TSYMBRYLA, Volodymyr, BARYLYAK, Liliya, ŻUKOW, Xawery and POPOVYCH, Igor. Metabolic accompaniment of plasma lipoproteins profile in persons with maladaptation. Journal of Education, Health and Sport. 2023;42(1):174-188. eISSN 2391-8306. https://dx.doi.org/10.12775/JEHS.2023.42.01.016 https://apcz.umk.pl/JEHS/article/view/49678 https://zenodo.org/records/10867732

The journal has had 40 points in Ministry of Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 17.07.2023 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines as signed: Health Sciences (Field of medical and health sciences); Medical sciences (Field of medical and health sciences) Punkty Ministerialne z 2019 - aktualny rok 40 punktów. Załącznik do komunikatu Ministra Edukacji i Nauki a nati Archa o Induca nana natu activity. Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki medyczne (Dziedzina nauk medycznych i nauk o zdrowiu). The Authors 2023:

© The Authors 2023; This article is published with open access at Licensee Open Journal Systems of Nicolaus Copernicus University in Torun, Poland Open Access. This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author (s) and source are credited. This is an open access article licensed under the terms of the Creative Commons Attribution Non commercial license Share alike. (http://creativecommons.org/licenses/by-nc-sa/4.0/) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited. The authors declare that there is no conflict of interests regarding the publication of this paper. Received: 14.06.2023. Revised: 11.07.2023. Accepted: 27.07.2023.

Metabolic accompaniment of plasma lipoproteins profile in persons with maladaptation

Volodymyr V. Tsymbryla<sup>1,2</sup>, Liliya G. Barylyak<sup>1,2,3</sup>, Xawery Żukow<sup>4</sup>, Igor L. Popovych<sup>1,2,3</sup>

# <sup>1</sup>Ukrainian Scientific Research Institute of Medicine of Transport, Odesa, Ukraine <sup>2</sup>Scientific group of Balneology of Hotel&Spa Complex "Karpaty", Truskavets', Ukraine liliabaryliak@gmail.com; cymbryla@gmail.com

<sup>3</sup>OO Bohomolets' Institute of Physiology, Kyïv, Ukraine i.popovych@biph.kiev.ua <sup>4</sup>Medical University of Bialystok, Bialystok, Poland xaweryzukow@gmail.com

# **Summary**

Background. During the implementation of the project "The relationship between the lipoprotein profile of the blood plasma and the parameters of the neuroendocrine-immune complex, and the influence of the factors of the Truskavets' spa on them", we first divided observed cohort into 5 homogeneous groups that differed from each other by 6 discriminant variables. The **purpose** of this study is to identify the metabolic accompaniment of plasma lipoprotein profile in the same persons.

Material and research methods. The object of observation were 41 volunteers: 20 women aged 30-76 years and 21 men aged 24-69 years without clinical diagnose but with dysfunction of neuroendocrine-immune complex and dysmetabolism. We estimated lipoprotein profile of plasma, determined the levels of the proinflammatory cytokines, parameters of lipid peroxidation as well as routine biochemical and paraclinical parameters.

Results. The patients with increased, normal and decreased levels of Dobiásová's&Frohlich's Atherogenic Index of Plasma (D&FAIP) are characterized, together with levels of Triglycerides and HDLP Cholesterol by definition, by specific constellations of levels of IL-6, IL-1, Diene conjugates, Malondialdehyde, Katalase, Glucose, and Alanine aminotransferase (classification accuracy is 98.8%). A close canonical correlation was found between the parameters of the plasma lipoprotein profile, on the one hand, and metabolism and erythroon, on the other (R=0.920).

**Conclusion.** Atherogenic, normal and anti-atherogenic blood plasma is characterized by specific levels of markers of inflammation, lipid peroxidation, cytolysis and erythroon.

**Keywords:** lipoprotein profile of plasma, atherogenic indexes, metabolic parameters, males, females, cluster analysis.

# Introduction

During the implementation of the project "The relationship between the lipoprotein profile of the blood plasma and the parameters of the neuroendocrine-immune complex, and the influence of the factors of the Truskavets' spa on them", we [2] first divided observed cohort into 5 homogeneous groups that differed from each other. It was found that 11 members of the V cluster, the oldest in the sample, exclusively women, had the maximum for sampling increased total Cholesterol, HDL-Ch and Triglycerides levels. At the opposite pole localized 11 members of I cluster, the youngest in the sample, in whom the levels of listed variables as well as LDL-Ch and Dobiásová&Frohlich atherogenic index of plasma (AIP) was decreased and gender representation was almost the same. The intermediate positions of the members of the other three clusters reflect, as a rule, the intermediate levels of the listed variables. Overall classification accuracy by 6 discriminant variables was 96.3%. Thus, the plasma lipoprotein profile of persons with maladaptation is characterized by a wide range of values, from increased to decreased.

