ISSN 0362-1197, Human Physiology, 2015, Vol. 41, No. 4, pp. 437–443. © Pleiades Publishing, Inc., 2015.
Original Russian Text © O.V. Filatova, A.A. Sidorenko, S.A. Agarkova, 2015, published in Fiziologiya Cheloveka, 2015, Vol. 41, No. 4, pp. 110–118.

Effects of Age and Sex on Rheological Properties of Blood

O. V. Filatova, A. A. Sidorenko, and S. A. Agarkova

Altai State University, Barnaul, Russia

e-mail: ol-fil@mail.ru

Received October 15, 2014

Abstract—We have studied rheological properties of blood (viscosity, concentration of erythrocytes, erythrocyte sedimentation rate, prothrombin index, and fibrinogen and lipid concentration) in healthy men and women at the age of 1 to 75 years. We have found an increase in blood viscosity from childhood to adult age. Blood viscosity decreased in elderly men; but it progressively increased with age in women. Three age groups have been distinguished: (1) from infancy to childhood (3.6 ± 0.07 mPa s regardless of age); (2) from adolescence to the adult age (5.1 ± 0.06 mPa s in men and 4.3 ± 0.05 mPa s in women); (3) elderly and old age (4.7 ± 0.13 mPa s in men and 4.4 ± 0.09 mPa s in women). In adult subjects, blood viscosity values were significantly different in men and women ($p < 0.001$). There were also sex-related differences in determination coefficients of the relationship between blood viscosity and the concentration of erythrocytes ($R^2_M = 0.41$, $p < 0.001$; $R^2_F = 0.35$, $p < 0.001$) and viscosity and cholesterol level ($R^2_M = 0.47$, $p < 0.001$; $R^2_F = 0.68$, $p < 0.001$). The factor analysis has shown that blood viscosity depends on the concentration of erythrocytes by 28%, fibrinogen level by 23%, and cholesterol level by 20%.

Keywords: blood viscosity, erythrocytes, fibrinogen, cholesterol, age, sex

DOI: 10.1134/S0362119715030044

Rheological properties of blood undergo certain changes during ontogenesis in humans due to the age-related involution [1]. Age-related changes of rheological properties of blood, together with factors on which they depend, are still studied insufficiently despite their importance for understanding the mechanisms of aging and associated vascular pathology. The results of the studies of the change in blood viscosity depending on age are controversial [2, 3]. Moreover, subjects under 18 years of age have not been previously studied. Therefore, the investigation of blood rheological parameters at different stages of human ontogenesis is important [2].

The aim of our study was to investigate blood viscosity in different age periods in men and women. Our results revealed the blood viscosity values in children, showed sex-related difference, and provided more details of age-related changes in this parameter.

METHODS

We have studied blood samples from 536 patients (245 men and 291 women) at the Altai Children Clinical Hospital and Altai Clinical Hospital (Barnaul, Russia). The subjects did not have any acute or chronic diseases, and their parameters of the complete blood count were within the normal range. The subjects included in the study met the following criteria: their age was in the range from 1 to 75 years; adult subjects or legal representatives of underage subjects gave an informed consent. We excluded subjects with conditions that could affect the results of the study. The number of subjects of each age group and the total number of subjects is shown in the Table 1. The age groups were formed according to the Table of Age Periods in Human Ontogenesis approved at the VII All-Union Conference on challenges in age-related morphology, physiology, and biochemistry of the Academy of Pedagogic Sciences of the Soviet Union (Moscow, 1965). This table is based on morphological, functional, and psychological criteria and includes the whole postnatal ontogenesis of a human: the newborn period, from 1 to 10 postnatal days; infancy, from 10 days to 1 year; early childhood, 1–3 years; the first childhood, 4–7 years; the second childhood, 8–12 years in boys and 8–11 years in girls; adolescence, 13–16 years in boys and 12–15 years in girls; youth, 17–21 years in men and 16–20 years in women; adult age, the first period, 22–35 years in men and 21–35 years in women; adult age, the second period, 36–60 years in men and 35–55 years in women; middle age, 61–74 years in men and 56–74 years in women; old age, 75–90 years in men and women; long-livers, over 90 years.

