Series on Biomechanics, Vol.37, No.3 (2023), 11-18
DOI: 10.7546/SB.02.03.2023

The relationship between the non-Newtonian properties of blood, its fluidity and transport potential in patients with arterial hypertension

E. Volkova[a], A. Zamyshliaev[a], P. Mikhailov[a], I. Tikhomirova[a], I. Osetrov, A. Muravyov[a]*, N. Antonova[b]

[a]*State Pedagogical University, Yaroslavl, Russia; kaprovchuk@rambler.ru- ORCID: 0009-0006-4211-02293; dr.avz@mail.ru - ORCID: 0000-0001-9329-0497; ORCID:0000-0003-1491-3882; tikhom-irina@yandex.ru - ORCID: 0000-0001-9521-4017; igos.yar@yandex.ru - ORCID: 0000-0002-3269-2262; alexei.47@mail.ru - ORCID: 0000-0002-5502-9164*
[b]*Department of Biomechanics, Institute of Mechanics to the Bulgarian Academy of Sciences, Sofia, Bulgaria, antonova@imbm.bas.bg; ORCID:0000-0003-1707-0235*

Received: 18 August 2023 Accepted: 12 October 2023 **Corresponding Author*

Abstract

In different parts of the circulation, blood exhibits the properties of a Newtonian and non-Newtonian fluid. Changing the shear conditions and the vascular bed geometry can contribute to a greater manifestation of the non-Newtonian behavior of blood. The latter is combined with a decrease in blood fluidity and its transport potential. The aim of the study was to estimate the effect of changes in non-Newtonian characteristics of blood on its fluidity and transport potential in patients with arterial hypertension (AH).

In two groups (group 1 of healthy subjects, n=22 and group 2 of 20 patients with AH) hemorheological profile parameters were recorded, including blood viscosity (BV) at five increasing shear stresses (SS). At the same SS, the red blood cell (RBC) elongation index (EI) and their ghosts were determined. The data obtained indicate that the flow of blood as a viscous liquid can have a non-Newtonian character both under normal conditions and especially in pathology, for example, in arterial hypertension. The non-Newtonian behavior of blood is very well described by the power-law fluid model. It can be obtained by registering blood viscosity at several, at least five, shear stresses. It was found that the most significant characteristic of the change in the degree of non-Newtonian behavior of blood is the index of consistency, "*k*" from this equation: $y = kx^{-n}$. It strongly correlated with blood fluidity and its transport potential mostly in AH patients. In addition, it was found that an increase in the RBC deformation, which is close to a linear type, with a gradual increase in shear stress in the microchamber, is better predicted by the power-law pseudoplastic fluid model.

Keywords: Blood viscosity, non-Newtonian properties, red blood cell deformability, arterial hypertension

---

1. Introduction

It follows from the Poiseuille equation that volume blood flow, perfusion of organs and tissues depend on the blood pressure gradient, vessel radius and blood viscosity [1]. The transport potential of blood is associated with its fluidity, the value of inverse viscosity ($\varphi=1/\eta$), which in turn depends not only on such hemorheological characteristics as: hematocrit (Hct), plasma viscosity, deformability and aggregation of erythrocytes, but also on shear conditions [2, 3]. As for shear conditions, in a flow with different shear rates, the blood exhibits non-Newtonian properties, which affects the efficiency of transport [4, 5]. This flow behavior of blood corresponds to pseudoplastic characterized as power law fluids [6, 7]. Systems of this type can be described by the rheological equation: $y = kx^{-n}$, where $\boldsymbol{y}$ is blood viscosity, $\boldsymbol{x}$ is shear stress, k is the consistency index and n is the exponent. An increase in these parameters of the equation points to the increasing of the degree of non-Newtonian behaviour of blood [8]. It is important to note that this leads to a decrease in the O_2-transport potential of the blood [2]. On the other hand, with an increase in shear stress, the flow deformation of red blood cells (RBCs) can increase [9]. This has a positive effect on the apparent viscosity of the blood and increases its fluidity [10].

