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ABSTRACT

of the dissertation for the degree of Doctor of Philosophy

LATENT HEMOSTASIS DISORDERS IN PATIENTS WITH BETA-THALASSEMIA AND IRON DEFICIENCY ANEMIA

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GENERAL DESCRIPTION OF THE STUDY

Relevance of the study. Thrombotic complications are one of the main causes that significantly and negatively affect the clinical course of many diseases, often leading to disability and death of patients[1]. These complications are diagnosed after the development of the first episode of thrombosis, and the patient's predisposition to early occurrence of thromboses is not taken into account. However, a patient may have a prethrombotic state, in which there are no clinical manifestations of thrombosis, but the circulating blood is in a state of increased readiness for coagulation (latent DIC)[2]. A constant increase in the intensity of intravascular blood coagulation, not manifested by changes in the clinical picture of the disease, may be observed in many chronic diseases with latent hypercoagulation[3].

Arterial and venous thrombotic complications are also observed in patients with anemia of various origins. There are reports of the occurrence of such complications in patients with beta-thalassemia[4] and in patients with low serum iron level[5]. In patients with beta-thalassemia, thrombotic complications are associated both with the

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[1] *Бокарев, И.Н., Попова, Л.В.* Современные проблемы тромбозов артерий и вен // Практическая медицина. Кардиология, – 2014. №6 (82), – с. 13-17.

[2] *Verigou, E.* Disseminated intravascular coagulation: An uncontrolled explosion of coagulation leading to consumptive coagulopathy / E.Verigou, K.-Ch.Valera, T. Chatzilygeroudi et al. // ACHAIKI IATRIKI, – 2024. 43(1), – p. 23-38.

[3] *Керимов, А.А.* Латентные гиперкоагуляционные нарушения гемостаза // – Баку: Современные достижения азербайджанской медицины, – 2014. №4, – с.116-122.

[4] *Bou-Fakhredin, R.* Hypercoagulability in hemoglobinopathies: Decoding the thrombotic threat / R.Bou-Fakhredin, M.D.Cappellini, A.T.Taher et al. // Am. J. Hematol., – 2025. Jan. 100 (1), – p. 103-115. doi: 10.1002/ajh.27500.

[5] *Livesey, A.* Low serum iron levels are associated with elevated plasma levels of coagulation factor VIII and pulmonary emboli/deep venous thromboses in replicate cohorts of patients with hereditary haemorrhagic telangiectasia / A.Livesey, R.M.Richard, J.H.Meek et al. // Thorax, – 2012. 67(4), – p. 328-333. doi: 10.1136/thoraxjnl-2011-201076.

platelet link of hemostasis[6] and with chronic (latent) hypercoagulation[7]. In patients with iron deficiency anemia (IDA) and anemia of chronic diseases, latent hypercoagulation is noted, with possible prethrombotic readiness of hemostasis in these patients[8]. At the same time, before the moment of exposure of provoking factors, such patients usually do not have thrombotic complications. At present, the search for new predictors of thrombosis and methods for timely correction of thrombus formation continues. The data have appeared that primary hypercoagulation and the formation of blood vessel thrombi in patients may be associated with magnesium deficiency, which can be considered an additional significant risk factor for thromboembolism. However, in case of a high risk of thromboembolism, the administration of antiplatelet agents and anticoagulants cannot in any way compensate for the magnesium deficiency in the blood[9].

Timely detection of increased predisposition to thrombosis in patients with beta-thalassemia and IDA is important for the effective treatment of these widely spread anemias in the world[10].

Hypomagnesemia and magnesium deficiency previously detected in patients with beta-thalassemia[11] and IDA[12] actualized the study of

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[6] *Musallam, K.M., Taher, A.T., Rachmilewitz, E.A.* β-Thalassemia intermedia: a clinical perspective // Cold Spring Harb Perspect. Med., – 2012. Jul. 2(7), – a013482. doi: 10.1101/cshperspect.a013482.

[7] *Taher, A.T.* Thalassemia and hypercoagulability / A.T.Taher, Z.K.Otrock, I.Uthman et al. // Blood Rev., – 2008. Sep. 22 (5), – p. 283-292. doi: 10.1016/j.blre.2008.04.001.

[8] *Копина, М.Н., Гаевский, Ю.Г.* Гиперкоагуляционные нарушения гемостаза у больных с впервые выявленной железодефицитной анемией // Вестник Новгородского Государственного Университета, – 2013. №71, – Т.1, – с.21-24.

[9] *Fritzen, R.* Magnesium deficiency and cardiometabolic disease // Nutrients, – 2023. May. 15(10), – 2355. doi: 10.3390/nu15102355.

[10] *Al-Samkari, H., Kessler, C.M., Auerbach, M.* Recognition of thrombotic risk of thrombocytosis in iron deficiency // Haematologica, – 2021. Mar; 1. 106(3), – p.661-663. doi: 10.3324/haematol.2020.270496.

[11] *Qafarova, S.N.* β-Talassemiyanın müxtəlif formalarında mineral mübadiləsinin öyrənilməsi: / Biol. elm. nam. ... dis. / – Bakı, – 2007. – 142 s.

the nature of thrombotic complications, thrombogenic risk factors, the presence and specificity of latent hypercoagulation in these patients, which determined the purpose and objectives of this study.

Object of the study. 420 female patients aged 18-40 years, including 285 patients with beta-thalassemia (130 patients with major beta-thalassemia, 95 patients with intermediate beta-thalassemia, 60 patients with minor beta-thalassemia) and 135 patients with IDA. The control group consisted of 30 female blood donors.

Purpose of the study. To study hypercoagulation disorders of hemostasis against the background of magnesium bioelement content in patients with beta-thalassemia and iron deficiency anemia.

Objectives of the study:

1. To investigate clinical manifestations and anamnestic signs of hypercoagulation in patients with beta-thalassemia and IDA.
2. To carry out adaptation and validation of the questionnaire of predisposition to increased thrombosis (PIT) and magnesium deficiency questionnaire (MDQ).
3. To study hemostasis indicators and magnesium level in patients with beta-thalassemia and IDA.
4. To identify latent hypercoagulation disorders of hemostasis in patients with beta-thalassemia and IDA.
5. To study the effect of magnesium therapy on hemostasis indicators in patients with beta-thalassemia and IDA.

Main provisions of the thesis submitted for defense:

– In patients with beta-thalassemia, compared to patients with IDA, thrombotic complications are significantly more frequently detected.

– A significant part (about one third) of patients with homozygous beta-thalassemia and with IDA have latent hypercoagulation, the so-called prethrombotic readiness of hemostasis.

– Magnesium deficiency was detected in a significant part of patients with homozygous beta-thalassemia and with IDA, and this bio-

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[12] *Shi, Z.* Joint association of magnesium and iron intake with anemia among Chinese adults // Nutrition, – 2008. Oct. 24 (10), – p. 977-984. doi: 10.1016/j.nut.2008.05.002.

element can be considered as a predictor of thrombogenic risk in patients with homozygous beta-thalassemia and IDA.