The comprehensive study of rheological properties of blood included measurements of blood viscosity, erythrocyte concentration, and total blood cholesterol concentration. Blood samples were taken from the

Table 1. Age- and sex-related grouping of subjects

Age period		Number of subjects	
		men	women
Early childhood		15	15
First childhood		15	15
Second childhood		20	25
Adolescence		25	25
Youth		25	25
Adulthood	First period	35	65
	Second period	65	68
Middle age		30	31
Old age		15	22
Total number of men and women		245	291
Total number of subjects		536	

cubital veins; in some cases blood was retrieved from smaller veins of hands or forearms. The volume of blood samples used for the analysis was 1 mL. Blood viscosity was evaluated using a VK-4 medical capillary viscometer by Hess's method under standard conditions. This method is the most precise for measuring blood viscosity [4]. Considering that the erythrocyte sedimentation rate (ESR) correlates with their mobility in the electric field [5] and reflects the rate of cell aggregation [6], we also took ESR values into account. Coagulogram of the venous blood was analyzed: the prothrombin index (PTI) and fibrinogen concentration were measured.

All results were statistically analyzed; mean values (M), standard deviation (SD), standard error of the mean (m), and 95% confidence interval (95% CI) were calculated. Data are shown as $M \pm m$. The normal distribution of the data samples was verified using the Kolmogorov–Smirnov test, $p < 0.05$. Mean values of blood parameters with normal distribution were obtained in the study. The differences between independent samples were evaluated using Student's t-test. The difference was considered statistically significant at $p < 0.05$. 95% CI was set as $M \pm 2m$ [7]. Pearson's correlation analysis was carried out. The integrated effect of plasma and cell factors on blood viscosity was studied using the factor analysis: strongly correlated variables were united in a single factor. Variables from different factors were not correlated. The aim of the factor analysis was to find integrative characteristics that would fully explain the observed relationships between the studied variables. Only the parameters included into a factor with positive values were considered; negative values indicated that the parameter had the weakest effect [8]. For better and more detailed understanding of the relationships between rheological, cellular, and plasma parameters of the blood, the regression analysis was run on the significant correlations with a dominating factor. The data was analyzed considering the subjects' sex. The statistical analysis was carried out using the SPSS 20.0 software.

RESULTS AND DISCUSSION

Investigation of blood viscosity in subjects aged from 1 to 75 years showed that this parameter depends on sex and age. Blood viscosity was low during the period from the early childhood to the second childhood; it significantly increased in adolescence ($p < 0.001$) and remained at the same level till the second adulthood. In men, blood viscosity decreased by the elderly age ($p < 0.001$) (Fig. 1). In women, blood viscosity increased at the elderly age (Fig. 1). During the period from the adolescence to the second adulthood, the values of blood viscosity were significantly different in men and women (Fig. 1).

Three periods of stable blood viscosity were found: (1) from the early childhood to the second childhood (we further refer to this period as the childhood); (2) from adolescence to the second adulthood (the adult age); (3) middle and old ages (elderly age). Blood viscosity, erythrocyte, fibrinogen, and cholesterol concentrations in these three periods are shown on Fig. 2. The trend of blood viscosity change (Fig. 2a) was the same as the trend of erythrocytes (Fig. 2b) and fibrinogen (Fig. 2c) in men and women. Cholesterol concentration tended to increase with age (Fig. 2d).

Apparently, adolescence is a specific period in the dynamics of the studied rheological parameters of blood. During this period, the processes of an intense increase in the somatic growth parameters take place, including abrupt changes in blood viscosity (Fig. 1). This age was also characterized by the changes of shear stress, a parameter of the blood flow near arterial walls depending on blood viscosity, as well as the vascular resistance index in the internal carotid artery [9]. Therefore, this fact emphasizes the specificity of adolescence as the period of physiologic changes in blood and hemodynamics, which could explain the manifestation of many functional deficits and disorders known to pediatricians during this period.