The aim of the study was to estimate the effect of changes in non-Newtonian characteristics of blood on its fluidity and transport potential in patients with arterial hypertension (AH).

2. Materials and methods

2.1. Patients and study design

From the total mass of the examined volunteers (n=42; aged 35 to 70 years) two groups were formed: group 1 (n=22) – healthy individuals. In this group, systolic arterial pressure (SAP) averaged 122.0 ± 7.6 mm Hg, while diastolic arterial pressure (DAP) was 73.3 ± 4.9 mm Hg. Group 2 (n=22) – hypertensive patients with grade II AH with a mean blood pressure of 103.7 ± 7.1 mm Hg. At the same time, SAP was from 138 to 184 mm Hg, and diastolic one – from 88 to 106 mm Hg. The use of human blood was in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki). The study was approved by the local ethical committee of the university (protocol No. 6 dated April 20, 2023) and informed consent was obtained from all study participants. Blood samples were obtained by venipuncture into EDTA vacutainers. RBCs were separated from plasma by centrifugation (15 min, 3000 rpm), washed three times in isotonic NaCl solution, and resuspended in Ringer's solution.

2.2. Hemorheological measurements

Hemorheological profile parameters were recorded: blood viscosity (BV) and RBC suspension viscosity (SV with hematocrit 40%) at five shear stress levels high (0.36, 0.72, 1.08, 1.44 and 1.80 N/m^2), together with plasma viscosity (PV) and hematocrit measurement. Viscosities were measured using a capillary viscometer at room temperature. The hematocrit index was determined on an Elmi SM-70 hematocrit centrifuge (Latvia). The hemorheological efficiency of oxygen transport was assessed by the ratio of hematocrit/viscosity (Hct/BV) [2]. To assess the degree of non-Newtonianity of blood and RBC suspension, flow equations were obtained by plotting blood viscosity data measured at five shear stresses (Fig. 1*A*). For every individual, a personal profile of viscous blood flow was built, and an equation was obtained that describes this flow. As shown in Fig. 1A the equation for the flow of a non-Newtonian fluid of a power-law of the form: $y = kx^{-n}$. The accuracy of approximation (R^2) of the experimental data with this equation is more than 95%. Indicators of non-Newtonian behaviour of the fluid are k - consistency coefficient and n - exponent, obtained from the blood flow equation [8].

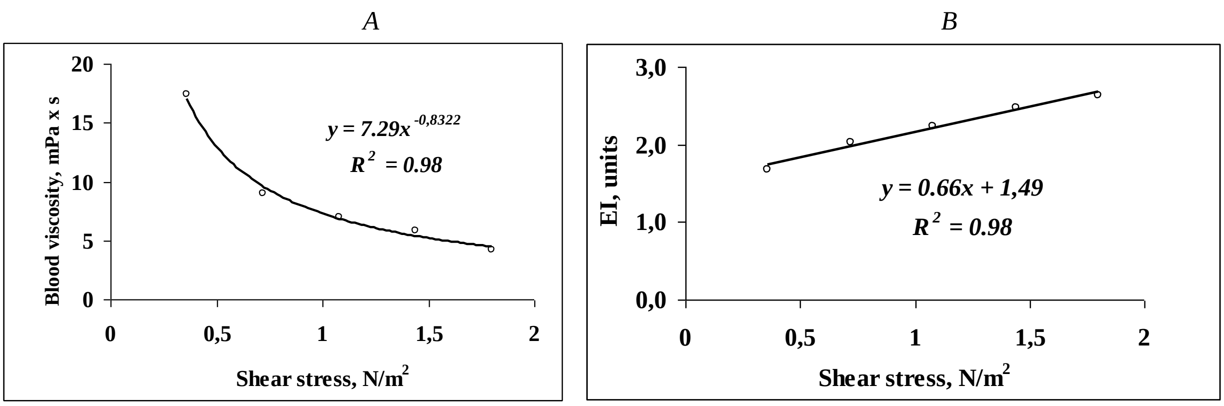


Fig. 1. Profiles of non-Newtonian blood flow in healthy subjects (*A*) and plot of erythrocyte elongation index (EI) versus shear stress (*B*)

Red blood cell aggregation was assessed by the Myrenne Aggregometer. The resulting index, termed «M1» by the manufacturer and «RBCA» herein, increased with enhanced RBC aggregation. To assess red blood cell deformability (RBCD), the cell elongation index (EI) was recorded in a flow microchamber [11].

