

The Relevance of Inflammatory Markers in Metabolic Syndrome

Genel SUR^{a,b}; Emanuela FLOCA^a; Liana KUDOR-SZABADI^a;
Maria Lucia SUR^a; Daniel SUR^a; Gabriel SAMASCA^{a,b}

^a"Iuliu-Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania

^bDepartment of Laboratory and Immunology, Emergency Clinical Hospital for Children, Cluj-Napoca, Romania

ABSTRACT

Objectives: To identify how severe is inflammation in metabolic syndrome using as inflammatory markers: C-reactive protein and leukocytes. To assess these markers considering the diversity of metabolic syndrome elements.

Material and method: We performed a study that enrolled 258 patients registered to a family physician and diagnosed with metabolic syndrome. The subjects included in the study were divided in two groups: group A-137 subjects diagnosed with metabolic syndrome that was defined by 3 elements: abdominal obesity+arterial hypertension+diabetes mellitus; group B-121 patients diagnosed with metabolic syndrome based on 5 elements: abdominal obesity+arterial hypertension+diabetes mellitus+decreased high density lipoprotein cholesterol (HDL-C)+increased triglycerides.

Results: We observed increased values of CRP and leukocytes for group B in comparison to group A: 0.9 ± 0.8 mg/dl vs 0.79 ± 0.8 mg/dl ($p=0.02$, significantly statistic). Leukocytes value was higher for group B, but not significantly statistic.

Conclusions: Inflammation in patients with metabolic syndrome depends on the number and association of elements that define this entity and it is more accentuated for subjects who associate more elements.

Keywords: metabolic syndrome, inflammation, markers

INTRODUCTION

Metabolic syndrome (MetS) is an entity that represents a global health problem; in our country there is an increased prevalence of metabolic syndrome (1,2). It is a multiplex risk factor that arises from insulin resistance accompanying abnormal adipose tissue (3-8). Clinical manifestations of the syndrome may include: abdominal obesity, hy-

per-tension, diabetes mellitus, hypertriglyceridemia, reduced high density lipoprotein cholesterol. According to International Diabetes Federation (IDF) and the National Heart, Lung and Blood Institute metabolic syndrome is diagnosed when a patient has at least 3 of the following 5 conditions (2005): obesity – waist circumference ≥ 94 cm in men and ≥ 80 cm in women (European population); blood pressure $\geq 130/85$ mmHg (or receiving drug therapy

Address for correspondence:

Sur Genel, Department of Laboratory and Immunology Emergency Clinical Hospital for Children, Cluj-Napoca, Romania.
E-mail: surgenel@yahoo.com.

Article received on the 27th of March 2012. Article accepted on the 31st of January 2014.

for hypertension); fasting glucose ≥ 100 mg/dl (or undergoing therapy); tryglicerides ≥ 150 mg/dl (or receiving treatment); HDL – C < 40 mg/dl in men and < 50 mg/dl in women (or receiving drug therapy) (9-13). Abundent data suggests that patients meeting these diagnostic criteria have a greater risk for significant clinical consequences: doubled risk of coronary artery disease, increased risk of stroke, fatty liver disease, diabetes and cancer (14-17). □

MATERIALS AND METHODS

The study included 250 people with metabolic syndrome enrolled on the lists of family physician. The group of study included patients from both urban and rural areas. The study was carried on from 2007 to 2009. Patients agreement for participation to the study was obtained. Subjects admitted in the study were divided in two groups: first group consists of 137 subjects diagnosed with metabolic syndrome that was defined by 3 elements: abdominal obesity+arterial hypertension + hyperglycemia; the second group consists of 121 patients diagnosed with metabolic syndrome based on 5 elements: abdominal obesity +arterialhypertension + hyperglycemia + decreased high density lipoprotein + increased triglycerides. There was an even distribution of patients in terms of age, obesity degree and sex in the study groups. We assessed inflammatory status for patients from the two study groups using as inflammatory markers: C-reactive protein and leukocytes. We considered as normal values for leukocytes: 5000-10000/ μ l. C-reactive protein was evaluated through a quantitative technique and we considered as normal values: 0.1-0.8 mg/dl. Inflammatory markers values obtained were compared for the two study groups. Patients diagnosed with other diseases beside metabolic syndrome were excluded from the study as there was a possibility to interfere with the results obtained for inflammatory markers: chronic pulmonary disease, chronic kidney failure, records of neoplasm or actual neoplasia, pulmonary microembolism (diagnosed by various procedures: chest X-ray, spiral computerized tomography scan, ultrasound, magnetic

resonance imaging), chronic focal infections, recent acute infections, collagenous diseases, nonsteroidian antiinflammatory therapy or cortisone therapy, surgery in the past six months, acute myocardial infarction or stroke.

