

Ethnic features of the incidence rheumatoid arthritis population Republic of Dagestan

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Objective. Assessment of the incidence of rheumatoid arthritis (RA) of various ethnic populations of the Republic of Dagestan (RD).

Materials and methods. The epidemiological study included all cases of arthritis (80 531 cases with the disease code according to ICD-10 M00-M14) and RA (41 141 cases with the code M05-M06) registered in the RD for 2014-2018.

Results. An analysis of the ethnic composition of the population of the RD showed that more than 90% of representatives of one ethnic group (Avars, Dargins, Laks, Lezgins, Aguls) live mainly in mountainous areas in half of rural areas. The specific gravity of RA in the structure of arthritis ranged from 24.7% among Nogais to 84.0% among Rutuls. The average incidence rate of RA over 5 years among representatives of the Dargin, Lak and Rutul ethnic groups was above 1000 cases per 100,000 population, and among Tabasarans, Kumyks and Azerbaijanis below the level of 500 patients per 100,000 population. In 12 regions of the RD, the level of the disease of women exceeds the rate of men more than 2 times. The incidence rates of RA among men of Rutuls, Dargins, and Didos at working age were maximum, and among women of the same age, Dargin, Lak, and Rutul were the leaders. At retirement age, the maximum incidence of RA was observed in Dargin, Lak, and Rutul men, and in the female population, in Dargin, Lak, and Tabasaran.

Conclusion. The results of the study demonstrated the importance of the ethnicity of the population, along with gender and age, as a risk factor in the development of autoimmune diseases of joints.

Keywords: postmenopause, gene polymorphism, plasminogen activator inhibitor, methylenetetrahydrofolate reductase, cardiovascular complications

For citation: Saidova Z.M., Ataeva Yu.M. Ethnic features of the incidence rheumatoid arthritis population Republic of Dagestan. *Ecological Medicine* 2019;2(1):74-85. DOI: 10.34662/2588-0489.2019.2.1.74-85.

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Translated from *Ecologicheskaya medicina* 2019. Vol. 2, N 1, pp. 79-90.

Translated by Kakvaeva S.B.

Rheumatoid arthritis (RA) is an autoimmune disease with a number of risk factors, including both genetic and environmental ones [15]. It should be noted that the problems considered from the point of view of environmental medicine

are currently gaining special relevance. The occurrence of risk factors, their participation in the onset of diseases and poor health is one of the tasks of ecological physiology. It should be borne in mind that health is the result of a complex interaction

of the hereditary-constitutional qualities of an individual with specific natural environmental factors [4]. The modern definition of an ethnos as a group of people connected by the unity of their origin and community of culture, including language, is practically universally recognized and largely goes back to the definition given in 1923 by S. M. Shirokogorov: "Ethnos is a group of people" children who speak the same language, recognize their common origin, have a complex of customs, a way of life, kept and sanctified by tradition and distinguished by it from those of other groups. "He considered an ethnos as the main form of existence of local groups of humanity, and considered it the main signs of "unity of origin, customs, language and lifestyle" [12]. The long process of adaptation could not but leave an original imprint on the genetic apparatus, morphological, functional and metabolic characteristics of representatives of one or another ethnic group. Ethnic groups have arisen as a result of the accumulation of many genetic differences in people living in a certain area, the manifesting mutations spread throughout the group. The number of accumulated differences between groups is proportional to the time elapsed since the moment of their separation. Ethnicity is more or less stable, although it arises and disappears in historical time [6].

Currently, more and more researchers are inclined to the idea of preserving a unique gene pool that separates an ethnic group as a population, studying ethnic diseases, a differentiated approach to providing medical care, and taking into account national traditions in the provision and consumption of medical services [2, 9].

The study of the ethnic characteristics of adaptation to natural and climatic conditions and the adaptation of representatives of various ethnic groups to physical and other types of influences is a priority biomedical direction [3, 8]. Available materials indicate the presence of ethnic characteristics of the manifestation of adaptive reactions and their biochemical foundations.

The study included 204 patients with RA and 324 individuals from the control group from the Republic of Bashkortostan. In the

study of the -592C>A polymorphic locus of the IL10 gene, it was found that the CC genotype is a marker of an increased risk of developing RA ($p = 0.042$, odds ratio - OR = 1.467, 95% confidence interval - CI 1.015-2.122), while the CA genotype is associated with a reduced risk of disease variations ($p = 0.017$, OR = 0.634, 95% CI 0.436-0.922). After stratification according to ethnicity, both associations were characteristic of representatives of the Bashkir ethnic group (CC genotype: $p = 0.036$, OR = 3.221, 95% CI 1.070-9.879 and CA genotype: $p = 0.008$, OR = 0.224, 95% CI 0.071-0.692). Differences between patients with RA and individuals of the control group of the Russian ethnicity reached the level of statistical significance only for the CA genotype ($p = 0.027$, OR = 0.470, 95% CI 0.239-0.923) [7].