As well as blood viscosity, RBCD was recorded at the same five shear stress values. (EI, Fig. 1B). For a more accurate analysis of changes in RBC deformability, their recovered ghosts were prepared according to the Dodge method [12]. RBCs were destroyed by osmotic shock. To do this, 7 ml of chilled distilled water (at 4°C) was added to 1 ml of cells, followed by washing twice in phosphate buffer. Then the ghosts concentrate was incubated in Ringer's solution with the addition of 30% dextran 150 kDa (the ratio of buffer and dextran was 7 : 3 by volume) and measured their deformability (RBCgD) in a flow microchamber.

2.4. Statistics and data presentation

Statistical processing included obtaining the mean (M) and standard deviation (SD). The sampling distribution was tested using the Shapiro–Wilk test. Nonparametric statistics of the program Statistica 10.0 (StatSoft Inc., USA) was used. When conducting paired comparisons of indicators within groups during repeated measurements, the Wilcoxon test was used. Differences at $p < 0.05$ and $p < 0.01$ were taken as statistically significant. The data correlation hypothesis was tested using Pearson's correlation coefficients.

3. Results

The main parameters of hemorheological profiles of healthy individuals and patients with hypertension are given in Table. 1. As can be seen, most of the hemorheological characteristics in AH patients were negatively changed compared to healthy individuals.

Table 1

Parameters of the hemorheological profile in AH patients and healthy individuals (M± σ)

Parameters	Group 1 (n=22)	Group 2 (n=20)
BV_1, mPa.s	4.64±0.42	6.56±1.32**
BV_2, mPa.s	6.30±0.74	7.88±1.79*
BV_3, mPa.s	7.48±0.62	8.79±2.00*
BV_4, mPa.s	9.20±1.04	10.63±2.85**
BV_5, mPa.s	18.40±1.18	25.89±7.76**
PV, mPa.s	2.12±0.15	2.56±0.15**
SV, mPa.s	4.18±0.41	5.10±0.48**
Hct, %	43.34±1.30	44.34±5.12
Hct/BV1, units	9.04±0.82	7.14±0.76*
RBCD, units	2.02±0.04	1.87±0.06**
RBCgD, units	1.82±0.04	1.74±0.05*
RBCA, units	11.09±4.12	16.64±4.46**
k, units	7.65±1.30	9.92±2.65*
n, units	0.92±0.19	0.94±0.16

Notes: BV_1 – BV_5 – blood viscosity at different shear stress (from 1.80 to 0.36 N/m2; see “Methods”); PV – plasma viscosity; VS – RBC suspension viscosity (Hct=40%), at high shear stress (1.80 N/m^2); Hct/BV_1 ratio – an index of blood O_2-transport efficiency; RBCD – red blood cell deformability; RBCgD – red blood cell ghost deformability RBCA – red blood cell aggregation; *k* –consistency index, as an index of the blood non-Newtonian behaviour, *n* – exponent, obtained from the blood flow equation
*p<0.05, *vs*. group 1; ** p<0.01, *vs*. group 1.

At the same time, in AH patients, the integral rheological characteristic – blood viscosity was 41% (p<0.01) higher than in healthy individuals. This is primarily due to the increased PV in group 2, which was by 21% (p<0.01) more than this parameter in group 1 (Table 1). At the same time, PV correlated more pronouncedly with BV_1 and BV_5 in AH patients (Table 2). The consistency index (*k*) was also significantly greater by 30% (p<0.05) in patients with AH, as an indicator of a greater non-Newtonian blood in these individuals (Table 1, Fig. 2).

