

ABO-BLOOD GROUPS SYSTEM AND MORBIDITY

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Peculiarities of metabolic profile and blood cell composition were studied on the basis of the examination of clinically healthy individuals with 0 (I) – AB (IV) blood groups. It was shown that the majority of molecular processes were associated with genetically determined group affiliation of the blood, the specifics of which can serve as a prerequisite for the formation of different health quality. The obtained data can be the basis for creating the individual health passport based on a personalized indicator of the AB0 blood groups.

Keywords: AB0 blood groups, cellular composition of the blood, metabolism, blood group associated diseases

Nowadays to justify an individual approach to the diagnosis and treatment of diseases in personalized medicine it is necessary to find objective criteria for the state of molecular processes genetically. There is an evidence that such external markers are stable during the life and can be considered as a unique variety and a unique combination of blood groups for the livelihoods of the human body [1, 2, 3, 4, 5, 6, 7, 8]. It is known, that the AB0 blood group system consists of two agglutinogens, which are presented on red blood cells, and two corresponding agglutinins in plasma – anti-A and anti-B. Group antigens are the foundation of a balanced polymorphism, one of the main cell structure “architects” in our body; blood plasma is the red blood cells external environment, which interacts with individual and unique topographical collection of glyco – and lipoproteins in the cytoplasmic membrane of each population of red blood cells and can affect their physical and chemical interactions. We studied the peculiarities of the metabolism and cellular composition of blood for each AB0 blood group, and the blood group associated diseases [9, 10, 11].

Materials and methods of research

The research was conducted at the department of fundamental and clinical biochemistry with laboratory diagnostic of Samara State Medical University and in the Samara State Medical University Clinics. We analyzed the 40 parameters of protein, carbohydrate, lipid metabolism and cell composition of the blood at the 21 setting on the clinical material more than 180,000 donations. Material for the study was venous blood.

AB0 blood groups were determined by the cross method and using monoclonal antibodies anti-A, anti-B, anti-AB by direct agglutination in the plane with an automated analyzer for conducting immune hematological studies “Chemosil SP” II company BIO-Rad, reagents TransCloneAnti-AB01 (A), TransCloneAnti-AB02 (B), TransCloneAnti-AB03 (AB) (Bio-Rad, USA). Distribution of the blood group were as following: 0 (I) blood group was 29,6%, A(II) blood group was 31,8%, B(III) blood group – 24,3%, AB (IV) blood group was 14,3%.

General blood analysis was performed on an automatic Hematology analyzer “Sysmex KX – 21”, “SysmexXT 2000i” (Japan) using a commercial set of reagents firm “Roch-Diagnostics” (Japan). Expanded differential count leukocyte formula was performed in stained blood preparations using light microscope “Zeiss”. The erythrocyte sedimentation rate was determined by the unified Panchenkov method.

Biochemical studies were performed on the automatic biochemical analyzer “Hitachi – 902” (Roch-Diagnostics, Japan), Cobas Integra 400 plus (Roche Diagnostics, Japan), “BIOSEN C_line” (Germany). The concentration of sodium, potassium, chloride were determined by ion-selective method. Analysis of protein fractions was carried out on the apparatus for electrophoresis “Astra” (Russia). Quality control was carried out using control sera of two levels of “Precinorm”, “Precipat” company “Roch-Diagnostics” (Switzerland) with the construction of control charts and application of the Westgard criteria.

Statistical processing of the results was performed using the statistical package SPSS12.0 and MicrosoftExcel 2010.

Results of research and their discussion

The obtained results indicate the biological variability of cellular and molecular composition of AB0 blood groups [12]. It was found that individuals with 0(I) blood group had lower number of erythrocytes comparing to the general population and other blood groups (Me $5,17 \cdot 10^{12}/l$) with relatively small average cell volume (Me 85,50 fl). Men with the 0(I) blood group had the lowest level of hemoglobin (Me 146,50 g/l). The intensity of hemoglobin synthesis was maximum (Me –33,90 g/dl). The hemoglobin content in the blood is one of the most conservative constants, not changing for long periods. Thus, at relatively low number of erythrocytes and the majority of cells in the average size, the full exchange of blood gases is possible due to fairly high degree of cells saturation with hemoglobin (Me –29,10 pg).