The **purpose** of this study is to identify the metabolic accompaniment of plasma lipoproteins profile in the same persons.

## Material and research methods

The object of observation were 41 volunteers: 20 women aged 30-76 years and 21 men aged 24-69 years without clinical diagnose but with dysfunction of neuro-endocrine-immune complex and dysmetabolism, characteristic for maladaptation and premorbid state.

We estimated lipoprotein profile of plasma: total cholesterol (by a direct method after the classic reaction by Zlatkis-Zack) and content of it in composition of HDL (by the enzyme method by Hiller [13] after precipitation of VLD&LD Ls particles in the infranatant with heparin manganese chloride).

VLDLCh was calculated by the level of triglycerides (estimated by meta-periodate method) as ratio TG/2.1834); LDLCh was calculated with the Friedewald et al. [8] formula. Based on them, two AIPs were calculated: TG/HDLCh [4,5,6,20] named as Dobiásová's&Frohlich's, and previously widely used Klimov's AIP as ratio (VLDLCh + LDLCh)/HDLCh [17].

In addition, after determining the percentage of lipoproteins (Lipoproteinogram) we calculated the Entropy of Lipoproteinogram (hLPG) using Popovych's [12] formula based on classic Shannon's [24] formula:

 $hLPG = - (HDLCh \cdot log_2 HDLCh + LDLCh \cdot log_2 LDLCh + VLDLCh \cdot log_2 VLDLCh)/log_2 3.$ 

We determined also the levels of the proinflammatory cytokines IL-1 and IL-6 (ELISA, analyzer "RT-2100C", reagents from "Vector-Best"); products of lipid peroxidation: diene conjugates (spectrophotometry of heptane phase of lipids extract) [10] and malondialdehyde (test with tiobarbiture acid) [1], the activity of antioxidant enzymes: katalase serum (by the speed of decomposition hydrogen peroxide) [18] and superoxide dismutase erythrocytes (by the degree of inhibition of nitroblue tetrazolium recovery in the presence of N-methylphenazone metasulfate and NADH) [7,19]; routine biochemical parameters: glucose (glucose-oxidase method), creatinine (by Jaffe's color reaction by Popper's method), urea (urease method by reaction with phenolhypochlorite), uric acid (uricase method), bilirubin (by diazoreaction using the Jedrashik-Kleghorn-Grof method), asparagine and alanine transaminase as well as  $\gamma$ -glutamiltranspeptidase according to instructions [11] with the use of analyzers "Reflotron" (BRD) and "Pointe-180" (USA) and corresponding sets of reagents. By default, a general blood test was performed.

Each volunteer was tested twice with a 4-day interval.

Reference values of variables, taking into account sex and age, are borrowed from the instructions and handbooks [11,15].

Statistical processing performed using a software package "Microsoft Excell" and "Statistica 6.4 StatSoft Inc" (Tulsa, OK, USA).

# **Results and discussion**

Adhering to the previously tested algorithm [22,23] for the purpose of correct comparison, registered variables (V) expressed as Z-scores calculated by formula:

Z = (V/N - 1)/Cv, where

N is mean of normal (reference) Variable, Cv is coefficient its variation.

Further, the characteristic variables were selected and condensed into 7 patterns (Fig. 1).

In the first pattern, triglycerides and IL-6 are collected, the levels of which are significantly increased in members of cluster V, moderately increased in clusters IV&III, normal in II and moderately decreased in members of cluster I. The members of clusters V and I occupy polar positions also in the second pattern, in which HDLP Cholesterol, IL-1, Lipoproteinogram entropy are collected, instead, members of cluster III rose to the second position; Glucose was also included in the pattern structure. The hierarchy of the third pattern is headed by the members of clusters IV due to the maximum levels of Dobiásová's&Frohlich's AIP and HDLP Cholesterol as well as Hemoglobin.