Statistics used Epilnfo 6 (ANOVA). A value of $p < 0.05$ was considered with a statistical significance.

Our study complies with Ethical Principles for Medical Research Involving Human Subjects stated by the Declaration of Helsinki. □

RESULTS

Females predominate in our study, 55.5% (142) vs. 45.5% (116) male. The average age is higher in women, 61.5 + / -10 versus men 55.1 + / - 11.5 years, with a statistically significant difference ($p = 0.03$).

In the second group C-reactive protein is higher than in the first group with statistical significance ($p = 0.02$).

Leukocytes have a less important value in establishing proinflammatory and cardiovascular risk contribution in patients with metabolic syndrome compared with C-reactive protein. □

DISCUSSION

In the present conditions that obesity is increasing at global level metabolic syndrome will always be in the top of medical problems. Our study is very actual as metabolic syndrome is very important for current medical practice due to a progressive increasing frequency and atherogenic risk. Metabolic syndrome may affect most of the population and it may generate both vascular and metabolic complications (1-2, 18-19). The severity of inflammation in the metabolic syndrome measured by determining C-reactive protein and leukocytes is influenced by the number of criteria that make up metabolic syndrome.

Pro-inflammatory mechanisms can be considered as a base of increased cardiovascular risk. Proinflammatory activity is more significant if metabolic syndrome is characterised by more elements (group B is defined by 5 elements and group A by 3 elements). The results we obtained ascertain that inflammatory status is increased in patients diagnosed with metabolic syndrome (significantly statistic in subjects that associate more than 3 elements). Inflammatory injury has different severity depending

	CRP (mg/dl)	Leukocytes (/ μ l)
First group	0.79 \pm 0.8	12600 \pm 1000
Second group	0.9 \pm 0.8	14100 \pm 1000
p	0.02	0.07

TABLE 1. Leukocytes and CPR values in the two groups.

on the elements that define metabolic syndrome and on their association. Once the inflammation level increases there is a differentiated prognostic impact for cardiovascular events (20-22).

Metabolic syndrome frequency is progressively increasing and evaluation of proinflammatory risk of this entity is valuable, as assessment of some inflammatory biomarkers implies minimum costs and it can be repeated (23). In our study CRP proved to be an accurate indicator of inflammation for patients with metabolic syndrome. In subjects with acute coronary syndrome, stroke, periferic vascular disease and sudden death, recent epidemiological data ascertained a positive association between CRP levels and clinic manifestations of atherothrombosis. Increased values of CRP represent a predictive marker for unfavourable evolution in patients with unstable angina pectoris after myocardial revascularisation, as well as in patients with metabolic syndrome and diabetes – that suggests its role in atherogenesis (24-25).

Leukocytes increase more evidently in acute vascular complications that may occur in these subjects. They seem to be less valuable for chronic inflammatory character (26-30). In our study leukocytes value, even if it was increased for group B in comparison to group A, was not significantly statistic. □

CONCLUSIONS

Obesity is the central factor of the metabolic syndrome. Patients diagnosed with metabolic syndrome present an activated inflammatory status. Inflammatory syndrome is expressed according to the number of metabolic syndrome components. Bioumoral components of metabolic syndrome have a higher proinflammatory contribution. Proatherogenic impact in those with metabolic syndrome is uneven and increased.