In the evaluation of blood serum total protein and protein spectrum of the patients with 0(I) blood group the tendency to lower content of albumin (Me50,8%) comparing to the

other blood groups drew attention: patients with A(II) – 52,7%; B(III) is 54,3%; AB(IV) – 53,6%. It is characteristic that the percentage of α_1 , α_2 , β -globulins was greater than the median in A(II)-AB(IV) blood groups: 3,93; 16,16 and 10,89% respectively. In addition, we noticed a high level of γ -globulin – Me 19,07%, due to that the albumin-globulin ratio had the lowest value. The content of C-reactive protein and other studied metabolic parameters were within the reference values, confirming the adequacy of the formed control groups, i.e. clinically healthy individuals. However, for patients with 0(I) blood group in the “gray zone” this parameter (Me 3,02 mg/l) was significantly higher than in the other blood groups. Relatively high values of IgA (Me 3,60 g/l), IgG (Me of 11,55 g/l) complement the specificity of the protein spectrum of patients with 0(I) blood group – reduced content of fine albumins and an increase of particulate protein fractions of globulins.

We found that the blood serum of patients with 0(I) blood group had the lowest comparing to the other blood groups glucose concentration (Me 3,8 mmol/l), magnesium (Me 0,82 mmol/l), calcium (Me 2,14 mmol/l) and iron (Me 16,8 μ mol/l). Low iron levels can be

the basis for studying the risk of developing iron-deficient conditions, assessment of this factor as a predictor of the development of iron deficiency conditions.

Men and especially women with the 0(I) blood group had relatively low compared to the other blood groups the leucocytes level: Me $6,00 \cdot 10^9/l$ and $5,85 \cdot 10^9/l$, respectively. The absolute content of neutrophils was sufficient; women had the lowest concentration of lymphocytes (Me 32%).

There is the literature based information about the connection 0 (I) blood group with some diseases, such as gastric ulcer and duodenal ulcer, gastritis, gastric cancer, dysplasia (Table 1). The team of the biochemistry chair received information about the anemia in hemophilic patients with 0(I) blood group [13, 14]. From Table 1 it follows that patients with 0 (I) blood group have a preferential relationship with somatic pathology. It is possibly depends on the characteristics of metabolism – the tendency to leukopenia, lymphocytopenia with relatively high concentrations of CRP, IgA, IgG. Apparently, this is the evidence of immunological memory to previous antigen-antibody interactions and lower potential immunological regulatory cellular link.

Table 1

Link between blood groups 0(I) and diseases

| Possibility of pathological process development | Authors |
|---------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------|
| Peptic ulcer disease | U. Altuhov (1983) [15], G. Drannik, G. Dizik (1990) [1], A. Tananyan (2001) [16], S. Garmonov et al. (2004) [17], N.N. Bogdanov (2012) [18] |
| Stomach cancer | B. Bjorkholm et al (2001) [19], M. Aspholm-Hurtig et al (2006) [20] |
| Hip joint dysplasia | I. Taboridze (1991) [21] |
| Myasthenia | B. Gehte(1995) [22] |
| Mutation (F7) | T. Subbotina (2012) [23] |
| Women papillomavirus infection Acute inflammatory processes in women reproductive system | E. Shevchenko (2010) [5] |
| Sympathetic oftalmia | L. Arkhipova (2012) [24] |
| Hemophilicpatient sanemia | U. Kosyakova, F. Gilmiarova (2015) [13] |
| Chronic prostatitis with benign prostatic hyperplasia | M. Shatohin, A. Konoplya, C.A. Dolgareva, (2011) [25] |
| Bladder cancer | I. Mayskov, (2013) [26] |
| The increased spontaneous platelet aggregation | E. Gergesova, (2011) [27] |
| Chronic heart disease | S. Biswas, P.K. Ghoshal, B. Halder, N. Mandal (2013) [28] |