We found highly significant differences in blood viscosity between adults, children, and elderly people (Fig. 2a). Blood viscosity increased in adult age in comparison with childhood; then it decreased in elderly men (Fig. 2a). In women, blood viscosity progressively increased with age (Fig. 2a). The data on blood viscosity change in elderly people are controversial. No dependence of blood and plasma viscosity on the age was found in [3]. At the same time, other authors

showed an increased blood viscosity in elderly people [2]. However, the authors of [2] studied blood viscosity in a wide age range and did not consider the subjects' sex.

Blood viscosity is the most important rheological parameter, which depends on hematocrit, plasma factors (lipid and fibrinogen concentrations), erythrocyte aggregation and deformation capacity, and changes in adhesive and aggregation properties of thrombocytes [10–14]. Therefore, for further discussion of mechanisms underlying the blood viscosity changes, we should note that significant differences in the number of erythrocytes were found between 7 age groups (Fig. 2b). Our results on erythrocyte concentration are in agreement with other authors [15]. Authors of [15] showed that erythrocyte and hemoglobin concentrations changed with age. These parameters increased from infancy to the age of 13–14 years independently of the sex. The number of erythrocytes in children was $3.8–4.9 \times 10^{12}$ cells/L [15]. In our study, the numbers of erythrocytes were similar in boys and girls from the early childhood to the second childhood (4.0 ± 0.05; Min, 3.6; Max, 4.8 in boys; 3.8 ± 0.04; Min, 3.5; Max, 4.3×10^{12} cells/L in girls). In men, the concentration of erythrocytes was $4–5.6 \times 10^{12}$ cells/L; in women, $3.5–5.1 \times 10^{12}$ cell/L [15]. We obtained the similar results: during the period from adolescence to the second adulthood the concentration of erythrocytes was $5.0 \pm 0.04 \times 10^{12}$ cells/L (Min, 3.8; Max, 5.8×10^{12} cells/L in male subjects; this parameter was $4.3 \pm 0.05 \times 10^{12}$ cells/L (Min, 3.5; Max, 5.1×10^{12} cells/L) in female subjects. According to the same authors [15], the erythrocyte concentration decreased from 4.51×10^{12} cells/L to 4.39×10^{12} cells/L in 65–70 year old men ($p < 0.001$) [15]. In our study, the erythrocyte concentration in men decreased to $4.8 \pm 0.08 \times 10^{12}$ cells/L ($p \le 0.1$); at the same time, it increased to $4.6 \pm 0.08 \times 10^{12}$ cells/L ($p \le 0.01$) in women. The authors of [2] did not find significant differences in hematocrit values among the subjects of both sexes aged from 20 to 70 years.

The age range studied in our work provided a wide variability of cells and plasma parameters. The number of erythrocytes varied from 3.5 to 5.8×10^{12} cells/L. An increase in blood viscosity in men was described by the following equation: $y = 0.867x + 0.836$ at a 41% significance of data approximation (Fig. 3a). In women, an increase in blood viscosity depending on erythrocyte concentration was described by the regression equation: $y = 0.777x + 0.811$ at a 35% significance of data approximation (Fig. 3a). Blood viscosity depended on the erythrocyte concentration by 41% in men ($R^2_M = 0.41$, $p < 0.001$) and 35% in women ($R^2_F = 0.35$, $p < 0.001$). R^2 value indicates a moderate power of relationship between these parameters [16]. Blood viscosity is affected by other factors besides erythrocyte concentration. The factor analysis showed that concentrations of erythrocytes and hemoglobin and ESD characterizing cell aggregation [5] were included in the first factor with the highest factor loading, which determined blood viscosity by 28% (Table 2). So, we confirmed that the erythrocyte concentration had the most significant impact on blood viscosity, especially in large blood vessels [17].

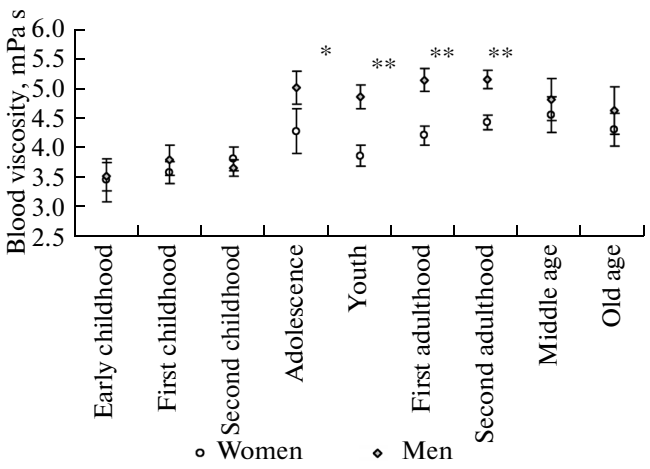

Fig. 1. Age dynamics of blood viscosity in men and women (*M*, 95% confidence interval). Statistically significant differences are indicated with * ($p < 0.05$) and ** ($p < 0.01$).

