

**INFLUENCE OF PSYCHOLOGICAL AND PERSONALITY CHARACTERISTICS OF
PATIENTS WITH CORONARY ARTERY DISEASE ON THE PHENOTYPE OF
PLATELETS**¹*Abdumalikova Feruza Bakhtiyarovna and ¹Nurillaeva Nargiza Muhtarkhanovna¹Tashkent Medical Academy, Tashkent, Uzbekistan.

*Corresponding Author: Dr. Abdumalikova Feruza Bakhtiyarovna

¹Tashkent Medical Academy, Tashkent, Uzbekistan.

Article Received on 21/03/2019

Article Revised on 10/04/2019

Article Accepted on 01/05/2019

ABSTRACT

To assess the influence of psychological distress on the morphological characteristic of the blood platelets depending on the level of anxiety-depressive syndrome in patients with cardiac pathology, examined 112 persons, of whom 84 patients with coronary artery disease, angina pectoris FC II-III, whose age average was 60.9 ± 1.46 years. Assessment of the level of psychoemotional status was conducted using hospital scale of anxiety and depression - HADS. To determine the personality type D was used a questionnaire - DS14. Study of the phenotype of platelets was performed using flow cytometry. The patients were divided into 2 groups: I group (n=40) patients with anxiety-depressive syndrome and the II group (n=44) without anxiety and depression. When assessing the interrelated effects of anxiety-depressive syndrome and psychological distress at the performance of platelet profile in patients, the differences in the groups according to the platelet phenotype. The patients of the I group the average platelet (PLT) made up $312,1 \pm 17,17 \times 10^9/L$, while in patients with type D value to PLT averaged $316,7 \pm 17,54 \times 10^9/L$, which was dominated by above average PLT- $220,4 \pm 10,48 \times 10^9/L$ in the II group ($p < 0,001$). The average value of the width of the platelets distribution (PDW) was significantly higher in I group patients at a mean of $17.0 \pm 0,94$ fL vs $13,6 \pm 0,76$ fL compared with patients of II group ($p < 0,05$). The average platelet volume (MPV) of the I group on the background of anxiety and depression were statistically significantly prevailed the value MPV, which amounted to an average of $11.3 \pm 0,42$, in contrast to performance II and control group of $9.7 \pm 0,23$ and $8.7 \pm 0,28$ fL, respectively ($p < 0,001$). Increased functional activity of platelets in patients with ischemic heart disease, due to the influence of anxiety and depression associated with personality.

KEYWORDS: coronary artery disease, arterial hypertension, anxiety-depressive syndrome, personality type D, platelets profile, phenotype of blood platelets.

INTRODUCTION

Currently, with the prevalence of coronary artery disease (CAD) and arterial hypertension (AH) and anxious-depressive syndrome (ADS) among the population, are increasingly common comorbid combination of these diseases. Thus, according to the EUROASPIRE III, among 8580 patients from 22 European countries observed within 6 months after hospitalization for CAD, the prevalence of depression ranged from 8.2 to 35.7% among men and from 10.3 to 62.5 % among women. The frequency of anxiety disorders ranged from 12.0 to 41.8 % among men and from 21.5 to 63.7 % in women. Meanwhile, according to clinical research conducted in our country, the general prevalence of ADS among patients with CAD, particularly stable angina pectoris (SAP) without myocardial infarction (MI) is 40-48%.^[1]

In the guideline developed by the experts of the European society of cardiology for the diagnosis and treatment of stable angina, noted the importance of

examining psychosocial stress as a risk factor (RF) of cardiovascular disease (CVD), and also they are based on the strategy of preventive interventions to identify, control and correction of cardiovascular and psychosocial factors.^[2] The largest evidence base confirming the adverse impact of psychosocial factors on the risk, course and prognosis of CAD with a class of evidence (IIA), levels of evidence (B) and the degree of evidence according to GRADE (strong) presented in relation to factors such as psychosocial stress, depression, anxiety, aggression, low socioeconomic status, social isolation, type D personality.^[3] To chronic psychological RF recently began to include personality type D (distressing), including negative anxiety (the tendency to experience negative emotions) and social inhibition (suppression of emotions and behavioral reactions in social interactions).^[4]