Fig. 1. The patterns of Lipids-Metabolic-Erythrocyte variables of lipoprotein clusters

The fourth pattern is led by members of cluster III due to the maximum levels of alanine transaminase and  $\gamma$ -glutamyltranspeptidase as well as bilirubin free and Erythrocytes sedimentation rate. The structure of the remaining patterns is unclear.

In order to identify among the registered parameters, those for which the clusters differ from each other, a discriminant analysis was performed [16]. The program forward stepwise included in the discriminant model 10 parameters. The rest of the variables were left out of the model (Tables 1 and 2).

**Table 1.** Discriminant Function Analysis Summary for Variables, their actual levels for Clusters as

 well as Reference levels and Coefficients of Variability

	Clust	ers (n)				Param	Parameters of Wilk's Statistics					
Variables	Ι		III	IV	V	Wilks	Parti-	F-re-	p-	Tole-	Refe-	Cv
currently	(11)	(27)	(26)	(7)	(11)	Λ	al $\Lambda$	move	value	rancy	rence	
in the model								(4.68)			(41)	
Triglycerides,	0.39	1.16	1.79	1.93	2.62	0,012	0,427	22,8	10-6	0,063	1.13	0.587
mM/L	0.04	0.06	0.05	0.09	0.12						0.10	
Dobiásová's &	0.37	0.81	1.03	1.34	1.21	0,019	0,267	46,7	10-6	0,052	0.82	0.442
Frohlich's AIP	0.03	0.04	0.02	0.11	0.07						0.06	
Klimov's Athero-	2.81	2.52	2.40	3.21	2.26	0,013	0,398	25,7	10-6	0,306	2.89	0.245
genic Ind Plasma	0.09	0.06	0.03	0.14	0.07						0.11	
Interleukin-6,	7.23	6.07	5.90	4.90	3.81	0,006	0,871	2,52	0,049	0,075	4.25	0.324
ng/L	0.28	0.24	0,12	0,14	0.26						0.22	
Interleukin-1,	5.56	4.63	5.16	4.87	4.42	0,009	0,590	11,8	10-6	0,076	4.51	0.173
ng/L	0.41	0.31	0.28	0.27	0.44						0.12	
Malondialdehyde,	68.5	87.2	76.6	81.1	75.6	0,005	0,925	1,37	0,253	0,778	77.5	0.339
μM/L	4.8	5.1	3.4	3.0	3.7						4.1	
Diene conjugates,	1.15	1.08	1.17	1.11	1.10	0,006	0,907	1,75	0,149	0,610	1.90	0.279
E <sup>232</sup> /mL	0.06	0.08	0.04	0.04	0.04						0.08	
Katalase,	101	145	112	152	141	0,006	0,903	1,83	0,133	0,751	125	0.458
µM/L∙h	13	18	9	10	15						9	
Glucose,	6.56	4.93	5.31	5.14	5.14	0,006	0,838	3,27	0,016	0,908	5.22	0.171
mM/L	0.55	0.14	0.15	0.09	0.10						0.14	
Alanine amino-	22.1	14.9	43.5	25.8	17.6	0,006	0,854	2,91	0,028	0,895	23.0	0.372
transferase, IU/L	3.3	2.6	6.3	3.6	1.9						1.3	
Variables	Ι		III	IV	V	Wilks	Parti-	F to	p-	Tole-	Refe-	Cv
currently not	(11)	(27)	(26)	(7)	(11)	Λ	al $\Lambda$	enter	value	rancy	rence	
in the model											(41)	
HDLP Choleste-	1.06	1.45	1.73	1.47	2.20	0,005	0,977	0,400	0,808	0,438	1.39	0.298
rol, mM/L	0.03	0.03	0.03	0.08	0.08						0.06	
LDLP Choleste-	2.76	3.07	3.32	3.77	3.72	0,005	0,981	0,322	0,863	0,892	3.46	0.192
rol, mM/L	0.08	0.04	0.04	0.13	0.07						0.10	
Lipoproteinogram	0,91	0,84	0,87	0,81	0,68	0,005	0,986	0,234	0,918	0,819	0.781	0.104
entropy	0,01	0,01	0,01	0,01	0,01						0.012	
Superoxide dis-	66.4	73.9	64.5	76.2	83.2	0,005	0,986	0,227	0,923	0,591	62.0	0.286
mutase, units/mL	4.7	5.8	3.8	2.6	6.5						2.8	

Step 10, N of vars in model: 10; Grouping: 5 grps; Wilks' Λ: 0.0050; appr. F<sub>(40)</sub>=19.7; p<10<sup>-6</sup>

