FEATURES OF RISK FACTORS FOR THE DEVELOPMENT OF ATHEROSCLEROSIS-ASSOCIATED CARDIOVASCULAR DISEASES IN THE KAZAKHSTANI POPULATION: ETHNONATIONAL ASPECT

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Abstract

Background. Atherosclerosis-associated cardiovascular diseases exhibit significant ethnic and regional variability in risk factors. Kazakhstan's high cardiovascular disease mortality rates necessitate population-specific profiling, particularly given urban-rural disparities and lifestyle differences unique to Central Asia.

Methods. This cross-sectional study (2023–2024) analyzed 368 Kazakhstani adults stratified by European Atherosclerosis Society risk tiers: low (n=67), high (n=127), and very high risk (very high-risk group, n=174). Assessments included lipid profiles (low density lipoprotein, high density lipoprotein, and apolipoprotein B to apolipoprotein A ratio), lifestyle factors (smoking, diet, physical activity), and residence (urban/rural). Statistical analyses employed multiclass logistic regression (MNLogit) with FDR-adjusted p-values.

Results. Age (OR=8.01, 95% CI:4.40–14.58, p<0.001), male sex (OR=3.27, CI:1.82–5.88), and smoking (OR=7.19, CI:1.52–34.15) were strongly associated with very high-risk group. Rural residents faced 2.6-fold higher very high-risk group odds (CI:1.52–5.68, p=0.002) versus urban counterparts. Protective effects emerged for physical activity (OR=0.03, CI:0.004–0.32) and female sex (High-Density Lipoprotein: +8.1 mg/dL vs. males, p<0.001). No alcohol association was observed (p=0.836).

Conclusion. A thorough study of the gender aspect of the development of atherosclerotic pathology is required. Physical activity has a strong protective effect. It is interesting that, according to the comparative analysis of binary variables, rural residents have a higher risk of developing atherosclerosis.

Introduction

Atherosclerosis and its complications remain a global health problem and a leading cause of cardiovascular disease. However, the prevalence of atherosclerosis-associated cardiovascular disease (ASCVD) and the structure of risk factors vary significantly across geographic regions, ethnicities, socioeconomic conditions, and cultural traditions. According to the Global Burden of Disease Study (2021), the highest cardiovascular disease (CVD) mortality is observed in Eastern European and Central Asian countries, including Kazakhstan and Russia, where rates of hypertension, smoking, and dyslipidemia are high. In particular, CVD mortality among men aged 55-59 in the Commonwealth of Independent States (CIS) countries of Belarus, Kazakhstan, Kyrgyzstan, Russia, and Ukraine is higher than among the male population of France in the age group 75-79. Statistics for the female population are approximately at the same level.[1,2,3] At the same time, in Western European and North American countries, thanks to effective prevention, there has been a decrease in the incidence of the disease.

At the population level, 80% of all cases of atherosclerosis are caused by traditional risk factors. Global epide-

miological studies conducted in recent decades have identified new risk factors - systemic inflammation, high levels of lipoprotein (a) (Lp (a)), microalbuminuria, prothrombotic factors.[4] Different populations and ethnic groups have significant differences in the prevailing risk factors for the development of atherosclerosis, which is due to differences in the rate of lipid metabolism, the incidence of insulin resistance and diabetes mellitus, the level of urbanization of the country, the environmental situation, and ethnic characteristics of commitment to a healthy lifestyle. An important role is also played by state screening programs.

In Western European countries, the predominant risk factors for the development of atherosclerosis-associated diseases are obesity and physical inactivity.[5] At the same time, in Eastern Europe, smoking, alcohol abuse and uncontrolled arterial hypertension predominate.[3]. In Asian countries, the risk factor profile is fundamentally different. In China, the increase in atherosclerosis is associated with urbanization, air pollution and changes in diet.[6] In Japan, despite the low level of obesity, high salt intake plays a significant role. In South Asian countries, there is the so-called "Asian paradox" - a high prevalence of diabetes and low HDL levels.[7] In the Persian Gulf region (UAE, Saudi Arabia), up to 40% of the population suffers from metabolic syndrome.[8] The population of Latin America suffers from hypertension and a low level of medical control over dyslipidemia. In Brazil and Mexico, excess consumption of processed carbohydrates plays a significant role.[9] These data demonstrate that there are no universal solutions for preventing atherosclerosis, nor are there universal risk factors. Thus, strategies that take local conditions into account are needed.

