original version, available on:
http://www.revhabanera.sld.cu/index.php/rhab/article/view/1978/1914

ABSTRACT

Introduction: The presence of arterial hypertension in patients with systemic lupus erythematosus is a health problem that has not been studied in Holguín.

Objective: To determine the cardiovascular risk factors associated with hypertension in patients with systemic lupus erythematosus.

Material and Methods: A cross-sectional study was conducted. The universe was composed of 193 patients with lupus who were treated in the Rheumatology Consultation of the Clinical-Surgical Hospital of Holguín from March 3, 2014 to January 1, 2015. The sample was made up of 81 patients who were randomly selected according to a 95 % confidence interval, a population size of 193, an estimated proportion of arterial hypertension of 0,20, a precision of a 7 %, and a design effect of 1. The

recommendations of the American College of Rheumatology were followed for the diagnosis of lupus erythematosus, and national guidelines were used for the diagnosis of hypertension. Clinical, anthropometric, and laboratory variables were determined. Odds Ratio (OR), and 95 % confidence intervals (IC95%) for risk determined factors were.

Results: The risk factors associated with hypertension in patients with lupus erythematosus are: age (OR=1,04; IC95%:1,01-1,08), age of the lupus onset (OR=1,04; IC95%:1,01-1,08), diabetes mellitus (OR=8,50; IC95%:1,63-44,33), metabolic syndrome (OR=5,09; IC95%:1,87-13,84), hyperuricemia (OR=4,08; IC95%:1,07-15,44), and microalbuminuria (OR=19,81; IC95%:4,24-92,39).

Conclusions: The patients with systemic lupus erythematosus presented cardiovascular risk factors associated with arterial hypertension, which are identifiable in the primary health care with variables of relatively easy realization.

Keywords: systemic lupus erythematosus, metabolic syndrome, hypertension, risk factors, adults.

RESUMEN

Introducción: La presencia de hipertensión arterial en pacientes con lupus eritematoso sistémico constituye un problema de salud no estudiado en Holguín.

Objetivo: Determinar factores de riesgo cardiovascular asociados a la hipertensión arterial en pacientes con lupus eritematoso sistémico.

Material y Métodos: Estudio transversal de un universo de 193 pacientes con lupus atendidos en la consulta de Reumatología del Hospital Clínico Quirúrgico de Holguín desde el 3 de marzo de 2014 al 1 de enero de 2015. La muestra de 81 pacientes seleccionados por muestreo aleatorio simple según nivel de confianza de 95%, tamaño poblacional de 193, proporción estimada de hipertensión arterial de 0,20, precisión de 7% y efecto de diseño de 1. Para el diagnóstico de lupus eritematoso se siguieron las recomendaciones de American College of Rheumatology y de la hipertensión arterial por las guías nacionales. Se determinaron variables clínicas, antropométricas y de laboratorio. Se determinaron Odds Ratio (OR) e intervalos de confianza de 95% (IC95%) de los factores de riesgo.

Resultados: Los factores de riesgo asociados a la hipertensión en pacientes con lupus son edad (OR=1,04; IC95%:1,01-1,08), edad de debut del lupus (OR=1,04; IC95%:1,01-1,08), diabetes mellitus (OR=8,50; IC95%:1,63-44,33), síndrome metabólico (OR=5,09; IC95%:1,87-13,84), hiperuricemia (OR=4,08; IC95%:1,07-15,44) y microalbuminuria (OR=19,81; IC95%:4,24-92,39).

Conclusiones: Los pacientes con lupus eritematoso sistémico presentaron factores de riesgo cardiovascular asociados a la hipertensión arterial, identificables en la atención primaria de salud con variables de relativa fácil realización.

Palabras claves: Lupus eritematoso sistémico, síndrome metabólico, hipertensión arterial, factores de riesgo, adultos.

INTRODUCTION

Systemic lupus erythematosus (SLE) is the autoimmune disease of greatest heterogeneity due to its clinical and immunological manifestations and evolution.[1] It is considered a chronic inflammatory disease of multifactorial etiology; whose frequency presents some discrepancies among countries.[2]

The metabolic syndrome (MS) comprises risk factors characterized by central obesity, glucose intolerance, arterial hypertension (AHT), hypertriglyceridemia, low concentrations of high density lipoprotein (HDL), and insulin resistance (IR).This syndrome favors a proinflammatory and protrombotic state that leads to the appearance of cardiovascular diseases and Type 2 Diabetes Mellitus. (DM2).[3-5]

As a basic component of MS, AHT is a cardiovascular risk factor, and a chronic non-communicable disease (CNCD). Its presence in patients with SLE results in a higher risk of morbidity and mortality since it accelerates atherosclerosis and cardiovascular disease, although the mechanisms remain uncertain.[6-8]

SLE is also associated with increased levels of cytokines, a characteristic found in IR and endothelial dysfunction, which are also related to cardiovascular diseases in the general population.[9] Besides the inflammation markers used for the evaluation of cardiovascular risk in these patients, atherogenic indexes are also used.

At present, much research is conducted on MS, AHT, and associated factors in several countries,[10-15] in Cuba16-25, and in the province of Holguín.26-36 Research on patients with lupus is also carried out, up to a certain point.[1,2,37-39] However, the studies about AHT conducted in Cuba in patients with SLE are insufficient[40,41] and in Holguín there are no precedents of these studies.

Hypertensive patients with SLE present an increase on the prevalence of cardiovascular morbidity and mortality with regard to the general population, so it is important to identify the risk factors to apply promotion and prevention measures that reduce its complications.

OBJECTIVE

The objective of this research is to determine the risk factors associated with arterial hypertension in patients with systemic lupus erythematosus.

MATERIAL AND METHODS

A cross-sectional study was conducted with a total universe of 193 patients with SLE treated in the Rheumatology Consultation of the Clinical-Surgical Hospital of Holguín from March 3 to January 1st, 2015.