Erythrocytes sedi-	7.5	3.9	8.5	5.0	4.6	0,005	0,945	0,98	0,424	0,890	7,0	0.395
mentat. rate, mm/h	1.4	1.0	1.6	0.8	0.9						0.4	
Hemoglobin,	141	151	138	141	134	0,005	0,959	0,72	0,583	0,882	139	0.056
g/L	5	2	3	3	3						1.2	
Bilirubin free,	10.7	9.65	11.9	10.2	9.44	0,005	0,973	0,466	0,760	0,834	8.55	0.450
μM/L	1.4	1.11	1.0	0.6	0.72						0.60	
Γ-glutamiltrans-	33	21	61	37	26	0,005	0,983	0,297	0,879	0,121	49	0.372
peptidase, IU/L	6	3	9	4	2						3	

Note: Mean±SE are given for variables. Reference values are not subject to discriminant analysis.

Table 2. Summary of Stepwise Analysis for Variables, ranked by criterion Lambda

Variables	F to	p-	Λ	F-va-	p-
currently in the model	enter	value		lue	value
Interleukin-6, ng/L	148,3	10-6	0,115	148,3	10-6
Klimov's Athe-rogenic Index	17,26	10-6	0,060	58,42	10-6
Dobiásová's & Frohlich's AIP	9,15	10-5	0,040	39,10	10-6
Triglycerides, mM/L	29,74	10-6	0,016	41,23	10-6
Interleukin-1, ng/L	15,24	10-6	0,008	39,09	10-6
Glucose, mM/L	2,60	0,043	0,007	32,42	10-6
Alanine aminotransferase, IU/L	2,41	0,057	0,007	27,95	10-6
Katalase, µM/L•h	1,89	0,123	0,006	24,57	10-6
Diene conjugates, E <sup>232</sup> /mL	1,41	0,241	0,005	21,85	10-6
Malondialdehyde, µM/L	1,37	0,253	0,005	19,73	10-6

Next, the 10-dimensional space of discriminant variables transforms into 4-dimensional space of a canonical roots, which are a linear combination of discriminant variables. The canonical correlation coefficient is for Root 1 0,965 (Wilks'  $\Lambda$ =0,0050;  $\chi^2_{(40)}$ =389; p<10<sup>-6</sup>), for Root 2 0,890 (Wilks'  $\Lambda$ =0,0738;  $\chi^2_{(27)}$ =192; p<10<sup>-6</sup>), for Root 3 0,744 (Wilks'  $\Lambda$ =0,3546;  $\chi^2_{(16)}$ =76; p<10<sup>-6</sup>) and for Root 4 0,455 (Wilks'  $\Lambda$ =0,793;  $\chi^2_{(7)}$ =17; p=0,017). The first root contains 72,0% of discriminative opportunities, the second 20,1%, the third 6,5%, and the last 1,4% only.

The calculation of the discriminant root values for each person as the sum of the products of raw coefficients to the individual values of discriminant variables together with the constant (Table 3) enables the visualization of each individual in the information space of the roots.

Coefficients	Standar	dized		Raw		
Variables currently in the model	Root 1	Root 2	Root 3	Root 1	Root 2	Root 3
Interleukin-6, ng/L	-0,694	-1,040	0,711	-1,890	-2,834	1,937
Klimov's Atherogenic Index Plasma	-0,618	-0,977	-1,199	-2,453	-3,881	-4,759
Dobiásová's & Frohlich's AIP	1,887	3,637	0,763	10,23	19,71	4,137
Triglycerides, mM/L	-0,867	-3,192	-0,796	-3,095	-11,39	-2,840
Interleukin-1, ng/L	1,702	1,713	-0,671	6,759	6,802	-2,665
Glucose, mM/L	0,005	-0,434	0,034	0,006	-0,521	0,040
Alanine aminotransferase, IU/L	-0,012	0,214	0,294	-0,001	0,010	0,014
Katalase, µM/L•h	-0,122	0,285	0,026	-0,003	0,006	0,001
Diene conjugates, E <sup>232</sup> /mL	-0,138	0,325	0,277	-1,476	3,476	2,968
Malondialdehyde, µM/L	-0,223	0,216	-0,099	-0,014	0,014	-0,006
	Constan	ts		-2,830	3,400	5,448
	Eigenva	lues		13,67	3,808	1,237
	Cumula	tive propo	ortions	0,720	0,921	0,986

Table 3. Standardized and Raw Coefficients and Constants for Variables

Table 4 presents the full structural coefficients, that is, the coefficients of correlation between the discriminant root and variables. There are also average values (centroids) of Roots and Z-scores of Variables, both discriminant and not included in the model due to duplication/redundancy of information.