Erythrocyte deformability and aggregation capacity are among the mechanisms of the influence of erythrocytes on blood viscosity [2]. Several studies showed that the increased erythrocyte aggregation and blood viscosity were closely related in patients with cardiovascular pathology [18–21]. The authors of [2] found that aggregation capacity and rigidity of erythrocytes increased and erythrocyte deformability index decreased with age. These factors determined the increase of blood viscosity with age [2].

Other parameters affecting blood viscosity include plasma parameters. In older subjects, changes in lipid and fibrinogen levels were found. Concentration of fibrinogen in boys and girls (Fig. 2c) corresponded to the mean values of this parameter (3.0 ± 0.1 g/L) in children in the Altai region [22]. We found a tendency to an increase in the fibrinogen level ($p < 0.1$) in women (Fig. 2c) of elderly age in comparison with the adult women. In men, on the contrary, the fibrinogen concentration tended to decrease at the elderly age ($p < 0.1$) (Fig. 2c). Factor analysis showed that the second factor with the highest factor loading, which was 23% of the total variance, included PTI and fibrinogen concentration (Table 2). The relationship between fibrinogen and viscosity can be described by a power-mode model: $y = 1.658x^{0.857}$ in men and $y = 2.217x^{0.511}$ in women with the similar $R^2 \approx 0.44$ ($p_M \le 0.001$, $p_F \le 0.001$, Fig. 3b).

The authors of [2] previously found an increase in the fibrinogen concentration in blood plasma at the age of 60–69 years (3.76 ± 0.04 g/L) in the subjects of