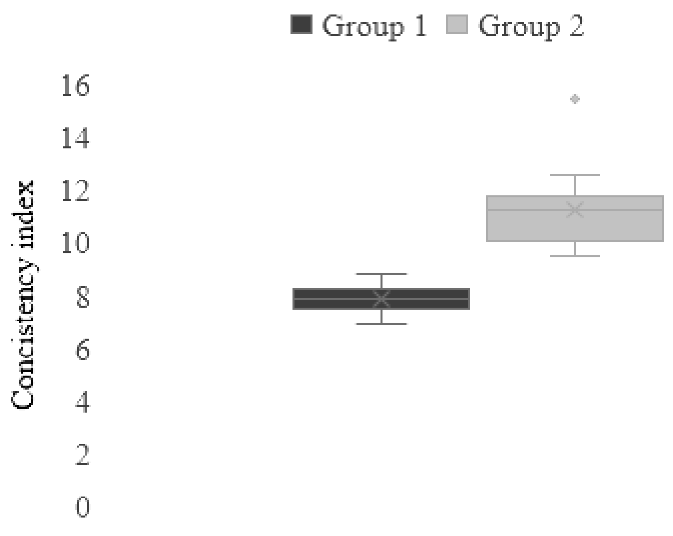


Fig. 2. The difference in the values of the consistency index in healthy individuals (Group 1) and in patients with arterial hypertension (Group 2).
Note: Data are presented as median (Me) [Q25:Q75].

Table 2
Correlation coefficients in two groups of individuals

Correlations	Group 1 (n=22)	Group 2 (n=20)
$1/BV_1$ – RBCD	0.36*	0.52**
$1/BV_1$ – PV	–0.38*	–0.64**
$1/BV_1$– Hct	–0.370*	–0.67**
$1/BV_5$–SV	–0.42**	–0.64**
BV_5/BV_1 – k	0.29	0.59**
BV_5/BV_1 – n	0.99**	0.99**
$1/BV_1$– k	–0.80**	–0.85**
$1/BV_1$ – n	–0.22	–0.67**
$1/BV_5$ – k	–0.79**	–0.82**
$1/BV_5$ – n	–0.75**	–0.90**
Hct/Hct – k	–0.77**	– 0.79**
Hct/Hct – n	–0.23	– 0.340*
The average of the correlation value coefficient	0.53±0.24	0.70±0.17

Notes: * p<0.05; **p<0.01;
$1/BV_1$ – blood fluidity at higher shear rate; $1/BV_5$ – blood fluidity at lower shear rate; other designations as in Table. 1.

In general, the analysis of correlations showed that 1) blood viscosity (or its fluidity) is more closely correlated with its determining factors in patients with hypertension (Table 2) and 2) indicators of non-Newtonian behavior of blood (*k* and *n*), in patients, are more strongly correlated with blood fluidity (1/BV) and its transport efficacy (Hct/BV1 ratio), then in healthy individuals. If we compare the average value of all correlation coefficients of groups 1 and 2, then in patients with AH this value will be significantly higher (group 1 - 0.53±0.24; group 2 – 0.70±0.17, p=0.04).

4. Discussion

The results of the study showed that in patients with hypertension, there is an increase in blood viscosity, with a negative change in the factors determining it, which is a typical hemorheological profile alteration [3, 13, 14]. It was shown that in individuals of both groups, blood is well described as a non-Newtonian thixotropic fluid of the power-law model [15]. Analysis of the use of several models (non-Newtonian models such as Bingham, Carreau, Carreau-Yasuda, Casson, modified Casson, Cross, modified Cross, simplified Cross, Herschel Bulkley etc.) to describe blood flow, both under normal and pathology, indicates that generalized power-law models were appeared to be superior for solving the blood flow at all shear rates [16-19]. Although consistency (*k*) and degree (*n*) are used to characterize the degree of non-Newtonianity of a fluid based on the power-law model [8], in our study we obtained a significant difference between the two comparison groups, only for (*k*) (Fig. 3).