The sample was composed of 81 patients who were selected by simple random sampling. To calculate the number of patients we used: 95 % confidence interval, a population size of 193, an estimated proportion of arterial hypertension of 0,20, a precision of a 7 %, and a design effect of 1.

The diagnosis of SLE was made according to the recommendations of the American College of

Rheumatology of 1997.[42] The patients should fulfill at least 4 of the 11 following requirements:

1. Malar exanthema: flat or raised fixed erythema over the malar eminences on the nasolabial folds.
2. Discoid lupus: raised erythematosus plaques with adherent keratotic scales and follicular plugs with presence of atrophic scars in old lesions.
3. Photosensitivity: skin rash as an abnormal reaction to sunlight.
4. Painless ulcers: oral or nasopharyngeal.
5. Arthritis: non erosive in ⩾ two peripheral joints.
6. Serositis: pleuritis: pleuritic pain, pleural rub or pleural effusion; pericarditis: pericardial friction rub, pericardial effusion and compatible electrocardiogram.
7. Renal affectation: proteinuria> 500 mg / 24 h greater than 3 crosses if not quantified; or cylinders composed of red blood cells or hemoglobin, granular, tubular or mixed.
8. Neurological disorders: convulsions or psychoses which are not explained by other causes.
9. Hematologic disorders: hemolytic anemia, leukopenia, <4x109/L in, at least, two determinations; lymphopenia <1,5x10^9/L in, at least, two determinations; thrombocytopenia <100x109 /L without drugs.
10. Immunological alterations: anti-native DNA to positive or anti-Sm positive titers or positive antiphospholipid antibodies: anticardiolipin, lupus anticoagulant, or false positive lueticserology during six months, confirmed by the immobilization of Treponema pallidum or Treponema l antibody-absorption[FTA-ABS] fluorescent test
11. Antinuclear antibodies: positive at any time in the absence of drug-induced lupuserythematosus. (DILE).

Operationalization of the variables:

Cuban guidelines were followed for the determination of arterial hypertension. [43] The patients who presented figures of blood pressure ⩾ 140/90 mmHg were considered hypertensive.

The patients should fulfill at least three criteria of the National Cholesterol Education Program (ATPIII) for the diagnosis of MS.[3]

- Abdominal obesity: waist circumference ⩾ 102 cm in men and ⩾ 88 cm in women.
- Hypertriglyceridemia: serum triglycerides ⩾ 1.70 mmol/L.
- Low levels of HDL- cholesterol: men <1,02mmol/L and women <1,29 mmol/L.
- Bloodpressure ⩾ 130/85 mmHg.
- Fasting blood glucose level ⩾ 5.55 mmol/L.

Diabetes Mellitus was diagnosed according to the criteria of the American Diabetes Association:[44]

- Fasting blood glucose level ⩾ 7 mmol/L with symptoms of diabetes.
- Casual glycemia ⩾ 11.1 mmol/L with symptoms of diabetes.
- Glycemia ⩾ 11.1 mmol/L at 2h of an oral load.

Ischemic heart disease: Patients had a history of angina, acute myocardial infarction or other manifestations of ischemic heart disease and electrocardiographic signs of ischemic heart disease, assessed by a specialist in Cardiology.

Body mass index (BMI) according to weight(kg) /height (m2).

For the classification of patients with regard to weight, the BMI according to WHO´s criterion was used.[45] Obesity was considered if BMI ⩾ 30.

The abdominal diameter or waist circumference was determined at the level of the median axillary line and the upper border of the iliac

crest.

The hip perimeter was measured at the level of the greater trochanter.

Anthropometric duplicate measurements were made and an average was taken to determine the values.

The waist/hip Ratio and waist/height Ratio were determined by dividing the respective values.

The skinfolds were measured on the right side, after a previous marking of the area with a crystallographic pencil, with a Holtain® brand caliper with a precision between 0,1-0,2 mm.

X1: Bicipital fold: at the mid-point of the radial acromion, in the anterior part of the arm, measured vertically in the meso-brachial ridge.

X2: Triceps fold: at the mid-acromion radial point, measured vertically on the posterior side of the arm.

X3: Subscapular fold: measured in the direction of the ribs on the inferior angle of the scapula.

X4: Suprailiac fold: measured above the iliac crest in the mid-axillary line.

To calculate the fat percentage, Siri´s equation was used:[46]

% of body fat = [(4,95/ density) – 4.5] x 100, where:

Density = 1.1776- 0.0744 x log (biceps + triceps + subscapular + suprailiac) for males.

Density = 1.1567- 0.0717 x log (biceps + triceps + subscapular + suprailiac) for women.

Body density was calculated with the Durnin & Womerley (1974) equation.[46]

The venous blood needed to determine duplicate laboratory variables was taken to the patients after 12-14 hours of fasting, and after diets low in lipids for 3 days. The reagents used were from national production (Finlay Laboratories, Havana):

Glycemia: Rapiglucotest.

Triglycerides: Triglitest for the enzyme determination of serum triglycerides.

Total cholesterol: Colestest. The patient had hypercholesterolemia when the concentrations were> 5.2 mmol / L.

HDL-cholesterol: homogeneous essay for HDL-C ImmunoFS.

C-reactive protein: turbidimetric method with high values> 8 mg / L.

Microalbuminuria: Microalb-Latex using a qualitative method with positive result if an agglutination occurs.

Uric acid: uric acid mono SL. Hyperuricemia when values were> 428 µmol /L in men and> 357 µmol /L in women.

Low-density lipoprotein cholesterol (LDL-cholesterol) according to the Friedewald formula: [47]

LDL-cholesterol = Total cholesterol - [triglycerides / 2.1] - HDL-cholesterol

For high values of atherogenic indexes, recommendations for secondary prevention were considered:

High Total cholesterol / HDL-cholesterol Ratio > 4.0 for men and> 3.5 for women.