The most important genetic risk factor for RA is the HLA genes. An increase in the frequency of HLA-DRB1*04 in the RA group was established compared with the control group ($p = 0.000003$, OR = 3.62), i.e. this specificity is positively associated with RA. HLA-DRB1*13, on the contrary, has a lower frequency in patients compared with the control group, i.e., this allele may have a protective effect against RA ($p = 0.001$, OR = 0.37). There is a statistically significant correlation between the variants of the HLA-DRB1 gene and resistance / sensitivity to RA in the Kazakh population [10].

Our study identified 221 novel RA-linked genes and specifically highlighted the importance of 20 genes selected for RA. As a result, differences in the ethnic genetic background of RA susceptibility between European and Asian populations were studied and a long list of overlapping or ethnic specific RA genes was found. The study not only significantly increases our understanding of genetic susceptibility to RA, but also provides important insights into the ethnogenetic homogeneity and heterogeneity of RA in both ethnic groups [23].

Sixty-four percent of patients with rheumatoid arthritis in Qatar were in remission or had low disease activity, while the remaining 36% had active disease, and

among these patients 29% were on biological drugs [17].

Interethnic differences in the incidence of certain classes of diseases in the North Caucasus [11], in particular in the Republic of Dagestan [1], were revealed.

Objective: to study the susceptibility to RA morbidity of various ethnic populations of Dagestan.

Material and methods

According to the 2010 All-Russian Population Census [5], the ethnic structure of the

population of the regions of Dagestan was compiled. 36 districts out of 42 were identified, where more than 50% of people of one ethnic group live. In the 21 mountain regions of the Republic of Dagestan, the mono-ethnicity of the region exceeds 90%, which mainly includes the Avar, Dargin, Lak, Agul and Lezgin districts. According to the ethnic composition, 7 population groups were formed: Avar, Dargin, Kumyk, Lezgin, Lak, Nogai and Azerbaijani (Table 1).

Table 1. Ethnic composition of the population of the regions of Dagestan according to the 2010 census (%)

Prevailing ethnos	District	Avars	Dido (ceses)	Dargins	Kumyks	Laks	Lezgins	Aguls	Tabasarans	Rutuls	Nogays	Azerbaijanis
Avar	Botlikh	75.9										
	Gergebil	99.2										
	Gumbet	98.6										
	Gunib	94.4	2.0	2.5								
	Shamil	98.7										
	Tlyarata	98.4										
	Untsukul	97.5										
	Kazbek	85.9	1.2									
	Kizilyurt	83.4			10.5	1.5						
	Khunzakh	97.5										
	Tsumada	94.9										
	Charoda	97.3				1.5						
Dido	Tsunta	2.9	56.8									
Dargin	Akusha			96.0		3.2						
	Dakhadaev			99.0								
	Kaitag			90.1	8.4							
	Sergokala			98.9								
	Levashi	22.4		76.5								
Kumyk	Kayakent			42.3	52.4			1.5	1.7			
	Karabudakhkent			32.4	64.9							
	Kumtorkala	18.7		8.4	67.0	1.1	1.2					
	Buinaksky	23.5		13.4	61.1							
Lak	Kuli					97.4						
	Lak	1.1		2.0		95.2						
Lezgin	Akhti						98.5					
	Kurakh						98.4					
	Magaramkent						96.1					1.6
	Dokuzpara						94.0	2.3		3.0		
	Suleiman-Stalsky						98.6					
Agul	Agul			5.9				92.5				
Tabasaran	Tabasaran								79.1			
	Khiv						38.9		59.4			
Rutul	Rutul	1.5				3.4	8.4			60.0		3.1
Nogai	Nogai			8.1							87.0	18.4
Azerbaijani	Derbent			7.9			18.8	2.2	9.9			58.0

For the study, a database on the incidence and treatment of arthritis (code for ICD-10 M00-M14) for medical care of the

rural population of Dagestan for 2014-2018 was compiled. Information about the appeal of patients was obtained from the da-

tabase of the Territorial Fund of Compulsory Medical Insurance of the Republic of Dagestan. Our epidemiological study includes all cases of RA registered in the Republic of Dagestan for 2014-2018. In just 5 years, 80 531 cases of arthritis (M00-M14) were registered, of which 41 141 cases of RA (M05-M06). The population of

the Republic of Dagestan is divided into 11 language groups, among which the most cases of RA were found among Dargins (36.1%) and Avars (26.5%). The share of Avars among arthritis patients was 28.7%, and the share of Dargins was 28.4% (Table 2).

Table 2. Distribution of patients with arthritis and rheumatoid arthritis by ethnic group

Ethnic group	M00-M14 Arthritis	M05-M06 Rheumatoid arthritis
Avar	23156	10903
Dido	1059	613
Dargin	22889	14875
Kumyk	6464	3859
Lak	2806	1307
Lezgin	13350	4644
Rutul	1403	1179
Agul	888	362
Tabasaran	3009	1465
Nogai	2063	509
Azerbaijani	3444	1425

Age groups included working age (15-59 years old) and retirement age (60 years and older) age distribution by gender.

