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# Metabolic Syndrome - A Bomb with Delayed Reaction

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## Abstract

**Premise:** According to the International Diabetes Federation (IDF) consensus worldwide 2013 the metabolic syndrome is a cluster of the most dangerous heart attack risk factors: diabetes and raised fasting plasma glucose, abdominal obesity, high cholesterol and high blood pressure. It is known that about 20-25% of the world population has metabolic syndrome. The risk of dying through complications such as heart attack or stroke is two to three times higher than the general population. Platinum standard definition (IDF) proposed for including metabolic syndrome in addition to other measurements determination of pro-inflammatory status.

**Objectives:** Identifying inflamation and its severity using inflamatory markers: C-reactive protein fibrinogen and leukocytes. Assesment of these markers considering the diversity of metabolic syndrome elements.

**Material and method:** We performed a study that enrolled 152 patients registered to a family physician and diagnosed with metabolic syndrome. The subjects included in study were divided in two groups: group A-78 subjects diagnosed with metabolic syndrome that was defined by 3 elements: abdominal obesity+arterial hypertension+diabetes mellitus; group B-74 patients diagnosed with metabolic syndrome based on 5 elements: abdominal obesity+arterial hypertension+diabetes mellitus+decreased high density lipoprotein+increased triglycerides. We also established a control group-30 healthy people to compare inflammatory markers values.

**Results:** We observed increased values of CRP fibrinogen 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)Fibrinogen increased in group B significantly in comparison to group A (442,35 versus 365,8 p=0,0006. Leukocytes level was less responsive in patients with metabolic syndrome; 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, being more accentuated for subjects who associate more elements.

**Keywords**: Metabolic syndrome; Inflammation; Markers

## Background

Metabolic syndrome (MetS) is an entity that represents a global health problem. It is a multiplex risk factor thar arises from insulin resistance acompanying abnormal adipose tissue [1]. According to the IDF definition (2013), for a person to be defined as having the metabolic syndrome, it must have central obesity plus any two of the following factors: raised triglycerides (≥ 150 mg/dL) or specific treatment for this lipid abnormality, reduced HDL cholesterol (<40 mg/dL in males, <50 mg/dL in females ) or specific treatment for this lipid abnormality, raised blood pressure (systolic BP ≥ 130 or diastolic BP ≥ 85 mm Hg) or treatment of previously diagnosed hypertension, raised fasting plasma glucose ((FPG) ≥ 100 mg/dL) or previously diagnosed type 2 diabetes [1,2]. In addition to clinical parameters, mentioned in the definition of metabolic syndrome, IDF describes the 'platinum standard' definition - additional metabolic measurements for research. These additional measurements include the following: abnormal body fat distribution (general body fat distribution, central fat distribution, adipose tissue biomarkers: leptin, adiponectin, and liver fat content),[3] insulin resistance (fasting insulin/proinsulin levels, HOMA-IR, insulin resistance by Bergman Minimal Model, elevated free fatty acids, M value from clamp), atherogenic dyslipidaemia (ApoB Small LDL particles), dysglycaemia (OGTT), pro-inflammatory state (elevated high sensitivity C-reactive protein, elevated inflammatory cytokines, decrease in adiponectin plasma levels), [4-7] vascular dysregulation (measurement of endothelial dysfunction, microalbuminuria), prothrombotic state (fibrinolytic factors, clotting factors), hormonal factors (pituitary-adrenal axis) [1-9]. Abundent data suggests that patients meeting these diagnostic criteria have a greater risk of having significant clinical consequences: doubled risk of coronary artery disease, increased risk of stroke, fatty liver disease, diabetes and cancer [10,11].

## Material and Methods

We performed a study that enrolled 152 subjects with metabolic syndrome registered to a family physician. The group of study is significant for Transylvania region as, to the family physician are registered people from both urban and rural areas, from Cluj county and also from bordered counties. The study was carried on from 2009 to 2010. We had patients agreement to participate in the study. Subjects admitted in the study were divided in two groups: group A – 78 subjects diagnosed with metabolic syndrome that was defined by 3 elements: abdominal obesity+arterial hypertension+diabetes mellitus; group B – 74 patients diagnosed with metabolic syndrome based on 5 elements: abdominal obesity+arterial hypertension+diabetes mellitus+decreased high density lipoprotein+increased triglycerides. Patients distribution in group A, considering the three elements , was unitary. We also formed a control group that consisted of 30 healthy