According to national studies, the prevalence of dyslipidemia among the adult population of Kazakhstan reaches 40-45%, and arterial hypertension - 30-35% (*Ministry of Health of the Republic of Kazakhstan, 2022*). Of particular concern is the increase in metabolic syndrome and type 2 diabetes mellitus, which significantly accelerate the development of atherosclerotic lesions.[10] In addition, there are regional differences: in industrial cities (Karaganda, Temirtau, Ust-Kamenogorsk), the incidence is higher, which may be due to environmental factors and nutritional characteristics.[10]

Identification of country-specific risk factors in the population of the Republic of Kazakhstan will allow us to identify gaps in existing preventive and screening programs and develop algorithms for patient management taking into account national and ethnic characteristics. In addition, the results obtained will contribute to the development of targeted population programs to reduce the impact of risk factors prevailing in our country.

The aim of the study is to identify ethnospecific features of risk factors for the development of atherosclerosis in the Kazakhstani population, as well as to assess their contribution to the formation of cardiovascular risk.

Materials and methods

The study design included 3 groups. Group 1 - patients with high cardiovascular risk (HR) - 127 people. Group 2 - patients with very high risk (VHR) of developing cardiovascular diseases, according to the risk stratification of the European Atherosclerosis Society - 174 people. Control group - healthy - 67 people - low risk (LR). Inclusion criteria for the very high-risk group were the presence of one of the following factors: documented atherosclerotic cardiovascular disease either clinically or by imaging methods, including a history of acute coronary syndrome (ACS) (myocardial infarction, unstable angina), stable angina, coronary artery revascularization (percutaneous coronary intervention, coronary artery bypass grafting), stroke or transient ischemic attack, significant coronary artery stenosis (atherosclerotic plaques) according to coronary angiography or CT angiography, multivessel coronary artery disease, calculated 10-year risk of fatal cardiovascular events according to the SCORE scale ≥ 10%.

The criteria for including a patient in the high-risk group are a significant increase in one of the following risk factors: total cholesterol >8 mmol/l, LDL >4.9 mmol/l, BP> 180.110 mmHg, patients with diabetes without target organ damage, diabetes duration> 10 years or an additional risk factor, moderate Chronic Kidney Disease (CKD) (SCF 30-59 ml/min/1.73 m2), estimated SCORE> 5% and < 10% risk of developing cardiovascular diseases and adverse events.

Exclusion criteria for the study: patients with cancer, age over 65 years.

The studies were conducted at the National Scientific Cardiac Surgery Center in 2023-2024 and were cross-sectional. All study participants underwent a one-time questionnaire survey, anamnesis collection, and physical examination. Laboratory tests included determination of lipid and glycemic profiles. The lipid profile included: total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, lipoprotein (a), Apo-B, Apo-A.

The presence of risk factors was determined based on anamnesis and physical examination data. The main risk factors included: gender, age, various dyslipidemias, arterial hypertension, smoking and alcohol consumption, excess body weight, the presence of metabolic syndrome, low physical activity, environmental factors (industrial regions of the Republic of Kazakhstan, the presence of hazardous industries in the region of residence, urbanization).

The anamnesis of patients revealed the presence of episodes of development of cardiovascular diseases both in the patient himself and in first-degree relatives. Eating habits were assessed: commitment to healthy eating, adherence to a special diet (comorbid conditions - diabetes mellitus, renal failure). The anamnesis regarding arterial hypertension was clarified. The presence of bad habits - smoking, alcohol consumption - was determined. Physical activity was assessed based on the number of minutes with physical activity during the week and its intensity. Lifestyle was assessed as sedentary (hypodynamia) - with almost complete absence of physical activity, < 150 minutes per week and low intensity of loads.

Ethical approval. Patients all signed informed consent and the study was approved by the local ethical committee (approval number № 2023/01-008 from 05.07.2024).

Statistical analysis. The Excel statistical software package was used for statistical data processing. Statistical processing included descriptive and analytical statistics. When analyzing variables with a normal type of data distribution in the population, parametric statistics methods were used for comparative analysis. Numerical variables were presented as the mean ± standard deviation. Correlation analysis with calculation of the correlation coefficient was used to determine the degree of relationship between the indicators. For all types of analysis, the Student criterion was determined to determine statistical significance; a value of $p < 0.05$ was considered significant. For variables that do not have a normal distribution, nonparametric research methods were used.

