тамина D и некоторыми факторами риска, в частности вероятность наличия дефицита витамина D в крови весной была в 11 раз выше, чем осенью - отношение шансов (OR)=11.3 95% CI (1.4-90.6); между типом работы (физическая инактивация) и дефицитом витамина OR=3.5 95% CI (1.1-12.6); стилем одежды (закрытая одежда и головные уборы) и дефицитом витамина OR=8.0 95% CI (1.0 -64.1).

Результаты проведенного исследования позволяют заключить, что во время менопаузы особое внимание следует уделять детерминантам уровня витамина D - пребывание женщин на солнце и связанные с этим различные аспекты.

რეზიუმე

სხვადასხვა ფაქტორის გავლენა ქვემო ქართლის რეგიონში მცხოვრები ქალების D ვიტამინის დონეზე მენოპაუზის პერიოდში

[1]მ.ფანჩულიძე, [2]თ. გრძელიძე, [1]რ.კვანჭახაძე

[1]საქართველოს უნივერსიტეტი; [2]აკაკი წერეთლის სახელმწიფო უნივერსიტეტი, ქუთაისი, საქართველო

კვლევის მიზანს წარმოადგენდა ქვემო ქართლის რეგიონში მცხოვრებ ქალთა პოპულაციაში მენოპაუზის დროს მზის სხივების ექსპოზიციის გავლენის შესწავლა D ვიტამინის დონეზე და მიზეზ-შედეგობრივი ეპიდემიოლოგიური კვლევის საფუძველზე ეფექტური პრევენციული ღონისძიებების რეკომენდაციების შემუშავება.

ჩატარდა ჯვარედინ-სექციური (პრევალენტობის) კვლევა ქ. რუსთავის მაღალი მიმართვიანობით გამორჩეულ სამედიცინო დაწესებულებებში. საკვლევ პოპულაციას წარმოადგენდა 47-54 წლის ასაკის 198 ქალბატონი,რომლებსაც ბოლო 2 თვის განმავლობაში არ მიუღიათ D ვიტამინის შემცველი პრეპარატები ან კვებითი დანამატები. კვლევის ინსტრუმენტებს წარმოადგენდა სტანდარტული კითხვარი, სადაც D ვიტამინის დონეზე მომქმედ სხვადასხვა ფაქტორებთან ერთად განისაზღვრა დემოგრაფიული მახასიათებლებიც. სისხლში D ვიტამინის სკრინინგი 99 (50%) ქალს ჩაუტარდა გვიან შემოდგომაზე, 99 (50%) - გაზაფხულზე.

სისხლში D ვიტამინის დონე ნორმის ფარგლებში (≥30ნგ/მლ) დაუფიქსირდა 47 (24%) რესპოდენტს, უკმარისობა (10.9-29.9 ნგ/მლ) – 139 (70%) და დეფიციტი (1-10ნგ/მლ) - 12 (6%) რესპოდენტს. სისხლში D ვიტამინის დეფიციტით გამოვლენილთა შორის უმრავლესობა (90%) იყო ქალაქის მაცხოვრებელი, მათგან 77% ფიზიკურ სამუშაოებს ასრულებს. ღია სივრცეში მომუშავე, ეთნიკურად აზერბაიჯანელ და შემოდგომაზე გამოკვლეულ არცერთ რესპოდენტს სისხლში D ვიტამინის დეფიციტი არ დაუფიქსირდა. ბივარიაციული ანალიზით გამოვლინდა სტატისტიკურად სარწმუნო კორელაცია D ვიტამინის დონის დეფიციტსა და ზოგიერთ რისკის-ფაქტორს შორის, კერძოდ, გაზაფხულზე სისხლში D ვიტამინის დონის დეფიციტის არსებობის ალბათობა 11-ჯერ აღემატება შემოდგომისას - შანსების თანაფარდობა (OR)=11.3 95%CI (1.4-90.6); სამუშაოს ტიპს (ნაკლებ ფიზიკურ დატვირთვას) და D ვიტამინის დონის დეფიციტს შორის (OR)= 3.5 95%CI (1.1-12.6); ჩაცმის სტილს (დახურული სამოსის და თავსაფრის მატარებელი პირები) და D ვიტამინის დონის დეფიციტს შორის (OR)= 8.0 95%CI (1.0 -64.1).