Clinically healthy examined people with A (II) blood group are characterized by the following features. It is established that they have a high level of triglycerides (Me 1,41 mmol/l), relatively low content of high density lipoprotein (Me 1,33 mmol/l) and higher content of low density lipoproteins (Me of 2,76 mmol/l) than in 0(I) and AB(IV) blood groups and, consequently, the high coefficient of atherogenicity. The level of lipid carriers A (II) blood can be roughly attributed to the lipid type. The content of total cholesterol by the median corresponds to the data in the General population (4,9 mmol/L). In addition, we noticed the low level of albumin (Me 40,8 g/l), which plays an important role in providing colloid osmotic homeostasis of blood, transport of exogenous and endogenous xenobiotics, fatty acids, trace elements.

Women with A (II) blood group had the highest content of erythrocytes compared with other blood groups – Me $4,55 \cdot 10^{12}/L$. Along with this, men had minimal relative to other blood groups the average volume of red blood cells – Me 85,20 fl. It is characteristic that the

average content of hemoglobin in one erythrocyte (Me of 28,65 pg) is less than the level in individuals with other blood groups. The erythrocyte sedimentation rate for women was higher comparing with the general population and with 0(I) blood group – Me 5 mm/h. Perhaps the uniformity of the volume of red blood cells, a sufficiently high coarse protein content – γ -globulin – is a significant factor in this process. Blood parameters in women of this blood group are also characterized by the highest content of leukocytes (Me $7,20 \cdot 10^9/l$), the absolute content of neutrophils (Me $3,65 \cdot 10^3/ml$) higher, and the stab neutrophils (Me 2%) lower than individuals with other blood groups. There is a tendency for women with A (II) blood group to the appealing small platelets (Me MPV 10,20 fl), functionally less complete than large cells. Men with A (II) blood group compared with other blood groups are characterized by the largest absolute content of lymphocytes – Me $2,40 \cdot 10^3/ml$.

There are the most common diseases for the patients with A (II) blood groups indicated in the Table 2.

Table 2

Link between blood groups A (II) and diseases

| Possibility of pathological process development | Authors |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------|
| Atherosclerosis of lower extremities Rheumatic diseases | S. Chubar (1980) [29], E. Meshalkin (1981) [30], M. Freidin et al. (2006) [31], E. Suslova (2012) [32] |
| Chronic heart disease | M. Rafalovich et al. (1982) [33] |
| Bronchial asthma | E. Chichenko, U. Koshel (1975) [34] |
| Cholecystitis, cholelithiasis | G. Dizik et al (1982) [35] |
| Meningococcal infection Secondary purulent meningitis | U. Rudometov et al. (1981) [36] |
| Leiden mutation (F5) Protrombin mutation (F2) | I. Danilov (2010) [37] |
| Platelet receptors mutation (GpIa, GpIIIa) | R. Vitkovskiy E. Gergesova (2011) [38] |
| HIV, The combined prevalence of HIV, Hepatitis C, Hepatitis B, Preeclampsia and fetal hypotrophy, Iron deficiency anemia, Onychomycosis, Chronic generalized periodontitis, Helicobacter pylori antibodies in oral fluid | F. Gilmiyarova, V. Radomskaya et al. (2007) [12] |
| Chronic prostatitis | M. Shatohin, A. Konoplya (2011) [25] |
| The combination of chronic prostatitis with benign prostatic hyperplasia | M. Shatohin, A. Konoplya(2011) [25] |
| Breast cancer | M. Yanchenko (2011) [39] |
| Tuberculosis | M. Bektasova, V. Kapcov (2014) [40] |
| Atherosclerosis with complications | E. Suslova, L. Vasilyeva (2012) [32] |
| Appendicular peritonitis in children | V. Gavrilyuk (2011) [41] |
| Hemolytic disease of the newborn with A-blood group mothers | B. Doyle, J. Quigley et al. (2014) [42] |
| Pancreatic cancer | C. Rizzato, D. Campa et al. (2013) [43] |
| Gastroesophageal reflux disease | M. Sadreddini, Y. Rasmi et al. (2011) [44] |