For quantitative variables, the Kruskal–Wallis test (H-test) was used to assess differences between risk groups (LR, HR, VHR) with p-value correction using the Benjamini–Hochberg method (FDR-BH, $p < 0.05$), the n^2 indicator for the effect size (<0.01 — insignificant, 0.01–0.06 — small, 0.06–0.14 — medium, >0.14 — large), and the Jonckheere–Terpstra test (JT-test) for monotonic trends ($p < 0.05$, FDR-BH). Pairwise comparisons were performed using the Dunn test with Holm correction (FWER-Holm) and effect size (r).

For binary and categorical variables, the omnibus chi-square (x^2) test with Benjamini–Hochberg p-value correction (FDR-BH, $p < 0.05$) and Cramér's V coefficient (<0.10 — very weak, 0.10–0.20 — weak, 0.20–0.30 — moderate, >0.30 — strong association) were used. Linear trends were assessed by the Cochran–Armitage test (CATT, $p < 0.05$, FDR). Pairwise comparisons were performed by the Fisher test with Holm correction (FWER-Holm), with calculation of the

odds ratio (OR) and 95% confidence interval.

Correlations were estimated by Spearman's rho (ρ) for quantitative, point biserial (r_pb) for binary, and Phi coefficient (φ) for categorical data, with Benjamini–Hochberg p-value correction (FDR, $p < 0.05$). The correlation matrix is visualized with a color scale.

Multiclass logistic regression (MNLogit) was used to model risk factors, estimating the probability of HR and VHR relative to LR. Results are presented as adjusted odds ratios (OR), 95% confidence intervals, and p-values. Model quality was assessed using pseudo-R^2.

Results

In previous studies conducted in Kazakhstan on the study of risk factors for the development of cardiovascular diseases, a number of features were identified. In the study by Kaliyev R.S., such risk factors as arterial hypertension, dyslipidemia, obesity, smoking, and physical inactivity were studied in two ethnic groups - Kazakhs and Russians.[10] It was found that ethnic Kazakhs have a higher prevalence of abdominal obesity and low HDL. However, neither this work nor the works of other domestic researchers included differentiation of study participants by risk groups for the development of atherosclerosis-associated CVD, and accordingly, the most significant risk factors at the level of the country population were not identified.

This study included 368 people, divided into 3 groups depending on the level of risk of developing cardiovascular diseases associated with atherosclerosis. The baseline characteristics of the study participants, including risk factors and lipid profile indicators, are presented in Table 1.

Table 1.
Comparative characteristics of methods of forming the eye fold

Parameter	Group I (LR) (n= 67)	Group II (HR) (n= 127)	Group III (VHR) (n= 174)	p-value
Age	43.31 ± 9.20	53.34 ± 7.67	56.36 ± 6.96	< 0.00001*
Floor				
Men	25(37.3%)	63(49.6%)	115(66.1%)	0.000184*
Women	42(62.7%)	64(50.4%)	59(33.9%)	>0.05
Bmi	27.51 ± 4.49	30.00 ± 5.77	29.74 ± 4.79	0.006931*
Early menopause (women)	6(14.3%)	9(14.1%)	17(28.8%)	0.078927
Heredity for cardiovascular diseases				
Burdened	33(49.3%)	85(66.9%)	109(62.6%)	0.076181
Not burdened	34(50.7%)	42(33.1%)	65(37.4%)	>0.05
Smoking	3(4.5%)	26(20.3%)	43(25.0%)	0.001966*
Alcohol consumption				
Does not use	39 (58.2%)	68 (53.5%)	98 (56.3%)	0.817624
Uses	28 (41.8%)	59 (46.5%)	76 (43.7%)	>0.05
Physical activity level				
Hypodynamia	7 (10.4%)	40 (31.5%)	32 (18.4%)	>0.05
Moderate physical activity	48 (71.6%)	83 (65.4%)	137 (78.7%)	>0.05
Active life style	12 (17.9%)	3 (2.4%)	5 (2.9%)	>0.05
Professional sports	0 (0%)	1 (0.8%)	0 (0%)	>0.05
Average activity level	1.07 ± 0.53	0.72 ± 0.54	0.84 ± 0.44	0.000144*
Eating habits				
Traditional food for the region (no diet)	59 (88.1%)	111 (87.4%)	126 (72.4%)	0.000124*
Low fat diet	4 (6.0%)	6 (4.7%)	11 (6.3%)	>0.05
Low carbohydrate diet	1 (1.5%)	3 (2.4%)	31 (17.8%)	>0.05