ჩატარებული კვლევის შედეგებზე დაყრდნობით ავტორებს გამოტანილი აქვთ დასკვნა, რომ სისხლში D ვიტამინის დეფიციტის ზემოაღნიშნულ ფაქტორებთან კორელაციის გათვალისწინებით განაკუთრებული ყურადღება უნდა გამახვილდეს კლიმაქსის პერიოდში D ვიტამინის დონეზე მომქმედ ისეთ დეტერმინანტებზე, როგორიცაა მზის ქვეშ ყოფნის ექსპოზიცია და მასთან დაკავშირებული სხვადასხვა ასპექტები.

ASSOCIATION OF IL-10 AND RESISTIN IN APPARENTLY HEALTHY ELDERLY POPULATION

Jgarkava M., Pantsulaia I., Rukhadze R., Karanadze N., Chikovani T.

Tbilisi State Medical University, Vl. Bakhutashvili Institute of Medical Biotechnology, Georgia

There is a growing body of evidence suggesting that the elderly population is characterized by chronic low-grade inflammation (“inflammaging”), which is may contribute to the development of cardiovascular, autoimmune, cancerous and other medical disorders. Age associated inflammation can be caused by a decrease in the level of IL-10, one of the anti-inflammatory cytokines during aging [2,8]. IL-10 is mainly produced by macrophages and is responsible for suppressing inflammation. It inhibits macrophage activation, antigen presentation and pro-inflammatory cytokine (IL-6, TNF-α, IL-1β) secretion and activation. Moreover, the results of various studies show that IL-10 attenuates the inflammation associated with aging and improves insulin signal and glucose metabolism in skeletal muscle. IL-10 also is involved in pathogenesis of many autoimmune inflammatory diseases such as chronic inflammatory bowel disease, rheumatoid arthritis,

systemic lupus erythematosus, and multiple sclerosis [25]. Therefore, IL-10 may be one of the important biomarkers for the detection of inflammatory processes during aging [25]. In addition to its anti-inflammatory properties, the binding of IL-10 to adipose tissue is very important. In rats, IL-10 also affects adipocytes and may be considered as a therapeutic agent for the prevention of age-related glucose metabolism. Adipocytes, which increase in overweight individuals, synthesize various adipokines that directly or indirectly affect the number and balance of cytokines, which in turn further aggravates the inflammatory status.

Circulating resistin is one of the pleiotropic adipokine, impairing endocrine, paracrine and autocrine mechanisms. It participates in inflammation, as well as in pathologic processes such as endothelial dysfunction, thrombosis, angiogenesis and smooth-muscle cell damage [1,10,20,26].

Expression and secretion of resistin by mononuclear cells is due to inflammatory factors [22] that increase circulating resistin levels. A vicious circle is formed where resistin exacerbates inflammation [16,27]. It is also involved in developing atherosclerotic and cardiovascular diseases [3,7,13,18], non-alcoholic fatty liver, osteoporosis, cancer, asthma, Crohn disease, chronic kidney failure, metabolic and autoimmune pathologies (Diabetes mellitus type 2, systemic lupus erythematosus [13].

Resistin expression in cancer cells is associated with their aggressive nature [9]. Moreover, resistin regulates the production of MMPs and the secretion of VEGF, which is important in the process of neoangiogenesis and metastasis [18].

Moreover, several studies have found that metabolic disorders are less likely to be detected in the children of centenarians expressed lower prevalence of metabolic disturbances compared with age-matched control group [23]. According to Ostan et al. children of centenarians showed more “healthy aging” and different metabolic disruptions [15,29]. Regulation of circulating adipokines, cytokines and metabolic mediators was also diverse compared with children of non-long-lived parents. In addition, it is supposed that protective phenotype against metabolic disturbances and insulin resistance could be inherited from long-lived parents and be relevant for healthy aging process. Although metabolic disturbances were equally shown in offspring of centenarians and control group, children of long-lived parents with metabolic defects appeared healthier and their resistin levels were lower. Centenarian offspring with MetS had lower grade of resistin compared with a control group, but there was no difference between other inflammatory mediators(CRP, IL-6, TNF-α and TGF-β1), adiponectin, leptin, IGF-1, leptin-adiponectin ratio and resistin-IGF-1 ratio.