High LDL/HDL- cholesterol Ratio > 3.0 for men and > 2.5 for women.

High Triglycerides / HDL-cholesterol Ratio > 2.75 for men and > 1.65 for women according to the recommendations of Cordero et al.49 for the diagnosis of MS.

The atherogenic index of plasma was calculated as the logarithm of the molar Ratio between the concentration of serum triglycerides and HDL-cholesterol, according to:[50]

= log (triglycerides/HDL-cholesterol). It was considered high if> 0.21.

The waist / height Ratio for identifying risk ⩾ 0.53.51

Menopause when women were> 45 years and had consecutive absence of menstruations for at least one year.

Smoking habit was considered as a dichotomous variable: smoker and non-smoker.

Hypothyroidism when they presented clinical symptoms and hormonal alterations (TSH, T3 and T4) 30

Statistical analysis:

Quantitative variables were expressed as mean ± standard deviation.

The mean comparisons were madewith the Mann-Whitney U test or t-test. Odds Ratio (OR) and their 95% confidence intervals (IC95%) of risk factors were calculated. The level of significance chosen was 5%.

The EPIDAT program V. 4.1 was used (Xunta de Galicia, Spain, PAHO, CES University, Colombia, 2014).

Ethical aspects:

The patients gave their informed consent in written form to participate in this research, which was approved by the Scientific Council and Ethics Committee of the University of Medical Sciences of Holguín, Cuba. The authors did not present conflict of interests.

RESULTS

Of the 81 patients with SLE,75 were female for a 92,59%. The prevalence of AHT was 34,56%.

Some clinical and anthropometric variables differed between patients with AHT and without AHT. (Table 1)

Table 1. Clinical-anthropometric and laboratory indicators of patients with Systemic Lupus Erythematosus according to the presence of arterial hypertension

Variables	Arterial Hypertension		Total (n=81)	p
	Yes (n=28)	No (n=53)		
Age (years)	46.46 ± 11.49	40.69 ± 12.23	42.69 ± 12.22	0.04*
Age of diagnosis SLE (years)	36.50 ± 12.29	30.75 ± 11.85	32.74 ± 12.24	0.04*
Time of Evolution SLE (years)	9.96 ± 9.90	9.94 ± 8.47	9.95 ± 8.23	0.99
Systolic blood pressure (mmHg)	124 ± 11.03	115 ± 11.70	118 ± 12	0.00*
Diastolic blood pressure (mmHg)	81 ± 6.61	73 ± 8.59	76 ± 8.0	0.00*
Weight(kg)	69.07 ± 15.36	64.87± 11.76	66.32 ± 13.17	0.17
Size (cm)	160 ± 7.87	161 ± 7.19	160 ± 7.40	0.52
BMI (kg/m^2)	26.88 ± 5.06	24.95 ± 4.32	25.62 ± 4.65	0.07
Waist circumference (cm)	89.96 ± 10.63	90.13 ± 11.10	91.71 ± 10.24	0.94
Hip perimeter (cm)	108 ± 10.33	106 ± 9.64	107 ± 9.85	0.47
Waist/hip Ratio	0.86 ± 0.07	0.84 ± 0.07	0.85 ± 0.07	0.41
Waist/height Ratio	0.58 ± 0.07	0.56 ± 0.06	0.57 ± 0.06	0.11

Bicipital fold (mm)	16.39 ± 3.62	13.92 ± 3.46	14.43 ± 3.56	0.07
Triceps fold (mm)	15.60 ± 3.22	14.62 ± 3.71	14.96 ± 3.56	0.23
Subscapular fold (mm)	14.82 ± 4.79	13.43 ± 4.10	13.91 ± 4.37	0.17
Suprailiac fold (mm)	15.75 ± 5.46	15.05 ± 3.96	15.29 ± 4.51	0.55
% of fat	27.17 ± 6.37	25.17 ± 6.07	25.86 ± 6.21	0.16
Glycemia (mmol/L)	5.14 ± 0.95	5.44 ± 2.03	5.34 ± 1.73	0.46
Triglycerides (mmol/L)	2.20 ± 0.95	2.08 ± 1.18	2.12 ± 1.10	0.65
Total cholesterol (mmol/L)	5.60 ± 1.68	5.20 ± 1.54	5.34 ± 1.58	0.29
LDL-cholesterol (mmol/L)	3,29 ± 1,79	2,78 ± 1,47	2,95 ± 1,60	0,17
HDL-cholesterol (mmol/L)	1.40 ± 0.96	1.66 ± 1.73	1.54 ± 1.53	0.54
Cholesterol/HDL-cholesterol Ratio	5.15 ± 3.61	4.21 ± 2.97	4.54 ± 3.21	0.21
LDL-cholesterol/HDL-cholesterol Ratio	3.19 ± 3.09	2.36 ± 2.33	2.65 ± 2.63	0.18
Triglycerides /HDL-cholesterol Ratio	1.97 ± 1.39	1.71 ± 1.50	1.80 ± 1.46	0.45
Atherogenic index of plasma	0.21 ± 0.25	0.10 ± 0.33	0.14 ± 0.13	0.14
Uric acid (µmol/L)	318 ± 123	284 ± 79	296 ± 97	0.13
C-reactive protein (mg/L)	8.34 ± 2.81	7.87 ± 2.29	8.03 ± 2.47	0.41

Mean ± mean standard deviation
* Significant value when compared with the other group (Mann-Whitney U tests or t-test, α=0.05)

Table 2 shows the significantly associated risk factors or not associated ones to AHT in patients with Systemic Lupus Erythematosus.