– Latent hypercoagulation in patients with homozygous beta-thalassemia and IDA may occur against the background of magnesium deficiency and is characterized by a number of clinical manifestations, anamnestic signs, and specificities of hemostasis indicators.

– Therapy with magnesium citrate preparation (Magne B_6 forte) improves hemostasis parameters in patients with homozygous intermediate beta-thalassemia and IDA, who have magnesium deficiency and latent hypercoagulation.

Scientific novelty of the study. For the first time in Azerbaijan, the incidence of thrombotic complications among women with major and intermediate forms of beta-thalassemia and IDA was studied.

For the first time, latent hypercoagulation was studied in these patients as a variant of increased thrombotic readiness of the hemostatic system. The specificity of latent hypercoagulable states according to hemostasis parameters against the background of magnesium deficiency was determined, on the basis of which a diagnostic algorithm was developed that facilitates the effective detection of latent hypercoagulation in patients with beta-thalassemia and IDA.

Hypercoagulation was expressed in an increase in thrombinemia markers – D-dimer and soluble fibrin-monomer complexes, fibrinogen levels, euglobulin clot lysis time, a decrease in activated partial thromboplastin time (APTT) and antithrombin III.

In some patients with homozygous beta-thalassemia and IDA, magnesium deficiency was detected, which is considered as a predictor of thrombogenic risk in these patients.

It has been established that the magnesium citrate preparation (Magne B_6 forte) improves hemostasis parameters in patients with intermediate beta-thalassemia and IDA, who have magnesium deficiency and latent hypercoagulation at the same time.

It has been established that the detection of latent hypercoagulation signs in patients plays an important role in the further pharmacological regulation of the intensity degree of constant intravascular blood coagulation and leads to an improvement of disease prognosis.

Practical significance of the study. Based on the results of the

research, a specialized questionnaire − PIT (predisposition to increased thrombosis) was developed to identify clinical and anamnestic signs of latent hypercoagulation in patients with anemia. Adaptation and validation of the PIT questionnaire was carried out.

Simultaneous investigation of serum magnesium content in patients and determination of magnesium deficiency using the standardized international MDQ questionnaire allows timely detection of this bioelement deficiency. For accessible implementation of the MDQ questionnaire in the republic's institutions, it was translated, adapted, and validated into the Azerbaijani language.

In some patients with beta-thalassemia and IDA who do not have clinical manifestations of thrombosis, such changes in hemostasis parameters were detected: an increase in the levels of the thrombinemia marker D-dimer, fibrinogen, fibrinolysis time, and a decrease in APTT and antithrombin III, increased induced platelet aggregation to ADP inducers and ristocetin (ASPI), which contributes to the early diagnosis of this pathology.

The use of magnesium citrate (Magne B_6 forte) positively influences some hemostasis parameters in patients with intermediate beta-thalassemia and IDA who have magnesium deficiency and latent hypercoagulation. Timely detection of thrombogenic risk predictors makes it possible to carry out the necessary correction of hypercoagulation and to optimize treatment in patients predisposed to thrombosis.

Approbation of the research results. The main provisions of the thesis were presented and discussed at the IX International Eurasian Hematology Oncology Congress (Istanbul, Turkey, 2018), the XI International Eurasian Hematology Oncology Congress (Istanbul, Turkey, 2020), the international conference dedicated to the 75th anniversary of the Research Institute of Hematology and Transfusiology "Actual Problems of Hematology" (Baku, 2019), the I Azerbaijan International Congress of Hematologists dedicated to the 10th anniversary of the Thalassemia Center (Baku, 2019), and the V International Scientific Congress on the topic "Modern Problems of Pharmacy" (Baku, 2021).

The initial discussion of the thesis was held at a meeting of the

Academic Council of the National Center of Hematology and Transfusiology (July 28, 2022, protocol No. 5). The results of the research were also reported and discussed at the Scientific Seminar on the specialty 3232.01 – "Hematology and blood transfusion" (June 30, 2025, protocol No. 1) operating under the BED 2.27 Dissertation Council of AMU.

Place of the study. The study was carried out at the B. Eyvazov Research Institute of Hematology and Transfusiology and the Thalassemia Center of the Ministry of Health of the Republic of Azerbaijan (now the National Center of Hematology and Transfusiology).

Connection of the study with the research plan of the institution. The thesis was carried out within the framework of the Research Institute project "Development at the modern level of organization of diagnostics, treatment, and prevention of hemoglobinopathy in Azerbaijan. Study of the molecular bases of thalassemia in Azerbaijan" (2014-2018, state registration No. 01144058).

Implementation of research results into practice. The research results were implemented into the daily work of the Thalassemia Center and the outpatient department of the National Center of Hematology and Transfusiology and also into the educational process of the Department of Hematology when teaching the course of hematology and transfusiology.

Publications. On the topic of the thesis, 22 works were published, including 14 articles (2 of them abroad), 7 materials of conferences (4 of them abroad), and 1 methodological guideline.

Structure and volume of the research work. The thesis is presented on 200 pages of computer text (240554 symbols), consists of an introduction (6 pages), a literature review (36 pages), a description of the material and research methods (21 pages), 4 chapters presenting the results of the author's own research (77 pages), a discussion of the obtained results in the form of a conclusion (24 pages), conclusions (2 pages), practical recommendations (1 page), a list of references (29 pages), containing 262 sources, of which 6 works are in the Azerbaijani language, the rest are in Russian and English. The thesis is illustrated with 31 tables, 15 graphs, and 3 figures.

MATERIAL AND METHODS OF THE STUDY

The present study included patients undergoing treatment and outpatient follow-up at the National Center of Hematology and Transfusiology. During 2014-2018, as medical documentation (outpatient medical records) was reviewed, patients with the following diagnoses were selected for the study: beta-thalassemia (D56.1 according to ICD-10); iron deficiency anemia (D.50). The study included patients with major beta-thalassemia, intermediate beta-thalassemia, minor beta-thalassemia, and primarily diagnosed iron deficiency anemia (IDA).

The study consisted of 3 stages. At the first stage, outpatient medical records were examined. In total, medical records of 420 female patients aged 18-40 years were reviewed: 285 patients with beta-thalassemia (average age 26.4±1.3 years) and 135 patients with IDA (average age 28.2±1.0 years). Among patients with beta-thalassemia, 130 patients had major beta-thalassemia (average age 26.2±1.4 years), 95 patients had intermediate beta-thalassemia (average age 28.6±1.2 years), and 60 patients had minor beta-thalassemia (average age 30.1±1.3 years). Clinically expressed cases of thrombotic complications were identified in splenectomized and non-splenectomized patients with beta-thalassemia and IDA. At this stage, a control group was also selected, consisting of 30 female primary blood donors, average age 29.7±1.2 years.

Cultural adaptation and validation of the PIT questionnaire – predisposition to increased thrombosis and the MDQ questionnaire – Menstrual Distress Questionnaire for assessing the risk of magnesium deficiency were carried out.