Based on above mentioned, the goal of our research was to study age-related changes in the anti-inflammatory cytokine IL-10 and adipokine circulating levels and their potential association.

Material and methods. The study was carried out on 150 apparently healthy volunteers (from 20 to 90 years old) in the Institute of Medical Biotechnology and Department of Immunology, Tbilisi State Medical University. Data were collected for each individual using a special questionnaire on age, sex, education, occupation, income, cigarette and alcohol consumption, physical activity, diet, body weight, height, transmitted infectious and chronic diseases, medical treatment, reproductive history in women. Individuals who were users of immunosuppressive drugs or alcohol and/or had pathologies affecting the immune system (infectious diseases, tumors, autoimmune and inflammatory pathologies, chronic liver pathologies, diabetes and asthma) were not included in the study. The study was conducted in accordance with the terms of the Helsinki Ethics Commission and was approved by the Bioethics Commission of the Tbilisi State Medical University. Each individual’s participation was voluntary and confirmed by the signature on the questionnaire.

Blood samples Collection. Blood samples were collected in vacutainers (10ml) in the morning after an overnight fast. Samples had been centrifuged at 1500-x g for 15 min, and plasma was aliquoted at 1 ml portions and was kept frozen -80C until their use in immunoassay.

Plasma levels of IL-10 and resistin were measured using commercial ELISA set (Thermofisher scientific, USA) according to the protocol. This assay employs the quantitative sandwich enzyme-immunoassay technique. The intra assay coefficient of variation was less than 5% and interassay coefficient of variation was 6%. Every sample was conducted in pairs and the mean value was used.

The general strategy of the quantitative traits analysis was included the following main stages: 1. Preliminary descriptive statistics. 2. Evaluation of statistically independent factors of the dependent variables.

Preliminary statistical calculations were performed by means of the STATISTICA 13.0 PC statistical package (Statsoft, Inc, USA). Initial analyses revealed that the biochemical indices were not distributed normally. Therefore, data were log transformed in the following analyses. To select potential covariates for the statistical analysis, all data were scanned for correlations with age, gender, body height, weight, and blood pressure. To make our study comparable to those reported by others men and women were divided into two age groups: I - ≤60 years; II - >60 years. Values of each variable that were not normally distributed therefore were log-transformed prior to analysis. A P-value of 0.05 or less was deemed significant for all analyses.

Results and discussion. In the first stage of the statistical analysis the studied biochemical parameters were scanned by gender. The results of the obtained descriptive statistics are presented in Table 1, where all data are shown in the original units according to gender before their logarithmic transformation. The results of our study correspond to the standards of healthy individuals offered by the immunoenzyme kits used in the study and fit within the norm.

The results of analysis revealed that there’s a statistically reliable difference in every parameter between female and male except of resistin (table 1). In addition, it is important to note that an increase in IL-10 is observed in postmenopausal women ($P<0.05$, Figure 1).

In the next phase of the study, the correlation between IL-10 and resistin plasma levels with age and other anthropometric parameters (weight, height, SBP, DBP) was evaluated.No statistically significant positive correlation was found between circulating IL-10 and age in both groups ($P>0.05$). However, the level of IL-10 in postmenopausal women shows an increasing trend. It should be noted that IL-10 levels in men correlated reliably with height and diastolic blood pressure readings (Table 2).

At the final stage of statistical analysis, the relationship between IL-10 and resistin was assessed in various groups. The results indicate that there is a direct statistically significant correlation between these studied variables only in women (Table 3).