Among other things, the study of the relationship of psychosocial, anxiety and depressive disorders and CVD

due to their high prevalence, social significance, impact on work capacity and is determined by the results of clinical, neurochemical, neurophysiological studies, indicating some of their common pathogenic mechanisms.^[5] There are several pathways that are potentially associated with negative psycho-emotional disorders with CAD through indirect mechanisms in the form of behavioral reactions manifested by low adherence of patients to the basic treatment, and more direct pathophysiological mechanisms, such as autonomic imbalance, activation of inflammatory reactions, increased platelet aggregation and endothelial dysfunction, which contribute to the manifestation of other cardiovascular RF and progression of atherosclerosis^[6].

The dysregulation of neuroendocrine function is another possible way through which depressive symptoms and psychological distress, can influence the development and course of CVD. Both components of type D personality are associated with greater reaction of cortisol in response to stress, for example, in patients with acute coronary syndrome (ACS) with type D was observed higher level of cortisol after awakening ($p=0.007$) and higher production of cortisol during the day ($p=0.044$), than patients without type D.^[5,7] Thus, the "distressing" type of personality leads to a more prolonged dysfunction of the hypothalamic-pituitary-adrenal axis, due to excessive release of cortisol, leading to hemostatic changes.^[7] Elevated levels of catecholamines in blood of patients with ADS, is associated with increased risk of platelet activation, aggregation and further thrombosis.^[8]

Thus, CVD and depression have a bilateral relationship, in which inflammatory processes, endothelial dysfunction, increased platelet activity, and neurohormonal dysfunction of the autonomic nervous system related to depression mutually potentiate each other.^[6] The accumulated evidence points to the feasibility of using the personal approach to identify patients with risk of thrombogenic cardiac complications due to stress. In this regard, a complex assessment of the interrelated effects of psychological distress and associated ADS on the performance of platelet profile blood to predict risk of development of thrombotic events in patients with major CVD.

The present study was conducted with the aim of to evaluate the impact of psychological distress on the morphological characteristic of blood platelets, depending on the level of ADS in patients with CAD.

MATERIAL AND METHODS

The study examined 112 persons, from them 84 patients with an established diagnosis of CAD, stable angina pectoris (SAP) FC II-III and arterial hypertension of I-III degree, of both sexes, whose age average was 60.9 ± 1.46 years under treatment 1 and 2 - cardiology department 1-clinic of Tashkent medical academy. The control group

consisted of 28 almost healthy persons. In the study not included the patients with acute coronary syndrome, myocardial infarction and stroke in anamnesis, diabetes mellitus and CHF FC IV.

Determination of the level of psychoemotional status was conducted using hospital scale of anxiety and depression - HADS (Hospital Anxiety and Depression scale). The questionnaire is designed to identify and assess the severity of depression and anxiety in the conditions of general medical practice, has high discriminant validity with respect to two disorders: anxiety and depression. The scale is composed of 14 statements that serve 2 subscore. In interpreting the data was taken into account, the total figure for each subscore (HAS and HDS), highlighting 3 areas of values: 0-7 points - norm, 8-10 points - subclinically pronounced anxiety/depression, 11 points and above — clinically pronounced anxiety /depression.