At the second stage of the study, latent hypercoagulable activity and magnesium levels were studied in patients with beta-thalassemia and IDA and age-matched, practically healthy female blood donors (visit 1). For this purpose, a questionnaire was administered to patients and donors during visit 1; studies of complete blood count, hemostasis indicators, platelet aggregation capacity (in patients with intermediate beta-thalassemia), and serum magnesium level were carried out. Detection of latent prethrombotic state was conducted

using the PIT questionnaire. The increased risk of magnesium deficiency was identified using the questionnaire.

At the third stage, the magnesium level and hypercoagulable activity were studied in patients with intermediate beta-thalassemia and IDA during treatment (visit 2). Visit 2 was carried out after prior invitation of the patient for examination one month after the start of treatment. During the outpatient appointment, a laboratory examination was repeated and the patient's answer to the PIT and MDQ questionnaires was taken again.

To adapt and validate the PIT questionnaire, the questionnaires were distributed (sent) to 307 patients (70 with major beta-thalassemia, 55 with intermediate beta-thalassemia, 60 with minor beta-thalassemia, 122 with IDA) and 30 female blood donors. The subjects had no clinically expressed thrombotic complications during examination or in their medical history, and they had not undergone splenectomy. Due to the absence of informed consent, the study using the PIT questionnaire was conducted in only 150 women with beta-thalassemia: 50 with major beta-thalassemia, 40 with intermediate beta-thalassemia, 60 patients with minor beta-thalassemia. Of the 135 patients with IDA under observation, 13 patients were excluded (various thrombotic complications were detected in 7 patients, and 6 patients were excluded due to the absence of informed consent).

The MDQ questionnaire was administered to 420 patients (130 patients with major beta-thalassemia, 95 patients with intermediate beta-thalassemia, 60 patients with minor beta-thalassemia, 135 with IDA) and 30 female blood donors.

Comparison of the MDQ questionnaire results with the serum magnesium content was carried out in a total of 312 women. Of these, 154 patients with beta-thalassemia (58 with major beta-thalassemia, 46 with intermediate beta-thalassemia, 50 patients with minor beta-thalassemia) and 128 patients with IDA (7 patients with IDA who had various thrombotic complications were excluded from the analysis). Obtaining blood plasma samples for analysis was carried out by taking venous blood from the cubital vein strictly on an empty stomach into test tubes/device of the Vacutainer type of syringes with vacuum inside, containing an anticoagulant.

A complete blood count was performed using a SysmexXN-1000 automatic analyzer. Additionally, a manual platelet count was carried out using the Fonio method.

The serum magnesium level was determined using the BioScreenMS-2000 spectrophotometer, HUMEN GBD mbH kit.

Hemostasis indicators were studied according to generally accepted standards. *Activated partial thromboplastin time (APTT)* was studied using the SysmexCA-50 coagulometer. *Prothrombin time (according to Quik)* was determined using the SysmexCA-50 coagulometer, HUMEN GBD mbH. kit. *INR (International Normalised Ratio)* is calculated using the formula: INR = (patient's prothrombin time / control prothrombin time) x ISI, where ISI (International Sensitivity Index) is the sensitivity coefficient of thromboplastin relative to the international standard. *Plasma fibrinogen level (according to Clauss)* was determined using the SysmexCA-50 coagulometer, HUMEN GBD mbH. kit. *D-dimer level* was determined by the method of immunochromatographic express diagnostics using the SelexOn reflectometer and the INFOPIA Co., Ltd. diagnostic kit. *Fibrinolytic activity* was determined by euglobulin clot lysis time under the action of plasmin *in vitro*. *Antithrombin III activity* was determined using the BioScreenMS-2000 spectrophotometer. *Platelet aggregation* was determined using the multiplate analyzer (SW Version 2.04 Operator's Manual). Multiplate^{R} reagents were used – ASPI test (lyophilized arachidonic acid preparation, initial concentration 15 mM). The reagent kit was used to monitor inhibitors in routine platelet aggregation studies to assess normal platelet function on the Multiplate^{R} analyzer.

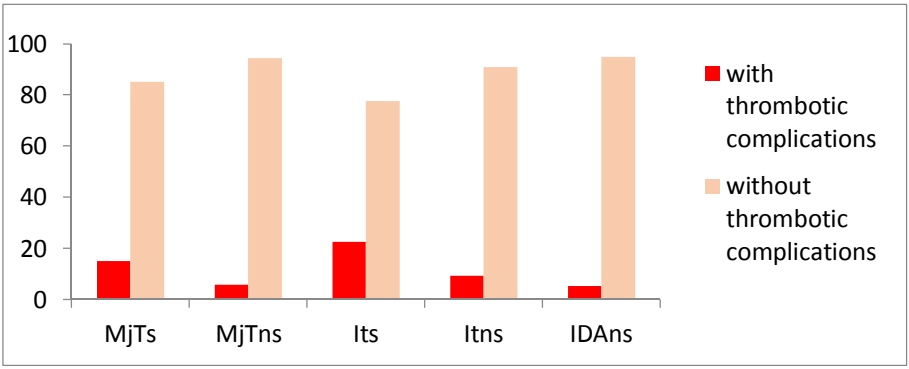
During the therapy, patients with intermediate beta-thalassemia (n=46) and IDA (n=80) were under observation. Patients with intermediate beta-thalassemia received metabolic therapy: per os Folic acid 5 mg/day for 30 days, Vitamin E 400 IU/day for 30 days. Patients with IDA received basic therapy per os "Sorbifer Durules" Fe 2+, Egis, Hungary, for 30 days. Groups of patients received only basic therapy – patients with intermediate beta-thalassemia (n=32) and IDA (n=40). Patients with intermediate beta-thalassemia (n=14) and patients with IDA (n=40) with magnesium deficiency and latent

hypercoagulation were additionally prescribed Magne B_6 forte (magnesium citrate, Mg2+, 100 mg, pyridoxine hydrochloride 10 mg) at 300 mg/day for 30 days for a course of 9,000 mg of the drug.

Statistical analysis. Statistical data processing was carried out using Microsoft Excel 2013, Microsoft Access 2013, and SPSS18.0 software. During statistical processing of the material, data entry was performed in the Excel Office system. Descriptive numerical characteristics of the studied variables: means, standard deviations, and standard errors were obtained using the Statistika 6.0 program. The assessment of the relationship between two variables was carried out using nonparametric correlation analysis by the Spearman method.

RESEARCH RESULTS AND THEIR DISCUSSION

We conducted a study of clinical manifestations of thrombotic complications in women with hereditary and acquired anemias. The medical records of 420 patients were examined: 130 (31.0±2.3%) patients with major beta-thalassemia, 95 (22.6±2.0%) patients with intermediate beta-thalassemia, 60 (14.3±1.7%) patients with minor beta-thalassemia, and 135 (32.1±2.3%) with IDA (Graph 1).



Graph 1. Frequency of thrombotic complications in patients with anemias

Note: MjTs − splenectomized patients with major beta-thalassemia (n=60); MjTns − non-splenectomized patients with major beta-thalassemia (n=70); ITs − splenectomized patients with intermediate beta-thalassemia (n=40); ITns – non-splenectomized patients with intermediate beta-thalassemia (n=55); IDAns – non-splenectomized patients with iron deficiency anemia (n=135).

