

## Original Article

### Characteristic Features of Hemostasis System Indicators in Patients with Inflammatory Periodontal Diseases Associated with Metabolic Syndrome

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#### ABSTRACT:

The purpose of this study was to study the characteristics of indicators of the hemostasis system in patients with chronic inflammatory periodontal disease associated with metabolic syndrome. 70 patients of both sexes (43 women and 27 men) aged from 30 to 58 years old were examined. They were diagnosed with MS for the first time by an endocrinologist at the Clinic TGSI. The main group included patients -27 people with moderately severe CGP, 20 patients with CGP combined with MSIMT>25 kg/m<sup>2</sup>, and 23 patients with CGP combined with MS BMI> 25 kg/m<sup>2</sup>. The control data used the survey of 20 healthy people. It was revealed that the course of CGP with its combination with persons with a high body mass index is complicated by not only dysfunction of vascular endothelial cells, but also by increased consumption of hemocoagulation system factors and the risk of thrombohemorrhages. In response to the conditions created in the plasma link of the hemostasis system, the organism adaptively activates the platelet (cellular) link of the hemostasis system, thereby increasing the aggregation activity of the platelets. It is proved that the revealed violations in the hemostasis system must be considered when taking therapeutic measures in dental practice.

**Key words:** hemostasis; periodontitis; metabolic syndrome; atherogenic coefficient; hepatitis C.

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#### INTRODUCTION

In a number of domestic and foreign studies, data are presented on various pathogenetic mechanisms of the interrelation of periodontitis and metabolic syndrome - these are dysbiotic disorders, a systemic inflammatory reaction, phenomena of oxidative stress, which are aggravated by the periodontal state. Systemic inflammatory reaction and endothelial dysfunction arising on its background, in turn, are risk factors for the development of vascular atherosclerosis and its clinical manifestations: coronary heart disease, myocardial infarction and stroke. Recently, the prevalence of metabolic syndrome (MS) is becoming global among the population of almost all developed countries of the world (1,2,3,4). The high risk of early development of coronary heart disease (CHD), type 2 diabetes mellitus and atherosclerosis in patients with MS gives this syndrome particular medical and social importance (8). Statistics show that the largest percentage of disability and mortality in this group is associated with vascular complications, impaired blood clotting processes with the development of intravascular thrombosis (9,10). Despite the close attention paid to this problem by the biomedical sciences, many issues of the pathogenesis of the metabolic syndrome, including the mechanism for the development of

hemostasiological disorders, the connection of these changes with endothelial dysfunction, remain unresolved (5,6,7). In this regard, the study of the indicators of vascular platelet hemostasis in patients with the presence of inflammation in periodontal disease with MS, as well as the search for effective corrective therapy aimed at maximizing the reduction of the blood thrombogenic potential, and, consequently, the risk of developing cardiovascular diseases, is very relevant. The purpose of this study was to study the characteristics of indicators of the hemostasis system in patients with chronic inflammatory periodontal disease associated with metabolic syndrome.

#### MATERIAL AND METHODS

The study group of patients was formed from 70 patients of both sexes (43 women and 27 men) aged from 30 to 58 years old who were diagnosed with MS for the first time by an endocrinologist at the TGSI clinic. The main group included patients -27 people with moderately severe CGP, 20 patients with CGP combined with MS BMI> 25 kg / m<sup>2</sup> and 23 patients with CGP combined with MS BMI> 25 kg / m<sup>2</sup> .. As a control, we used the data from 20 healthy people donors with an intact

periodontal disease of the corresponding sex (11 women and 9 men) and age, thin build, without bad habits.