Variables	Correlat	tions		Ι		III	IV	V
	Variable	es-Roots		(11)	(27)	(26)	(7)	(11)
Root 1 (72,0%)	R 1	R 2	R 3	-7,4	-1,3	1,5	3,1	5,0
Interleukin-6	0,730	-0,326	-0,001	-0,32	0,47	1,20	1,32	2,16
Interleukin-1	0,715	-0,294	-0,057	-0,11	0,46	0,83	0,15	1,34
Triglycerides	0,626	-0,233	-0,008	-1,02	0,20	0,78	1,41	1,98
Dobiásová's & Frohlich's AIP	0,404	0,121	-0,216	-1,05	0,20	0,37	1,65	0,78
HDLP Cholesterol				-0,85	<b>0,16</b>	0,87	0,25	1,99
Lipoproteinogram entropy				-1,26	0,39	1,09	0,68	1,59
Superoxide dismutase				1,19	0,80	0,14	0,67	0,25
Root 2 (20,1%)	R 1	R 2	R 3	-2,3	1,4	0,4	2,5	-3,6
Malondialdehyde	-0,018	0,151	-0,097	-0,08	0,13	-0,04	0,36	-0,35
Katalase	-0,065	0,112	-0,109	0,28	0,48	-0,22	0,34	-0,42
LDLP Cholesterol				-0,66	-0,31	-0,41	0,62	-0,12
Hemoglobin				-0,67	-0,22	-0,14	1,71	1,43
Glucose	0,088	-0,241	0,049	0,04	-0,06	0,02	-0,31	1,18
Bilirubin free				0,23	0,43	0,86	0,29	0,56
Erythrocyte sedimentation rate				-1,05	-0,61	0,46	-1,22	-0,32
Root 3 (6,5%)	R 1	R 2	R 3	-0,8	0,4	0,9	-3,0	-0,3
Klimov's Atherogenic Index	-0,104	0,185	-0,797	0,40	-0,27	-0,84	0,52	-1,18
Alanine aminotransferase	0,036	0,050	0,339	-0,64	0,32	2,40	-0,95	-0,11
Diene conjugates	0,045	-0,055	0,221	-1,50	-1,50	-1,37	-1,55	-1,41
Γ-glutamiltranspeptidase				-1,22	-0,90	0,62	-1,48	-0,34

Table 4. Correlations Variables-Canonical Roots, Means of Roots and Z-scores of Variables

The localization along the first root axis in the extreme left (negative) zone (Fig. 2) the members of cluster No.1 reflects theirs minimum for sampling normal IL-6 and IL-1 levels as well as decreased Triglycerides, HDLP Cholesterol, Entropy of Lipoproteinogram and Dobiásová's&Frohlich's AIP levels, on the one hand, and maximally increased activity of SOD - on the other hand. At the opposite pole of information field localized members of cluster No.5, in whom the levels of listed variables are maximally increased, while activity of SOD is norm. The intermediate positions of the members of the other three clusters reflect, as a rule, the intermediate levels of the listed variables. At the same time, the projections of members of cluster No.4 and No.3 are mixed, but they are clearly demarcated along the axes of the next two roots. In particular, top position members of cluster No.4 along the second root axis reflects theirs maximum for sampling levels of Malondialdehyde, Katalase, LDLP Cholesterol and Hemoglobin as well as minimum for sampling levels of Glucose, Bilirubin free and Erythrocyte sedimentation rate. The lowest position of members of this cluster along the third root axis

reflects theirs maximum for sampling level of Klimov's AIP as well as minimum for sampling levels of Diene conjugates, Alanine aminotransferase and  $\Gamma$ -glutamiltranspeptidase.



Fig. 2. Scattering of individual values of the discriminant Lipids-Metabolic-Erythrocyte roots of patients of different lipids clusters

In general, all clusters are clearly delineated on the planes of three roots, which is documented by calculating the Mahalanobis distances (Table 5).