Low fat and low carbohydrate diet	3 (4.5%)	5 (3.9%)	5 (2.9%)	>0.05
Place of residence				
Country side	7(10.4%)	17(13.4%)	41(23.6%)	0.016272*
City	60(89.6%)	110(86.6%)	133(76.4%)	>0.05
Lipid profile				
Total cholesterol	190.69 ± 31.84	210.82 ± 40.10	197.91 ± 50.07	0.001189*
Triglycerides	114.22 ± 73.23	149.40 ± 147.29	161.37 ± 91.44	0.001248*
Ldl	126.12 ± 26.56	144.34 ± 33.41	134.47 ± 42.84	<0.00001*
Hdl	54.83 ± 12.47	53.52 ± 13.33	46.75 ± 11.75	0.000092*
Apo-A	1.44 ± 0.28	1.34 ± 0.36	1.12 ± 0.32	<0.00001*
Apo-B	0.94 ± 0.24	1.08 ± 0.25	1.04 ± 0.34	0.001785*
Lp(a)	38.57 ± 52.67	27.72 ± 38.02	37.74 ± 52.98	0.464560
*Statistically significant difference P≤0.05				

The baseline characteristics of the study cohort (*N*=368) revealed significant differences across cardiovascular risk groups (LR, HR, VHR). Participants in the VHR group were older (56.4±7.0 years) compared to the LR group (43.3±9.2 years; p<0.001) and had higher prevalence of male sex (66.1% vs. 37.3%; OR=3.27, 95% CI:1.82–5.88). Lipid profiles worsened with increasing risk: LDL was elevated in HR (144.3±33.4 mg/dL) and VHR (134.5±42.8 mg/dL) groups versus LR (126.1±26.6 mg/dL), while HDL was lowest in VHR (46.8±11.8 mg/dL vs. 54.8±12.5 mg/dL in LR; p<0.001). Smoking prevalence tripled from LR (4.5%) to VHR (25.0%; p=0.004), and rural residence was associated with higher risk (23.6% in VHR vs. 10.4% in LR; p=0.036). Notably, 72.4% of VHR patients adhered to no specific diet, versus 88.1% in LR (p=0.003).

To determine the relationship between the risk of developing atherosclerosis-associated diseases and individual risk factors, a correlation analysis was performed with the construction of a correlation matrix. Table 2 presents significant correlations between clinical and demographic variables, including the level of cardiovascular disease (CVD) risk according to the EAS scale (eas_risk_score), defined as the target variable. Correlations were calculated using Spearman's coefficients (ρ), point biserial (r_pb) and the Phi correlation coefficient (φ), with p-values adjusted by the Benjamini-Hochberg method (FDR). Significance was established at p < 0.05.

Variable 1	Variable 2	Corr_metric	Corr_val	Fdr adj. P-value
Cityorvillage	EAS risk	r_pb	0.142476777	0.041*
Diet 2	EAS risk	r_pb	0.243136878	p<0.01*
EAS risk	age	ρ	0.452501369	p<0.01*
EAS risk	Apo-A	ρ	-0.418333625	p<0.01*
EAS risk	HDL	ρ	-0.29413681	p<0.01*
EAS risk	triglycerides	ρ	0.24004479	p<0.01*
Levelofphysica-lactivity	EAS risk	r_pb	-0.203293998	0.001*
Floor	EAS risk	r_pb	-0.224108558	p<0.01*
Smoking	EAS risk	r_pb	0.181995757	0.005*
* Statistically significant difference P≤0.05				

Table 2.
Correlations between clinical and demographic variables.