A *B*

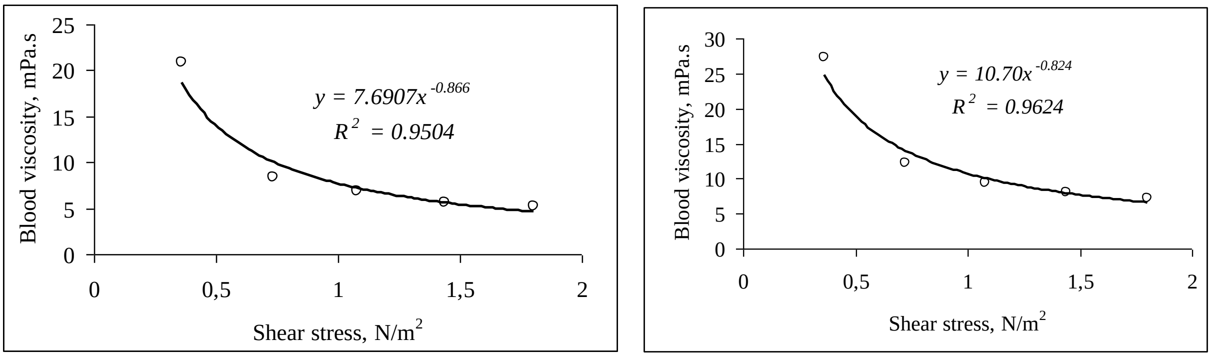


Fig. 3. Profiles of non-Newtonian blood flow in healthy persons (*A*) and in patients with arterial hypertension (*B*), represented by the power-law fluid model.

However, both indicators of the non-Newtonian behaviour of blood (*k* and *n*) are pronounced and negatively correlated with blood fluidity and transport efficiency. Moreover, the correlations were stronger in the group of patients with AH. This may be evidence of a greater negative effect of the non-Newtonian properties of blood on its O_2-transport potential.

A *B*

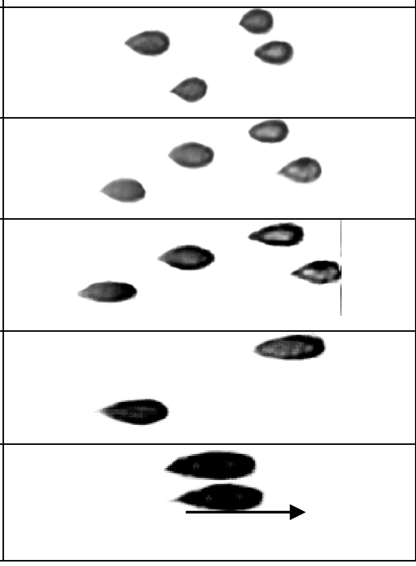
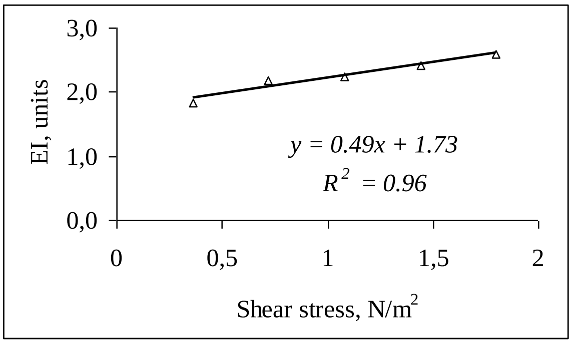
Shear stress (N/m^2)	Red blood cell elongation	Plot of elongation index (EI) versus shear stress
0.36		
0.72		
1.08		
1.44		
1.80		

Fig. 4. Change in RBC elongation index upon application of increasing shear stress (*A*), which is well described by a linear regression equation of the form (*B*): $y = ax + b$, at a high experimental data approximation 96% ($R^2 = 0.96$).