Table 2. Risk factors associated with arterial hypertension in patients with Systemic Lupus Erythematosus

Risk factors	***Odds Ratio***	**95% Confidence Interval**	**p**
Quantitative Variables			
Age	1.04	1.01-1.08	0.04*
Age of onset of SLE	1.04	1.01-1.08	0.04*
Time of evolution of SLE	1.00	0.94-1.05	0.99
Total cholesterol /HDL-cholesterol Ratio	1.49	0.59-3.75	0.39
LDL-cholesterol/HDL-cholesterol Ratio	1.49	0.57-3.90	0.49

Triglycerides/HDL-cholesterolRatio	1.73	0.67-4.48	0.25
High AtherogenicIndex of plasma	1.58	0.61-4.08	0.33
Qualitative Variables			
Menopause	2.64	0.96-7.25	0.06
Smoking Habit	0.94	0.16-5.49	0.94
Diabetes Mellitus	8.50	1.63-44.33	0.01*
Ischemic Heart Disease	8.66	0.91-81.73	0.06
Metabolic Syndrome	5.09	1.87-13.84	0.00*
Obesity	1.95	0.65-5.81	0.23
Abdominal Obesity	1.27	0.50-3.24	0.60
Hypothyroidism	0.63	0.18-2.22	0.47
Hypertriglyceridemia	1.49	0.57-3.92	0.41
Hypercholesterolemia	1.75	0.69-4.43	0.23
High LDL-cholesterol	2.62	0.83-8.23	0.09
Hyperuricemia	4.08	1.07-15.44	0.04*
Positive Microalbuminuria	19.81	4.24-92.39	0.00*
High C-reactive protein	1.27	0.50- 3.24	0.60
Total cholesterol /HDL-cholesterol Ratio	1.49	0.59-3.75	0.39
LDL-cholesterol/HDL-cholesterol Ratio	1.49	0.57-3.90	0.49
Triglycerides/HDL-cholesterol Ratio	1.73	0.67-4.48	0.25
High Atherogenic Index of plasma	1.58	0.61-4.08	0.33
High Waist/Height Ratio	1.67	0.60-4.66	0.32

* Significance level (α=0.05) in simple binary logistic regression

DISCUSSION

Age constituted a significant cardiovascular risk factor in patients with AHT and SLE; that is,the older you get, the greater your risk; which is due to the ageing process that favors atherosclerosis, inflammation, oxidative stress, and endothelial dysfunction.[52]

On the other hand, SLE affects the arterial walls and causes atherosclerosis due to its systemic and chronic nature. Also, some medications administered such as steroids retain water and electrolytes at a kidney level, which favors the venous return and cardiac output, factors that influence on the elevation of blood pressure.8 This explains, at least, part of the role of the onset age of SLE as a risk factor strongly associated with AHT.

Diabetes Mellitus increased the risk of AHT (about 8,5 times), which is explained by the close links between DM2 and AHT, which coincides with the majority of researchers who find higher levels of blood pressure in diabetic patients.[53,54]

MS includes a group of cardiovascular risk factors characterized by AHT, dyslipidemias, glucose intolerance, and a proinflammatory and prothrombotic state that favors atherosclerosis and its long-term sequelae, and the appearance of DM2. 3As high levels of blood pressure constitute a basic feature of MS; it is not surprising that MS constitutes a risk factor associated with hypertension in patients with lupus.

Serum concentrations of uric acid are increased in MS and IR; [55] this metabolite is associated with AHT,[55] which partially explains that hyperuricemia constitutes a risk factor associated with AHT in patients with SLE. The concentration of uric acid is related to autoimmune diseases as it was demonstrated in a Peruvianstudy that found an association between age, fat percentage, and uric acid with MS in patients with lupus.[56] Besides, this metabolite is a circulating marker of oxidative damage in diseases such as hepatic ischemia, hyperlipemia, atherosclerosis, and Diabetes Mellitus.[57] This means that its determination in patients with SLE is of great importance to assess the risk of presenting cardiovascular and other complications.

Patients with SLE and cardiovascular risk factors also present a low-grade chronic inflammatory state due to the quantity of adipokines synthetized by the visceral adipose tissue, among which the tumor necrosis factor alpha (TNFα) and interleukin 6 (IL-6) stand out. In the health care, two markers of inflammation are used: microalbuminuria, which is considered an early marker of kidney damage, and C-reactive protein. In this research, positive microalbuminuria was considered a risk factor associated with AHT in patients with lupus, but not high C-reactive protein, without presenting significant differences between both groups of patients.

The role of C-reactive protein in SLE is still unclear. Generally, when there is no infection, the C-reactive protein concentrations are lower or normal than in other systemic diseases like rheumatoid arthritis, despite the high levels of activity of the disease.[58]

The smoking habit did not constitute a risk factor associated with AHT due to the low number of smoking patients (7, 41% of the total). Other risk factors and CNCDs, such as ischemic cardiopathy, obesity, abdominal obesity, hypothyroidism, and risk lipid profile did not indicate a significant association; which could be due to the influence of factors that were not studied, and the prolonged evolution of SLE.

The identification of cardiovascular risk factors in patients with SLE is a challenge because of the close links established among them, the long period of evolution of the disease, the use of steroids and immunosuppressive drugs, and the appearance of complications that make the cause-effect more complex.

The identification of risk factors in patients with CNCDs is important for the evaluation of the risk of cardiovascular morbidity and mortality; for the prevention, diagnosis, and effective treatments of these disorders; and for the calculation and distribution of material human resources.[59,60]

The main limitations of this study are related to the cross-sectional design of this research, which

limits the cause-effect analysis; and the small number of patients. However, the authors consider that this fact does not demerit the extrapolation of this research which has the merit of studying AHT in patients with SLE in the province of Holguín.

CONCLUSIONS

The patients with SLE presented cardiovascular risk factors associated with AHT, which were identifiable in primary health care with relatively easy variables.