Statistical processing was performed using SPSS 20.0 and Excel 2010.

Results and its discussion

The study included patients with arthritis (codes according to ICD-10: M00-M14), identified in the first life years of 2014-2018 in the RD. Of these, RA was diagnosed in

24.7-84.0% of cases, depending on ethnicity.

A comparative analysis showed that the share of RA among arthritis in the Rutul, Dargin, Dido and Kumyk populations is greater than in the Nogai. The share of RA in the structure of arthritis is significantly greater among Dargins and Rutuls, than among Lezgins (Table 3).

Table 3. The incidence rate of arthritis and rheumatoid arthritis of the male and female population

Ethnos	Incidence, per 100,000 population		% RA of M00-M14	RA incidence: Women / Men
	M00-M14	RA		
Dargin	2031.7	1320.3	65.0	1.5
Laks	2434.9	1134.1	46.6**	1.9
Rutul	1315.1	1105.1	84.0	0.8
Agul	1771.3	722.1	40.8**	1.2
Dido	1111.8	643.6	57.9	0.9
Avar	1180.6	555.9	47.1**	1.8
Nogai	2161.0	533.2	24.7* **	1.5
Lezgin	1466.4	510.1	34.8* **	1.4
Tabasaran	856.7	417.1	48.7**	1.6
Kumyk	537.6	320.9	59.7	2.1
Azerbaijani	668.6	276.6	41.4**	1.8

* - significant difference ($P < 0.05$ for the Fisher z-test) in comparison with the Dido, Dargin, and Kumyk ethnic groups; ** - $P < 0.05$ compared with the Rutul ethnic group. M00-M14 - arthritis; RA - rheumatoid arthritis.

The incidence of RA in the female population of the RD prevailed over the rate of men. In Kumyks and Laks, women were 2 times more likely to get RA than men. An exception to this rule were Dido and Rutul ethnic groups with a prevalence of male RA incidence over that of women.

An analysis of the incidence of RA, carried out by sex, showed several differences

between ethnic groups. At the same time, among the Dargins, Laks, and Rutuls, the incidence of RA was above 1000 cases per 100,000 population, and among Tabasarians, Kumyks and Azerbaijanis, it was below the level of 500 patients per 100,000 population (Figure 1).