The greater degree of non-Newtonian blood requires a higher shear stress for tissue perfusion [20-22] and, consequently, an increase in blood pressure. With a gradual increase in the shear stress in the flow microchamber, a close to linear increase in the RBC elongation index is observed (Fig. 4).

Since the RBC elongation index (EI), as ratio L/W, increases linearly with increasing shear stress, the slope of the regression line in the equation (Fig. 5*B*) is proportional to the shear modulus of the membrane [23]. Thus, EI measurements can characterize the shear modulus of the cell membrane [24]. At the same time, if the experimental data of RBC elongation indices are presented not by a linear equation, but by a power-law model, then the reliability of the data approximation approaches 100% (Fig.5; $R^2 = 0.99$).

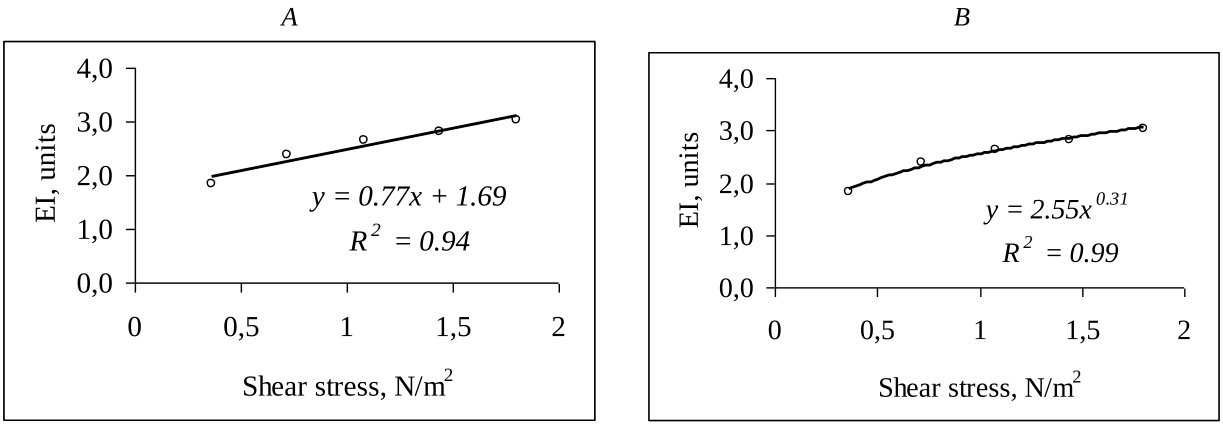


Fig. 5. Comparison of two models describing the change in the RBC elongation index in a flow microchamber with a gradual increase in the applied shear stress: *A* - a linear regression model; *B* – a power regression model (Figures *A* and *B* are the same experimental values EI)

With exponents n<1.0 in the equation, this is the behaviour of a pseudoplastic body [8]. The RBC ghosts exhibit the same variant of deformation behaviour with an increase in shear stress (Fig. 6).