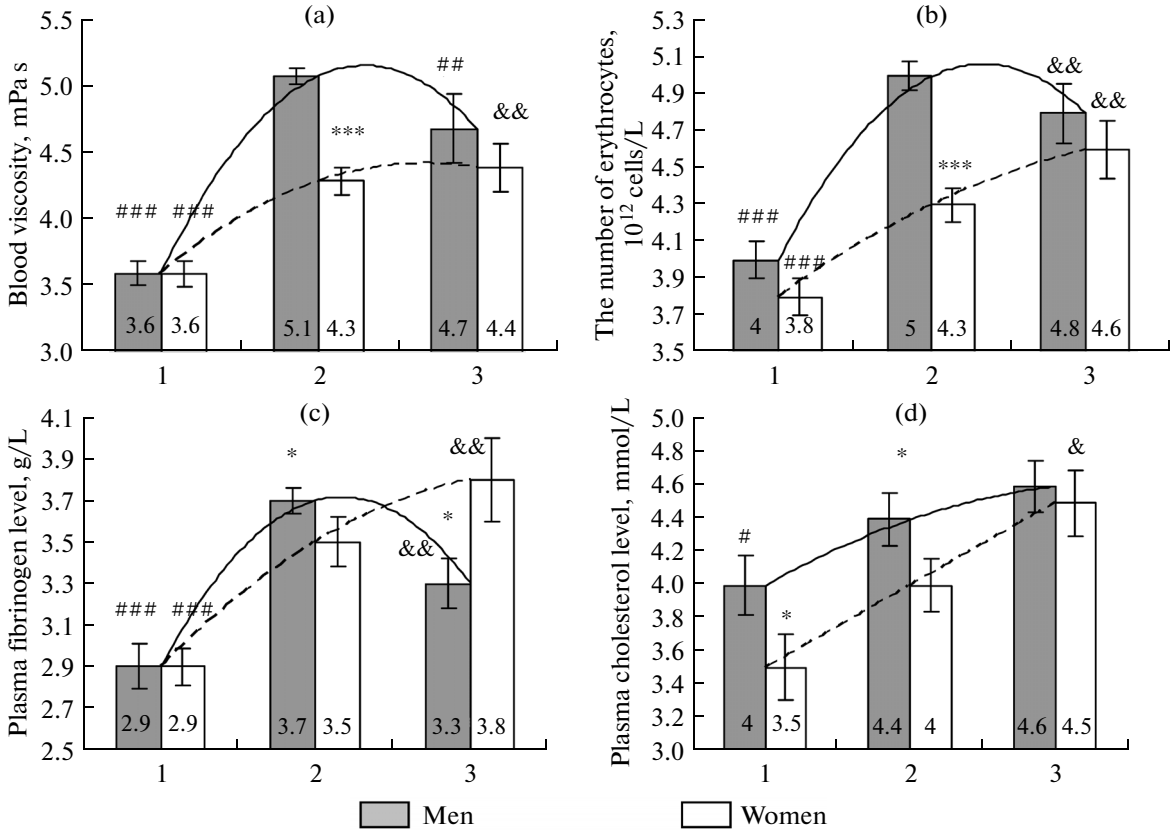

Fig. 2. Age-related changes in blood viscosity and cellular and plasma components of blood (M, 95% confidence interval). Age groups are shown on the X axis: (1) from the early childhood to the second childhood; (2) from adolescence to the second period of the adult age; (3) middle and old age. In Fig. 2b, the number of erythrocytes is on the Y axis (10^{12} cells/L). Statistically significant sex-related differences are indicated with * ($p < 0.05$), ** ($p < 0.01$), and *** ($p < 0.001$). Statistically significant age-related differences (in comparison with the second group) are indicated with # ($p < 0.05$), ## ($p < 0.01$), and ### ($p < 0.001$). Age-related tendencies are indicated with & ($p \le 0.2$) and && ($p \le 0.1$).

both sexes. A possible mechanism of the effect of fibrinogen concentration on blood viscosity could be an activation of erythrocyte aggregation in response to increased fibrinogen concentration leading to the viscosity increase [23]. Higher fibrinogen concentrations led to an increase in plasma viscosity [10].

We found an increase in cholesterol (ChS) levels in subjects of both sexes (Fig. 2d). The cholesterol level was included into the third factor, which had a 20% effect on blood viscosity (Table 2). Dynamics of blood viscosity in men can be described by a regression equation: $y = 0.672x + 2.102$ at a 47% significance of data approximation ($p < 0.001$, Fig. 3c). In women, dynamics of blood viscosity can be described by the regression equation: $y = 0.793x + 1.102$ at a 68% significance of data approximation ($p < 0.001$, Fig. 3c).

Our results on the ChS levels in different age groups (Fig. 2d) are within the normal range for children (3.11–5.18 mmol/L) and adults (3.63–6.48 mmol/L) in the Altai region [22]. Subjects with increased cholesterol levels were absent in our study. An increase in cholesterol and cholesterol of low density lipoproteins levels and a decrease in cholesterol of high density lipoproteins at the age of 60–69 years have been previously reported [2]. Some authors found that the change in blood lipid concentrations, particularly cholesterol, can affect blood viscosity, change the laminar blood flow to the turbulent flow, and increase plasma viscosity [12, 24].

The shifts in blood lipid levels can have an effect on the age-related increase in blood viscosity [2]. Our study confirmed these findings for female subjects (Figs. 1, 2a). The decrease in blood viscosity in male subjects of elderly age (Fig. 2a) could be caused by a decrease in the number if erythrocytes (Fig. 2b) and the fibrinogen level in this age range (Fig. 2c) as factors defining blood viscosity by 51% (Table 2). The results of the correlation analysis in the three age groups (Table 3) also support this hypothesis. In adult men, the strongest correlation was found between blood viscosity and cholesterol level (Table 3). It became slightly stronger with age, while the role of erythrocytes and fibrinogen concentrations increased almost