Analysis of clinical manifestations of thrombotic complications in women with hereditary and acquired anemias based on medical records revealed various thrombotic complications in 10.0% of patients with major beta-thalassemia, 14.7% of patients with intermediate beta-thalassemia, and 5.2% of patients with IDA. No thrombotic complications were detected among patients with minor beta-thalassemia and women in the control group.

The most common thrombotic complications were cases of chronic venous insufficiency – 19 (5.3%), and the rarest were cases of arterial thrombosis – 4 (1.1%), and the difference between the indicators under consideration was statistically significant.

When analyzing the data of splenectomized and non-splenectomized patients with major and intermediate beta-thalassemia, as well as patients with IDA, it was found that in patients with major beta-thalassemia, venous thrombosis was detected 2 times more often than arterial thrombosis, but the data were statistically insignificant (4 and 2 cases, respectively). In intermediate beta-thalassemia, venous thrombosis was also detected 2.4 times more often than arterial thrombosis, but it was also statistically insignificant (5 and 2 cases, respectively). Absolute rates of detection of chronic venous insufficiency were almost identical in major and intermediate forms of beta-thalassemia – 7 cases each. In women with IDA, venous thrombosis was detected in 1.5% of cases, signs of chronic venous insufficiency – in 3.7% of cases. Episodes of arterial thrombosis, trophic ulcer, or venous eczema were not observed in patients with IDA.

Currently, various algorithms and scales are used to assess the risk of thrombosis in patients in various clinical situations. However, the assessment of the predisposition to a prethrombotic state based on both clinical signs and medical history had not been carried out prior to our study, and therefore a questionnaire was developed to identify latent hypercoagulable activity in patients with beta-thalassemia and iron deficiency anemia. Cultural adaptation and validation of the PIT questionnaire were carried out, and its reliability was assessed using the Cronbach's Alpha coefficient.

The predisposition to increased thrombosis was studied in 302

women without splenectomy and clinically expressed thrombotic complications: 50 with major beta-thalassemia, 40 with intermediate beta-thalassemia, 60 with minor beta-thalassemia, 122 with IDA and a control group of 30 female blood donors. The data of patients with a predisposition to hypercoagulation (Group 1, total score >30) and without an increased level of thrombotic risk factors (Group 2, total score <30) were analyzed based on the responses to 39 symptoms and signs included in the questions of the proposed questionnaire and the following results were obtained. In major beta-thalassemia and IDA, statistically significant differences were observed both in the number of patients and in the total score. In intermediate beta-thalassemia, only the average score values (32.9 points and 14.9 points) were statistically significant. In patients with minor beta-thalassemia and in female blood donors, a predisposition to hypercoagulation was not revealed according to the PIT questionnaire. For patients with major, intermediate, and minor forms of beta-thalassemia with a preserved spleen, as well as for patients with IDA, the Cronbach's Alpha coefficient in the PIT questionnaire developed by us had a value of on average = 0.75 (0.78 - 0.79 - 0.74 - 0.68). The data obtained by us indicate construct validity and internal consistency in this questionnaire.

When comparing frequently identified risk factors in patients with beta-thalassemia and IDA of Groups 1 and 2, it was found that in patients with major beta-thalassemia in Group 1, 96 risk factors for latent hypercoagulation were noted, in Group 2 – 33 factors, the difference was statistically significant. The most statistically significant factors of latent hypercoagulation were increased blood pressure, constantly cold extremities (72.2% and 21.9%, respectively).

As for patients with intermediate beta-thalassemia, in Group 1 a total number of risk factors for latent hypercoagulation was 100 cases, in Group 2 – 35 cases, which was also statistically significant. In this category of patients, the most common factor was fatigue – 20.7%, less often – pregnancy at the time of the survey – 2.2%, and a catheter in the central vein in the medical history – 2.2%.

In patients with IDA in Group 1, the risk factors for latent hypercoagulation were 69.7%, in Group 2 – 30.3%, the difference was sta-

tistically significant. For Group 1, the following indicators were the highest – physical inactivity (83.3%), high blood pressure (73.3%), and visible veins on the legs (66.7%). In Group 2, the highest indicators were physical inactivity (16.3%), frequent stressful situations (15.2%), and cardiovascular diseases (14.1%). It should be noted that when comparing the risk factors in Groups 1 and 2 in patients with IDA, statistically significant differences were observed in almost all indicators.

Thus, the results of the first stage of the study showed that thrombotic complications were observed in women with homozygous beta-thalassemia and were not detected in heterozygous beta-thalassemia. The detection rate of thrombotic episodes in patients with major and intermediate forms of beta-thalassemia was almost identical. Thrombotic complications were significantly more frequent in patients with beta-thalassemia than in patients with IDA. In some patients with major and intermediate beta-thalassemia and IDA, in contrast to patients with minor beta-thalassemia and donors, a predisposition to latent hypercoagulation was found.

Due to the presence of thrombotic complications in a significant number of patients with beta-thalassemia and IDA, it is evidently important to determine the predisposition to latent hypercoagulation, namely by studying laboratory indicators (predictors) of thrombogenic risk in these patients. In clinical practice, possible latent hypercoagulation can be assessed by examining the indicators of the coagulation and fibrinolytic systems of the blood and platelets, as well as the thrombinemia marker D-dimer.

The hemostasis indicators of 282 women with anemia (including 154 women with beta-thalassemia and 128 women with IDA) were studied. The control group consisted of 30 age-matched blood donors. The women studied did not have clinically expressed thrombotic complications. As a result of our investigations, some of the examined patients with anemia were found to have increased activation of intravascular blood coagulation (Tables 1-3).

Table 1

Hemostasis indicators in patients with major beta-thalassemia

Index	Patients with major beta-thalassemia			Blood donors n=30
	all, n=58	with LH, n=22	without LH, n=36	
Platelet count x10^9/L	230,0±20,8	253,1±22,4	213,6±14,5	220,1±1,2
APTT sec R=	30,4± 2,4 0,99± 0,08	27,3±1,2* 0,89±0,09	32,4±0,97* 1,06±0,03	33,3±0,8 0,98
PT, Quick activity, %	99,2±2,7	99,2±3,07	99,2±2,4	100,1±0,9
INR	1,02±0,02	1,0±0,02	1,03±0,02	1,01±0,1
Plasma fibrinogen, mg/dl	338,1± 84,5	449,5±25,0 **	270,0± 12, 6**	288,1±2,0
D-dimer, ng/ml	439,2±161,3	651,8±75,3 **	309,8±47,2 **	299,1±4,8
Euglobulin clot lysis time, min	7,0±1,8	9,0±1,7	5,6±0,92	7,0±0,5
Antithrombin III, activity, %	101,1±6,0	94,7±4,4	102,8±4,5	107,5±1,8

Note: significance between patients with latent hypercoagulation (LH) and without LH: *p≤0.005; **p≤ 0.001

According to the identified thrombinemia marker, patients with beta-thalassemia and IDA were divided into two groups: Group 1 with hypercoagulation (D-dimer above normal, i.e. >500 ng/ml) and Group 2 without hypercoagulation (D-dimer within normal limits, i.e. <500 ng/ml). When comparing the D-dimer level in Group 1 with Group 2, significant differences in its indicators were obtained: on average, in major beta-thalassemia 651.8 ng/ml and 309.8 ng/ml; in intermediate beta-thalassemia – 679.5 ng/ml and 373.0 ng/ml; in IDA – 610.0 ng/ml and 341.1 ng/ml, respectively.