Table 1. Descriptive statistics of studied traits according to gender

	Mean±SD (Min–Max)			
	Total	**Men**	**Women**	
Age	57.373±16.696 (21.000 - 83.00)	58.429±14.154 (24.000±78.00)	57.012±17.55 (21.000±83.00)	NS
Height	167.600±6.832 (155.000-193.00)	175.429±5.978 (165.000±193.00)	164.927±4.74 (155.000±176.00)	P<0.05
Weight	77.827±16.736 (38.000-121.00)	87.286±18.439 (51.000-121.00)	74.598±14.90 (38.000-113.00)	P<0.05
SPB	132.817±17.151 (100.000-180.00)	139.444±18.867 (101.000-180.00)	130.634±16.08 (100.000-180.00)	P<0.05
DPB	77.606±9.956 (55.000-105.00)	82.556±11.085 (65.000±105.00)	75.976±9.05 (55.000±101.00)	P<0.05
IL-10	4.209±10.498 (1.211-66.55)	1.848±0.683 (1.385-4.58)	5.147±12.30 (1.211-66.55)	P<0.05
Resistin	1447.261±757.076 (436.830-4883.19)	1414.554±614.043 (668.550-2899.46)	1469.934±812.63 (436.830-4883.19)	NS

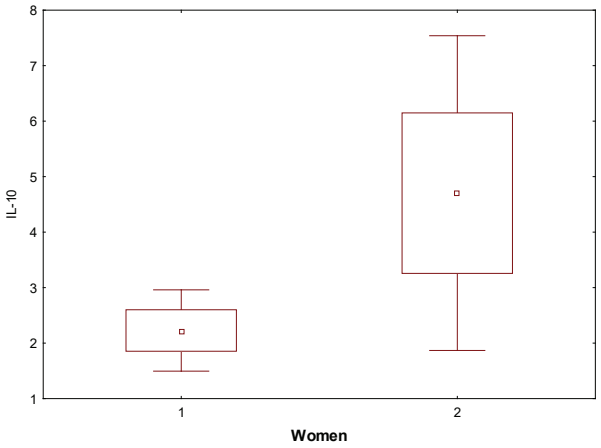

Fig. 1. Interleukin-10 levels in pre- and postmenopausal women

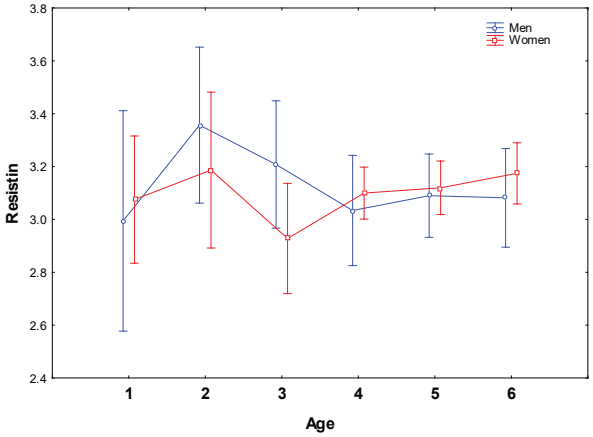

Fig. 2. Age and gender related changes of circulating resistin

Table 2. Relationship between IL-10 and resistin plasma levels according to gender

Parameters	**Total**		**Men**		**Women**	
	IL-10	**Resistin**	**IL-10**	**Resistin**	**IL-10**	**Resistin**
Age	.0163 p=.886	.0256 p=.823	-.0912 p=.687	-.2507 p=.260	.0154 p=.908	.1281 p=.342
Height	-.0006 p=.996	.0312 p=.785	**.5889 p=.004**	.0431 p=.849	.1518 p=.255	.0381 p=.778
Weight	-.0291 p=.798	-.0181 p=.874	.2642 p=.235	-.0112 p=.960	.0055 p=.967	-.0244 p=.857
Systolic blood pressure	-.1425 p=.213	.0915 p=.428	.2852 p=.210	-.1733 p=.452	-.1627 p=.222	.2101 p=.117
Diastolic blood pressure	-.0862 p=.453	-.0158 p=.891	**.4662 p=.033**	-.0865 p=.709	-.1158 p=.387	-.0577 p=.670

Table 3. Correlation between IL-10 and resistin considering sex

	Resistin		
	Total	**Men**	**Women**
IL-10	.1946 p=.084	-.2751 p=.215	.2537 p=.050