Examination of selected patients with obesity and overweight included laboratory diagnostics: biochemical analysis of blood with lipidogram, determination of fasting glucose, determination of the level of immunoreactive insulin in fasting plasma, calculation of insulin resistance indexes (HOMO-IR, Caro); The laboratory examination of patients of the selected group was carried out on the basis of the clinical diagnostic laboratory TSHS. The examined group of patients according to the diagnostic criteria for MS (World Health Organization, 1998 and the International Diabetes Organization, 2005) had: body mass index (BMI)  $37.42 \pm 2.8$  kg/m<sup>2</sup>; the ratio of waist to hip (OT/ON)  $0.94 \pm 0.03$ ; fasting glucose level  $6.12 \pm 0.05$  mmol/l; insulin level (IRI)  $19.64 \pm 1.0$   $\mu$ IU/l; Caro index  $0.31 \pm 0.02$ ; atherogenic coefficient (CA)  $3.15 \pm 0.16$ ; blood pressure (BP)  $145 \pm 10/95 \pm 5$ . Determination of glucose was performed on an empty stomach in the venous blood by the glucose oxidase method using standard sets of the Olvex company (St. Petersburg); the content of insulin - sets "IRI" on the automatic analyzer of the closed type COBAS-411 of the firm ROSH. Biochemical analysis of blood with the quantitative determination of indicators reflecting the lipid spectrum of blood serum: OH, TG, HDL-C, LDL-C was performed on an ROSH COBAS-311 automatic biochemical analyzer.

Content of desquamated endotheliocytes in the blood plasma (J. Hladovic method, (1978), Rutberg fibrinogen content, (1961), prothrombin time (PV), partially activated thromboplastin time (APTT), thrombin time (TV), plasminogen activator inhibitor and Willebrand factor (FW) using the HUMAN kits, and the functional state of the platelets relative to the ADP (hemolysation / aggregation test) according to the method of Barkagan ZS (1988).

Statistical processing of the results was performed using the Exel 8.0 and Statistica 5 programs. The significance of the differences between the studied values was determined by the Student's t-test. Differences were considered significant at  $p < 0.05$ .

## RESEARCH RESULTS AND DISCUSSION

All studied medical documents of patients with inflammatory diseases of periodontal tissues were divided into two subgroups depending on the patient's body mass index (BMI) values. The value of BMI is a characteristic of the correspondence of body weight to the average population values for a given height. This index allows you to determine whether body weight is low, normal or excessive (obesity), as well as using international WHO criteria (WHO, 1995) to assess the risk of CVD, which increases in proportion to the severity of overweight. 42.8% cases of BMI in patients were within the normal range ( $< 25$  kg/m<sup>2</sup>), and in (57.2%) cases, patients showed an excess of this indicator ( $> 25$  kg/m<sup>2</sup>), which indicated a high-risk development of metabolic syndrome and its complications.

For an objective assessment of the clinical condition of the periodontium, the hygiene index Silness-Loe was determined; Muhlemann bleeding index in the Cowell modification; at the same time, Miller's tooth mobility was recorded in the Flezar modification and the depth of periodontal pockets was measured.

Most of the examined patients had poor oral hygiene. The mean values of the Silness-Loe hygiene index were  $2.23 \pm 0.14$  in patients in the study group and  $2.01 \pm 0.12$  in the comparison group; no significant differences between the groups were observed ( $p > 0.05$ ).

One of the main signs of inflammation of periodontal tissues is bleeding gums, the degree of which is estimated using

the Muhlemann-Cowell index. According to the results of the Muhlemann-Cowell index assessment, signs of inflammation of periodontal tissues in the form of bleeding of varying severity were observed in all the examined patients. The average value of the bleeding index in patients of the study group was  $2.39 \pm 0.13$ , and in patients of the comparison group -  $1.76 \pm 0.11$ , the differences between the groups were statistically significant ( $p < 0.05$ ). The degree of destruction of the periodontal complex, which was reflected by such indicators as the depth of the PC and the mobility of the teeth, also differed significantly, which was due to the different ratio of patients with severe CGP in the study group and the comparison group.

Numerous studies have shown that mobilization of hemomicrocirculation during mechanical stress on periodontal tissues during inflammation does not meet the increased demand of tissues for the effective elimination of metabolic products and oxygen delivery from them. From this it follows that one of the causes of dystrophic processes in periodontal tissues during inflammation is structural and functional disorders of microcirculation and hemocoagulation. In turn, dyslipidemia contributes to the increase of oxidative stress and dysfunction of vascular endothelial cells. Oxidative stress in dyslipidemia adversely affects the functional state of platelets, since the latter is involved in the transport of lipoproteins.