To determine the personality type D was used 14-point questionnaire "The Type D scale" (DS14), which was successfully validated in many countries of Western Europe and Asia.^[4,9] The questionnaire DS14 consists of two subscales: negative affectivity (NA) and social inhibition (SI) containing 7 questions for each of the subscales. If there are 10 or more points in each of the scales was diagnosed with a personality type D.^[4]

Current research methods allow the study of virtually every phase of the participation of platelets in the process of thrombus formation. General blood analysis with a gross morphological pattern of platelets is highly informative and highly sensitive method of quantitative and qualitative evaluation of thrombogenic potential of blood in routine practice, in contrast to the costly and time-consuming methods of assessing the functional status of platelets. Hemobiological studies using fluorescent - cytometric techniques, including a detailed analysis of the quantitative and qualitative characteristics of platelets was carried out on high-tech hematology analyzer series XN. This unit explores the formed elements of blood with the help of innovative technology of flow cytometry, the concept of which is that blood cells are evaluated not only by external parameters – size, volume, etc., and internal, i.e., the internal content of the cells, nucleus, DNA. In addition, the cell count is not in sight, and the blood volume. This blood test includes in addition to the main standard indicators haemogram 3 additional modules: reticulocytosis, leukocyte and platelet. platelet profile includes the following indicators: the number of platelets (PLT, $10^9/L$), the platelet distribution width (PDW, fL), mean platelet volume (MPV, fL), the ratio of large platelet (P-LCR, %), thrombocrit (PCT, %) and the immature platelet fraction (IPF, %).

Statistical processing of the results was performed using the calculation of standard distribution characteristics, incl. averages, standard deviations, standard errors. For a

statistical description of the relationship between the various parameters, the Spearman rank correlation coefficient was calculated. The reliability of differences between the two groups was tested using Student's t-test, the level of statistical significance was considered to be $p < 0.05$; $p < 0.01$; $p < 0.001$.

RESULTS

To identify characteristics of thrombogenic potential of blood in patients with CAD and AH depending on the presence and severity of psycho-emotional condition investigated are divided into two groups: the I group – 40 (47,6 %) patients with ADS and the II group – 44 (52,4 %) patients without ADS. According to the results of the survey using the HADS questionnaire, the first group scored an average of 11.5 ± 0.55 points subscore HAS and 11.4 ± 0.41 points for HDS, which was dominated by above average values in the comparison group ($p < 0.001$), which was 4.9 ± 0.37 and 5.7 ± 0.36 points, respectively. In the control group recruited average score was for HAS 4.5 ± 0.40 and for HDS 4.8 ± 0.29 points, which also exclude the presence of anxiety and depression in healthy individuals. An important is the fact that among patients with CAD and AH for the I group in 60% of cases were diagnosed clinically pronounced level of anxiety and depression, and in 25% cases subclinical pronounced level, which indicates prevalence pronounced degree of combined ADS in patients with CVD. At the time of inclusion in the study between the formed groups were not observed statistically significant differences in age, sex, severity of SAP and the degree of AH, the duration and the severity of the previous CAD and the incidence of associated diseases.

The results of the survey with the aim to compare personality characteristics of patients with CAD

combined with AH, was noted: personality type D had the prevailing most patients of the I group – 34 (85 %) studied, whereas in the II group at 22.7 % of cases were detected in patients with type D ($p < 0.0001$), which corresponds to the occurrence of "distressing" type among patients with CVD (25-30 %).^[5] The least number of persons with personality type D was in the control group, 4 (14,2 %) healthy subjects. The feature of persons with the presence of this type is the tendency to experience negative emotions in daily life and suppress their expression in social interactions, as manifested by a predisposition to manifestations of psychological distress.^[4] Evaluation of indicators on scales of negative affectivity and social inhibition of the questionnaire DS-14 established significant differences of the components, the combination of which characterizes a type D. So, the severity of social inhibition was least in the control group ($SI-8,7 \pm 0.64$ points), than in the II group ($SI-10,8 \pm 0.60$ points) and highest among patients of the I group ($SI-13,7 \pm 0.72$ points) ($p < 0.01$). Values on the scale of negative affectivity was 15.5 ± 1.07 , $8,0 \pm 0.73$ and 7.2 ± 0.75 points, respectively ($p < 0.001$).

When performing correlation analysis among the examined there was a statistically significant relationship between the severity of distressing of personality traits on scales of NA and SI and comorbid ADS. A positive correlation of moderate strength was observed between levels of anxiety and NA ($r=0,60$), SI ($r=0,48$) and the presence of personality type D ($r=0,62$). Similar degree of correlation relationship with these indicators were also noted for level of depression ($r=0,61$ $r=0,58$ and $r=0,64$ respectively), indicating reliable association of ADS and psychological distress.