Table 2

Hemostasis indicators in patients with intermediate beta-thalassemia

Index	Patients with intermediate beta-thalassemia			Blood donors n=30
	All, n=46	with LH, n=14	without LH, n=32	
Platelet count x10^9/L	233,6±16,8	230,3±20,6	235,0±15,1	220,1±1,2
APTT sec R=	30,3±2,1 0,99±0,07	27,3±0,88* 0,9±0,03*	31,7±1,3* 1,04±0,04*	33,3±0,8 0,98
PT, Quick activity, %	94,3±6,1	95,7±5,3	93,7±6,3	100,1±0,9
INR	1,03±0,03	1,02±0,02	1,03±0,03	1,01±0,1
Plasma fibrinogen, mg/dl	340,0±73,1	460,0±25,0**	287,4±11,6**	288,1±2,0
D-dimer, ng/ml	466,3±134,9	679,5±75,1*	373,0±47,9*	299,1±4,8
Euglobulin clot lysis time, min	6,2±1,6	8,5±1,0*	5,2±0,92*	7,0±0,5
Antithrombin III, activity, %	102,5±5,6	99,6±5,6	103,8±5,4	107,5±1,8

Note: significance between patients with latent hypercoagulation (LH) and without LH: *p≤0.05; **p≤0.01

In the course of the study, a retrospective analysis of the studied hemostasis indicators in patients with beta-thalassemia and IDA was performed. When comparing the obtained data of the patients of Groups 1 and 2, statistically significant differences in the coagulation properties of the patients' blood were revealed. Thus, in patients with major beta-thalassemia of Group 1, compared with Group 2, APTT was shortened (27.3 sec and 32.4 sec); fibrinogen was increased

Table 3

Hemostasis indicators in patients with minor beta-thalassemia

Index	Patients with minor beta-thalassemia n=50	Blood donors n=30
Platelet count x10^9/L	237,2± 17,8	220,1±1,2
APTT sec R=	30,2± 1,2* 0,99±0,04	33,3±0,8* 0,98±0,04
PT, Quick activity, %	101,0±1,0	100,1±0,9
INR	1,02±0,03	1,01±0,1
Plasma fibrinogen, mg/dl	290,4± 12,9	288,1±2,0
D-dimer, ng/ml	320,1± 35,6	299,1±4,8
Euglobulin clot lysis time, min	6,73± 1,22	7,0±0,5
Antithrombin III, activity, %	108,7± 5,3	107,5±1,8

Note: significance between patients with MT and the norm: *p≤0.05

(449.5 mg/dl and 270.0 mg/dl); fibrinolysis time was slightly prolonged (9.0 min and 5.6 min); antithrombin III activity was decreased (94.7% and 102.8%, respectively). In patients with intermediate beta-thalassemia of Group 1, compared with Group 2, a statistically significant difference was obtained for the following parameters: shortened APTT (27.3 sec and 31.7 sec); increased fibrinogen (460.0 mg/dl and 287.4 mg/dl); slightly prolonged fibrinolysis time (8.5 min and 5.2 min, respectively). In patients with IDA of Group 1, compared with Group 2, a statistically significant difference was found only for APTT, which was shortened (30.2 sec and 34.0 sec, respectively).

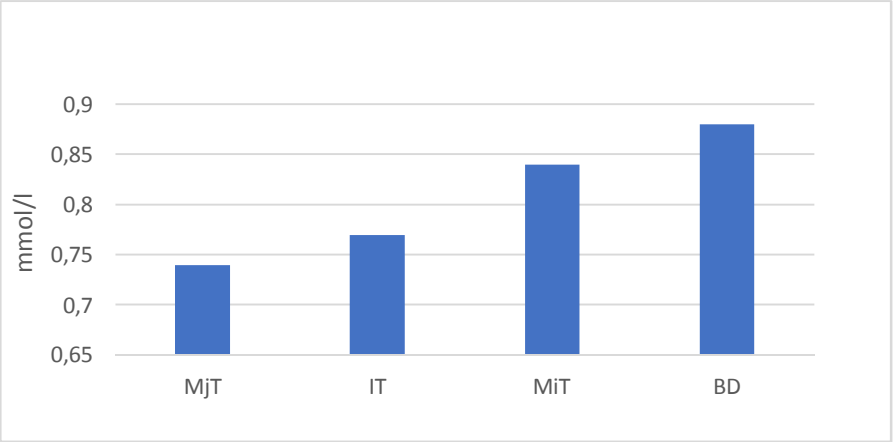
The obtained data indicate a hypercoagulation orientation of hemostasis in some patients with major and intermediate forms of beta-

thalassemia and IDA. At the same time, in patients with latent hypercoagulation, a significant change in some hemostasis indicators was detected compared to the control group (taken as 100%). Thus, in major beta-thalassemia, intermediate form and IDA, the D-dimer level was 218%, 227%, and 204%, respectively; fibrinogen level – 156%, 160%, and 106%, respectively; fibrinolysis time – 129%, 121%, and 120%, respectively; APTT – 82%, 82%, and 90%, respectively; antithrombin III activity – 88%, 93%, and 92%, respectively.

Recent studies show that magnesium deficiency, or hypomagnesemia, is an underestimated risk factor – magnesium deficiency is increasingly associated with enhanced platelet aggregation and an increased risk of thrombosis and embolism, in connection with which we conducted a study of the magnesium content in the blood serum of 312 women (including 58 women with major beta-thalassemia, 46 women with intermediate beta-thalassemia, 50 women with minor beta-thalassemia, and 128 women with IDA) and 30 blood donors.

The average serum magnesium level in patients with major beta-thalassemia was 0.74 mmol/l, in women with intermediate beta-thalassemia – 0.7 mmol/l, in patients with minor beta-thalassemia – 0.84 mmol/l, in patients with IDA – 0.79 mmol/l. In the control group, the magnesium level was 0.88 mmol/l (Graph 2).

A comparison of the magnesium level in the blood serum of patients with anemias, having latent hypercoagulation (Group 1) and patients without latent hypercoagulation (Group 2) was made. It was found that in patients with latent hypercoagulation, the content of the magnesium bioelement in the blood was significantly lower. Thus, in Group 1, compared with Group 2, the serum magnesium level in major beta-thalassemia was 0.64 mmol/l and 0.80 mmol/l, respectively; in intermediate beta-thalassemia – 0.62±0.02 mmol/l and 0.84±0.03 mmol/l, respectively; in IDA – 0.66 mmol/l and 0.85 mmol/l, respectively. According to WHO recommendations, serum magnesium level less than 0.7 mmol/l indicates magnesium ion deficiency in the body, therefore, we regarded a decrease in serum magnesium level below 0.7 mmol/l as hypomagnesemia.