**Table 5.** Squared Mahalanobis Distances between Lipids Clusters and **F-values** (df=11; for all  $p<10^{-6}$ )

Lipids	V	III	I	Ι	IV
Clusters	(11	(26)	(27)	(11)	(7)
V (11)	0	30.6	65.6	157	48.5
III (26)	20.9	0	10.5	88.5	22.2
II (27)	45.3	12.2	0	51.2	33.4
I (11)	76.2	60.4	35.6	0	137
IV (7)	18.3	10.8	16.4	51.9	0

The same discriminant parameters can be used to identify the belonging of one or another person to one or another cluster. This purpose of discriminant analysis is realized with the help of classifying functions and constants (Table 6).

We can retrospectively recognize members of four lipids clusters unmistakably and members of cluster No.2 with one mistake only. Classification accuracy is 98.8% (Table 7).

Lipids Clusters	V	Ш		Ι	IV
Variables currently in the model	p=.134	p=.317	p=.330	p=.134	p=.085
Interleukin-6, ng/L	94,48	94,35	93,41	114,7	77,19
Klimov's Atherogenic Index	55,35	45,26	48,25	84,27	51,20
Dobiásová's & Frohlich's AIP	-88,87	-44,53	-52,80	-192,6	-2,467
Triglycerides, mM/L	12,38	-24,18	-26,58	37,20	-42,02
Interleukin-1, ng/L	-67,84	-70,78	-78,36	-143,3	-34,42
Glucose, mM/L	8,937	6,440	6,384	7,791	5,347
Alanine aminotransferase, IU/L	-0,032	0,053	0,026	0,002	0,011
Katalase, µM/L•h	0,079	0,102	0,127	0,111	0,111
Diene conjugates, E <sup>232</sup> /mL	113,4	138,2	141,8	136,8	130,7
Malondialdehyde, µM/L	0,620	0,729	0,773	0,826	0,756
Constants	-359,2	-320,4	-301,4	-339,4	-348,5

Table 6. Coefficients and Constants for Classification Functions for Lipids Clusters

	Rows: Observed classifications Columns: Predicted classifications									
	Percent	V		II		IV				
Group	Correct	p=,13415	p=,31707	p=,32927	p=,13415	p=,08537				
V	100,0	11	0	0	0	0				
III	100,0	0	26	0	0	0				
II	96,3	0	1	26	0	0				
I	100,0	0	0	0	11	0				
IV	100,0	0	0	0	0	7				
Total	98,8	11	27	26	11	7				

Table 7. Classification Matrix

At the final stage, the canonical correlation between the parameters of the plasma lipoprotein profile, on the one hand, and the parameters of metabolism and erythroon, on the other hand, was analyzed. The lipid canonical root receives the maximum factor loadings from the elements of Dobiásová's & Frohlich's AIP formula as well as calculated on their basis Lipoproteinogram entropy, while Klimov's AIP gives the minimum loading, even more, with the opposite sign (Table 8).

Table 8. Factor structure	of Lipids and M	letabolic&Erythron	canonical Roots
---------------------------	-----------------	--------------------	-----------------

Left set	R
Triglycerides, mM/L	0,956
HDLP Cholesterol, mM/L	0,912
Lipoproteinogram entropy	0,893
Dobiásová's & Frohlich's AIP	0,786
LDLP Cholesterol, mM/L	0,734
Klimov's Atherogenic Index Plasma	-0,381
Right set	R
Interleukin-6, ng/L	0,978
Glucose, mM/L	0,367
Interleukin-1, ng/L	0,263
Diene conjugates, E <sup>232</sup> /mL	0,208
Erythrocyte sedimentation rate, mm/h	0,178
Hemoglobin, g/L	0,169
Bilirubin free, µM/L	0,163
Alanine aminotransferase, IU/L	0,128
Γ-glutamiltranspeptidase, IU/L	0,121
Superoxide dismutase, units/mL	-0,370
Katalase, µM/L•h	-0,277

The lion's share of loads on the metabolic root is obtained from IL-6, which correlates most closely with the parameters of the lipoprotein profile (Table 9). A much smaller loads is given by IL-1 and ESR as modern and good old markers of inflammation, respectively. Another constellation of the root factor structure consists of three parameters of lipid peroxidation, with opposite signs. This situation is consistent with the current view of atherosclerosis as chronic low-grade inflammation and oxidative stress [9,14,21,25]. The presence of glycemia in the structure of the root as a component of the metabolic syndrome is quite understandable as well as AlT and  $\gamma$ -GTP as markers of cytolysis, which in turn is a consequence of oxidative stress.