Table 1: Quantitative and qualitative characteristics of blood platelets in the groups.

Indicators of platelets profile	I group (n=40)	II group (n=44)	Control group (n=28)	p
Number of platelets (PLT)	$312,1 \pm 17,17$	$220,4 \pm 10,48$	$242,6 \pm 19,81$	$< 0,001$
Platelet distribution width (PDW)	$17,0 \pm 0,94$	$13,6 \pm 0,76$	$11,2 \pm 0,58$	$< 0,05$
Mean platelet volume (MPV)	$11,3 \pm 0,42$	$9,7 \pm 0,23$	$9,7 \pm 0,32$	$< 0,001$
Ratio of large platelet (P-LCR)	$31,2 \pm 1,49$	$27,7 \pm 1,19$	$25,9 \pm 1,9$	$> 0,05$
Immature platelet fraction (IPF)	$0,3 \pm 0,02$	$0,2 \pm 0,01$	$0,23 \pm 0,02$	$< 0,01$
Platelet crit (PCT)	$2,4 \pm 0,35$	$1,9 \pm 0,30$	$2,1 \pm 0,39$	$> 0,05$

When assessing the interrelated effects of ADS and psychological distress at the performance of platelet profile peripheral blood of patients with main CVD, the differences between the groups studied according to the morphological characteristics of peripheral platelets, which are presented in the table 1. It is known that high levels of platelet factor thrombogenic risk involved in the cellular mechanisms of primary hemostasis.^[3] Patients of the I group the average number of platelet (PLT) made up $312,1 \pm 17,17 \times 10^9/L$, in particular, in patients with D type value of PLT averaged $316,7 \pm 17,54 \times 10^9/L$, which was prevailed over PLT - $220,4 \pm 10,48 \times 10^9/L$ in the II group ($p < 0.001$), despite the corrective standard antiplatelet therapy in both groups. Among healthy

individuals of the control group were not taking antiplatelet drugs the average number of platelets made $242,6 \pm 19,81 \times 10^9/L$, whereas in healthy recipients, with "distressing" type, was a predisposition to increased PLT $298,7 \pm 14,9 \times 10^9/L$, evidence of independent predictive value of psychological distress in a deterioration of the thrombogenic potential of blood.

It is noted the relationship of the size of platelets with functional activity content in the granules of platelets biologically active compounds, propensity of cells to adhesion, volume changes of platelets before aggregation. As a result of activation of platelets discoid form of platelets is changed to spherical, appear

pseudopodia, which leads to an increase in the size of cells and the degree of anisocytosis, which is reflected in the indicators PDW, MPV.^[6] Thus, the average values of PDW, increased heterogeneity of platelets based on their size, indicates the degree of anisocytosis, was significantly higher in the I group patients compared with patients with no ADS, an average of 17.0 ± 0.94 fL vs 13.6 ± 0.76 fL ($p < 0.05$). The average volume of platelets (MPV) indirectly reflects the appearance in the blood of big reticular platelets with a high content of procoagulant factors, high functional activity and the development of the inflammatory process also revealed differences between the study groups. Patients of the I group on the background ADS is statistically prevailed the value MPV, which amounted to an average of 11.3 ± 0.42 , in contrast to performance II and control

groups of 9.7 ± 0.23 and 8.7 ± 0.28 fL, respectively ($p < 0.001$). However, in terms of P-LCR, PCT, and IPF prevalence in the group of patients with ADS, there was a slight and significant differences between the groups were not established, as in the I group of them averaged 31.2 ± 1.49 %, 0.3 ± 0.02 %, 2.4 ± 0.35 %, in the II group 27.7 ± 1.19 %, 0.2 ± 0.01 %, 1.9 ± 0.30 % and in the control group 25.9 ± 1.9 %, 0.23 ± 0.02 %, 2.1 ± 0.39 %, respectively.