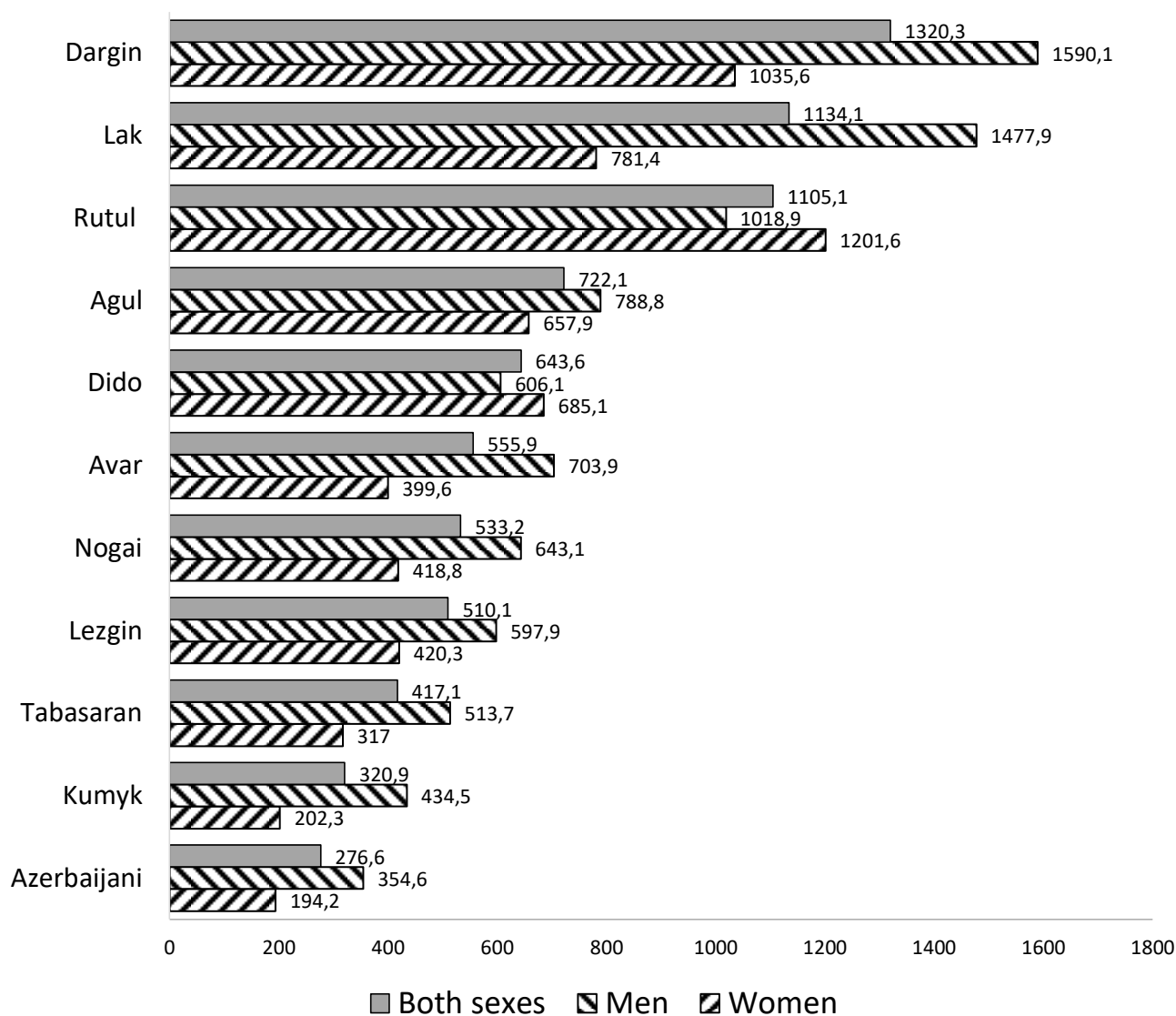


Figure 1. The incidence rates (per 100,000 of the population) of rheumatoid arthritis of ethnic groups, ranked in descending order.

A comparative analysis of the regional incidence of RA showed that within ethnic groups the indicator differed significantly between regions. Thus, the incidence of RA in the Botlikh district was characterized by the lowest level among the Avar districts, and in contrast to this region, the incidence in the Charoda district was 39.9 times higher, in Tlyarata - 22.5 times, in

Gergebil - in 19.8 times. Among Dargin districts, the minimum incidence rate of RA was noted in Sergokala district (434.9 cases per 100,000 population), the maximum level in Levashi district was 3.9 times higher than the previous one. In areas where more than 50% of the population of the Kumyk ethnic group lived, there was also a significant difference between the areas.

Thus, the maximum value of the indicator in the Kayakent district exceeded the minimum level in the Kumtorkala district by 7.2 times.

Among Laks, the multiplicity of exceeding the indicator in the Kuli district over the Lak district was 19.8 times. The Lezghin language group also showed a significant

inter-district difference with a maximum in Kurakh and a minimum in Dokuzpara (the difference was 76.9 times). Thus, the average ethnic characteristics of the incidence of RA had a significant amplitude of fluctuations in a comparative analysis of areas among one ethnic group.

Table 4. The incidence rate of arthritis and rheumatoid arthritis in the male and female population of the districts of Dagestan (per 100,000 population)

Ethnos	District	Incidence		% RA or M00-M14	RA incidence		Women / Men
		M00-M14	RA		Men	Women	
Avar	Botlikh	388.5	66.5	17.1	39.4	94.4	2.4
	Gergebil	2480.4	1317.2	53.1	1085.2	1538.3	1.4
	Gumbet	873.0	318.8	36.5	234.9	399.2	1.7
	Gunib	716.0	317.0	44.3	151.1	476.7	3.2
	Shamil	1147.7	247.1	21.5	155.1	333.9	2.2
	Tlyarata	2768.0	1494.5	54.0	1009.9	1950.1	1.9
	Untsukul	1303.1	810.7	62.2	495.9	1100.1	2.2
	Kazbek	575.4	394.4	68.5	270.7	509.9	1.9
	Kizilyurt	843.8	174.2	20.6	163.9	184.0	1.1
	Khunzakh	1635.6	996.7	60.9	590.3	1378.8	2.3
	Tsumada	1715.1	486.3	28.4	411.3	561.0	1.4
	Charoda	3004.5	2652.0	88.3	2349.0	2935.6	1.2
Dido	Tsunta	1111.8	643.6	57.9	685.1	606.1	0.9
Dargin	Akusha	3162.3	1542.3	48.8	1298.7	1782.6	1.4
	Dakhadaev	2061.0	1478.7	71.7	967.5	1963.7	2.0
	Kaitag	1237.5	728.1	58.8	444.9	993.0	2.2
	Sergokala	927.8	434.9	46.9	251.7	613.9	2.4
	Levashi	1984.8	1679.3	84.6	1441.8	1896.8	1.3
Kumyk	Kayakent	1050.2	852.4	81.2	487.6	1197.7	2.5
	Karabudakhkent	327.4	208.1	63.6	154.5	259.7	1.7
	Kumtorkala	274.3	204.2	74.5	146.1	261.6	1.8
	Buinaksk	492.8	118.0	24.0	79.4	155.1	2.0
Lak	Kuli	3764.1	2196.9	58.4	1571.9	2787.9	1.8
	Lak	1154.9	110.7	9.6	41.3	182.3	4.4
Lezgin	Akhti	1229.3	304.3	24.8	209.2	400.0	1.9
	Kurakh	1129.4	784.4	69.5	529.2	1035.5	2.0
	Magaramkent	1420.9	630.4	44.4	580.6	679.3	1.2
	Dokuzpara	618.6	10.2	1.7	7.8	15.1	1.9
	Suleiman-Stalsky	1968.9	557.4	28.3	449.3	660.3	1.5
Rutul	Rutul	1315.1	1105.1	84.0	1201.6	1018.9	0.8
Agul	Agul	1771.3	722.1	40.8	657.9	788.8	1.2
Tabasaran	Tabasaran	1073.2	535.4	49.9	405.4	662.3	1.6
	Khiv	324.1	126.1	38.9	93.0	158.1	1.7
Nogai	Nogai	2161.0	533.2	24.7	418.8	643.1	1.5
Azerbaijani	Derbent	668.6	276.6	41.4	194.2	354.6	1.8