Graph 2. Magnesium level indicators in patients with beta-thalassemia

Note: MjT – non-splenectomized patients with major beta-thalassemia (n=58); IT – non-splenectomized patients with intermediate beta-thalassemia (n=46); MiT – patients with minor beta-thalassemia (n=50); BD – blood donors (n=30)

We translated the MDQ questionnaire into Azerbaijani, performed its cultural adaptation, and assessed reliability using the Cronbach's alpha coefficient. The study using the MDQ questionnaire was conducted in 154 patients with beta-thalassemia and 128 patients with IDA. High probability of magnesium deficiency was detected in 10 (9.6%) patients with homozygous beta-thalassemia, including 6 (10.3%) patients with major beta-thalassemia and 4 (8.7%) with intermediate beta-thalassemia. Average risk of magnesium deficiency was detected in 35 (33.6%) patients: 20 (34.5%) and 15 (32.6%) cases, respectively. No risk of magnesium deficiency was detected in the remaining examined patients with anemia and in the control group. Thus, in patients with major beta-thalassemia, the risk of magnesium deficiency according to the MDQ questionnaire was determined to be 44.8%, and serum magnesium deficiency in 37.9% of cases; in patients with intermediate beta-thalassemia, these indicators were 41.3% and 30.4%, respectively, and in both forms of thalasse-

mia, statistically significant differences between the indicators were not noted. The correlation between the indicators of the serum magnesium level and the risk of magnesium deficiency according to the MDQ questionnaire was inversely proportional and strong.

In patients with IDA, a high probability of magnesium deficiency was detected in only 12 patients (9.4%); the average risk of magnesium deficiency was found in 47 patients (36.7%). The remaining patients with IDA did not have a risk of magnesium deficiency. Out of 128 patients with IDA, the risk of magnesium deficiency according to the MDQ questionnaire was revealed in 46.1% of cases, while serum magnesium deficiency was detected in 31.3% of cases, which is statistically significant. The correlation between the severity of magnesium deficiency symptoms according to the questionnaire score and the blood magnesium level was strongly negative.

According to our data, the most frequently observed symptoms among patients with beta-thalassemia (39.3-78.6% of cases) included: need for carbohydrates, poor memory, frequent consumption of unhealthy "fast food", inattentiveness, need for salt, hyperactivity, cramps, chronic fatigue, muscle weakness, low mood, irritability, tics. Among patients with IDA, the following symptoms were most frequently identified (29.0-50.0% of cases): hyperactivity; poor memory; irritability; cramps; chronic fatigue; need for carbohydrates; frequent consumption of unhealthy "fast food"; decreased activity; chronic depression; high blood pressure; diarrhea/constipation; headache.

Thus, the study of the magnesium content in the blood serum and the results of the MDQ questionnaire indicate that some patients with beta-thalassemia and IDA have magnesium deficiency. The identified magnesium deficiency and the risk of deficiency of this bioelement are more pronounced in patients with latent hypercoagulation. In some cases, patients without latent hypercoagulation were found to have normal levels of the bioelement with high scores according to the MDQ questionnaire.

A study was also conducted of the magnesium level and hypercoagulable activity in 46 patients with intermediate beta-thalassemia and 80 with IDA during treatment with a magnesium preparation.

The magnesium level in patients with intermediate beta-thalassemia before treatment was 0.62 mmol/l, and after treatment – 0.88 mmol/l; in patients with IDA – 0.66 mmol/l and 0.90 mmol/l, respectively, with the difference being statistically significant. After treatment with Magne B_6 forte, both in Group 1 and 2 of patients with intermediate beta-thalassemia and patients with IDA, the average questionnaire score decreased, but these indicators did not statistically differ from those of the control group – healthy blood donors. It should be noted that after using Magne B_6 forte in patients with intermediate beta-thalassemia and IDA, who had magnesium deficiency before treatment, the overall well-being significantly improved and complaints decreased. During and after treatment of patients with intermediate beta-thalassemia and IDA with Magne B_6 forte, no cases of side effects were noted in patients.

According to our data, positive dynamics of some hemostasis indicators was observed in patients with intermediate beta-thalassemia and IDA with latent hypercoagulation during treatment with Magne B_6 forte. In Group 1 of patients with intermediate beta-thalassemia, the levels of plasma fibrinogen (from 446.0 mg/dl to 300.7 mg/dl) and D-dimer (from 679.5 ng/ml to 396.4 ng/ml) statistically significantly decreased. In Group 1 of patients with IDA, the level of plasma fibrinogen (from 306.7 mg/dl to 261.8 mg/dl) and D-dimer (from 610.0 ng/ml to 323.6 ng/ml) in the blood significantly decreased.

The results of our studies showed that therapy with Magne B_6 forte improves the aggregation capacity of platelets in both patients with intermediate beta-thalassemia and patients with IDA who have magnesium deficiency. In patients with intermediate beta-thalassemia with magnesium deficiency, the initially elevated platelet aggregation activity in the spontaneous agglutination test, as well as in the ADP test and the ASPI test, statistically significantly decreased to normal. Thus, in patients with intermediate beta-thalassemia, the ADP test value before treatment averaged 141.4 U, after treatment – 89.5 U, the ASPI test – 140.1 U and 93.1 U, respectively. Spontaneous platelet agglutination (+++) detected before therapy in Group 1 of patients with intermediate beta-thalassemia was not observed after treatment with the magnesium preparation (–) (Table 4, 5).

Table 4

Dynamics of hemostasis indicators and platelet aggregation activity in patients with intermediate beta-thalassemia before and after therapy

Index	IT patients (Group 1) n=14		IT patients (Group 2) n=32		Control group (BD) n=30
	before	after	before	after	
Platelet count x10^9/L	228,5±21,6	228,7±20,7	235,0±15,1	230,5±12,9	220,1±1,2
APTT sec R=	27,3±0,86 0,90±0,03	29,5±0,9 0,92±0,03	31,7±1,3 1,04±0,04	30,7±1,3 1,03±0,04	33,3±0,8 0,98
PT,%	95,4±5,4	97,8±5,1	93,4±6,3	96,8± 5,7	100,1±0,9
INR	1,02±0,02	1,03±0,03	1,03±0,03	1,01±0,02	1,01±0,1
Plasma fibrinogen, mg/dl	446,0±41,0*	300,7±31,4*	287,4±11,6	280,7±12,0	288,1±2,0
D-dimer, ng/ml	679,5±75,1*	396,4±61,9*	373,0±47,9	362,1±47,7	299,1±4,8
Euglobulin clot lysis time, min	8,5±1,0	7,0±0,3	5,23±0,92	5,9±0,9	7,0±0,5
Antithrombin III, activity, %	99,6 ±6,0	102,6±5,6	103,7±5,5	105,7± 5,3	107,5±1,8
ADP test, U	141,4±10,2* (115-162)	89,5±21,8* (58-113)	91,3±9,2 (70 -111)	87,2±14,2 (65-110)	85,0 ±6,8 (57-113)
ASPI test, U	140,1±7,2** (129-156)	93,1 ±6,2** (80-110)	93.8±8,1 (75-115)	93,0±7,8 (77-112)	86,1±7,4 (71-115)
Thrombin (TRAP test), U	94,8±6,1 (88-120)	93,9±6,3 (84-107)	109,1±11,7 (84-126)	106,7±9,5 (88-122)	105,5±10,8 (84-128)
Ristomycin (Risto high), U	143,4±20,3 (112-178)	140,7±22,1 (110-170)	147,5±20,3 (98-180)	139,5±12,5 (99-180)	139,0±20,0 (98-180)
Ristomycin (Risto low), U	13,5±3,5 (9-18)	13,6±3,7 (7-19)	12,0±4,3 (2-19)	10,5±3,8 (4-17)	10,2±4,9 (0-20)
Spontaneous agglutination test	+ + +	–	– /+	–	–