REFERENCES

1. Kokuina E. Autoanticuerpos como biomarcadores de actividad de la enfermedad del lupus eritematoso sistémico. Rev Cub Med [Internet]. 2014 Jun [Cited: 2017 Mar. 9]; 53(2):201-223. Available from: http://scieloprueba.sld.cu/scielo.php?script=sci_arttext&pid=S0034-75232014000200009&lng=es

2. Scolnik M, Marin J, Valeiras SM, Marchese MF, Talani AS, Avellaneda NL, et al. Incidence and prevalence of lupus in Buenos Aires, Argentina: a 11-year health management organisation-based study. Lupus SciMed[Internet]. 2014 [Cited: 2016 Feb. 11]; 1(1) Available from: www.ncbi.nlm.nih.gov/pmc/articles/PMC4213830/pdf/lupus-2014-000021.pdf

3. Grundy SM, Brewer HB, CleemanJI, Smith SC, Lenfant C. Definition of metabolic syndrome: Report of the National Heart, Lung and Blood Institute/American Heart Association conference on scientific issues related to definition. Circulation [Internet]. 2004 [Cited: 2016 Feb. 11]; 109:433-438. Available from: http://circ.ahajournals.org/content/109/3/433.full.pdf+html

4. Kip KE, Marraquin OC, Kelley DE, Johnson BD, Kelsey SF, Shaw LJ, et al. Clinical importance of obesity versus the metabolic syndrome in cardiovascular risk in women: A report from the Women's Ischemia Syndrome Evaluation (WISE) study. Circulation [Internet]. 2004[Cited: 2016 Feb. 11]; 109:706–713. Available from: http://circ.ahajournals.org/content/109/6/706.full.pdf+html

5. Tarragó Amaya E, Miguel Soca PE, Cruz Lage LA, Santiesteban Lozano Y. Factores de riesgo y prevención de la cardiopatía isquémica. CCM [Internet]. 2012 [Cited: 2015 Jul.12]; 16 (2). Available from: http://www.revcocmed.sld.cu/index.php/cocmed/article/view/505

6. Magadmi ME, Ahmad Y, Turkie W, Yates AP, Sheikh N, Bernstein RM, et al. Hyperinsulinemia, insulin resistance and circulating oxidized low density lipoprotein in women with systemic lupus erythematosus. J Rheumatol [Internet]. 2006[Cited: 2016 Feb. 11]; 33:50-56. Available from: http://www.jrheum.org/content/33/1/50.long

7. Chung CP, Avalos I, Oeser A, Gebretsadik T, Shintani A, Raggi P, et al. High prevalence of the metabolic syndrome in patients with systemic lupus erythematosus: association with disease characteristics and cardiovascular risk factors. Ann Rheum Dis [Internet]. 2007 [Cited: 2016 Feb. 11]; 66(2):208-14.Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1798504

8. Medeiros MM, Xavier de Oliveira ÍM, Ribeiro ÁT. Prevalence of metabolic syndrome in a cohort of systemic lupus erythematosus patients from Northeastern Brazil: association with disease

activity, nephritis, smoking, and age. RheumatolInt [Internet]. 2016 [Cited: 2016 Feb. 11]; 36(1):117-24. Available from: http://link.springer.com/article/10.1007/s00296-015-3316-z/fulltext.html

9. Uslu AU, Kucuk A, Icli A, Cure E, Sakiz D, Arslan S, et al. Plasma Atherogenic Index is an Independent Indicator of Subclinical Atherosclerosis in Systemic Lupus Erythematosus. Eurasian J Med[Internet]. 2017 [Cited: 2017 Nov. 13]; 49(3):193-197.Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5665629/?report=reader

10. Vicente-Herrero MT, Ramírez Íñiguez de la Torre V, Capdevila García LM, López-González ÁA, Terradillos García MJ. Consumo de alcohol en población trabajadora española y repercusiones metabólicas. Rev Cub Sal Púb [Internet]. 2014 Mar [Cited: 2016 Mar.14]; 40(1):40-46. Available from: http://scieloprueba.sld.cu/scielo.php?script=sci_arttext&pid=S0864-34662014000100005&lng=es

11. Donato M. ¿La diabetes mellitus y el síndrome metabólico interfieren con el efecto cardioprotector del poscondicionamiento isquémico? Rev Argent. Cardiol. [Internet]. 2013[Cited: 2016 Feb. 11]; 81(6). Available from: http://www.scielo.org.ar/scielo.php?script=sci_arttext&pid=S1850-37482013000600019&lng=es&nrm=iso

12. Srikanthan K, Feyh A, Visweshwar H, Shapiro JI, Sodhi K. Systematic Review of Metabolic Syndrome Biomarkers: A Panel for Early Detection, Management, and Risk Stratification in the West Virginian Population. Int J Med Sci [Internet]. 2016 [Cited: 2016 Feb. 11]; 13(1):25-38. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26816492

13. Lee S, Ko Y, Kwak C, YimES. Gender differences in metabolic syndrome components among the Korean 66-year-old population with metabolic syndrome. BMC Geriatr [Internet]. 2016[Cited: 2016 Feb. 11]; 16(1):27 Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4724404

14. Wong-McClure RA, Gregg EW, Barceló A, Lee K, Abarca-Gómez L, Sanabria-López L, Tortós-Guzmán J. Prevalence of metabolic syndrome in Central America: a cross-sectional population-based study. Rev Pana Sal Publ [Internet]. 2015[Cited: 2016 Feb. 11]; 38(3):202-8. Available from: http://www.scielosp.org/scielo.php?script=sci_arttext&pid=S1020-49892015000800004&lng=en

15. Fernández-Bergés D, Cabrera de León A, Sanz H, Elosua R, Guembe MJ, Alzamora M, et al. Síndrome metabólico en España: prevalencia y riesgo coronario asociado a la definición armonizada y a la propuesta por la OMS. Estudio DARIOS. RevEspCardi [Internet]. 2012 [Cited: 2016 Feb. 11]65(3):241-248. Availablefrom: https://www.clinicalkey.es/ui/service/content/url?eid=1-s2.0-S0300893211008840