M00-M14 - arthritis; RA - rheumatoid arthritis.



Figure 2. Monoethnic districts of Dagestan are highlighted in color. The incidence of rheumatoid arthritis of Avars is shown in shades of red; Dargins - in blue; Kumyks — green; Laks — brown; Lezgins, Rutuls, Aguls, Tabasarans - purple; Azerbaijanis and Nogais - blue. A light shade indicates a level of less than 500 per 100,000 population, an average intensity of 500–1300, and a dark color of more than 1300.

Probably, these significant fluctuations in the incidence of RA in the population of

certain regions were also reflected in the structure of detection of arthritis.

According to the study, significant fluctuations in the proportion of RA in the structure of arthritis in regional values were noted. In the Avar group of districts, the specific gravity of the RA ranged between 17.1% in the Botlikh district and 88.3% in the Charoda district, in the Dargin group - between 46% in the Sergokala district and 84.6% in the Levashi district, in the Kumyk districts - between 24% in Buinaksk and 81.2% in the Kayakent district, in the Lak group - between Lak (9.6%) and Kuli districts (58.4%). In the Lezgin group, between Dokuzpara (1.7%) and Kurakh districts (58.4%).

Therefore, if there are similar significant differences between ethnic groups, regions within an ethnic group, then it makes sense to study the incidence of RA in individual settlements. A study of the gender characteristics of the incidence of RA in the population of certain regions showed that the ratio of the incidence of women is higher than that of men.

So, in the Gunib district women became ill with RA 3.2 times, and in the Lak district

4.4 times more often than men. In 10 districts of the RD, the level of disease in women exceeds that of men from 2 to 3 times. The exceptions were indicators of the Tsunta and Rutul districts, where the ratio of the incidence rates of men and women showed the prevalence of the male rate over women (Table 4).

Mapping of the incidence of RA in populations of areas with different ethnicities is shown in Figure 2.

Areas with high incidence of RA are mainly located nearby in the highlands of the RD.

The incidence of RA in the retirement age exceeds that of the able-bodied population in all ethnic groups, except for the Agul people, among whom the incidence of the working-age population is higher than that of the pensionable population. According to the RA morbidity rating, in all age groups of the population, Dargins were in the first place, Rutuls were in the second, Laks were in the third. The minimum incidence of RA was observed among Azerbaijanis (Table 5).

Table 5. The incidence rate of rheumatoid arthritis in the age groups of the population of Dagestan in ethnic groups (per 100,000 population)

Ethnos	Age group, years			Ratio
	15+	15-59	60+	60+ / 15-59 years old
Dargin	1755.4	1555.8	2751.9	1.8
Rutul	1500.8	1451.2	1768.4	1.2
Lak	1424.5	1352.9	1689.1	1.2
Dido	974.8	975.6	997.9	1.0
Agul	932.0	991.6	754.3	0.8
Avar	750.7	653.1	1251.3	1.9
Nogai	721.6	607.4	1235.8	2.0
Lezgin	645.0	559.0	1152.3	2.1
Tabasaran	592.6	393.9	1436.3	3.6
Kumyk	442.2	376.8	861.5	2.3
Azerbaijani	372.1	340.9	579.8	1.7

The detection rate of RA in men and women differed depending on the age and ethnic group of the population. From the data in Table 6, it can be seen that the incidence rates of RA in men of Rutuls, Dargins, and Didos of working age ranked first 3 places, and among women of this age, Dargin, Lak, and Rutul were in the

lead. At the age of retirement, the leaders in the incidence of RA in men were Dargins, Laks, and Rutuls, and in the female population, dargins, lacques, and tabarana. It is noteworthy that the incidence of RA among women is higher than that of men. Nevertheless, in some ethnic groups, the gender ratio of the indicators

revealed a higher incidence of RA in men compared with the indicator of women, which included the Rutul and Dido ethnic

groups in both age groups, as well as the Agul ethnic group in the pension age (Table 6).