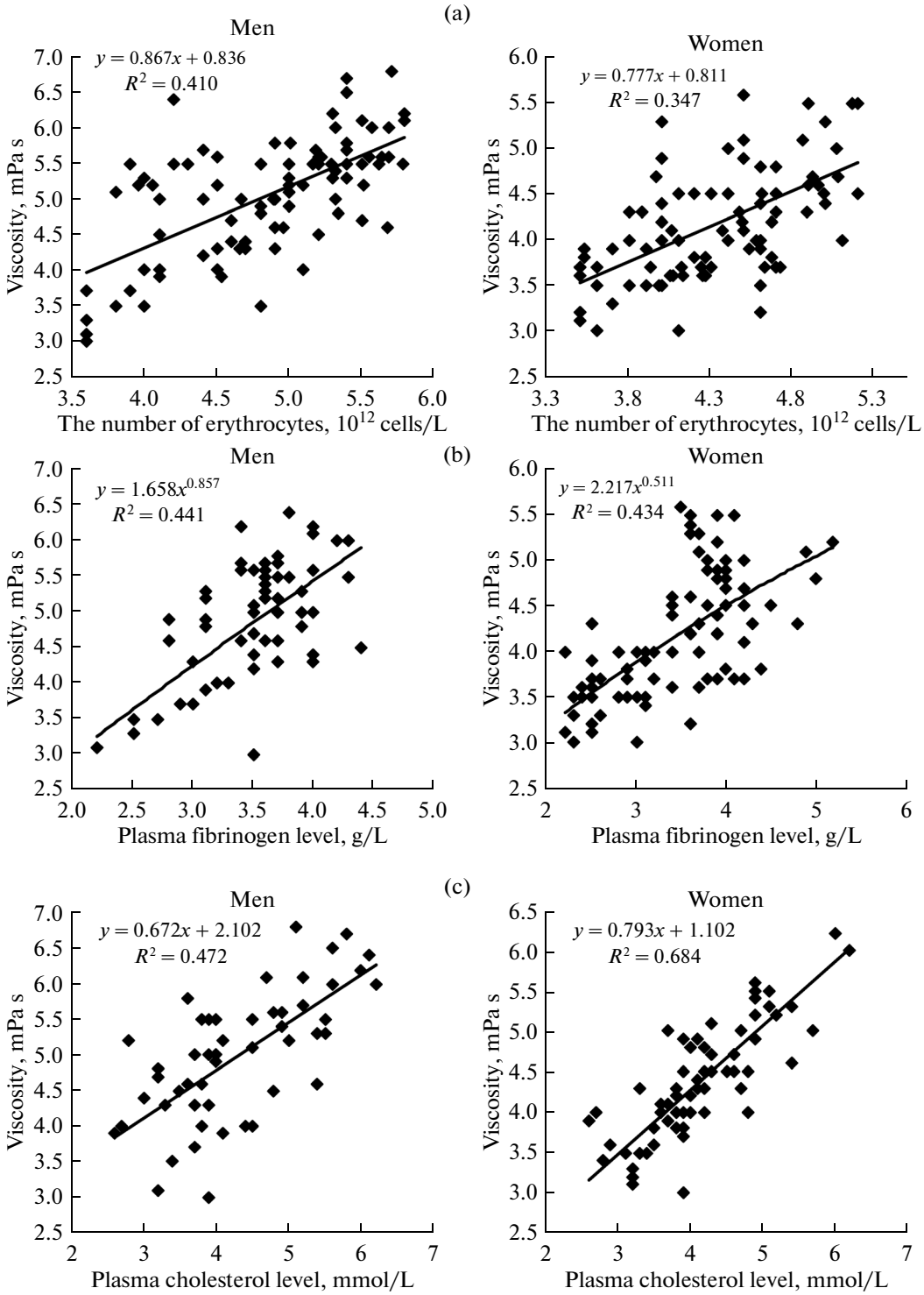

Fig. 3. The relationship between blood viscosity and blood cell and plasma components. The equations are shown on the charts. (a) The number of erythrocytes is shown on the *X* axis, 10^{12} cells/L.

two times (Table 3). In women, the role of erythrocytes and fibrinogen also slightly increased, while the effect of cholesterol became weaker (Table 3).

Factor analysis showed that the total variance of the studied parameters together with age and sex was 71% (Table 2); i.e., blood viscosity was 71% determined by these parameters. Other factors including aggregation and deformability of erythrocytes and changes in adhesive and aggregation properties of thrombocytes could be responsible for the rest 29% of blood viscosity [2].