	Correlations							
Variable	ALP	TG	BLP	KAIP	DFAIP	hLPG		
ALP	1,00	0,79	0,64	-0,68	0,48	0,77		
TG	0,79	1,00	0,63	-0,25	0,90	0,92		
BLP	0,64	0,63	1,00	0,04	0,53	0,46		
KAIP	-0,68	-0,25	0,04	1,00	0,08	-0,43		
DFAIP	0,48	0,90	0,53	0,08	1,00	0,85		
hLPG	0,77	0,92	0,46	-0,43	0,85	1,00		
SOD	-0,33	-0,30	-0,26	0,16	-0,24	-0,32		
Katalase	-0,32	-0,18	-0,20	0,22	-0,05	-0,16		
DC	0,20	0,20	0,15	-0,14	0,13	0,20		
Glucose	0,33	0,36	0,19	-0,19	0,23	0,29		
Hb	0,09	0,15	0,07	0,00	0,19	0,18		
Bilir free	0,13	0,16	0,08	-0,04	0,16	0,19		
ALT	0,13	0,15	-0,01	-0,21	0,13	0,25		
GGTP	0,12	0,14	0,02	-0,17	0,11	0,22		
ESR	0,17	0,16	0,09	-0,13	0,12	0,19		
IL-6	0,81	0,87	0,66	-0,30	0,73	0,80		
IL-1	0,31	0,15	0,23	-0,23	0,04	0,16		

Table	9	Correl	lation	Matrix
Lanc	).	COLLE	auon	IVIALIA



R=0.920; R<sup>2</sup>=0.847; χ<sup>2</sup>(66)=193; p<10<sup>-6</sup>; Λ Prime=0.069

**Fig. 3.** Scatterplot of canonical correlation between Lipids (X-line) and Metabolic&Erythron (Y-line) parameters

Finally, the presence of hemoglobin in the structure of the root is associated, apparently, with erythrocytes, or rather with their sedimentation rate. Overall, the canonical correlation between the two sets is very strong (Fig. 3).

Against this background, Klimov's Atherogenic Index Plasma [17] looks like a "foreign body", because it is only weakly correlated with the main marker of atherogenicity such as triglycerides/VLDLPCh, and negatively correlated with markers of inflammation.

The following articles will analyze the relationship between the parameters of the plasma lipoprotein profile and the parameters of the neuroendocrine-immune complex at same patients.

#### Acknowledgment

We express sincere gratitude to administration of clinical sanatorium "Moldova" for help in conducting this investigation.

## Accordance to ethics standards

Tests in patients are conducted in accordance with positions of Helsinki Declaration 1975, revised and complemented in 2002, and directive of National Committee on ethics of scientific researches. During realization of tests from all participants the informed consent is got and used all measures for providing of anonymity of participants.

## Reference

1. Andreyeva LI, Kozhemyakin LA, Kishkun AA. Modification of the method for determining the lipid peroxide in the test with thiobarbituric acid [in Russian]. *Laboratornoye Delo*. 1988;11:41-43.

2. Barylyak LG, Tsymbryla VV, Zukow W, Popovych IL. Variants of plasma lipoprotein profile in persons with maladaptation. *Journal of Education, Health and Sport.* 2015;5(3):381-394. doi.org/10.12775/JEHS.2015.05.03.032

3. Barylyak LG, Tsymbryla VV, Zukow W, Popovych IL. Relationships between parameters of plasma lipoproteines profile and heart rate variability. *Journal of Education, Health and Sport*. 2019;9(12):238-253. doi.org/10.12775/JEHS.2019.09.12.025

4. Dobiásová M & Frohlich J. The plasma parameter log (TG/HDL-C) as an atherogenic index: correlation with lipoprotein particle size and esterification rate in apoB-lipoprotein-depleted plasma (FER(HDL)). *Clin Biochem.* 2001;34(7):583-588. doi:10.1016/s0009-9120(01)00263-6

5. Dobiásová M. AIP - aterogenní index plazmy jako významný prediktor kardiovaskulárního rizika: od výzkumu do praxe [AIP - atherogenic index of plasma as a significant predictor of cardiovascular risk: from research to practice]. Vnitr Lek. 2006;52(1):64-71. Czech. PMID: 16526201.

6. Dobiásová M, Frohlich J, Sedová M, Cheung MC, Brown BG. Cholesterol esterification and atherogenic index of plasma correlate with lipoprotein size and findings on coronary angiography. *J Lipid Res.* 

2011;52(3):566-571. doi:10.1194/jlr.P011668.