Table 6. The incidence rate of rheumatoid arthritis of age and ethnic groups of male and female population of Dagestan (per 100,000 population)

Ethnos	15-59 years old			60 years old and older		
	Men	Women	Women / Men	Men	Women	Women / Men
Rutul	1545.3	1367.4	0.9	2061.7	1552.8	0.8
Dargin	1249.2	1861.3	1.5	2324.2	3018.2	1.3
Dido	1072.9	888.2	0.8	1175.3	888.3	0.8
Lak	930.5	1805.1	1.9	1217.4	2021.6	1.7
Agul	891.1	1096.8	1.2	818.7	721.2	0.9
Nogai	508.9	708.0	1.4	923.8	1458.8	1.6
Avar	491.6	810.5	1.6	895.0	1495.0	1.7
Lezgin	472.9	646.0	1.4	993.2	1267.7	1.3
Tabasaran	304.3	485.5	1.6	1287.3	1543.3	1.2
Azerbaijani	238.0	436.4	1.8	492.1	647.1	1.3
Kumyk	236.2	512.6	2.2	620.1	1035.7	1.7

The discussion of the results

Thus, the incidence of RA is affected not only by gender and age, but also by ethnicity of the population. A significant difference between the incidence rates of RA in the population of certain regions within the ethnic group indicates the presence of genomic features in mountain populations, which will probably also occur when the incidence of residents of certain settlements is compared.

In studies on fundamental medicine, much attention is paid to molecular genetic methods of analysis with identification of polymorphic regions that increase the risk of disease development, therefore, the study of genetic predictors of the development of diseases in various ethnic groups in specific environmental regions is relevant and promising, especially in terms of preventive measures developed on the basis of these data [4].

As a result of adaptation to the environment, the population of the evolutionary mechanisms appear that determine the adaptive capabilities and the course of adaptation processes in different populations under conditions of permanent residence. The indigenous population of various regions is the natural population of Homo sapiens with certain strictly specific morphological and functional features and a unique

culture, a peculiarity of socio-economic, genetic and environmental factors. Many diseases have special metabolic manifestations and specifics, which must be taken into account in the pathogenesis of the disease [4]. Preliminary data show differences in survival strategies, perceptions of illness, self-efficacy, beliefs in avoiding fear, locus of control and attitude to pain in different population groups. Further prospective and longitudinal studies are needed using standard definitions of race, ethnicity or culture and valid questionnaires for each population group to study racial, ethnic, and cultural differences in pain, knowledge, and behavior [18]. Our current study shows that CTLA-4 +49 G/A (rs231775) is associated with susceptibility to autoimmune disease. Therefore, rs231775 can be used as a diagnostic biomarker for both the Asian and Caucasian populations [20]. Recently, one new RA susceptibility gene (RAD51B) has been identified in Korean and European populations. The common variant, rs911263, was successfully identified as being significantly associated with the disease status of RA ($P = 4.8 \times 10^{-5}$, OR = 0.64). In addition, this SNP has been shown to be associated with erosion, a clinical assessment of the severity of a disease in RA ($P = 2.89 \times 10^{-5}$, OR = 0.52). These

data shed light on the role of RAD51B in the onset and severity of RA [22].

A meta-analysis showed a significant association between the TGF- β 1 +869T/C polymorphism and the development of RA [16].

Three loci (HLA region, intergenic 5q13 and 17p13 in SMTNL2 / GGT6) reached genomic significance in association assays with RA and seropositive RA, and evidence of independent replication was demonstrated for all 3 loci. In accordance with the conclusions set forth in European and East Asian populations, the association of RA with the HLA variant of the DRB1 gene of amino acid position 11 received a strong effect ($P = 4.8 \times 10^{-16}$), and the weighted result of genetic risk, previously associated RA of loci and a relationship was established with RA ($P = 3.41 \times 10^{-5}$) and with seropositive RA ($P = 1.48 \times 10^{-6}$) in this population [19].

With an increase in the statistical power and size of the effect compared to individual studies, we present a more reliable profile of the association of HLA-DRB1 variants with RA in Arab ethnicity and contribute to the global geo-ethnic picture in this context [13].

In our study, we studied the demographic features (gender, age, ethnos) of patients with RA. Recent scientific papers contain very scarce data on the ethnic aspects of this disease, although there are a lot of epidemiological data. As for age and gender, the data from our study correlate with recent publications [14, 21].

Conclusions

1. Half of the rural areas of the Republic of Dagestan are mono-ethnic, with one ethnic group (Avars, Dargins, Laks, Lezgins, Aguls).

They are mainly located in mountainous areas.

2. The proportion of RA in the structure of arthritis ranges from 24.7-84.0%, depending on the ethnicity of the population, with a maximum among Rutuls and a minimum among Nogais.