Table 2. The factor structure of blood rheological parameters

Parameters	Factors		
	1	2	3
Age	0.894		
Concentration of erythrocytes, $\times 10^{12}$ cells/L	0.741		
Mean concentration of hemoglobin in an erythrocyte, g/L	0.587		
Erythrocyte sedimentation rate	0.577		
Prothrombin index		0.865	
Plasma fibrinogen level, g/L		0.764	
Sex		–0.711	
Plasma cholesterol level, mmol/L			0.904
Variance, %	28	23	20

Table 3. Correlation coefficients between blood viscosity and the parameters that can affect it in healthy people of various ages

Age groups	Sex	*N*	Correlation coefficient	Parameters		
				fibrinogen	cholesterol	erythrocytes
1	M	50	*r*	0.983	0.942	0.536
			p	<0.001	0.001	0.073
	F	55	*r*	0.828	0.967	0.725
			p	0.002	<0.001	0.012
2	M	150	*r*	0.386	0.722	0.388
			p	0.012	<0.001	0.002
	F	183	*r*	0.667	0.837	0.543
			p	<0.001	<0.001	<0.001
3	M	45	*r*	0.863	0.783	0.632
			p	<0.001	0.001	0.009
	F	53	*r*	0.761	0.623	0.630
			p	0.004	0.030	0.016

Age groups: (1) from the early childhood to the second childhood; (2) from adolescence to the second period of the adult age; (3) middle and old ages.

CONCLUSIONS

The study conducted on subjects of a wide age range clarified age- and sex-related specificity of blood viscosity. An increase in blood viscosity in the period from childhood to adolescence and later decrease at the elderly age in men was found. In women, blood viscosity progressively increased with age. Three age periods with stable blood viscosity were found: (1) from the early childhood to the second childhood; (2) from adolescence to the adult age; (3) the middle and old age. Blood viscosity values were different in adult men and women. Sex-related differences also appeared between determination coefficients (R^2) of the relationship between blood viscosity and erythrocyte concentrations in men and women.

Analysis of blood rheological parameters showed that blood viscosity depended on the concentration of erythrocytes by 28%, on the fibrinogen level by 23%, and on the cholesterol concentration by 20%.