16. García Guerra LA, Beatón Lovaina YB, CousoSeoane C. Morbilidad oculta del síndrome metabólico en ancianos con diabetes mellitus de tipo 2. MEDISAN [Internet]. 2013 Dec. [Cited: 2016 Jan 27]; 17(12):9044-9050. Available from: http://scieloprueba.sld.cu/scielo.php?script=sci_arttext&pid=S1029-30192013001200003&lng=es

17. Ortiz Pérez G, Pérez Salas VL, Abalos Fernández EY, De la Fe Batista LE. Incidencia del síndrome metabólico en una comunidad del municipio de II Frente oriental "Frank País García". MEDISAN [Internet]. 2013 Oct [Cited: 2016 Jan. 27]; 17(10):6039-6045. Available from: http://scieloprueba.sld.cu/scielo.php?script=sci_arttext&pid=S1029-30192013001000004&lng=es

18. Zaldívar Ochoa JR, Domínguez Redondo D. Niños y adolescentes obesos con síndrome metabólico. MEDISAN [Internet]. 2012 Jul [Cited:

2016 Jan. 27]; 16(7):1098-1104. Available from: http://scieloprueba.sld.cu/scielo.php?script=sci_arttext&pid=S1029-30192012000700011&lng=es

19. Valdés Ramos E, Bencosme Rodríguez N. Síndrome metabólico y enfermedad cardiovascular en personas con diabetes mellitus tipo 2. Rev Cub Endo [Internet]. 2013 Aug.[Cited: 2016 Jan. 27]; 24(2): 125-135.].Available from: http://scieloprueba.sld.cu/scielo.php?script=sci_arttext&pid=S1561-29532013000200003&lng=es

20. ParláSardiñas J, Cabrera Rode E, Marichal Madrazo S, Arranz Calzado C, Domínguez Alonso E, González Fernández P, et al. Frecuencia y caracterización del síndrome metabólico según criterios de la Federación Internacional de Diabetes en familiares de primer grado de personas con diabetes tipo 1. Rev Cub Endoc [Internet]. 2011 Dec. [Cited: 2016 Jan. 27]; 22(3):196-209. Available from: http://scieloprueba.sld.cu/scielo.php?script=sci_arttext&pid=S1561-29532011000300003&lng=es

21. Bojorges Velázquez LA, Castillo Herrera JA, Jiménez Tamayo R. Factores de riesgo de síndrome metabólico en estudiantes de la universidad Pablo Guardado Chávez, año 2013. Rev Cub Invest Bioméd [Internet]. 2013 Dec.[Cited:2016 Jan. 27] 32(4):379-388. Available from: http://scieloprueba.sld.cu/scielo.php?script=sci_arttext&pid=S0864-03002013000400001&lng=es

22. Valdés Ramos ER, Espinosa Benítez Y. Factores de riesgo asociados con la aparición de enfermedad arterial periférica en personas con diabetes mellitus tipo 2. Rev Cub Med [Internet]. 2013 Mar [Cited: 2016 Jan. 27]; 52(1):4-13]. Available from: http://scieloprueba.sld.cu/scielo.php?script=sci_arttext&pid=S0034-75232013000100002&lng=es

23. González Sotolongo O, Arpa Gámez Á, Hernández Sierra Y. Influencia del síndrome metabólico sobre la evolución de pacientes hospitalizados en salas de Medicina Interna. Rev Cub Med Mil. 2014 Dec.[Cited: 2016 Jan. 27]; 43(4):449-458. Available from: http://scieloprueba.sld.cu/scielo.php?script=sci_arttext&pid=S0138-65572014000400005&lng=es

24. Hinojosa Romero I, Solís Alfonso L. Caracterización de la aterosclerosis carotídea en pacientes con síndrome metabólico. Rev Cub Med Mil [Internet]. 2014 Mar [Cited: 2016 Jan. 27] ; 43(1): 23-32. Available from: http://scieloprueba.sld.cu/scielo.php?script=sci_arttext&pid=S0138-65572014000100004&lng=es

25. Picos Nordet S, Pérez Clemente LM. Resistencia insulínica y los componentes del síndrome metabólico en niños y adolescentes obesos. Rev Cub Ped [Internet]. 2015 Dec[Cited: 2016 Jan. 27]; 87(4):449-459. Available from: http://scieloprueba.sld.cu/scielo.php?script=sci_arttext&pid=S0034-75312015000400007&lng=es

26. Ochoa Expósito K, Rivas Estévez M, Miguel-Soca PE, Batista Hernández A, Leyva Sicilia Y. Ensayo no aleatorizado: impacto de cambios en la dieta y ejercicios físicos en pacientes adultos con síndrome metabólico. CCM [Internet]. 2015 Sep. [Cited:2016 Jan. 27]; 19(3):465-482. Available from: http://scieloprueba.sld.cu/scielo.php?script=sci_arttext&pid=S1560-43812015000300008&lng=es

27. Miguel-Soca PE. Riesgo de diabetes mellitus en pacientes con resistencia a la insulina. Rev Ciencias Médicas [Internet]. 2015 Jun.[Cited: 2016 Jan. 27]; 19(3):396-399. Available from: http://scieloprueba.sld.cu/scielo.php?script=sci_arttext&pid=S1561-31942015000300002&lng=es

28. Mariño Soler AL, Miguel Soca PE, Ochoa Rodríguez M, Cruz Font JD, Cruz Batista Y, Rivas Estévez M. Caracterización clínica, antropométrica y de laboratorio de mujeres con diabetes mellitus tipo 2. Rev. Med. Elect [Internet]. 2012 Feb.[Cited:2016 Jan. 27]; 34(1):57-67. Available

from: http://scieloprueba.sld.cu/scielo.php?script=sci_arttext&pid=S1684-18242012000100006&lng=es