Note 1: IT – intermediate beta-thalassemia; statistical significance of differences between indicators before and after therapy: *p≤0.05. Note 2: IT – intermediate beta-thalassemia; statistical significance of differences between indicators before and after therapy, *p≤0.05; **p≤0.005

Table 5

Hemostasis and platelet aggregation activity indicators in patients with IDA before and after treatment

Parameter	IDA patients				Control group (BD) n=30 M±m (interval)
	Group 1, n=40 M±m (interval)		Group 2, n=40 M±m (interval)		
	Before	After	Before	After	
Platelet count x10^9/L	235,7±16,6	252,3±26,5	228,5±16,4	223,1± 13,5	220,1±1,2
APTT sec R=	30,1±1,3 0,96±0,04	31,3±1,4 0,97±0,04	33,9±0,9 1,03±0,03	33,02±0,98 1,0±0,03	33,3±0,8 0,98
PT,%	95,8±5,1	96,9±4,3	93,6±5,2	95,1±5,2	100,1±0,9
INR	1,02±0,02	1,01±0,02	1,04±0,02	1,03±0,02	1,01±0,1
Plasma fibrinogen, mg/dl	306,7±27,7*	261,8±31,6*	266,8±12,2	278,2± 12,0	288,1±2,0
D-dimer, ng/ml	610,0±78,1*	323,6±66,4*	340,1±47,6	309,3±47,9	299,1±4,8
Euglobulin clot lysis time, min	8,4±0,9	6,9±0,9	5,8±1,04	6,3±1,04	7,0±4,8
Antithrombin III, activity, %	99,05±5,6	100,4±5,2	107,6±4,8	106,6±4,8	107,5±0,5
ADP test, U	135,0±10,9* (100-158)	86,3±15,2* (59-110)	94,5±5,4 (80 -105)	92,8±6,7 (65-102)	85,0 ±6,8 (57-113)
ASPI test, U	139,0±13,2* (120-158)	88,6±5,6* (79-110)	90,7±7,8 (74-112)	89,3±7,1 (75-109)	86,1±7,4 (71-115)
Thrombin (TRAP test), U	94,6±6,7 (90-110)	90,7±6,5 (84-106)	103,3±3,8 (98-115)	100,2±7,8 (89-111)	105,5±10,8 (84-128)
Ristomycin (Risto high), U	127,3±12,4 (100-160)	122,2±14,8 (98-150)	139,6±16,0 (99-160)	129,2±16,7 (100-170)	139,0±20,0 (98-180)
Ristomycin (Risto low), U	13,6±4,2 (9-20)	11,2±3,0 (7-19)	10,4±4,3 (3-19)	10,0±3,7 (3-18)	10,2±4,9 (0-20)
Spontaneous agglutination test	+ + +	–	–	–	–

Note: statistical significance of differences between indicators before and after therapy: *p≤0.05.

The conducted therapy with Magne B_6 forte improved the aggregation capacity of platelets in patients with IDA who had magnesium deficiency. Thus, after the use of Magne B_6 forte in patients with IDA, platelet aggregation activity significantly decreased, reaching normal values. Thus, in patients with IDA, the ADP test before treatment averaged 135.0 U, after treatment – 86.3 U; the ASPI test – 139.0 U and 88.6 U, respectively. Spontaneous platelet agglutination (+++) detected in Group 1 of patients with IDA before therapy was not detected after treatment with the magnesium preparation (–). After the use of Magne B_6 forte in Group 1 of patients with intermediate beta-thalassemia and IDA, platelet aggregation activity almost did not differ from normal reference values.

Thus, as a result of treatment with Magne B_6 forte, patients with intermediate beta-thalassemia and IDA showed an increase in serum magnesium levels, a decrease in the severity of some magnesium deficiency symptoms according to the MDQ questionnaire; in patients with intermediate beta-thalassemia and IDA who have magnesium deficiency and latent hypercoagulation, along with normalization of magnesium levels, elevated platelet aggregation to adenosine diphosphate acid and arachidonic acid inducers decreased, and elevated levels of D-dimer and fibrinogen decreased. Under the influence of treatment there was a tendency to normalization of APTT, euglobulin clot lysis time, and antithrombin III activity. Our studies showed that treatment with Magne B_6 forte in patients with intermediate beta-thalassemia and IDA, along with the elimination of magnesium deficiency, led to a decrease in hypercoagulable activity in the patients' blood.

Our studies highlighted the need to develop an accessible diagnostic algorithm for latent hypercoagulation for its implementation in routine medical practice in the republic. The algorithm is carried out in the following sequence. After collecting anamnesis and examination, the patient with anemia undergoes clinical evaluation and is sent for laboratory and instrumental studies. The patient's diagnosis is verified. Next, after obtaining the patient's informed consent, a survey is conducted to identify latent thrombogenic risk factors. We use the PIT questionnaire (predisposition to increased thrombosis) devel-

oped by us and the standardized MDQ questionnaire for diagnosing magnesium deficiency. An answer to the MDQ questionnaire in the amount of > 30 points is interpreted as a predisposition to magnesium deficiency, and the patient's serum magnesium level is tested. An answer to the PIT questionnaire in the amount of > 30 points is interpreted as a predisposition to thrombus formation, and the following hemostasis indicators are evaluated in the patient: D-dimer level (thrombinemia marker); APTT, fibrinogen concentration, fibrinolytic activity, antithrombin III activity, platelet count using the Fonio method. In each specific case, the need for additional in-depth studies is decided, as well as the correction of hypercoagulation against the background of basic therapy. Additional studies: genetic thrombotic risk factors, platelet aggregation ability – spontaneous agglutination test, ADP test (aggregation to adenosine diphosphate acid inducer), ASPI test (aggregation to arachidonic acid inducer), etc. It is proposed to correct hypercoagulation with magnesium citrate preparations (in particular, Magne B_6 forte) and, if necessary, with anticoagulants and antiplatelet agents. In our opinion, the use of the proposed algorithm will allow timely detection of pre-thrombotic readiness in patients and adequate correction of hemostasis.

