International Journal of
Health Systems and Medical Sciences

ISSN: 2833-7433
Volume 2 | No 3 | March -2023

Features of Violations of the Hemostasis System in Patients with Type 2 Diabetes Mellitus with Kidney Damage

Madasheva Anajan Gazkhanovna [1], Gaffarov Fazliddin Ergashevich [2], Dadajanov Uktam Utkirovich [3]

[1] PhD of the department of hematology, Samarkand State Medical University

[2] Head of the reception department of the Multidisciplinary medical center of Samarkand region

[3] Assistant of the department of Hematology, Samarkand State Medical University

Abstract: This article discusses the characteristics of hemostasis system disorders in patients with type 2 diabetes with kidney damage. In the article, the problems and difficulties that arise in the process of treatment of hemostasis disorders in patients with diabetes and the pathology of the disease are studied.

Keywords: Himostasis, diabetes 2, process of treatment, microangiopathy.

Introduction.

In almost half of the cases, diabetes mellitus (DM) is detected only after complications have developed; nephropathy is determined in 25% newly diagnosed patients, and this complication manifests itself in the form of persistent microalbuminuria (MAU). According to the State Register of Patients with Diabetes Mellitus 2010–2020, the prevalence of diabetic nephropathy (DN) averages 19% in type 1 DM and 8% in type 2 DM, which is 2 and 5 times lower than world values, respectively. . In Tashkent and the Tashkent region (according to the registry for 2015), the prevalence of DN is the closest to world statistics and is 33% for type 1 DM and 25% for type 2 DM. According to the registry for the city of Tyumen, the prevalence of DN is 23.3%; in patients with type 1 diabetes - 32.5%, type 2 diabetes - 22% (data for 2015). However, with active screening, the true prevalence of DN in Russia exceeds the registered one by 2–8 times.

Literary review.

It is known that a decrease in the production of nitric oxide (NO) and a violation of the functional state of the endothelium, as well as a change in platelet-coagulation hemostasis, play a role in the development of microangiopathy in DM [3]. Endothelium-dependent processes include vascular tone and permeability, adhesion of leukocytes and platelets, angiogenesis, thrombogenicity and thromboresistance. Endothelial dysfunction is considered as a significant link in the pathogenesis of atherosclerosis, hypertension and DM [4].

NO causes relaxation of vascular muscles and thus has a vasodilating effect [2]. In normal blood vessels, the endothelium regulates the tone of smooth muscle cells, adhesion of platelets and neutrophils through the release of mediators, of which NO and endothelin-1 (ET-1), which is a

vasoconstrictor, can be considered the main ones. With pathological changes in the vessels, the formation of NO decreases, and ET-1 increases, which can change the reactivity of the vessels and affect the aggregate state of the blood [5]. A decrease in NO content in the endothelium may be associated with impaired expression or transcription of eNOS, a decrease in the availability of L-arginine reserves for eNOS, and/or accelerated NO metabolism (with increased formation of free radicals). The reasons for the decrease in eNOS activity may be hypercholesterolemia and an increase in the level of oxidized LDL [6,7].

Of particular interest is the study of the functional state of the endothelium and coagulation-platelet hemostasis in patients with newly diagnosed type 2 diabetes.

Object and methods of research

For the study, 3 groups of patients were formed (comparable in age, sex, degree of obesity and hypertension): 1) patients with newly diagnosed type 2 DM with DN at the stage of MAU (33 people), 2) with newly diagnosed type 2 DM without DN (28 people), 3) control group - people without carbohydrate metabolism disorders (34 people) with obesity (BMI - 31.24±4 kg/m2) and AH I-II degree according to the WHO classification (BP 139.3±11/89 .33±9 mm Hg). There were 82% women, 18% men. The average age of the surveyed was 50.96±11 years.

Glycated hemoglobin (HbA1c) and MAU were determined using a Nycocard rider 2 apparatus. To assess the platelet link of hemostasis, a photometric method was used, the dynamics of changes in plasma light transmission was evaluated on a laser aggregometer Biola. The platelet count and fibrinogen level were determined; von Willebrand factor (WF), prothrombin ratio (PO), and recalcification time were measured using a Trombostat II device. Ristomycin (15 mg in 0.5 ml of solvent) was used as an inducer in the determination of VW. The level of NO metabolites in blood plasma was determined by the method of V.B. Karpyuk (2000), xanthine oxidase (XO) activity according to the method of Dyachina (1973).