From Table 2 follows that for persons with A (II) blood group are common infectious diseases, such as viral hepatitis B and C, HIV infection. We found it possible to associate it with features of metabolic and cellular composition of the blood: a tendency to lymphocytosis in this patients are visualized with hypergammaglobulinemia (γ -globulin Me of 19,59%) and higher concentration of immunoglobulin G (Me of 11,56 g/l), as a reflection of the earlier response, immune response, immunological memory of old and fresh contacts with bacterial and viral agents. Apparently, the structure of agglutinin A is similar to the antigenic structure of many bacterial and viral agents, and we can observe the phenomenon of "antigenic mimicry" when antigen penetrating to the body do not cause an immune response.

Patients with B (III) blood group are identified with low total protein level (Me 71,6 g/l) relatively to the general population level and persons with other blood groups. They are characterized by a low percentage of α 1 – (Me 3,45%), β -globulin (Me 14,85%), IgA (Me 2,76 g/l), IgM (Me 0,84 g/l), IgG (Me of 11,01 g/l); the concentration of albumin exceed the level in the other groups (Me 54,3%). There are some specificities of the lipid spectrum: the highest concentration of high-density lipoproteins (Me 1,45 mmol/l) and low-density lipoprotein (Me of 2,81 mmol/l); also we can notice a sufficiently high concentration of the general serum cholesterol of blood (Me 5,1 mmol/l), which is higher than in the general population and all other patients. Characterized by the highest supply of magnesium (Me 0,93 mmol/l) and calcium (Me 2,36 mmol/l), which is quite physiological with association of significant albumin content (Me 54,3%). The tendency to decreasing an iron content is similar to persons with A (II) blood group: they are determined by the lowest values – Me 16,80 μ mol/L.

For men with (III) blood group it was discovered the highest number of erythrocytes (Me of $5,29 \cdot 10^{12}/l$), average volume (Me 86,85 fl), hematocrit (Me of 45,85%), significantly increased the content of hemoglobin in the blood (Me 158,50 g/l; $p < 0,05$) in one erythrocyte (Me 30,15 pg; $p < 0,05$) comparing with O (I), A (II), AB(IV) blood groups. Women had the lowest number of erythrocytes (Me of $4,40 \cdot 10^{12}/l$) hematocrit (Me 38,6%), the content of hemoglobin in the blood (Me 129 g/l) in one erythrocyte (Me 29,2 PG). The erythrocyte sedimentation rate in men (Me 2 mm/h; $p < 0,05$) was significantly lower in 2 times than the female B (III) blood group

(Me 4 mm/h). In addition, compared with O (I), A (II), AB (IV) blood groups revealed a number of features in males: the highest number of leukocytes (Me $6,7 \cdot 10^9/l$) due to a more considerable Fund of neutrophils (Me 56,35%). The absolute content of neutrophils is also at the highest level – Me $3,75 \cdot 10^3/ml$, and the relative number of lymphocytes characterized by the lowest rate – Me of 32,5%. Men with this blood group had the highest average volume of platelets (Me 11,4 fl), the average width of the distribution of platelets in volume (Me 14,9%), significantly increased the content of monocytes (9,0%; $p < 0,05$).

Table 3 shows data on associated with B (III) blood group diseases. It is clearly visible that this blood group is associated with a minimal amount of diseases. We identified that individuals with blood group B (III) are characterized by a minimal risk of developing preeclampsia, polyploidy, fetal malnutrition [12, 45]. Cellular blood composition of patients with B (III) blood group is characterized by severe quantitative and qualitative features, but in general we tend to believe that there are prerequisites for good health.

