1. INTRODUCTION

Diabetes mellitus type 2 indicates multi etiology and mono pathogenic health disorder. In diabetes mellitus there is a constant insulin resistance of target cells of the body, and their chronic inability to adequately respond to changes in the concentration of insulin in the blood, with consecutive relative insulin deficiency (1). Diabetes mellitus is the most common metabolic disease in humans, whose prevalence in the world is in the constant and dramatic rise. During 2000 in the world has registered about 150 million patients with diabetes (type 1 and 2), and projections suggest that this number could double by 2030 (2).

Biochemical parameters in serum of patients with type 2 diabetes mellitus represent a complex and heterogeneous group of laboratory indicators, whose task is indirectly presenting the current situation in individual organs and how the disease affects the general and specific metabolic processes throughout the body.

In terms of direct and indirect clinical implications of type 2 diabetes mellitus and certain pathophysiological changes, often associated with this disease, is described by a separate clinical entity known as the metabolic syndrome. Also called syndrome X, disability, insulin resistance syndrome, “big 4” and “deadly quartet”.

It occurs in people with android (visceral) form of obesity, characterized by cardiovascular vulnerability
to hypertension, hyperglycemia (caused by insulin resistance) and dislipidemia.

2. GOALS
To determine the number of leukocytes and erythrocyte sedimentation, the concentration of alpha 1 and alpha 2 globulin and fibrinogen in the blood of patients with type 2 diabetes mellitus and metabolic syndrome in the blood of patients with type 2 diabetes mellitus without metabolic syndrome.

Determine albumin-globulin relationship in patients with type 2 diabetes mellitus and metabolic syndrome and patients with type 2 diabetes mellitus without metabolic syndrome.

3. MATERIAL AND METHODOLOGY
3.1. MATERIAL
The study was conducted at the Clinic for Endocrinology, Clinical Center of Sarajevo University. The study included 100 patients diagnosed with type 2 diabetes mellitus aged 49 to 70 years. All patients were on insulin therapy or oral medications. According to ATP III definition from 2001 (3) the diagnosis of the metabolic syndrome can be set when there are three or more of the total of 5 criteria, namely: abdominal, central obesity based on the volume of the waist (men over 102 cm and women over 88 cm), fasting triglycerides more or equal to 1.69 mmol/L, HDL cholesterol than men 1.04 mmol/women to 1.29 mmol/L, blood pressure greater than or equal to 130/85 mm Hg and fasting glucose greater than or equal to 6.1 mmol/L (4). Patients were based on criteria from the ATP III definition are divided into two groups: DM2 Group, MS, the metabolic syndrome (n = 50) and DM2 Group, NMS, without metabolic syndrome (n = 50) as a control group.

In the group of patients with metabolic syndrome included are patients who had concentrations of fasting plasma glucose ≥ 6.1 mmol/L, triglycerides ≥ 1.69 mmol/L and blood pressure ≥ 130/85 mmHg.

3.2. METHODOLOGY
In all patients was done: anamnese, physical examination and laboratory tests, arterial blood pressure.

Laboratory results:
- To all patients are determined the concentration of glucose, total cholesterol, triglycerides, HDL, LDL and VLDL and calculated atherogenic index.
- Fibrinogen: reference values for plasma fibrinogen concentration above the laboratory were determined in subjects older than 30 years and amounted to 1,8-3,8 g/L. Serum levels of alpha-1 globulin and alpha 2-globulin; Reference values for alpha-1 globulin was 0.04 to 0.08 mg/dL, and alpha 2 globulin was 0.08 to 0.12 mg/dL.
- Erythrocyte sedimentation
- Determining the number of white blood cells was normal values are 6-8 x 10^9 in 1L.
- Albumin-globulin ratio is calculated as follows:
  - ALB/GLB where: ALB–albumin levels in blood (g/L) GLB–globulin levels in blood (g/L); Reference interval of albumin-globulin relationship is 1.2-1.5.

4. RESULTS
The average value of erythrocyte sedimentation in patients with type 2 diabetes mellitus and metabolic syndrome was higher (41.85 ± 4.99 mm) compared to the average value of erythrocyte sedimentation in patients with type 2 diabetes mellitus without metabolic syndrome (26.4 ± 3.1 mm). Determined the difference was statistically significant (p<0.05).

The average number of leukocytes in the blood of patients with type 2 diabetes mellitus and metabolic syndrome was higher (10.07 ± 0.52) compared to the average number of leukocytes in the blood of patients with type 2 diabetes mellitus without metabolic syndrome (9.25 ± 0.47), but the difference was not statistically significant.

The average concentration of alpha-1 globulin in the plasma of patients with type 2 diabetes mellitus and metabolic syndrome was higher (0.053 ± 0.003) compared to the concentration of alpha-1 globulin in the plasma of patients with type 2 diabetes mellitus without metabolic syndrome (0.042 ± 0.002). Determined the difference was statistically significant (p <0.05).