To our knowledge, this is the first study to demonstrate that the IL-10 is correlated with the resistin levels in postmenopausal women. IL-10 produced by a variety of immune cells, including macrophages, dendritic cells, T cells, and B cells [4] and is classically known to have anti-inflammatory properties. For example, it inhibits the action of Th1 cells by reducing the levels of various cytokines, including IL-6, interferon (IFN)-γ, and TNF-α [4]. Therefore, IL-10 is widely studied cytokine as well as an attractive candidate for the treatment of inflammatory diseases [30]. However, the role of IL-10 in white adipose tissue (WAT) metabolism as well as in the regulation of insulin sensitivity is controversial. A few experimental studies showed that IL-10 is increased in obesity [5,19], while after markedly reduction of WAT fat mass (very low-calorie diet and bariatric surgery) IL-10 levels downregulated [6]. Also, some studies suggested that anti-inflammatory properties of IL-10 can be associated with adipose tissue macrophages M2 polarization [14,31]. On the other hand, IL-10 ablation didn't lead to the insulin resistance, so it's importance in preventing or decreasing inflammation in the case of obesity wasn't confirmed [11,21].

Resistin is a fat-derived hormone that has anti-inflammatory properties [24]. It inhibits the expression of nitric oxide by endothelium, increases endothelial permeability, increases the expression of adhesive molecules and oxidative stress, and activates smooth muscle cell proliferation and migration. Resistin causes endothelial dysfunction leading to vascular abnormalities [12]. Several studies reported that resistin has an important role in different inflammatory conditions like ankylosing spondylitis, rheumatoid arthritis and others [17,32].

Despite experimental studies typically conducted in mouse models, further research in humans is needed, as direct interpolation of the results from experimental research on mice to humans is not easy.

Our study has several limitations, first of all the number of studied individuals, second - we have used frozen plasma. However, our finding is the first very important effort for clarification the direct association between IL-10 and resistin levels.

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SUMMARY

ASSOCIATION OF IL-10 AND RESISTIN IN APPARENTLY HEALTHY ELDERLY POPULATION

Jgarkava M., Pantsulaia I., Rukhadze R., Karanadze N., Chikovani T.

Tbilisi State Medical University, Vl. Bakhutashvili Institute of Medical Biotechnology, Georgia

There is a growing body of evidence suggesting that the elderly population is characterized by chronic low-grade inflammation ("inflammaging"). Age associated inflammation can be caused by a decrease in the level of IL-10, one of the anti-inflammatory cytokines during aging. The binding of IL-10 to adipose tissue is very important. In rats, IL-10 has also been shown to effect on adipocytes and may be considered as a therapeutic agent for the prevention of age-related glucose metabolism. Adipocytes, which increase in overweight individuals, synthesize various adipokines that directly or indirectly affect the number and balance of cytokines, which in turn further aggravates the inflammatory status.

The goal of our research was to study age-related changes of plasma levels of IL-10 and pleiotropic resistin and their potential association.

The study was carried out on 150 apparently healthy volunteers (from 20 to 90 years old). Anthropometric data were collected for each individual using a special questionnaire. Individuals who had pathologies affecting the immune system were not included in the study. Plasma levels of IL-10 and resistin were measured using commercial ELISA set (Thermofisher scientific, USA) according to the protocol.

The results revealed that there is a statistically significant difference in every parameter between female and male except of resistin. IL-10 levels are elevated in postmenopausal women ($P< 0.05$). While in men il-10 correlated reliably with height and diastolic blood pressure. The results indicate a direct statistically significant correlation between IL-10 and resistin only in postmenopausal women.

To our knowledge, this is the first study to demonstrate that the IL-10 is correlated with the resistin levels in postmenopausal women.

Keywords: aging, IL-10, resistin.

РЕЗЮМЕ

ВЗАИМОСВЯЗЬ ИНТЕРЛЕЙКИНА-10 И РЕЗИСТИНА У ЗДОРОВОГО НАСЕЛЕНИЯ

Джгаркава М.В., Панцулая И.Дж., Рухадзе Р.Г., Каранадзе Н.А., Чиковани Т.И.