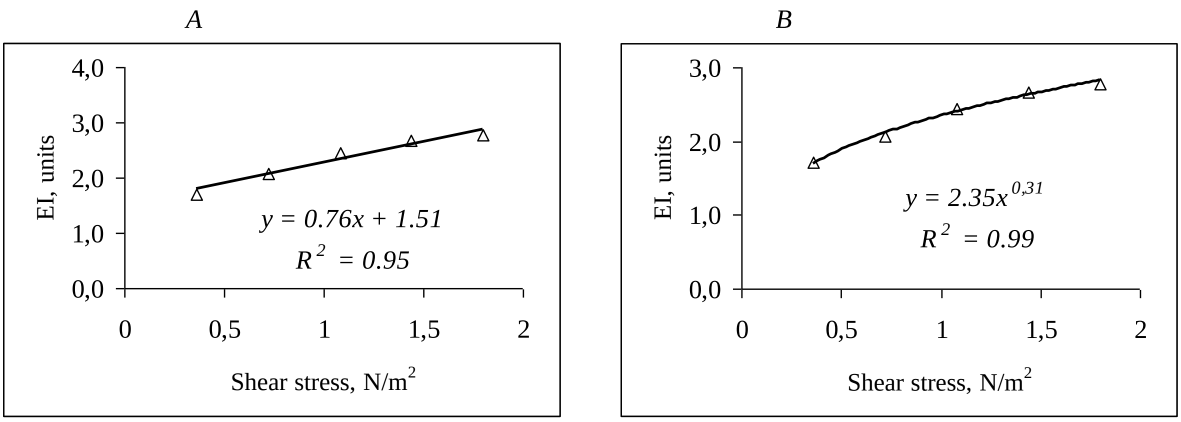


Fig. 6. Comparison of two models describing the change in the RBC ghost elongation index in a flow microchamber with a gradual increase in the applied shear stress: *A* - a linear regression model; *B* – a power regression model.

Comparative analysis showed that whole blood in a viscometer and erythrocytes in a flow microchamber exhibit very similar mechanical behavior when changing shear stress, which is very well described by the generalized power-law model [17]. At the same time, RBCs are well drawn along the bloodstream lines, with an increase in shear stress, and thereby contribute to a decrease in the blood apparent viscosity. This is supported by significant negative correlations between BV and EI (r= – 0.56, p<0.01) and consistency index *k* and EI (r= – 0.54, p<0.01).

5. Conclusion

The data obtained indicate that the flow of blood as a viscous liquid can have a non-Newtonian character both under normal conditions and especially in pathology, for example, in arterial hypertension. The non-Newtonian behavior of blood is very well described by the power-law fluid model. It can be obtained by registering blood viscosity at several, at least five, shear stresses. It was found that the most significant characteristic of the change in the degree of non-Newtonian behavior of blood is the index of consistency, "*k*" from this equation: $y = kx^{-n}$. It strongly correlated with blood fluidity and its transport potential and to a greater extent in AH patients. In addition, it was found that an increase in the RBC deformation, which is close to a linear type, with a gradual increase in shear stress in the microchamber, is better predicted by the power law pseudoplastic fluid model.

Acknowledgments

All work, except for data analysis was supported by the Russian Science Foundation grant (No. 22-15-00120)