The interrelated influence of psychological and personality characteristics of patients with CAD and AH with morphological changes of platelets confirms the assessment of correlation between these indicators (table 2).

Table 2: The correlation relationship between indicators of psychological distress, anxiety, depression and phenotype of blood platelets.

Indicators	NA		SI		Type D		Level of anxiety		Level of depression	
	r	p	r	p	r	p	r	p	r	p
PLT	0,41	<0,05	0,2	<0,05	0,52	<0,01	0,5	<0,01	0,57	<0,01
PDW	0,15	<0,01	0,17	<0,05	0,29	<0,01	0,1	<0,01	0,26	<0,01
MPV	0,35	<0,01	0,19	<0,05	0,44	<0,05	0,41	<0,05	0,34	<0,05
P-LCR	0,10	<0,05	0,15	<0,05	0,23	<0,05	0,11	<0,05	0,12	<0,01
PCT	0,08	<0,05	0,12	<0,01	0,26	<0,01	0,34	<0,05	0,45	<0,01
IPF	-0,06	<0,05	-0,08	<0,05	-0,18	<0,05	-0,07	<0,05	-0,19	<0,05

Note: NA- negative affectivity; SI - social inhibition; PLT - number of platelets; PDW - platelet distribution width; MPV - mean platelet volume; P-LCR - ratio of large platelet; PCT - platelet crit; IPF - immature platelet fraction.

So, a positive high degree of correlation was noted between the values of PLT and HDS, HAS ($r = 0.5$ and $r = 0.57$), and presence of personality type D ($r = 0.52$). Medium positive correlation was noted among the indices HDS and PDW, MPV, PCT ($r = 0.26$, $r = 0.34$ and $r = 0.45$ respectively), and also HAS and MPV, PCT ($r = 0.41$ and $r = 0.34$). Similar degree of correlation of the relationships with indicators of PDW, MPV, PCT was noted for the presence of type D ($r = 0.29$, $r = 0.44$ and $r = 0.26$, respectively). Except for the lack of connection, P-LCR with SI and HAS, among other personal-psychological indicators with values of thrombophilia showed weak and very weak correlation relationship.

DISCUSSION

Studies have shown that psychological RF's such as ADS are often combined within a single person, and the type D design is specifically designed to identify patients at risk of combining such factors.^[5] In the study, patients with CAD showed a comparable increase in the frequency and severity of combined ADS, which are associated with such components of personality type D, as negative excitability and social inhibition. The pathogenetic aspects of this associative relationship may be related to the presence of a biological substrate, common to depression and psychological distress. The data of some triple studies confirmed the hyperreactivity of the hypothalamic-pituitary-adrenal system with increased production of cortisol in depression, which is

also characteristic in the presence of personality type D.^[6,7,11] Chronic hypercortisolemia in turn increases the risk of functional activation of platelets, aggregation processes and further thrombus formation, which are closely associated with the development of cardiovascular complications.^[8]

Platelet dysfunction has been described in patients with varying degrees of severity of ADS. With depression, there are deviations in the level of serotonin in the platelets, an increased concentration of platelet serotonin receptors and a decrease in the level of platelet protein, a serotonin transporter, suggesting an increased sensitivity of platelets to serotonin and a decrease in the rate of its capture by blood plasma cells.^[12] Moreover, there is evidence that patients with depression have significant defects in the physiological characteristics of platelets, such as elevated levels of intracellular free calcium, hypersensitivity to serotonin (5-HT) and catecholamine receptors, hyperproduction of factor 4 and beta-thromboglobulin.^[13] In the blood of patients with depression, the number of reticular platelets, the average volume of platelets, as well as their functional activity is increased, which is accompanied by an increase thrombogenic potential of blood. Indirect reflection of the appearance in the blood of active platelets can serve as indicators of platelets profile, which are proposed to be used to predict the risk of thrombotic events in patients.^[10]

Existing research methods to date allow us to study almost every stage of the participation of platelets in the process of thrombus formation. In the diagnosis of disorders of platelet hemostasis, essential analysis can be provided by the analysis of the functional activity of platelets carried out using flow cytometry. Complete blood count with a detailed morphological characteristic of platelets is a modern informative and highly sensitive method for assessing the quantitative and qualitative thrombogenic potential of blood in routine practice, as opposed to expensive and time-consuming methods for assessing the functional state of platelets.