Институт медицинской биотехнологии им. Вл. Бахуташвили, Тбилисский государственный медицинский университет, Грузия

В последние годы все более доступны данные, свидетельствующие, что наличие хронического воспаления слабой степени характерно для пожилых людей. Воспалительное старение может быть вызвано в процессе старения уменьшением количества одного из противовоспалительных цитокинов - интерлейкина-10. Взаимосвязь интерлейкина-10 с жировой тканью чрезвычайно значима. Эксперименты на крысах показали способность влияния интерлейкина-10 на адипоциты и позволяют предположить, что его можно использовать для предотвращения возрастных изменений метаболизма глюкозы. Адипоциты, количество которых значительно увеличивается при ожирении, синтезируют различные адипокины, прямо или косвенно влияющие на баланс цитокинов, что, в свою очередь, усугубляет воспалительное состояние.

Целью исследования явилось определение возрастного изменения уровня интерлейкина-10 и резистина в плазме и выявление возможной корреляции между ними.

Исследование проведено на 150 практически здоровых добровольцах в возрасте от 20 до 90 лет. Данные собирались с помощью специального вопросника. В исследование не включали индивидов, которые принимали иммунодепрессанты, алкоголь и/или имели заболевания иммунной системы. Уровни интерлейкина-10 и резистина в плазме измеряли с помощью ELISA (Thermofisher Scientific, США) согласно протоколу.

Результаты исследования показали, что существует статистически значимая разница между всеми параметрами у женщин и мужчин. Исключение составляет уровень резистина в плазме. Повышение концентрации интерлейкина-10 наблюдалось у женщин в постменопаузном периоде ($P<0,05$). Количество интерлейкина-10 у мужчин коррелировало с ростом и показателями диастолического артериального давления. Результаты подтверждают наличие статистически значимой корреляции между резистином и интерлейкином-10 только у женщин.

Настоящее исследование является первым, подтверждающим наличие достоверной связи между интерлейкином-10 и резистином у женщин после 60 лет.

რეზიუმე

ინტერლეიკინ-10-ს და რეზისტინის ურთიერთკავშირი ჯანმრთელ პოპულაციაში

მ.ჯღარკავა, ი.ფანცულაია, რ.რუხაძე,
ნ.კარანაძე, თ.ჩიქოვანი

ვლ.ბახუტაშვილის სახ. სამედიცინო ბიოტექნოლოგიის ინსტიტუტი, თბილისის სახელმწიფო სამედიცინო უნივერსიტეტი, საქართველო

უკანასკნელ წლებში მატულობს ასაკოვან პოპულაციაში დაბალი ხარისხის ქრონიკული ანთების არსებობის დამადასტურებელი მონაცემები. ასაკთან ასოცირებული ანთებითი პროცესი შესაძლოა გამოწვეული იყოს ერთ-ერთი ანთებისსაწინააღმდეგო ციტოკინის - ინტერლეიკინ-10-ის რაოდენობის ცვლილებით. აღსანიშნავია ასევე ინტერლეიკინ-10-ს კავშირი ცხიმოვან ქსოვილთან. კერძოდ, ინ ვივო ექსპერიმენტში გამოვლინდა ინტერლეიკინ-10-ის გავლენა ადიპოციტებზე და ნავარაუდებია, რომ ის, შესაძლოა, გამოყენებული იყოს ასაკთან დაკავშირებული გლუკოზის მეტაბოლიზმის ცვლილებების პრევენციისათვის. ადიპოციტები, რომელთა რაოდენობა მნიშვნელოვნად არის მომატებული სიმსუქნის დროს, ასინთეზებს სხვადასხვა ადიპოკინს, რაც პირდაპირ ან არაპირდაპირ გავლენას ახდენს ციტოკინების ბალანსზე, რაც, თავის მხრივ, ანთებითი მდგომარეობის დამძიმებას განაპირობებს.

კვლევის მიზანს წარმოადგენდა პლაზმაში ინტერლეიკინ-10-ისა და რეზისტინის რაოდენობის ასაკზე დამოკიდებული ცვლილებების შესწავლა და მათ შორის შესაძლო ურთიერთკავშირის დადგენა.