Endothelial function was assessed on the brachial artery (BA). The response to reactive hyperemia (HR) was calculated as the difference in arterial diameter against the background of reactive hyperemia and the initial one [1,3]. Samples were performed using an ALOKA 1700 Duna View II ultrasonic device with a linear transducer with a frequency of 7.5 MHz. A normal reaction of PA is considered to be its expansion against the background of RG by 10% or more of its initial diameter [2, 3].

The Biostat program was used for statistical processing. Data in the text and tables are given as M±m. The significance of differences was assessed using the nonparametric paired Wilcoxon test (T) for linked samples and the Mann-Whitney test (U) for unrelated samples in a confidence interval of more than 95% with a normal distribution of the variation series. Differences were considered significant at $p<0.05$.

Results and its discussion

In patients with DM 2 with preserved kidney function, changes in the diameter of the VA in the sample with RG did not differ significantly from those in the control group: 7.9 and 7.96% ($p>0.05$), respectively. Consequently, individuals with hypertension and obesity already have disorders in the vasoregulatory function of the endothelium, which may contribute to the appearance of MAU [8]. Some authors [9] believe that endothelial dysfunction plays a major role in the pathogenesis of AH associated with metabolic disorders. In persons with obesity, the causes of which may be insulin resistance and hyperinsulinemia, there is a decrease in the response to vasodilatation and an increase in the vasoconstrictor effect, which is due to a decrease in NO activity, a decrease in the formation of prostacyclin and an increase in the production of vasoconstrictor substances (ET-1, thromboxane A2, prostaglandin F2). Of no small importance in the formation of endothelial dysfunction may be the increase in oxidative stress characteristic of such patients. Thus, the endothelial function is an integral aspect of the insulin resistance syndrome and contributes to its aggravation, increased vascular reactivity, and the formation of hypertension, which leads to cardiovascular complications.

It has been shown that arterial hypertension changes the morphology and functions of the endothelium [3]. Compared with patients with normal BP, these cases develop an increased interaction of platelets and monocytes with endothelial cells, and oxidative stress in elevated BP reduces endothelial-dependent vasodilation. With age, endothelial NO synthesis decreases and the response of the endothelium to vasoconstrictor factors increases. In patients with diabetes, a sharp acceleration of arteriosclerotic changes is often found. The reason for this may be endothelial dysfunction caused by chronically elevated blood sugar levels. Experimental studies have shown that elevated glucose concentrations lead to paradoxical vasoconstriction [10]. We found that the content of NO metabolites in plasma in individuals with DM 2 without DN was 45.4% lower, and the level of VWF was 21.8% higher than in controls. Other parameters of hemostasis in patients with DM without DN did not differ from those in controls (p>0.05) (Table 1).

Table 1

Investigated parameters in patients with type 2 diabetes without nephropathy and in the control group (without DM)		
Index	Control group	DM 2 without nephropathy
MAU, mg/l	17.31±03.99	19.61±0.51***
Spontaneous aggregation, %	2.87±0.27	3.06±0.24***
The number of platelets, thousand / µl	268.6±19.12	48.5±12.88***
Fibrinogen, g/l	3.38±0.06	3.39±0.05***
BY	0.95±0.02	0.92±0.02***
Recalcification time, s	92.3±4.3	83.05±3.54***
Willebrand factor,%	71.14±4.71	90.95±4.1*
NO, nmol/ml	5.42±0.45	2.96±0.23*
KSO, nmol/ml•min	3.37±0.37	3.43±0.13***

Note, here and in Table. 2 and 3: *p<0.01, **p<0.05, ***p>0.05.

Table 2

Investigated parameters in patients with type 2 diabetes without nephropathy and with nephropathy at the MAU stage		
Index	SD 2 with DN	SD 2 without nephropathy
HbA1c, %	8.55±0.35	7.95±0.27*
MAU, mg/l	215.5±15.83	19.61±0.51*
Spontaneous aggregation, %	3.91±0.46	3.06±0.24*
The number of platelets, thousand / µl	312.75±15.68	248.5±12.88*
Fibrinogen, g/l	3.65±0.05	3.39±0.05**
BY	1.02±0.02	0.92±0.02**
Recalcification time, s	98.85±3.75	83.05±3.54*
Willebrand factor,%	98.94±4.81	90.95±4.1**
NO, nmol/ml	2.59±0.16	2.96±0.23**
KSO, nmol/ml•min	4.17±0.27	3.43±0.13*