*Conflict of interests: none declared.
Financial support: none declared.*

REFERENCES

1. **Cinteza M, Pana B, Cochino E, et al.** – Prevalence and control of cardiovascular risk factors in Romania cardiozone national study. *Maedica* 2007; 2:277-88
2. **Sur G, Sur M, Kudor-Szabadi L, et al.** – Arterial Hypertension-Prevalence of Risk Factors and Morbide Associations that increase Cardiovascular Risk. *Maedica* 2010; 5:34-41
3. **Grundey SM** – Metabolic syndrome pandemic. *Arterioscler Thromb Vasc Biol* 2008; 28:629-636
4. **Kolovou GD, Anagnostopoulou KK, Salpea KD, et al.** – The prevalence of metabolic syndrome in various populations. *Am J Med Sci* 2007; 333:362-371
5. **Bentley-Lewis R, Koruda K, Seely EW** – The metabolic syndrome in women. *Nat Clin Pract Endocrinol Metab* 2007; 3:696-704
6. **Goossens GH** – The role of adipose tissue dysfunction in the pathogenesis of obesity-related insulin resistance. *Physiol Behav* 2008; 94:206-218
7. **Gustafson B, Hammarstedt A, Andersson CX, et al.** – Inflamed adipose tissue: a culprit underlying the metabolic syndrome and atherosclerosis. *Arterioscler Thromb Vasc Biol* 2007; 27:2276-2283
8. **Lann D, LeRoith D** – Insulin resistance as the underlying cause for the metabolic syndrome. *Med Clin North Am* 2007; 91:1063-1077
9. **Olufadi R, Byrne CD** – Clinical and laboratory diagnosis of the metabolic syndrome. *J Clin Pathol* 2008; 61:697-706
10. **Després JP, Lemieux I, Bergeron J, et al.** – Abdominal obesity and the metabolic syndrome: contribution to global cardiometabolic risk. *Arterioscler Thromb Vasc Biol* 2008; 28:1039-1049
11. **Banerjee D, Misra A** – Does using ethnic specific criteria improve the usefulness of the term metabolic syndrome? Controversies and suggestions. *Int J Obes* 2007; 31:1340-1349
12. **Blaha MJ, Bansal S, Rouf R, et al.** – A practical „ABCDE” approach to the metabolic syndrome. *Mayo Clin Proc* 2008; 83:932-941
13. **Vrolix R, van Meijl LE, Mensink RP** – The metabolic syndrome in relation with the glycemic index and the glycemic load. *Physiol Behav* 2008; 94:293-299
14. **Xue F, Michels KB** – Diabetes, metabolic syndrome, and breast cancer: a review of the current evidence. *Am J Clin Nutr* 2007; 86:823-835
15. **Grundey SM** – Metabolic syndrome: a multiplex cardiovascular risk factor. *J Clin Endocrinol Metab* 2007; 92:399-404
16. **Lutsey PL, Steffen LM, Stevens J** – Dietary intake and the development of the metabolic syndrome: the Atherosclerosis Risk in Communities study. *Circulation* 2008; 117:754-761
17. **Essah PA, Nestler JE** – The metabolic syndrome in polycystic ovary syndrome. *J Endocrinol Invest* 2006; 29:270-280
18. **Xu H, Barnes GT, Yang Q, et al.** – Chronic inflammation in fat plays a crucial role in the development of obesity-related insulin resistance. *J Clin Invest* 2003; 112:1821-1830
19. **Tilg H, Moschen AR** – Inflammatory mechanisms in the regulation of insulin resistance. *Mol Med* 2008; 14:222-231
20. **Cheng AY, Leiter LA** – Metabolic syndrome under fire: weighing in on the truth. *Can J Cardiol* 2006; 22:379-382
21. **Johnson RJ, Segal MS, Sautin Y, et al.** – Potential role of sugar (fructose) in the epidemic of hypertension, obesity and the metabolic syndrome, diabetes, kidney disease, and cardiovascular disease. *Am J Clin Nutr* 2007; 86:899-906
22. **Goldbacher EM, Matthews KA** – Are psychological characteristics related to risk of the metabolic syndrome? A review of the literature. *Ann Behav Med* 2007; 34:240-252
23. **Florez H, Castillo-Florez S, Mendez A, et al.** – C-reactive protein is elevated in obese patients with the metabolic syndrome. *Diabetes Res Clin. Pract* 2006; 71:92-100

24. **Hassinen M, Lakka T, Komulainen P, et al.** – C-Reactive Protein and Metabolic Syndrome in Elderly Women—a 12-year follow-up study. *Diabetes Care* 2006; 289:931-932
25. **Frohlich M, Imhof A, Berg G, et al.** – Association between C-reactive protein and features of the metabolic syndrome: a population-based study. *Diabetes Care* 2000; 23:1835-1839
26. **Tsai JC, Sheu SH, Chiu HC, et al.** – Association of peripheral total and differential leukocyte counts with metabolic syndrome and risk of ischemic cardiovascular diseases in patients with type 2 diabetes mellitus. *Diabetes Metab Res Rev* 2007; 23:111-118
27. **Shim WS, Kim HJ, Kang ES, et al.** – The association of total and differential white blood cell count with metabolic syndrome in type 2 diabetic patients. *Diabetes Res Clin Pract* 2006; 73:284-291
28. **Desai MY, Dalal D, Santos RD, et al.** – Association of body mass index, metabolic syndrome, and leukocyte count. *Am J Cardiol* 2006; 97:835-837
29. **Kempf K, Rose B, Herder C, et al.** – The metabolic syndrome sensitizes leukocytes for glucose-induced immune gene expression. *J Mol Med* 2007; 85:389-396
30. **Desai MY, Dalal D, Santos RD, et al.** – Association of body mass index, metabolic syndrome, and leukocyte count. *Am J Cardiol* 2006; 97(15):835-838.
-
- 