3. On average, over 5 years, the incidence of Dargin, Lak and Rutul ethnic groups in the RA was higher than 1000 cases per 100,000 population, and among Tabasarans, Kumyks and Azerbaijanis, it was below the level of 500 patients per 100,000 population.

4. In 12 regions of the Republic of Dagestan, the level of the disease of women exceeds the rate of men more than 2 times. The exceptions were the Tsunta and Rutul districts, where the incidence of men prevailed over that of women.

5. The incidence rates of RA in men of Rutuls, Dargins, and Didos at working age were maximum, and among women of the same age, Dargin, Lak, and Rutul were the leaders. In the retirement age, the maximum incidence of RA is noted among Dargins, Laks and Rulets men, and in the female population, by Dargin, lak, and Tabaran.

Funding and Conflict of Interest Information

The authors declare no apparent and potential conflicts of interest related to the publication of this article.

This study was carried out at the personal expense of members of the team of authors.

The participation of the authors: the concept and design of research, editing tech-hundred - Saidova Z.M.; collection and processing of materials, analysis of the data, writing text - Ataeva Yu.M.

References

1. Abuyazidov AM, Khachirov DG. The incidence of lymphogranulomatosis by ethnic groups in the countryside of the Republic of Dagestan. *News of the Dagestan State Pedagogical University. Natural and exact sciences* 2011;(1):82-88 [Abuyazidov AM, Khachirov DG. Zabolevayemye limfogranulematozom po etnicheskim gruppam v selskoi mestnosti respubliky Dagestan. *Izvestiya Dagestanskogo gosudarstvennogo pedagogicheskogo universiteta.*

Estestvennye i tochnye nauki 2011;(1):82-88 (In Russian)].

2. Avrusin SL, Chasnyk VG, Burtseva TE, Sinelnikova EV. Actual problems of the ethnic group in medicine. *Human ecology* 2010;(12):43-49 [Avrusin SL, Chasnyk VG, Burtseva TE, Sinelnikova EV. Aktualnye problemy etnosa v meditsine. *Ekologiya cheloveka* 2010;(12):43-49 (In Russian)].