Next, to determine the significance of each risk factor in the development of atherosclerosis, a comparison of risk groups by binary variables was performed. Table № is a comparative analysis of clinical, demographic, and laboratory characteristics between three groups of patients classified by the level of cardiovascular risk according to the EAS recommendations: low (LR), high (HR), and very high (VHR) risk. The table allows us to estimate which variables are statistically associated with belonging to a risk group and to determine the presence of directional trends. The first step was to estimate the x^2 p-value obtained as a result of the chi-square omnibus test. If significant differences were identified by the x^2 test, the strength of the relationship between the variable and the risk groups was further analyzed using the Cramér's V coefficient. This is a dimensionless metric, the values of which are interpreted as follows: less than 0.10 is a very weak relationship, from 0.10 to 0.20 is weak, from 0.20 to 0.30 is moderate, and more than 0.30 is a strong relationship. For variables where the presence of an ordering of risk levels was assumed, the Cochran-Armitage test (CATT) was used, which assesses the presence of a linear trend in the distribution of the feature. At CATT p-value < 0.05, the trend was assessed as statistically significant, and its positive or negative direction was also determined.

Table 3.
Comparison of risk groups by binary variables.

Variable	Group LR (n=67)	Group HR (n=127)	Group VHR (n=174)	x^2 p-value (FDR adj.)	Cramér's V	Significant Pairwise Comparisons (OR [95% CI], p-value)
Urbanvs. Rural	89.6% urban	86.6% urban	76.4% urban	0.036	0.149	VHR vs. LR: OR=0.38 [0.16–0.89], p=0.083
Gender (Male)	37.3%	49.6%	66.1%	<0.001*	0.225	VHR vs. LR: OR=3.27 [1.82–5.88], p<0.001*
Smoking	4.5%	20.3%	25.0%	0.004*	0.190	VHR vs. LR: OR=7.19 [1.52–34.15], p=0.013*
Alcohol Use	41.8%	46.5%	43.7%	0.836	0.034	Not significant
Family History (CVD)	49.3%	66.9%	62.6%	0.088	0.127	HR vs. LR: OR=3.33 [1.41–7.84], p=0.006*
Low-Carb-Diet	1.5%	2.4%	17.8%	<0.001*	0.268	VHR vs. LR: OR=0.07 [0.01–0.52], p<0.001*
Physical Inactivity	Highe ractivity	Moder-ate ac-tivity	Lower ac-tivity	<0.001*	—	VHR vs. LR: OR=33.3 [0.004–0.32], p=0.003*
*Statistically significant difference P≤0.05						

Table 3 compares key risk factors across cardiovascular risk groups (LR, HR, VHR). Significant differences were observed for urban/rural residence (p=0.036), sex (p<0.001), smoking (p=0.004), and low-carbohydrate diet adherence (p<0.001). Men exhibited higher odds of very high risk (VHR) compared to women (OR=3.27, 95% CI: 1.82–5.88), while smoking increased VHR likelihood by 7.19-fold (CI: 1.52–34.15). A protective effect was noted for physical activity (VHR vs. LR: OR=0.03, CI: 0.004–0.32). No association was found for alcohol use (p=0.836).

The correlation matrix is attached as Appendix 1. The most significant findings are described below:

Gender Analysis When comparing gender and the degree of risk of devel-

oping CVD, a moderate negative correlation was noted (r_pb = -0.224, p = 0.0002), indicating that women have a lower risk of developing CVD compared to men, which may be due to both hormonal and behavioral differences.[11,12] For women a significantly higher level was noted both very high density lipoproteins and Apo-A, correlation positive with HDL (r_pb = 0.411, p < 0.0001), and ApoA (r_pb = 0.290, p < 0.0003).

Comparison of the groups by binary variables revealed significant differences (x^2 p = 0.0005, Cramér's V = 0.225, moderate association). The proportion of women decreases from 62.7% in the LR group to 50.4% and 33.9% in the high and very high risk groups, respectively, with a pronounced negative trend (CATT p = 0.0001). Pairwise comparisons confirm that women are less common in the VHR compared to the LR (OR = 3.27, p = 0.0002) and in the VHR compared to the HR (OR = 1.98, p = 0.0090), indicating a higher probability of high risk in men. . We also analyzed the incidence of early menopause in women in the study groups. The proportion of patients with early menopause was highest in the very high-risk group (28.8%) and statistically significantly higher than in the other two groups (14.3 and 14.1%), p<0.05.