The blood of clinically healthy individuals with the AB (IV) blood group is characterized by a high content of total protein (Me 75,3 g/l), albumin (Me of 4,9 g/l), and the concentration of C-reactive protein in trace amounts (Me 0,9 mg/l), reflecting the lack of response to exogenous and endogenous pathogens, products of damaged tissues, atherosclerotic process. The amount of cholesterol (Me 4,6 mmol/l) and triglycerides (Me 0,96 mmol/l) were minimal. Providing tissues and organs with lipids, primarily cholesterol, unsaturated higher fatty acids, low density lipoproteins and destruction in the composition of lipoproteins of high density, obviously, balanced interconversions of lipoproteins, transport of lipid components to extrahepatic tissues to the liver, as evidenced by rather high content of lipoproteins of high density (Me of 1,42 mmol/l). Magnesium concentration (Me of 0,84 mmol/l) was similar to persons with A (II) blood group, which could serve as a prerequisite for the disorders of energy production in the body.

Based on the studied parameters of cellular blood composition in women with AB (IV) blood group it was revealed that they had 2 times more significant features than in men. They are characterized by a high content of erythrocytes – Me $4,54 \cdot 10^{12}/l$, the average volume is rather small – Me 87,20 fl, they are homogeneous according to this indicator, as evidenced by the small width of their distribution

Table 3

Link between blood groups B (III) and diseases

| Possibility of pathological process development | Authors |
|-------------------------------------------------------------------------------|------------------------------------------------------|
| Pneumonia Postoperative infection | M. Averbah (1985) [46] |
| Osteochondrosis with radicular syndrome Sciatica | G. Drannik (1990) [1] |
| MGTFR mutation | T. Subbotina (2012) [23] |
| Chronic inflammatory processes in women reproductive system | E. Shevchenko (2010) [5] |
| Damage of the coronary artery associated with Kawasaki disease | K. Jamamura (2012) [47] |
| Chronic prostatitis | M. Shatohin, A. Konoplya (2011) [25] |
| The combination of chronic obstructive bronchitis with coronary heart disease | E. Suslova, L. Vasilyeva (2013) [48] |
| Thrombosis | T. Subbotina, A. Petuhova (2012) [23] |
| Brain neoplasms | E. Stolbova, B. Bane (2009) [49] |
| Gingivitis | H. Mortazavi, G. Lotfi (2015) [50] |
| Periodontal disease | B. Ramamoorthy, S.S. Varghese (2015) [51] |
| Minimal risk of development of gestosis Polyploidy Low-birth-weight fetus | F. Gilmiyarova, V. Radomskaya et al. (2007) [12, 45] |

by volume Me 12,70%; high saturation of cells with hemoglobin (Me 29,80 pg) is also very common. It should be noted that for patients with AB (IV) blood group the highest concentration of iron in serum – Me 18,8 $\mu\text{mol/l}$ was revealed, which is a prerequisite to supply these micronutrients systems heme synthesis, iron-containing non-heme proteins. The erythrocyte sedimentation rate in females was the lowest (Me 3 mm/h), which indirectly shows the optimal ratio of the electrophysiological parameters of the outer topography of erythrocytes, proteins and other components of blood plasma; characterizes the health of the examined women. The number of cells corresponds to the data in the general population, and the relative content of neutrophils is lower than in individuals with (I) B (II), (III) blood group – Me 51,25%. The absolute content of neutrophils was the lowest Me $3,35 \cdot 10^3/\text{ml}$. We can notice the lowest level of segmented neutrophils (Me 47%), which characterizes the slow maturation of neutrophils

In addition, it was noticed the highest absolute (Me $2,30 \cdot 10^3/\text{ml}$) and relative content of lymphocytes (Me 38%), representing the basis of any of the immunological phenomena of cellular and humoral performing constant immunological control the antigenic composition of cells, macromolecules, and receipts of foreign material from outside. In those with AB (IV) blood group, the content of IgA (Me 3,64 g/l), M (Me of 1,16 g/l) than in those with other blood groups. Therefore, a low content

of C-reactive protein is an indicator of the absence of factors inducing the production of acute-phase response. Along with this tendency to lymphocytosis, a higher level of the entire studied range of immunoglobulins is used as an indication of tension specific resistance and a sufficient compensatory reserve in those with AB (IV) blood group is the result qualified them as healthy individuals.