3. Agadzhanian NA. Ethnic problems of adaptive physiology. Moscow: RUDN, 2007.57 c. [Agadzhanian NA. Etnicheskie problemy adaptatsionnoi fiziologii. M.: RUDN 2007.57 (In Russian)].
4. Agadzhanian NA, Makarova II. The ethnic aspect of adaptive physiology and morbidity of the population. *Human ecology* 2014;(3):3-13 [Agadzhanian NA, Makarova II. Etnicheskii aspekt adaptatsionnoi fiziologii i zabo-levaemosti naseleniia. *Ekologiya cheloveka* 2014;(3):3-13 (In Russian)].
5. All-Russian Population Census 2010. URL: www.gks.ru/free_doc/new_site/perepis2010/croc/perepis_itogi1612.htm [Vserossiiskaia perepis naseleniia 2010 goda. URL: www.gks.ru/free_doc/new_site/perepis2010/croc/perepis_itogi1612.htm (In Russian)].
6. Gumilev LN. Ethnosphere: the history of people and the history of nature. Saint Petersburg: Crystal Publishing House, 2003. 576 c. [Gumilev LN. Etnosfera istoriia liudei i istoriia prirody. SPb.: Izdatelskii Dom Kristall, 2003. 576 (In Russian)].
7. Danilko KV, Nazarova LSh, Khabibullina PP, Khayrullina RR, Slesarenko YaS, Shamieva MV, Mutalova EG, Viktorova TV. Gene polymorphism 1L10, CTLA4 and susceptibility to rheumatoid arthritis. The scientific result. *Medicine and pharmacy* 2018;4(2):18-25 [Danilko KV, Nazarova LSh, Khabibullina PP, Khairullina RR, Slesarenko YaS, SHamieva MV, Mutalova EG, Viktorova TV. Polimorfizm genov 1L10 CTLA4 i predispo-lozhennost k revma-toidnomu artritu. Nauchnyi rezultat. *Meditsina i farmatsiia* 2018;4(2):18-25 (In Russian)].
8. Kaznacheev VP, Aulov AI, Kisel'nikov AA, Mingazov IF. Survival of the population of Russia. Problems of the "Sphinx of the XXI century." Ed. V.P. Kaznacheev. Novosibirsk: Publishing House of Novo-Siberian University, 2002. 463 [Kaznacheev VP, Aulov AI, Kisel'nikov AA, Mingazov IF. Vyzhivanie naseleniia Rossii Problemy Sfinksa XXI veka. Red. Akad. V.P. Kaznacheeva. Novosibirsk: Izd-vo Novosibirskogo un-ta, 2002.463 (In Russian)].
9. Kolesnikova LI, Darenskaya MA, Grebenkina LA, et al. Problems of ethnos in medical research. *Bulletin of the All-Russian Scientific Research Center of Sociology* 2013;4(92): 153—171 [Kolesnikova LI, Darenskaia MA, Grebenkina LA, Labygina AV, Dolgikh MI, Natiaganova LV, Pervushina OA. Problemy etnosa v meditsinskikh issledovaniakh. *Biulleten VNSTS SO AN* 2013;4(92):153—171 (In Russian)].
10. Kuranov AB, Abisheva ST, Zhusupova AL, et al. HLA genes of class II and rheumatoid arthritis in the Kazakh population. *Immunology* 2016;37(4):188-193. DOI: 10.18821/0206-4952-2016-37-4-188-193 [Kuranov AB, Abisheva ST, Zhusupova AL, i dr. Geny HLA klassa II i revmatoidnyi artrit v Kazakhskoi populiatsii. *Immunologiya* 2016;37(4):188-193. DOI: 10.18821/0206-4952-2016-37-4-188-193 (In Russian)].
11. Khachirov DG, Dzhalilova NA, Kazieva HE, Ataev MG, Tereshchenko AG, Baigishieva ND, Musaeva ShM. The incidence of leukemia in the population of the South of Russia. *Fundamental Mental Studies* 2013;(12-3):554-562 [Khachirov DG, Dzhalilova NA, Kazieva KhE, Ataev MG, Tereshchenko AG, Baigishieva ND, Musaeva ShM. Zaboлеваemost leikemiiami naseleniia subiektov luga Rossii. *Fundamentalnye issledovaniia* 2013;(12-3):554-562 (In Russian)].
12. Shirokogorov SM. Ethnos. Vladivostok: Publishing House of Vladivostok University, 2004. 148 c. [Shirokogorov SM. Etnos. Vladivostok: Izd-vo Vladivostokskogo un-ta, 2004. 148 (In Russian)].
13. Bizzari S, Nair P, Al Ali MT, Hamzeh AR. Meta-analyses of the association of HLA-DRB1 alleles with rheumatoid arthritis among Arabs. *Int J Rheum Dis* 2017;20(7):832-838. DOI: 10.1111/1756-185X.12922.
14. Iltchev P, Śliwczyński A, Czeleko T, Sierocka A, Tłustochowicz M, Tłustochowicz W, Timler D, Brzozowska M, Szatko F, Marczak M. Epidemiology of Rheumatoid Arthritis (RA) in rural and urban areas of Poland - 2008-2012. *Ann Agric Environ Med* 2016;23(2):350-6. DOI: 10.5604/12321966.1203904.
15. Korani S, Korani M, Butler AE, Sahebkar A. Genetics and rheumatoid arthritis susceptibility in Iran. *J Cell Physiol* 2019;234(5):5578-5587. DOI: 10.1002/jcp.27379.
16. Lee YH, Bae SC. Association between circulating transforming growth factor-β1 level and polymorphisms in systemic lupus erythematosus and rheumatoid arthritis: A meta-analysis. *Cell Mol Biol (Noisy-le-grand)*. 2017; 63(1):53-59.
17. Lutf A, Poil AR, Hammoudeh M. Characteristics of patients with rheumatoid arthritis in Qatar: a cross-sectional study. *Int J Rheum Dis*. 2014;17(1):63-5. DOI: 10.1111/1756-185X.12135.
18. Orhan C, Van Looveren E, Cagnie B, Mukhtar NB, Lenoir D, Meeus M. Are Pain Beliefs, Cognitions, and Behaviors Influenced by Race, Ethnicity, and Culture in Patients with Chronic Musculoskeletal Pain: A Systematic Review. *Pain Physician* 2018;21(6):541-558.

19. Saxena R, Plenge RM, Bjornes AC, et al. A Multinational Arab Genome-Wide Association Study Identifies New Genetic Associations for Rheumatoid Arthritis. *Arthritis* 2017;69(5):976-985. DOI: 10.1002/art.40051.
20. Wang K, Zhu Q, Lu Y, Lu H, Zhang F, Wang X, Fan Y. CTLA-4 +49 G/A Polymorphism Confers Autoimmune Disease Risk: An Updated Meta-Analysis. *Genet Test Mol Biomarkers* 2017;21(4):222-227.
21. Yang DH, Huang JY, Chiou JY, Wei JC. Analysis of Socioeconomic Status in the Patients with Rheumatoid Arthritis. *Int J Environ Res Public Health* 2018;15(6):E1194. DOI: 10.3390/ijerph15061194.
22. Zhi L, Yao S, Ma W, Zhang W, Chen H, Li M, Ma J. Polymorphisms of RAD51B are associated with rheumatoid arthritis and erosion in rheumatoid arthritis patients. *Sci Rep.* 2017; 7:45876. DOI: 10.1038/srep45876.
23. Zhu H, Xia W, Mo XB, et al. Gene-Based Genome-Wide Association Analysis in European and Asian Populations Identified Novel Genes for Rheumatoid Arthritis. *PLoS One* 2016;11(11):e0167212. DOI: 10.1371/journal.pone.0167212.

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