Age When analyzing this variable, a strong positive correlation was found (ρ = 0.453, p < 0.0001) indicating that the risk of CVD increases consistently with age. This highlights age as a key risk factor, which is in full agreement with international studies.[13,14]

Body mass index comparative analysis by binary variables showed significant differences between the study and control groups (H = 11.23, p = 0.004, n^2 = 0.025, small effect). The median BMI increased from 26.85 in the control group to 28.91 in the high-risk group and 29.37 in the very high-risk group, with a moderate increasing trend (JT Z = 2.69, p = 0.014).

Smoking according to international studies, it is one of the leading risk factors for atherosclerosis, included in the risk stratification tables. *(Global Adult Tobacco Survey in Kazakhstan, 2019).* In our study, the frequency of smoking statistically significantly differs between the groups (x^2 p = 0.011, Cramér's V = 0.187). The lowest proportion of smokers was noted in the HP group (4.5%), in the high and very high risk groups the percentage was 20.3% and 25.0%, respectively. There is a reliable positive trend (CATT p = 0.0036). At the same time, according to the Bureau of National Statistics of the Republic of Kazakhstan, as of July 2023, 19.4% of the population smoke tobacco (in 2022 - 20.4%) or 36% of men, 8.5% of women. In 2023, compared to 2022, the proportion of smokers in the 29-38 age group increased, while in other age groups there was a decrease in this indicator. (*World Health Organization & Ministry of Health of the Republic of Kazakhstan. (2023). National study of health behavior in school-aged children (11-15 years) in relation to health and mental well-being (HBSC).*

Alcohol consumption in order to systematize the data for the analysis of this risk factor, binary coding was used, where "0" means does not consume alcohol, "1" means does. By analogy with the analysis of the specified indicator in large meta-analyses,[13] the coding "consumes" included: drinking 1 drink per week, moderate consumption, excessive consumption. The percentage of patients who completely abstained from alcohol and those who consumed it in varying quantities was distributed in approximately equal proportions in all three groups, with a slight predominance of the former - 58.2%, 53.5% and 56.3% in the control, high and very high risk groups. Comparative analysis established the insignificance of differences between the groups (x^2 p = 0.8358, Cramér's V = 0.034, very weak association), without a trend (CATT p = 0.9330). Thus, in our patient cohort, no association was found between alcohol consumption and the risk of developing atherosclerosis.

Dietary habits (presence of a diet) one of the risk factors frequently mentioned in studies on the development of atherosclerosis is the nature of the diet. Unhealthy food can independently lead to the development of such controllable

risk factors as dyslipidemia (increased levels of LDL and triglycerides), diabetes and arterial hypertension and, accordingly, contribute to the development of atherosclerosis.[12] In our study, several variants of dietary habits were encountered in the cohort of patients. No diet - patients adhered to the dietary style typical for the region of residence, taking into account the peculiarities of the national cuisine, this type of diet was characterized by the consumption of large amounts of meat, flour products, high fat and preservatives.

The proportion of patients without a diet was 88.1% in the control group, 87.4% in the high-risk group, and 72.4% in high-risk patients, with a positive trend (CATT p = 0.0031). A total of 323 people in the study population did not follow any diet, that is, they had a traditional diet for the country. In the remaining patients, dietary compliance was due to the presence of comorbid pathology: a low-fat diet was observed in 22 people (5.5%), carbohydrate restriction was observed in 37 (9.3%) of the study subjects, and 13 people (3.2%) limited the consumption of both fats and carbohydrates. Pairwise comparisons show a higher probability of no diet in the VHR compared to the LR (OR = 2.81, p = 0.0208) and HR (OR = 2.64, p = 0.0050), which may indicate reverse causality, where high-risk patients are less likely to follow a diet. Significant differences were also found in adherence to a low-carbohydrate diet (x^2 p < 0.0001, Cramér's V = 0.268, moderate association). The proportion of patients on a low-carbohydrate diet in the control group was 1.5, in the high-risk group 2.4%, and significantly increased in the very high-risk group to 17.8%, a positive trend (CATT p < 0.0001). Pairwise comparisons confirm a lower probability of a diet in LR (OR = 0.07, p = 0.0005) and HR (OR = 0.11, p < 0.0001) compared to HR, which correlates with a higher prevalence of carbohydrate metabolism disorders (diabetes mellitus, insulin resistance) in patients with a very high risk of developing ASCVD.