The results of this study demonstrate that in patients with CAD, the presence of personality type D was associated with higher levels of anxiety and depression on the HADS scale, which correlate with blood platelet profile parameters, such as PLT, PDW and MPW, reflecting the blood thrombogenic potential. This suggests that when combined with ADS and psychological distress components, the summation of their effect is expected, which may be accompanied by worsening of the clinical course of CAD according to the morphological characteristic of platelets, in the direction of enhancing the activity of the thrombocyte link of the hemostasis cascade.

CONCLUSIONS

Thus, changes in the morphological characteristic of platelets are due to the combined effect of distress through hypercortisolemia, associated with the personality type D and the dominant ADS in patients with CAD and AH. The study showed a significant predominance of the mean values of PLT, PDW and MPW in patients with clinically significant ADS. During the work was established the predictive value of psychological and personal characteristics of patients with CAD in the growth thrombogenic potential of blood, based on a comparable correlation of type D, anxiety and depression with indicators of thromboprofile. It can be assumed that the type of personality D is an independent chronic psychological RF for the manifestation of CAD, the development of severe anxiety and depression, which indicates the need to identify it in a timely manner as a negative prognostic factor in patients with CVD. Investigation of the ability of platelets to activation, structural and functional changes, the understanding of the mechanisms underlying them, expands the possibilities of prevention and correction of disorders in thrombocytic link of hemostasis system, not only aggravating the disease, but often determines the outcome.

REFERENCES

1. Nurillaeva NM. Analysis of the prevalence and significance of behavioral risk factors in patients with ischemic heart disease in outpa conditions. Preventive medicine, 2011; 1: 11-15.

2. ESC Guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J., Sep, 2012; 33(17): 2126.
3. Garganeeva NP, Petrova MM. The Influence of depression on the course of coronary artery disease and quality of life of patients. Wedge. Med., 2014; 12: 30-37.
4. Denollet J. DS14: Standard assessment of negative affectivity, social inhibition, and Type D personality. Psychosom Med, 2005; 67(1): 89-97.
5. Sumin AN. et al. The Prevalence of personality type D and the relationship with the presence and risk factors of cardiovascular disease according to the study "ESSAY". Rational pharmacotherapy in cardiology, 2015; 11(3): 261-266.
6. Vinokurov EV, Sobennikov VS. The Relationship of depression to cardiovascular disease. Acta scientifica biomedica, 2017; 2(5): 124-128.
7. Daisy LW, Linda P. Cortisol awakening response is elevated in acute coronary syndrome patients with type-D personality. Journal of Psychosomatic Research, 2007; 62: 419– 425.
8. Nemeroff C. Are platelets the link between depression and ischemic heart disease? Am. Heart J., 2000; 140(4): 57–62.
9. Lim H, Lee M. et al. Assessment of the Type D personality construct in the Korean population: A validation study of the Korean DS14. J Korean Med Sci., 2011; 26(1): 116-23.
10. Philippova OI etc. Methods of the study of the functional activity of platelets. Transfusion medicine, 2012; 13: 493-514.
11. Denollet, J., Kupper, N. Type-D personality, depression, and cardiac prognosis: Cortisol dysregulation as a mediating mechanism. Journal of Psychosomatic Research, 2007; 62(6): 607-609.
12. Gehi A., Musselman D. et al. Depression and platelet activation in outpatients with stable coronary artery disease: findings from the heart and soul study. Psychiatry Res., 2010; 175(3): 200-204.
13. Pogosova G. V. Depression new risk factor for coronary artery disease and a predictor of coronary death. Cardiology, 2002; 4: 86–91.