29. Santiago Martínez Y, Miguel Soca PE, Ricardo Santiago A, Marrero Hidalgo MM, Peña Pérez I. Caracterización de niños y adolescentes obesos con síndrome metabólico. Rev Cub Ped [Internet]. 2012 Mar.[Cited:2016 Jan. 27]; 84(1):11-21. Available from: http://scieloprueba.sld.cu/scielo.php?script=sci_arttext&pid=S0034-75312012000100002&lng=es

30. Sarmiento Teruel Y, Miguel Soca PE, Almaguer Herrera A, García Niebla LA, Mariño Soler AL, Edwards Scringer I. Caracterización del síndrome metabólico en mujeres con hipotiroidismo clínico. AMC [Internet]. 2013 Feb.[Cited:2016 Jan. 27]; 17(1):51-64. Available from: http://scieloprueba.sld.cu/scielo.php?script=sci_arttext&pid=S1025-02552013000100009&lng=es

31. Hernández Tamayo M, Miguel Soca P, Marrero Hidalgo M, Pérez López L, Peña Pérez I, Rivas Estévez M. Comportamiento de variables clínicas, antropométricas y de laboratorio en pacientes con síndrome metabólico. Medisur [Internet]. 2011 Apr. [Cited: 2016 Jan. 27]; 9(2):102-109. Available from: http://scieloprueba.sld.cu/scielo.php?script=sci_arttext&pid=S1727-897X2011000200004&lng=es

32. Hernández Tamayo M, Miguel Soca PE, Marrero Hidalgo M, Rodríguez Graña T, Niño Escofet S. Caracterización del síndrome metabólico en pacientes adultos con obesidad. MEDISAN [Internet]. 2012 Mar.[Cited: 2016 Jan. 27]; 16(3):341-348. Available from: http://scieloprueba.sld.cu/scielo.php?script=sci_arttext&pid=S1029-30192012000300005&lng=es

33. Miguel Soca PE, Peña Pérez I, Niño Escofet S, Cruz Torres W, Niño Peña A, Ponce De León D. Ensayo clínico aleatorio: papel de la dieta y ejercicios físicos en mujeres con síndrome metabólico. Aten Prim [Internet]. 2012[Cited: 2016 Feb. 11]; 44 (7):387–393. Available from: http://www.sciencedirect.com/science/article/pii/S0212656711004252

34. Miguel Soca PE, Niño Escofet S, Rodríguez López M, Almaguer Herrera A. Pesquisaje de síndrome metabólico en mujeres obesas. CCM [Internet]. 2004[Cited: 2016 Feb. 11]; 8 (4). Available from: http://www.cocmed.sld.cu/no84/n84ori5.htm

35. Miguel Soca PE, Cruz Torres W, González Ferrer J, Cardona Cáceres X, Cruz Lage LA, Hernández Tamayo M. Efectos beneficiosos de cambios en la dieta y ejercicios físicos en mujeres obesas con síndrome metabólico. Panorama Cuba y Salud [Internet]. 2009[Cited:2016 Feb. 11]; 4 (3). Available from: http://www.revpanorama.sld.cu/index.php/panorama/article/view/121/pdf

36. Rivas Vázquez D, Miguel Soca PE, Llorente Columbié Y, Marrero Ramírez GM. Comportamiento clínico epidemiológico del síndrome metabólico en pacientes adultos. Rev Cub Med Gen Integr [Internet]. 2015[Cited:2016 Feb. 18]; 31(3). Available from: http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S0864-21252015000300001&lng=es

37. Solís Cartas U, Amador García DM, Crespo Somoza I, Pérez Castillo E. Síndrome de Guillain Barré como forma de debut en el lupus eritematoso sistémico. Rev Cub Reum [Internet]. 2015[Cited: 2016 Jan. 27]; 17(suppl.1) Available from: http://scieloprueba.sld.cu/scielo.php?script=sci_arttext&pid=S1817-59962015000300007&lng=es

38. García-Villegas EA, Lerman-Garber I, Flores-Suárez LF, Aguilar-Salinas C, Márquez González H, Villa-Romero AR. Prognostic value of metabolic syndrome for the development of cardiovascular disease in a cohort of premenopausal women with

systemic lupus erythematosus. Med Clin (Barc) [Internet]. 2015[Cited: 2016 Feb. 11]; 144 (9):289-96. Available from: http://www.elsevier.es/en-revista-medicina-clinica-english-edition--462-pdf-90393415-S300

39. Parker B, Bruce IN. The Metabolic Syndrome in Systemic Lupus Erythematosus. Rheum Dis Clin N Am [Internet].2010 [Cited: 2016 Feb. 11]; 36 (1): 81-97. Available from: https://www.clinicalkey.es/ui/service/content/url?eid=1-s2.0-S0889857X09001252

40. Guibert Toledano ZM, Reyes Llerena GA, Hernández Muñiz Y, Ugarte Moreno D, MiñosoArafi Y. Morbilidad cardiovascular y evaluación de aterosclerosis en pacientes con lupus eritematoso sistémico. Rev Cub Reum [Internet]. 2016 Aug.[Cited: 2017 Nov. 13]; 18(2):102-110. Available from: http://scieloprueba.sld.cu/scielo.php?script=sci_arttext&pid=S1817-59962016000200002&lng=es

41. Hernández Muñiz Y, Guibert Toledano ZM, Reyes Llerena GA. Correlación de las cifras de proteína C reactiva y aterosclerosis en pacientes con lupus eritematoso sistémico. Rev Cub Reum [Internet]. 2015 Aug.[Cited: 2017 Nov. 13]; 17(2):126-131. Available from: http://scieloprueba.sld.cu/scielo.php?script=sci_arttext&pid=S1817-59962015000200005&lng=es

42. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum [Internet]. 1997[Cited: 2016 Feb 11]; 40 (9): 1725. Available from: http://onlinelibrary.wiley.com/doi/10.1002/art.1780400928/pdf

43. Comisión Nacional Técnica Asesora del Programa de Hipertensión Arterial. Hipertensión arterial. Guía para la prevención, diagnóstico y tratamiento. La Habana: Editorial de Ciencias Médicas; 2008.