Table 3

Investigated parameters in patients with DM 2 and DN and in the control group		
Index	SD 2 with DN	Control group
MAU, mg/l	215.5±15.83	75.61±13.99*
Spontaneous aggregation, %	3.91±0.46	2.87±0.27*
The number of platelets, thousand / μl	312.75±15.68	268.6±19.12*
Fibrinogen, g/l	3.65±0.05	3.38±0.06**
BY	1.02±0.02	0.95±0.02**
Recalcification time, s	98.85±3.75	92.3±4.3**
Willebrand factor,%	98.94±4.81	71.14±4.71*
NO, nmol/ml	2.59±0.16	5.42±0.45*
KSO, nmol/ml•min	4.17±0.27	3.37±0.37**

In patients with DM 2 and DN at the MAU stage, endothelial dysfunction was more pronounced: PA response=6.92% ($p<0.05$). The level of NO metabolites in blood plasma in patients with DM 2 with DN at the stage of MAU was 12.5% lower than in patients with DM 2 without DN, and 45.4% lower than in controls. The concentration of HbA1c in the group with DN was 0.6% higher than in the group with DM 2 without MAU. Protein excretion in the urine in patients with DN was 90.9% (11 times) higher than in patients with DM without DN.

The level of EF in patients with DM 2 with MAU was 8.8% higher than in the group without nephropathy, and 39% higher than in patients without DM. Violations of hemostasis in type 2 diabetes are manifested by thrombosis and DIC, which is a consequence of increased platelet aggregation and hypercoagulability. In individuals with DN, compared with controls and patients without DN, the level of fibrinogen, PO, recalcification time, platelet count, and spontaneous aggregation were increased (Tables 2 and 3).

Thus, in DN, the development of endothelial dysfunction was established, which is expressed not only in violation of vasoregulation, but also in violation of fibrinolytic and anticoagulant activity of the blood.

In patients with DM, a negative correlation was found between the level of NO metabolites in plasma and MAU ($r=-0.51$; $p<0.05$). Flow-dependent vasodilation parameters correlated with the level of NO metabolites ($r=0.44$; $p<0.05$). Previously [1, 2], using ultrasound, a decrease in endothelial regulation of peripheral arterial tone was found in patients with AH compared with healthy people.

Conclusions.

1. In patients with newly diagnosed DM 2, the response of PA to RG in the presence of DN at the MAU stage is less than in patients without DN.
2. DM 2 is characterized by changes in platelet-oagulation hemostasis, which is manifested by an increase in the number of platelets with an increase in their spontaneous aggregation.
3. Platelet-coagulation changes are most pronounced in patients with DM 2 with DN at the MAU stage.
4. The level of NO metabolites in patients with obesity and hypertension without type 2 diabetes is higher than in type 2 diabetes. This may indicate a decrease in endothelial NO production in chronic hyperglycemia.

5. A correlation has been established between changes in the hemostasis system and disorders of endothelial regulation of vascular tone.

REFERENCES:

1. Epstein M, Sowers JR: Diabetes mellitus and Hypertension 2012; 19:403-418.
2. Zateishchikova A.A., Zateishchikov D.A. Endothelial regulation vascular tone research methods and clinical significance // Cardiology - 2008. - No. 9. - p. 68-76.
3. Mogensen CE, Hansen KW: Preventing and postpoing renal disease in insulin depedent diabetes by glycemic and non-glycemic intervention. Ivanova O.V., Rogoza A.N., Balakhonova T.V. etc. Definition sensitivity of the brachial artery to shear stress on endothelium as a method for assessing the state of endothelium-dependent vasodilation with high-resolution ultrasound patients with arterial hypertension //Kardiology. – 2008. – No. 3. - P. 37–41.
4. Petrishchev NN, Vlasov TD. Physiology and pathophysiology of the endothelium. IN: Petrishchev NN, red. endothelial dysfunction. Causes, mechanisms, pharmacological adjustment. Publishing House of St. Petersburg State Medical University, St. Petersburg, 2013; 4-38
5. Robert MF, Rabelink TJ. Atherosclerosis and two faces of endothelial nitric oxide synthase. circulation. 2008; 97:108-112.
6. Warner T.D. Relationships between the endothelin and nitric oxide pathways, Clinical and Experimental Pharmacology and Physiology. 2009; 26:247-252.
7. Watts GF, Herrmann S, Dogra GK et al. Vascular function of peripheral circulation in patients with nephrosis. Kidney International. 2001; 60(1): 182-188. Luscher T.F. Endothelial dysfunction as a therapeutic target: the ENCORE trials // Europ. Heart J. - 2000. - Vol. 2, (Suppl. D). – P. 20-26. contrib Nephrol 2009; 78:73-100.
8. Stehouwer CDA, Fisher HRA, Kuijk AWR van, et al. Endothelial dysfunction precedes the development of microalbuminuria in IDDM. Diabetes 1995:44:561-4.
9. Zadionchenko V.S., Adasheva T.V., Demicheva O.Yu. etc. Arterial hypertension in metabolic syndrome: pathogenesis, basics therapy. Consilium-medicum, T. 06/N 9/2014, www.consilium medicum.com
10. Baer F.M. Clinical significance of endothelial dysfunction. Magazine Top Medicine, 2010, No. 3.
11. Khakimova, M. S., & Allayarov, A. T. (2022). DIAGNOSIS AND TREATMENT OF ACCOMMODATION SPAZM IN CHILDREN. In *НАУКА, ОБЩЕСТВО, ОБРАЗОВАНИЕ В УСЛОВИЯХ ЦИФРОВИЗАЦИИ И ГЛОБАЛЬНЫХ ИЗМЕНЕНИЙ* (pp. 163-165).
12. Allayarov, A. (2020). THE HYPOTENSIVE EFFECT AND TOLERABILITY TAFLOPRESS IN PATIENTS WITH OPEN-ANGLE GLAUCOMA. *Теория и практика современной науки*, (4), 218-220.
13. Аллаяров, А. Т. (2020). ГИПОТЕНЗИВНЫЙ ЭФФЕКТ И ПЕРЕНОСИМОСТЬ ПРЕПАРАТА ТАФЛОПРЕСС У ПАЦИЕНТОВ С ОТКРЫТОУГОЛЬНОЙ ГЛАУКОМОЙ. In *НАУКА И ИННОВАЦИИ В XXI ВЕКЕ: АКТУАЛЬНЫЕ ВОПРОСЫ, ОТКРЫТИЯ И ДОСТИЖЕНИЯ* (pp. 228-230).
14. Мадашева, А. Г., & Жураева, М. З. (2019). Биохимические показатели и комплексное лечение больных псориазом с лечебным плазмаферезом. *Достижения науки и образования*, (10 (51)), 78-82.
15. Дадажанов, У., & Мадашева, А. (2019). Эритропоэтинлар. *Журнал вестник врача*, *1*(4), 153-155.
16. Мадашева, А. Г., Дадажанов, У. Д., Абдиев, К. М., Маматкулова, Ф. Х., & Махмудова, А. Д. (2019). Динамика электронейромиографических показателей и эффективность

электрической стимуляции мышц у больных гемофилией с мышечными атрофиями. *Достижения науки и образования*, (10 (51)), 26-30.

17. Madasheva, A. G., Yusupova, D. M., & Abdullaeva, A. A. EARLY DIAGNOSIS OF HEMOPHILIA A IN A FAMILY POLYCLINIC AND THE ORGANIZATION OF MEDICAL CARE. *УЧЕНЫЙ XXI ВЕКА*, *37*.
18. Жураева, М. З., Нурматова, И. Б., & Мадашева, А. Г. Псориаз билан касалланган беморлар биокимёвий кгрсаткичлари ва уларни комплекс даволашда плазмаферез усулини iгллашнинг самарадорлиги. *МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ РЕСПУБЛИКИ УЗБЕКИСТАН РЕСПУБЛИКАНСКИЙ СПЕЦИАЛИЗИРОВАННЫЙ НАУЧНО-ПРАКТИЧЕСКИЙ МЕДИЦИНСКИЙ ЦЕНТР АКУШЕРСТВА И ГИНЕКОЛОГИИ АССОЦИАЦИЯ ВРАЧЕЙ ЧАСТНОЙ ПРАКТИКИ УЗБЕКИСТАНА КЛИНИКА «MAHLIYO-SHIFO» & V «MAHLIYO-SHIFO» & V*, 13.