7. Dubinina YY, Yefimova LF, Sofronova LN, Geronimus AL. Comparative analysis of the activity of superoxide dismutase and catalase of erythrocytes and whole blood from newborn children with chronic hypoxia [in Russian]. *Laboratornoye Delo*. 1988;8:16-19.

8. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem.* 1972;18(6):499-502. PMID: 4337382.

9. Ganjali S, Gotto AM Jr, Ruscica M, Atkin SL, Butler AE, Banach M, Sahebkar A. Monocyte-to-HDLcholesterol ratio as a prognostic marker in cardiovascular diseases. *J Cell Physiol*. 2018;233(12):9237-9246. doi: 10.1002/jcp.27028.

10. Gavrilov VB, Mishkorudnaya MI. Spectrophotometric determination of plasma levels of lipid hydroperoxides [in Russian]. *Laboratornoye Delo*. 1983;3:33-36.

11. Goryachkovskiy AM. Clinical biochemistry [in Russian]. Odesa. Astroprint;1998:608.

12. Gozhenko AI, Korda MM, Popadynets OO, Popovych IL. *Entropy, Harmony, Synchronization and their Neuro-endocrine-immune Correlates* [in Ukrainian]. Odesa. Feniks;2021:232.

13. Hiller G. Test for the quantitative determination of HDL cholesterol in EDTA plasma with Reflotron®. *Klin Chem.* 1987;33:895-898.

14. Kılıç N, Tasci G, Yılmaz S, Öner P, Korkmaz S. Monocyte/HDL Cholesterol Ratios as a New Inflammatory Marker in Patients with Schizophrenia. *J Pers Med.* 2023;13(2):276. doi: 10.3390/jpm13020276.

15. Khmelevskyi YV, Usatenko OK. *Basic Biochemical Constants of Humans at Norm and at Pathology* [in Russian]. Kyïv. Zdorovya;1987:160.

16. Klecka WR. Discriminant Analysis [trans. from English in Russian] (Seventh Printing, 1986). In: *Factor, Discriminant and Cluster Analysis*. Moskva:Finansy i Statistika;1989:78-138.

17. Klimov AN, Nikulcheva NG. *Lipids, Lipoproteides and Atherosclerosis* [in Russian]. St-Pb. Piter Pres;1995:304.

18. Korolyuk MA, Ivanova MI, Mayorova IG, Tokarev VYe. The method for determining the activity of catalase [in Russian]. *Laboratornoye Delo*. 1988;1:16-19.

19. Makarenko YeV. A comprehensive definition of the activity of superoxide dismutase and glutathione reductase in red blood cells in patients with chronic liver disease [in Russian]. *Laboratornoye Delo*. 1988;11:48-50.

20. Niroumand S, Khajedaluee M, Khadem-Rezaiyan M, Abrishami M, Juya M, Khodaee G, Dadgarmoghaddam M. Atherogenic Index of Plasma (AIP): A marker of cardiovascular disease. *Med J Islam Repub Iran*. 2015;29:240. PMID: 26793631; PMCID: PMC4715400.

21. Petreski T, Piko N, Ekart R, Hojs R, Bevc S. Review on Inflammation Markers in Chronic Kidney Disease. *Biomedicines*. 2021;9(2):182. doi: 10.3390/biomedicines9020182.

22. Polovynko IS, Zajats LM, Zukow W, Yanchij RI, Popovych IL. Quantitative evaluation of integrated neuroendocrine and immune responses to chronic stress in rat male. *Journal of Education, Health and Sport*.

#### 2016;6(8):154-166. doi.org/10.5281/zenodo.60023

23. Popovych IL, Gozhenko AI, Korda MM, Klishch IM, Popovych DV, Zukow W (editors). *Mineral Waters, Metabolism, Neuro-Endocrine-Immune Complex*. Odesa. Feniks;2022:252.

24. Shannon CE. A mathematical theory of information. Bell Syst Tech J. 1948;27:379-423.

25. Zoubiri H, Tahar A, AitAbderrhmane S, Saidani M, Koceir EA. Oral Cholecalciferol Supplementation in Sahara Black People with Chronic Kidney Disease Modulates Cytokine Storm, Oxidative Stress Damage and Athero-Thromboembolic Risk. *Nutrients*. 2022;14(11):2285. doi: 10.3390/nu14112285.

26.