Thus, as a result of our studies, it was established that a certain proportion of patients with major and intermediate forms of beta-thalassemia and IDA have clinically expressed thrombotic complications in the form of arterial and venous thromboses, and chronic venous insufficiency. Patients with beta-thalassemia and IDA, without clinically expressed thrombotic complications may also be predisposed to increased thrombosis. Detection of magnesium deficiency and latent hypercoagulation in patients with beta-thalassemia and IDA should be considered as predictors of thrombogenic disorders in these patients. Treatment with Magne B_6 forte in patients with intermediate beta-thalassemia and IDA eliminates magnesium deficiency and reduces hypercoagulable activity in the blood of patients, inhibiting thrombosis. Effective and safe compensation of magnesium deficiency at the stage of latent hypercoagulation may be a promising direction for the prevention of thrombotic complications.

CONCLUSIONS

1. Thrombotic complications were detected in 10.0±2.6% of patients with major beta-thalassemia, in 14.7±3.6% of patients with intermediate beta-thalassemia, and in 5.2±1.9% of patients with IDA. Patients more often had chronic venous insufficiency (6.2±1.1% in beta-thalassemia, 5.2±1.9% of cases in IDA), less often – arterial thrombosis (1.1±0.55% in beta-thalassemia, 0% in IDA), t=3.2, p≤0.005; venous thrombosis was detected at almost the same frequency (3.1±0.91% in beta-thalassemia, 2.96±0.9% in IDA, p≥0.05). Thrombotic complications occurred more frequently in splenectomized patients with beta-thalassemia compared to non-splenectomized ones: respectively, in the major form – 15.0±4.6% and 5.7±2.8%, p≥0.05; in the intermediate form – 22.5±6.6% and 9.1±3.9%, p≥0.05. In patients with anemia who do not have thrombotic complications, a hypercoagulable tendency of hemostasis indicators was reliably established in 37.9% of patients with major beta-thalassemia (increased D-dimer, fibrinogen, fibrinolysis time; decreased APTT); in 30.4% of patients with intermediate beta-thalassemia (increased D-dimer, fibrinogen, fibrinolysis time); in 31.3% of patients with IDA (increased D-dimer content in the blood, decreased APTT) [1, 6, 8, 11, 13, 15, 18, 19].
2. The validity, reliability, and internal consistency of the developed PIT questionnaire were demonstrated (Cronbach's Alpha coefficient up to r= 0.79). According to the PIT questionnaire, the predisposition to increased thrombosis was detected in 36.0±6.8% of patients with major beta-thalassemia, in 40.0±7.7% with intermediate beta-thalassemia, and in 24.6±3.9% with IDA. The construct validity and reliability of the adapted MDQ questionnaire were also demonstrated (Cronbach's Alpha coefficient up to r=0.79). The risk of magnesium deficiency according to the MDQ questionnaire was detected in 44.1±6.5% of patients with major beta-thalassemia, in 41.3±7.3% of patients with intermediate beta-

thalassemia, and in 46.1±4.4% of patients with IDA [2, 7, 22].

3. In patients with anemia who do not have thrombotic complications, magnesium deficiency in the blood serum was detected in 37.9±6.4% of patients with major beta-thalassemia, 30.4±12.3% of patients with intermediate beta-thalassemia, and 31.3±4.1% of patients with IDA [5, 15, 16].
4. In patients with and without latent hypercoagulation, the most significant predictors according to the PIT questionnaire were: in major beta-thalassemia – increased blood pressure (72.2±10.6% and 21.9±7.3%, respectively, t= 4.0; p≤0.0001) and constantly cold extremities (72.2±10.6% and 21.9±7.3%, 95%, respectively, t=4.0; p≤0.0001); in intermediate beta-thalassemia – fatigue (81.2±9.8%, 95% and 62.5±9.9%, respectively, p≥0.05) and dry mouth (75.0±10.8%, and 20.8±8.3%, respectively, t=4.0; p≤0.005); in IDA – hypodynamia (83.3±6.8% and 16.3±3.9, respectively, p≤0.005), BP (73.3±8.1 and 7.6±2, respectively, p≤0.005), and visible veins on the legs (66.7±8.6% and 6.5±2.6, respectively, p≤0.005)) [7, 12, 22].

   The magnesium level and the average scores of the MDQ questionnaire are significantly lower in patients with latent hypercoagulation: in major beta-thalassemia, respectively, 0.64±0.02 mmol/l (p≤0.01), 44.1±7.1 points (p≤0.005); in intermediate beta-thalassemia 0.62±0.02 mmol/l (p≤0.005), 44.0±9.6 points (p≤0.005); in IDA 0.66±0.02 mmol/l (t=4.2; p≤0.005), 44.5±6.8 points (p≤0.05) [3-5, 10, 12, 14-16, 21].
5. During treatment with a magnesium preparation in patients with anemia with latent hypercoagulation, a significant normalization of elevated hemostasis indicators was observed: in patients with intermediate beta-thalassemia – D-dimer from 679.5±75.1 ng/ml to 396.4±61.9 ng/ml (p≤0.05), plasma fibrinogen from 446.0±41.0 mg/dl to 300.7±31.4 mg/dl (p≤0.05), spontaneous and induced platelet aggregation activity in ADP and ASPI tests (p≤0.05); in patients with IDA –

D-dimer from 610.0±78.1 ng/ml to 323.6±66.4 ng/ml ($p \leq 0.05$), plasma fibrinogen from 306.7±27.7 mg/dl to 261.8±31.6 mg/dl ($p \leq 0.05$), spontaneous and induced platelet aggregation activity in ADP and ASPI tests ($p \leq 0.05$) [9, 17, 20, 21].

PRACTICAL RECOMMENDATIONS

1. In patients with beta-thalassemia and IDA, it is necessary to take into account significant predictors of latent hypercoagulation – groups of clinical symptoms and anamnestic signs, including "chronic stress states", "unreasonable consumption of various foods", "comorbid conditions".
2. Patients with major and intermediate beta-thalassemia and IDA should undergo a diagnostic algorithm to detect latent hypercoagulation in them.
3. Patients with major and intermediate beta-thalassemia and IDA, who have latent hypercoagulation and magnesium deficiency, should be under regular medical supervision due to a high risk of thromboembolic complications.
4. Magnesium citrate preparation is recommended for wide use in the comprehensive therapy of patients with intermediate beta-thalassemia and IDA. Magne B_6 forte exhibits hypocoagulant (normalization of blood rheological parameters) and pleiotropic clinical effects.

LIST OF SCIENTIFIC WORKS, PUBLISHED ON THE TOPIC OF THE DISSERTATION

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LIST OF CONDITIONAL ABBREVIATIONS

APTT	– activated partial thromboplastin time
DASH scale	– DASH scale (D-dimer AgeSexHormones)
DIC	– disseminated intravascular coagulation
IDA	– iron deficiency anemia
ISTH	– International Society on Thrombosis and Haemostasis
SPT	– a tendency to increased thrombosis
MDQ	– Menstrual Distress Questionnaire, a questionnaire for detecting magnesium deficiency

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