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people with the same age as the subjects included in the study group. We assesed inflammatory status for patients from the two study groups and for the control group using as inflammatory markers: C-reactive protein fibrinogen and leukocytes. We considered as normal values for leukocytes: 5000-10000/µl. C-reactive protein was evaluated through a quantitative technique and we considered as normal values: 0.1-0.8 mg/dl. We considered as normal values for fibrinogen 200-400 mg% Inflammatory markers values obtained for the two study groups were compared with values obtained for the control group. We excluded from the study people who presented other morbide conditions beside metabolic syndrome as there was a posibility to interfere with the results obtained for inflammatory markers: chronic pulmonary disease, chronic kidney failure, (creatinine >1.2 mg/dl), record of neoplasm or actual neoplasia, pulmonary microembolism, chronic focal infections, recent acute infections, colagenous diseases, nonsteroidian antiinflammatory therapy or cortisone therapy, surgery in the past six months, acute myocardial infarction or stroke. Statistics used SPSS 13.0 Statistical Sofware Package (SPSS Inc Illinois USA). Data were expressed with standard life average. For testing differencies were used parameters Mann-Whitney and Kruskall-Valis. A value of $p<0.05$ was considered significant statistic.

## Results

Out of all 152 subjects submitted to the study, 89 were males, representing 44.5% and 63 were females, representing 55.5%. Average age was 55.9 ± 11 years. Men average age was 55.1 ± 11.5 years, while women average age was 61.5 ± 10 years, meaning a significantly statistic difference (p=0.03).

For inflammatory biomarkers we observed increased values of CRP for group B in comparison to group A, with a significant statistic difference (p=0.02). Fibrinogen increased for group B in coparison to group A with a significant statistic difference (442,35 versus 365,82 p=0,0006)

Leukocytes level was less responsive in patients with metabolic syndrome in comparison to CRP revealing that leukocytes have a less important value in establishing proinflammatory and cardiovascular risk contribution in patients with metabolic syndrome. Values of inflammatory markers in individuals from the control group consisting of 30 subjects aged approximately equal to the patients in the study were normal.

## Disscusion

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 [1,12-14].

Inflammation factors that define the metabolic syndrome are related to inflammatory cytokine produced by various cell types. These cytokines are released into the circulation and regulate various tissues, thus having the central and peripheral actions. In the literature is clear that cytokines play a major role in the development of type 2 diabetes, but the ability to reduce inflammation and thus the risk of developing type 2 diabetes is still under study.

Our study outlines an important mechanism: proinflammatory injury as a base of 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 find that inflammatory status is increased in patients diagnosed with metabolic syndrome (statistically significant, in subjects that associate more than 3 elements). Inflammatory injury has different severity depending on the elements that define metabolic syndrome and on their association. Out of these elements, hypertension has a less expressed contribution in comparison to triglycerides, HDL-C, glycemia values. Once the inflammation level increases there is a differentiated prognostic impact for cardiovascular events [15,16].

Metabolic syndrome frequency is progressively increasing and evaluation of proinflammatory risk of this entity is valuable, as assesment of some inflammatory biomarkers implies minimum costs and it can be repeated [17-20]. In our study CRP and fibrinogen proved to be an accurate indicator of inflammation existance 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, fibrinogen levels and clinic manifestations of atherosclerosis atherotrhtrombosis. Increased values of CRP and fibrinogen are a predictive marker for unfavourable/improper evolution at patients with unstable angina pectoris after myocardial revascularisation, as well as in patients with metabolic syndrome and diabetes – that suggests its role in atherogenesis [21-25].

Leukocytes increase more evidentely in acute vascular complications that may occur in these subjects. These markers seem to be a less valuable marker for chronic inflammatory character. In our study leukocytes value, even if it was increased for group B in comparison to group A, was not significantly statistic [26,27].

## Conclusions

Patients diagnosed with metabolic syndrome present an activated inflammatory status.

In subjects with metabolic syndrome, defined by more than 3 elements, inflammatory status is more increased. Bioumoral components of metabolic syndrome have a higher proinflammatory contribution. Inflammatory status in patients with metabolic syndrome increases the risk of atherogenesis, type 2 diabetes and heart complications.

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