კვლევა ჩატარდა 150 პრაქტიკულად ჯანმრთელ მოხალისეზე 20-დან 90 წლამდე. მონაცემები თითოეულ ინდივიდზე შეგროვდა სპეციალური კითხვარის მეშვეობით. კვლევაში არ იყვნენ ჩართული პირები, რომლებიც მოიხმარდნენ იმუნოსუპრესიულ წამლებს, ალკოჰოლს და/ან აღენიშნებოდათ იმუნური სისტემის დაავადებები. ინტერლეიკინ-10-ის და რეზისტინის რაოდენობა პლაზმაში იზომებოდა იმუნოფერმენტული მეთოდით პროტოკოლის შესაბამისად (Thermofisher scientific, USA).

კვლევის შედეგებმა აჩვენა, რომ ქალებსა და მამაკაცებში, პლაზმაში რეზისტინის შემცველობის გარდა, ყველა შესწავლილი პარამეტრი სტატისტიკურად სარწმუნოდ განსხვავდება. ინტერლეიკინ-10-ს რაოდენობის მატება აღინიშნებოდა პოსტმენოპაუზურ ქალებში ($P<0.05$). ინტერლეიკინ-10-ს დონე მამაკაცებში კორელირებდა სიმაღლესა და სისხლის დიასტოლური წნევის მაჩვენებლებთან. მიღებული შედეგები ადასტურებს რეზისტინსა და ინტერლეიკინ-10-ს შორის სტატისტიკურად სარწმუნო კორელაციის არსებობას მხოლოდ ქალებში.

რამდენადაც ჩვენთვის არის ცნობილი, წინამდებარე კვლევა არის პირველი ნაშრომი, რომელიც ადასტურებს ინტერლეიკინ-10-ს და რეზისტინის სარწმუნო ურთიერთკავშირს პოსტმენოპაუზური პერიოდის ქალებში.

ALPHA- AND BETA-GLOBIN GENE MUTATIONS IN GEORGIA AND ARMENIA

[1]Oberkanins C., [2]Pagava K., [3,4]Babikyan D., [2]Korinteli I.A., [5]Phagava H., [3,4]Hayrapetian H., [6,7]Kriegshäuser G., [3,4]Sarkisian T.

[1]ViennaLab Diagnostics, Vienna, Austria; [2]Tbilisi State Medical University, Department of Child & Adolescent Medicine, Georgia; [3]Center of Medical Genetics and Primary Health Care, Yerevan, Armenia; [4]Yerevan State Medical University, Department of Medical Genetics, Armenia; [5]Tbilisi State Medical University, Department of Epidemiology & Biostatistics, Georgia; [6]IHR LABOR, Medical Diagnostic Laboratories, Vienna, Austria; [7]Clinical Institute of Medical and Laboratory Diagnostics, Medical University of Graz, Graz, Austria

Georgia and Armenia are situated at the juncture of Eastern Europe and Western Asia. Bordering to countries with a known high prevalence of thalassemias (Turkey, Iran, Azerbaijan), they represent the Northern rim of the so-called thalassemia belt. There is scarce literature about the prevalence of thalassemias in Georgia and Armenia, and the publications are mainly case reports [1-6]. The aim of the present study was to review existing data and to analyze the spectrum and carrier frequency of 21 α-globin and 47 β-globin mutations in random population samples from both countries.

Material and methods. Blood samples were obtained from 202 Georgian and 190 Armenian individuals without symptoms or reported family history of thalassemia. Georgian samples came from unselected newborns, whose heel had been pricked to collect blood drops on filter cards (Protein Saver Cards, Whatman, UK) at various hospitals in Tbilisi. Armenian samples were collected from 190 consecutive adult patients (16-84 years old) visiting the Center of Medical Genetics and Primary Health Care in Yerevan for various medical reasons. None of them had hematological abnormalities indicating a hemoglobinopathy. The present study was approved by the local ethics committees of Yerevan State Medical University and Tbilisi State Medical University and is in accordance with the latest version of the Declaration of Helsinki. Patients or parents of newborns provided appropriate informed consent.