REFERENCES

1. Baev, V.M., Effect of age on rheological properties of blood in adults, *Tromb. Gem. Reol.*, 2001, no. 5, p. 40.
2. Korkushko, O.V., Lishnevskaya, V.Yu., and Duzhak, G.V., Rheological properties of blood in aging and the parameters affecting it, *Krovoobr. Gem.*, 2007, no. 1, p. 5.
3. Jung, F., Kiesewetter, H., and Roggenkamp, H.G., Bestimmung der referenzbereiche rheologischer parameter, *Klin. Wochenschr.*, 1986, no. 64(8), p. 375.
4. Sidorova, M.A. and Kalmykova, S.A., Analysis of methods and devices in measurement of blood viscosity in humans, in *Trudy Mezhdunarodnogo simpoziuma nadezhnost' i kachestvo* (International Symposium on Reliability and Quality), 2006, vol. 1, p. 358.
5. Khazipova, I.R., Bagautdinova, R.Sh., and Shamratova, V.G., Relationships between blood viscosity parameters at their various levels, *Vestn. ChGPU*, 2011, no. 10, p. 312.
6. Levtov, V.A., Rediger, S.A., and Shadrina, N.Kh., *Reologiya krovi* (Blood Rheology), Moscow: Meditsina, 1982.
7. Lang, T.A. and Sesik, M., *Kak opisyvat' statistiku v meditsine* (How to Report Statistics in Medicine), Moscow: Prakticheskaya Meditsina, 2011.
8. Nasledov, A.D., *SPSS komp'yuternyi analiz dannykh v psikhologii i sotsial'nykh naukakh* (SPSS Automated Analysis in Psychology and Social Sciences), St. Petersburg: Piter, 2007, 2nd edition.
9. Filatova, O.V., Sidorenko, A.A., and Skorobogatov, Yu.Yu., Age and sex dependence of hemodynamic parameters of human internal carotid arteries, *Hum. Physiol.*, 2014, vol. 40, no. 5, p. 554.
10. Barkagan, Z.S., *Diagnostika i kontroliruemaya terapiya narushenii gemostaza* (Diagnostics and Controlled Therapy of Hemostasis Disorders), Moscow: N'yudiamed, 2001.
11. Berkovskii, A.L., Vasil'ev, S.A., and Zherdeva, L.V., *Posobie po izucheniyu adgezivno-agregatsionnoi aktivnosti trombotsitov* (The Guide on Studies of Adhesive and Aggregation Activity of Thrombocytes), Moscow, 2002.
12. Volkov, V.I. and Zaproval'naya, O.E., Thrombocyte hemostasis and atherogenesis, *Krovoob. Gemostaz*, 2003, no. 1, p. 18.
13. Ami, R.B., Barshtein, G., Zeltser, D., et al., Parameters of red blood cell aggregation as correlates of the inflammatory state, *Am. J. Physiol. Heart. Circ. Physiol.*, 2001, vol. 280, no. 5, p. 1982.
14. Raddino, R., Ferrari, R., Scarabelli, T.M., et al., Clinical implications of rheology in cardiovascular diseases, *Recenti Prog. Med.*, 2002, no. 93, p. 186.
15. Isaeva, I.V., Shutova, S.V., Maksinev, D.V., and Medvedeva, G.V., Problems of sex- and age-related properties of blood, *Sovr. Nauk. Tekhn.*, 2005, no. 4, p. 45.
16. Sidorenko, E.V., *Metody matematicheskoi obrabotki v psikhologii* (Methods of Mathematical Analysis in Psychology), St. Petersburg: Rech', 2006.
17. Murav'ev, A.V., Tikhomirova, I.A., Bulaeva, S.V., et al., Role of certain rheologicalal parameters of blood in its fluidity and transport capacity, *Ross. Zh. Biomekh.*, 2012, vol. 16, no. 3, p. 32.
18. Kuryata, A.V., Geichenko, V.P., and Kudelya, I.V., Role of age-related changes of membranes of erythrocytes in regulation of microcirculation, in *Mikrotsyrkulyatsiya ta ii viiovi zminy* (Microcirculation and Its Age-related Changes) (Proc. 2nd Int. Conf.), Kyev, 2002, p. 180.
19. Smirnov, I.Yu., Effect of aggregation and electrostatic interactions between erythrocytes on the structure of blood flow, in *Mezhdunar. konf. po gemoreologii v mikro i makrotsirkulyatsii* (Int. Conf. on Hemorheology and Micro- and Macrocirculation), Yaroslavl, 2005, p. 37.
20. Katiukhin, L.N., The role of erythrocyte rheological determinants in the regulation of blood flow structure, *Klin. Lab. Diagn.*, 2001, no. 12, p. 22.
21. Mchedlishvili, G., Shakarishvili, R., Momtselidze, N., et al., Comparative Values of Erythrocyte Aggregability versus Other Indices of Hemorheological disorders in patients with ischemic brain infarcts, *Clin. Hemorheol. Microcirc.*, 2000, no. 22, p. 9.
22. Lobanov, Yu.F., Mal'chenko, A.M., and Skudarnov, E.V., *Osnovnye fizicheskie i paraklinicheskie konstanty detskogo vozrasta* (Basic Physical and Paraclinical Constants of Childhood), Barnaul: AltGMU, 2008, vol. 136.
23. Blokhina, T.A., Nazarov, S.B., and Chemodanov, V.V., Role of plasma parameters in regulation of rheological properties of erythrocytes in humans, *Mezhdunar. konf. po gemoreologii* (Int. Conf. on Hemorheology and Micro and Macrocirculation), Yaroslavl, 2001, p. 60.
24. Petrova, M.N., Hemorheological parameters in patients with type II and VI hyperlipidemia at early stages of hypolipidemic therapy, *Mezhdunar. konf. po gemoreologii v mikro i makrotsirkulyatsii* (Int. Conf. on Hemorheology and Micro and Macrocirculation) Yaroslavl, 2005, p. 33.

Translated by E. Suleimanova