However, women with AB (IV) blood group had the highest relative content of monocytes (Me 9%), which indicates the presence of stimuli that provoke their increased education for the phagocytosis of pathogens in tissues and integration of the production of cytokines, interleukins, interferons, and components of the complement of a complex mechanism of the immune response. Women with AB (IV) blood platelet count (Me $245 \cdot 10^9/\text{l}$) is lower than in the General population (Me $254 \cdot 10^9/\text{l}$) and patients with 0 (I) and a (II) blood group – Me of $268,5 \cdot 10^9/\text{l}$ and $254 \cdot 10^9/\text{l}$, respectively, and platelets are the most heterogeneous in size, as evidenced by the width of the distribution of platelets according to this indicator (Me 13,85%). Men with this blood group had the smallest number of leukocytes (Me of $5,75 \cdot 10^9/\text{l}$) due to the decrease in the absolute content of neutrophils (Me of $2,80 \cdot 10^3/\text{ml}$) lymphocytes (Me of $1,80 \cdot 10^3/\text{ml}$). For platelets it was typical to had the smallest average volume (Me 10,0 fl) and the large number of them in the blood (Me $262 \cdot 10^9/\text{l}$). Significantly reduced the average concentration of hemoglobin

in one erythrocyte (Me of 33,3 g/dl; $p < 0,05$), most pronounced anisocytosis of erythrocytes (Me 13,3%), and high erythrocyte sedimentation rate (Me 4 mm/h).

The specificity of the owners of AB(IV) blood group is the minimum number of diseases. It is known the predisposition of carriers of AB(IV) to have acute respiratory viral infections, sore throat, chronic tonsillitis, sinusitis (Table 4). Apparently, such parameters of metabolism and cellular composition, described earlier, provide a sufficiently high level of health.

The presented results show that there are group-specific peculiarities of metabolism, the knowledge of which is not only informative in theoretical way, but also applied on the basis of which we have composed the metabolic profile of individuals with O (I) – AB (IV) blood groups [53]. Summarizing the obtained data, it can be argued that a cer-

tain group of genetically determined specificity of the associated molecular processes [54, 55], which, in turn, are obviously a prerequisite for the formation of different health quality (Table 5).

Conclusions

The obtained data are the actual material, revealing individual characteristics of the features of many molecular processes in the personalized indicator – ABO blood group system. Biological variability of cellular composition of blood and metabolism in various blood groups, in our view, are a prerequisite for the formation of various quality health; serve as the basis for creating an individual health passport, providing increase of accuracy and expansion of the prospects for personalized and predictive medicine as markers of preclinical diagnostics of diseases and monitoring the effectiveness of treatment.

Table 4

Link between blood groups AB(IV) and diseases

| | |
|-------------------------------------------------|--------------------------------|
| Sore throat Chronic tonsillitis Sinusitis | S. Garmonov et al. (2004) [17] |
| Nasopharynx cancer | Sheng Liming (2013) [6] |

Table 5

| O (I) | A (II) | B (III) | AB (IV) |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> – High level of $\alpha 1$, $\alpha 2$, β-globulin, urea, CRP; – The lowest level of the uric acid, glucose, HDL, LDL; The lowest level activity of AST; – Low number of red blood cells; – Low level of hemoglobin in the blood | <ul style="list-style-type: none"> – Reduced level of albumin, γ-globulin, IgA; – Increased level Ig M, Ig G; – Low cholesterol, HDL; – The lowest value of hematocrit, average content of hemoglobin in one erythrocyte, the average volume of platelets; The maximum number of leukocytes, neutrophils, lymphocytes | <ul style="list-style-type: none"> The highest rates of albumin and albumin fractions, glucose, cholesterol; The highest level of activity of AST, LDH; The minimum value of SRB, Ig A, Ig M, Ig G; The minimum value of LDL cholesterol, triglycerides; – The largest volume of platelets, the average concentration of hemoglobin in one red blood cell | <ul style="list-style-type: none"> The highest protein content, uric acid; – The lowest value of urea, direct bilirubin, triglycerides; – The highest absolute and relative content of lymphocytes |
| ↓ | ↓ | ↓ | ↓ |
| propensity for somatic diseases | propensity for infectious diseases | high health level | high health level |

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