References

[1] Pries, A. R. Secomb T. W., 1997. Resistance to blood flow in vivo: from Poiseuille to the «in vivo viscosity law». Biorheology 34, 4-5, 369–373.
[2] Stoltz, J.F., Donner, M., Muller, S., Larcan, A., 1991. Hemorheology in clinical practice. Introduction to the notion of hemorheologic profile. J. Mal. Vasc. 6, 261-270.
[3] Ajmani, R.S., 1997. Hypertension and hemorheology. Clin. Hemorheol. Microcirc. 17, 6, 397–420.
[4] Liepsch, D., Sindeev, S.V., Frolov, S.V., 2018. Distinguishing between Newtonian and non-Nowtonian character of blood flow in vascular bifurcations and bends. Series on Biomechanics 32, 2, 3-11.
[5] Gallagher, M.T., Wain, RAJ, Dari, S., Whitty, J.P., Smith D.J., 2019. Non-identifiability of parameters for a class of shear-thinning rheological models, with implications for haematological fluid dynamics. J Biomech. 85, 230-238.
[6] How, T.V., Black, R.A., 1987. Pressure losses in non-Newtonian flow through rigid wall tapered tubes. Biorheology 24, 3, 337-351.
[7] Mazumdar, J., Ang, K.C., Soh, L.L., 1991. A mathematical study of non-Newtonian blood flow through elastic arteries. Australas Phys Eng Sci Med. 14, 2, 65-73.
[8] Wilkinson, W.L., 1960. Non-Newtonian fluids. Fluid Mechanics, Mixing and Heat Transfer. Pergamon Press. London, 138 pp.
[9] Dintenfass, L., 1981. Clinical applications of heamorheology. The Rheology of blood, blood vessels and associated tissues. New York: Oxford Press, 22–50.
[10] Baskurt, O.K., Meiselman, H.J., 1997. Cellular determinants of low shear blood viscosity. Biorheology 34, 30, 235–247.
[11] Muravyov, A.V., Antonova, N., Tikhomirova, I.A., 2019. Red blood cell micromechanical responses to hydrogen sulphide and nitric oxide donors: Analysis of crosstalk of two gasotransmitters (H_2S and NO). Series on Biomechanics 33, 2, 34-40.
[12] Dodge, J., Mitchell, C., Hanahan, D., 1963. The preparation and chemical characteristics of hemoglobin free ghosts of erythrocytes. Arch. Biochem. Biophys. 100, 119-130.
[13] Foresto, P., D'Arrigo, M., Filippini, F., 2005. Hemorheological alterations in hypertensive patients. Medicina (B Aires). 65, 2, 121–5. [Article in Spanish].
[14] Guedes, A.F., Moreira, C., Nogueira, J.B., 2019. Fibrinogen - erythrocyte binding and hemorheology measurements in the assessment of essential arterial hypertension patients. Nanoscale 11, 6, 2757–66. DOI: 10.1039/C8NR04398A.
[15] Neofytou, P., 2004. Comparison of blood rheological models for physiological flow simulation. Biorheology 41, 6, 693-714.
[16] Soulis, J.V., Giannoglou, G.D., Chatzizisis, Y.S., Seralidou, K.V., Parcharidis, G.E., Louridas, G.E., 2007. Non-Newtonian models for molecular viscosity and wall shear stress in a 3D reconstructed human left coronary artery. Med Eng Phys. 30, 1, 9-19. DOI: 10.1016/j.medengphy.2007.02.001.
[17] Abbasian, M., Shams, M., Valizadeh, Z., Moshfegh, A., Javadzadegan A., Cheng S., 2020. Effects of different non-Newtonian models on unsteady blood flow hemodynamics in patient-specific arterial models with in-vivo validation.

Comput Methods Programs Biomed. 186, 105-185. DOI: 10.1016/j.cmpb.2019.105185.
[18] Kannojiya, V, Das, A.K., Das P.K., 2021. Simulation of Blood as Fluid: A Review From Rheological Aspects. IEEE Rev Biomed Eng. 14:327-341. DOI: 10.1109/RBME.2020.3011182.
[19] Wajihah, S.A., Sankar D.S., 2023. A review on non-Newtonian fluid models for multi-layered blood rheology in constricted arteries. Arch Appl Mech. 93, 5, 1771-1796. doi: 10.1007/s00419-023-02368-6.
[20] Johnston, B.M., Johnston, P.R., Corney, S., Kilpatrick, D., 2004. Non-Newtonian blood flow in human right coronary arteries: steady state simulations. J Biomech. 37, 5, 709-20. DOI: 10.1016/j.jbiomech.2003.09.016.
[21] Mejia, J., Mongrain, R., Bertrand, O.F., 2011. Accurate prediction of wall shear stress in a stented artery: newtonian versus non-newtonian models. J Biomech Eng. 133, 7, 074501. DOI: 10.1115/1.4004408.
[22] Kandangwa, P., Torii, R., Gatehouse, P.D., Sherwin, S.J., Weinberg, P.D., 2022. Influence of right coronary artery motion, flow pulsatility and non-Newtonian rheology on wall shear stress metrics. Front Bioeng Biotechnol. 10, 962687. DOI: 10.3389/fbioe.2022.962687.
[23] Hochmuth, R.M., Mohandas, N., Blackshear, P.L., 1973. Measurement of the elastic modulus for red cell membrane using a fluid mechanical technique. Biophysical journal. 13, 747-762. 1.
[24] Chien, S., Sung, L.F., Lee, V.V., Skalak, R., 1992. Red cell membrane elasticity as determined by flow channel technique. Biorheology 29, 467-478. DOI: 10.3233/bir-1992-295-607.