The average concentration of alpha 2 globulin in plasma of patients with type 2 diabetes mellitus and metabolic syndrome was higher (0.10 ± 0.004) compared to the concentration of alpha 2 globulin in plasma of patients with type 2 diabetes mellitus without metabolic syndrome (0.10 ± 0.004). Determined the difference was statistically significant (p <0.05)
The average concentration of fibrinogen in the plasma of patients with type 2 diabetes mellitus and metabolic syndrome was higher (14.53 ± 0.65) compared to the concentration of fibrinogen in the plasma of patients with type 2 diabetes mellitus without metabolic syndrome (11.21 ± 0.50). Determined the difference was statistically significant (p <0.001).

Albumin-globulin ratio in the blood of patients with type 2 diabetes mellitus and metabolic syndrome was lower (1.06 ± 0.03) compared to albumin-globulin ratio in the blood of patients with type 2 diabetes mellitus without metabolic syndrome (1.11 ± 0.02), but the difference was not statistically significant.

5. DISCUSSION AND CONCLUSION

Inflammation, with its direct and indirect effects on the pathophysiological development of disease, plays an important role in the development and progression of type 2 diabetes mellitus (5). Number of leukocytes, sedimentation rate, the value of albumin-globulin ratio, and the concentration of fibrinogen and alpha globulin belong to the group of these parameters. (6).

Although the new definition of this disorder, published by the International Diabetes Federation excludes the inflammatory parameters (7), undoubtedly is that inflammation in the broader sense, marked as proinflammatory state plays a significant role in its pathogenesis, and therefore mentioned parameters include in supporting metabolic criteria in the diagnosis of metabolic syndrome (8).

Based on ATP III criteria, all diabetic patients are divided into two groups. We found that half of patients (50%) had diabetes and the metabolic syndrome, while the other half was without metabolic syndrome.

Analysis of serum concentration of fibrinogen in patients from both groups showed a statistically significant increase in concentration in the group with metabolic syndrome in relation to the group without metabolic syndrome (an average increase of 380% compared to the upper reference value). Barrazoni showed that in patients with type 2 diabetes mellitus increases the production of fibrinogen and that it has a key role in increasing the concentration of inflammatory markers in plasma of patients (9). Bruno and colleagues in cohort population study found that the value of fibrinogen in patients with type 2 diabetes mellitus increases with age, glycoside hemoglobin level (Hb1ac), smoking, hypertension and increasing the number of factors of the metabolic syndrome (10).

The results of our study showed significant increase in the concentration alpha1 and alpha2 globulin in plasma of patients with, compared to those without metabolic syndrome (an increase of 32.5% for alpha1 and 20% for alpha2 globulin in relation to the upper reference value). Anjuman Gul, et al found these changes as a result of the general process of glycation of serum proteins due to relative insulin deficiency (11). Their production is increased in order to increase the amount of glycation substrate, as well as compensatory response to reduce the concentration of free glucose in plasma, and consequently the level of hyperglycemia. According to research by L. Mati increase in the concentration of alpha globulin regularly is associated with cardiovascular complications and related cataracts (12). Frankl WS also found increased the value of both apostrophized globulin sub fraction in patients with diabetic neuropathy, nephropathy and retinopathy (13), while Berkman et al (14) found the increased alpha2 values and normal value of alpha1 globulin in the diabetic patient with chronic glomerulonephritis.

Number of leukocytes, as an important inflammatory parameter was not significantly different between patients with and without metabolic syndrome. These results differ from the results of study by Ford S. Earl according to which the number of leukocytes significantly elevated in patients with type 2 diabetes mellitus (15). Although it speaks in favor of inflammatory etiology of the disease, histology did not determine the presence of inflammatory infiltrates in and around the endocrine islet of pancreas. Therefore, it is unlikely that the leukocytes are directly responsible for the destruction of pancreatic beta cells. Their increased number is probably a consequence of increased production of cytokines by existing supporting T lymphocytes. The same author noted associated with frequent bacterial and fungal infections in these patients.

According to research by Peter C. Tong, leukocytosis in diabetic patients with and without metabolic syndrome is regularly associated with late complications in the form of micro and macroangiopathy (16).

The results of our study showed that the sedimentation rate increased significantly in the group of patients with
metabolic syndrome in relation to the other group (an increase of 109% compared to the upper reference value). This result is consistent with the results of research and Elias AN Domurat E who found a statistically significant association between elevated ESR, elevated values glyco-
side hemoglobin and plasma proteins (17). According to the authors Karr and Kalen, sedimentation rate in patients with diabetes is a reliable parameter in the diagnosis of osteomyelitis (18).

On the other hand, a group of authors gathered around Godsland IF considers that the parameters of inflammation, including sedimentation rate, elevated in diabetic patients without metabolic syndrome, and as such rep-
resent high-risk factor in the occurrence of coronary heart disease (19). Cohort study included 649 men from higher socio-economic strata (HDDRISC study).

Albumin-globulin ratio (A/G), as important biochemical parameters of chronic inflammation was not signifi-
cantly altered in comparison to the baseline between two groups of patients. Not stated in accordance with the study author Elias AN Domurat and E in their results showed reduction in A/G relations in patients with diabetes mel-
itus type 2 and above are put in correlation with elevated values of serum fibrinogen, increased sedimentation, and increased percentage of glycoside hemoglobin (17). The authors of these changes result in direct connection with inflammatory etiology and pathogenesis of the disease.

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