44. American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. Diabetes Care. 2012; 35(Suppl. 1): S64-71.

45. World Health Organization. Obesity: Preventing and managing the global epidemic. Report of a WHO Consultation. World Health Organ Tech Rep Ser. 2000; 894.

46. Martín Moreno V, Gómez GandoyJB, Antoranz González MJ. Medición corporal mediante impedancia bioeléctrica, pliegues de la grasa cutáneos y ecuaciones a partir de medidas antropométricas. Análisiscomparativo. Rev Esp Sal Públ [Internet]. 2001 May [Cited: 2013 Jul. 2]; 75(3):221-236. Available from: http://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S1135-57272001000300006&lng=es

47. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem. 1972; 18(6):499-502.

48. Millán J, Pintó X, Muñoz A, Zúñiga M, Rubiés-Prat J, Pallardo LF, et al. Lipoprotein Ratios: Physiological significance and clinical usefulness in cardiovascular prevention. Vascular Health and Risk Management. 2009; 5:757-765.

49. Cordero A, Laclaustra M, León M, Casasnovas JA, Grima A, Luengo E, et al. Comparison of serum lipid values in subjects with and without the metabolic syndrome. Am J Cardiol [Internet]. 2008[Cited:2016 Feb. 11]; 102(4):424-428. Available from: http://www.ajconline.org/retrieve/pii/S0002914908006565

50. Xiao-Wei Z, Fei-Yan D, Shu-Feng L. Meta-analysis of Atherogenic Index of Plasma and other lipid parameters in relation to risk of type2 diabetes mellitus. Primary Care Diabetes [Internet].

2015[Cited: 2016 Feb. 11]; 9:60–67. Available from: http://dx.doi.org/10.1016/j.pcd.2014.03.007
51. García AI, Niño-Silva LA, González-Ruiz K, Ramírez-Vélez R. Utilidad del índice de adiposidad corporal como indicador de obesidad y predictor de riesgo cardiovascular en adultos de Bogotá, Colombia. EndocNutr [Internet]. 2015[Cited: 2016 Feb. 11]; 62(3):130-137. Available from: http://dx.doi.org/10.1016/j.endonu.2014.11.007
52. Buford TW. Hypertension and Aging. Ageing Res Rev [Internet]. 2016; 26: 96-111.
53. Pinto MD, Viera García M, Agramonte Martínez IM, Cordero López G. Infarto agudo del miocardio en diabéticos relacionado con factores de riesgo Hospital Universitario Dr. Enrique Cabrera. Rev Hab de Cien Méd[Internet]. 2002-2004[Cited: 2017 Mar. 13];11(2):[approx. 0 p.]. Available from: http://www.revhabanera.sld.cu/index.php/rhab/article/view/1898
54. Almaguer Herrera A, Miguel Soca PE, Reynaldo Sera C, Mariño Soler AL, Oliveros Guerra RC. Actualización sobre diabetes mellitus. CCM [Internet]. 2012[Cited: 2015 Jul. 13]; 16(2). Availablefrom: http://www.revcocmed.sld.cu/index.php/cocmed/article/view/507
55. Vega Abascal J, Guimará Mosqueda MR, Vega Abascal L. Más allá de la definición de síndrome metabólico: ácido úrico, proteína c reactiva de alta sensibilidad y riesgo cardiovascular global. CCM [Internet]. 2017 Mar. [Cited: 2017 Nov. 13]; 21(1):70-86. Available from: http://scieloprueba.sld.cu/scielo.php?script=sci_arttext&pid=S1560-43812017000100007&lng=es
56. Ugarte Gil MF. Factores asociados al síndrome metabólico en pacientes con lupus eritematoso sistémico. [tesis de Maestría]. Lima, Perú: Universidad Nacional Mayor de San Marcos, Facultad de MedicIna. Unidad de Posgrado; 2014.
57. Billiet L, Doaty S, KatzJD, Velázquez MT. Review of hyperuricemia as new marker for metabolic syndrome. ISRNRheumatol [Internet]. 2014[Cited: 2016 Feb. 11]. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3945178
58. Batún Garrido JAJ, Radillo Alba HA, Hernández Núñez E. Riesgo cardiovascular en lupus eritematoso sistémico. Rev Colo Reum [Internet]. 2016 Dec [Cited: 2017 Nov. 13]; 23(4): 242-249. Available from: http://dx.doi.org/10.10167j.rcreu.2016.05.001
59. Vega Abascal J, Guimará Mosqueda MR, Garces Hernández Y, Vega Abascal LA, Rivas Estevez M. Predicción de riesgo coronario y cardiovascular global en la atención primaria de salud. CCM [Internet]. 2015 Jun.[Cited: 2016 Mar. 13]; 19(2):202-211. Available from: http://scieloprueba.sld.cu/scielo.php?script=sci_arttext&pid=S1560-43812015000200003&lng=es
60. Vega Abascal J, Guimará Mosqueda MR, Garces Hernández Y, García Bermúdez Y, Vega Abascal LA. Proteína C reactiva de alta sensibilidad y riesgo de enfermedad cardiovascular. CCM [Internet]. 2015 Jun.[Cited:2016 Feb. 7]; 19(2):190-201. Available from: http://scieloprueba.sld.cu/scielo.php?script=sci_arttext&pid=S1560-43812015000200002&lng=es

***Pedro Enrique Miguel-Soca*. Universidad de Ciencias Médicas de Holguín. Holguín, Cuba.**
E-mail: socahlg@infomed.sld.cu