Analysis of the results of the studies presented in the table shows a significant increase in the number of desquamated endotheliocytes in the blood plasma in patients with chronic hepatitis C associated with high and low body mass index ( $> 25$  kg/m<sup>2</sup>). The observed dynamics of endothelial cell dysfunction in patients with chronic hepatitis C associated with high and low body mass index, in our opinion, is due to hyperlipidemia and the influence of local inflammatory mediators. Endothelial cell dysfunction leads to an increase in the level of plasminogen activator inhibitor in the blood. Thus, in patients with chronic hepatitis C, the studied index exceeded the initial level of healthy individuals by 26%. The combined form of the disease was accompanied by an increase in the level of the plasminogen activator inhibitor by an average of 67% and 2.4 times when compared with the figures of healthy individuals. High levels of plasminogen activator inhibitor in the blood of the examined patients with the combined form of the disease apparently creates the conditions for the development of thrombohemorrhagic complications in this cohort of patients during surgical procedures. In support of this, we studied the index of the internal pathway of activating the hemostasis system in the APTT. As can be seen from the presented results of the study, the studied index of the hemostatic system over time lengthens with the combined form of the disease. The observed dynamics of the APTT index in the blood of the examined persons testified to an increased consumption of plasma factors of the hemocoagulation system and thus indicated the risk of thrombohemorrhages. Naturally, the consumption of plasma factors of the hemostatic system leads to increased consumption of fibrinogen for the formation of fibrin. A fibrin bridge is also required for platelets with endothelial dysfunction. The above is confirmed by an increase in the active forms of platelets and an increase in the number of platelets involved in the aggregates.

Studies of recent years proved the participation of platelets in the process of thrombus formation in vessels. The reason for this is the available platelet receptors for leptin, the level of which increases with increasing body weight. Platelets are also constantly in the interaction of plasma lipoproteins. Consequently, dyslipidemia is one of the reasons for the activation of blood platelets.

**Table**  
**Indicators of vascular-platelet system of hemostasis in patients with chronic hepatitis C associated metabolic syndrome**

Indicators	Healthy individuals with intact periodontal n = 20	Healthy individuals with intact periodontal n = 20	Patients with moderately severe CGP combined with MS BMI <25 kg / m2 (n = 20)	Patients with moderately severe HGP combined with MS BMI > 25 kg / m2 (n = 23)
The content of desquamated endotheliocytes in the blood is $1 \times 10^4 / l$	2,02+0,13	2,36+0,17	3,47+0,26*	4,01+0,35*
Plasminogen activator inhibitor, u/l	2,13+0,14	2,68+0,19	3,55+0,34*	5,12+0,44*
Plasminogen activator inhibitor, u/l	29,5+2,33	34,5+2,78	36,9+2,07*	38,1+2,18*
Fibrinogen blood plasma g/l	3,03+0,18	3,44+0,21	4,24+0,33*	5,78+0,49*
The amount of active forms of platelets%	12,8+0,56	16,9+1,07	21,9+1,27*	25,9+2,01*
The amount of active forms of platelets%	8,01+0,67	10,8+0,89	15,7+1,09*	18,1+1,34*
Hemolysate aggregation test (2 recon.) Sec.	12,3+0,87	11,2+0,77	9,78+0,88*	8,67+0,61*
Hemolysate aggregation test (6 recon.) Sec	32,4+2,43	29,5+2,01	25,8+1,56*	22,1+1,18*

Note: \* - significance of differences  $p < 0.05$

Simultaneously with platelet hyperactivity, we noted the state of thrombocytopeny, expressed in the activation of ADP induced aggregation activity of the platelets. As can be seen from the presented results of the study, under the influence of ADP derived from red blood cells, there is a decrease in the aggregation activity of blood platelets at different concentrations. The hyperaggregation of platelets induced by ADP makes it possible to judge the increase in their primary aggregation, which is reversible. Consequently, the course of CGP with its combination with individuals with a high body mass index is complicated not only by dysfunction of vascular endothelial cells, but also by increased consumption of hemocoagulation system factors and the risk of thrombohemorrhages. In response to the conditions created in the plasma link of the hemostasis system, the body adaptively activates the platelet (cellular) link of the hemostasis system, thereby increasing the aggregation activity of the platelets. This condition should be considered when carrying out therapeutic measures in dental practice.

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