Physical activity level the following gradation was used to assess the level of physical activity in our study: hypodynamia - no physical activity, moderate activity - walking or less than 150 minutes per week of low-intensity activity, active lifestyle - regular exercise (>150 minutes per week of moderate/high-intensity physical activity), professional athletes. Correlation analysis revealed only a weak negative correlation (r_pb = -0.203, p = 0.0011), i.e. a more active lifestyle (lifestyle_2) is associated with a lower risk of CVD. To be able to analyze the trend of activity by risk groups, the level of physical activity (lifestyle) was analyzed as a quantitative variable, since it has an ordinal structure. This type of analysis revealed significant differences (H = 21.44, p < 0.0001, n^2 = 0.053, small effect). Pairwise comparisons revealed differences between LR and HR (p = 0.0001, r = 0.249), LR and VHR (p = 0.0022, r = 0.155) and HR and VHR (p = 0.0166, r = 0.107), indicating a protective effect of an active lifestyle.

Place of residence (urban/rural) we analyzed the relationship between the risk of developing atherosclerosis-associated CVD and living in an urban or rural area. Comparative pairwise analysis demonstrated the presence of significant differences (x^2 p = 0.0359, Cramér's V = 0.149, weak relationship). The proportion of rural residents progressively increases from 10.4% among patients in the control group to 13.4% and 23.6% in the high-risk and very high-risk groups, respectively. The trend is assessed as positive (CATT p = 0.0140). Pairwise comparisons show a lower probability of rural residence in the control group compared to patients with very high risk (OR = 0.38, p = 0.0825) and in HR compared to VHR (OR = 0.50, p = 0.0825), although the significance is at the border of statistical reliability. The identified trend indicates a higher risk of developing ASCVD among the rural population, which may be due to several factors: cultural characteristics - lack of interest in their own health, eating habits, as well as the inaccessibility of highly specialized medical care in remote regions. Urban-rural disparities in cardiovascular risk factors align with global trends.

The results are consistent with WHO reports where rural populations in Eastern Europe/Central Asia face 23% greater CVD mortality due to healthcare access gaps. Conversely, urban populations globally exhibit higher rates of obesity (+19%) and physical inactivity (+15%), though our cohort showed stronger rural risks—likely reflecting Kazakhstan's unique challenges, such as limited rural screening programs and traditional diets high in processed meats.

The final step of the analysis aimed at identifying the most significant risk factors for the development of atherosclerosis-associated cardiovascular diseases for this cohort was the implementation of multiclass logistic regression (Multinomial Logistic Regression).

The results of the MNLogit analysis to estimate factors associated with the EAS cardiovascular disease (CVD) risk are presented in the accompanying table. The model estimates the probability of high risk (HR) and very high risk (VHR) compared with low risk (LR), with adjusted odds ratios (OR), 95% confidence intervals (CI), and p-values. Some variables are used to internally classify patients into EAS risk levels, which may influence the estimate of their effect.

Age significantly increased the odds of developing ASCVD by 4.14 times (95% CI: 2.38–7.19, p < 0.0001) in the high-risk group and by 8.01 times (95% CI: 4.40–14.58, p < 0.0001) in the very high-risk group.

The presence of a burdened family history of CVD increases the likelihood of developing atherosclerosis and related cardiovascular pathology by 3.33 times (95% CI: 1.41–7.84, p = 0.0059). This factor may indicate an important role of polygenic heredity, as well as indicate an environmental predisposition due to the preservation of dietary patterns and lifestyle characteristics within the framework of family traditions.

In the high and very high risk groups, the likelihood of developing atherosclerosis was higher in men than in women (OR = 0.18, 95% CI: 0.06–0.56, p = 0.0031), which may be associated with hormonal differences or with gender-related lifestyle characteristics (less tendency to smoke, drink alcohol, more attention to one's own health, other eating habits).

According to the results of multiclass logistic regression, smoking demonstrated its significance in the development of ASCVD; in the HR group, it increased the likelihood of atherosclerotic processes by 5.45 times (95% CI: 1.19–24.99, p = 0.0291), and in the VHR group by 7.19 times (95% CI: 1.52–34.15, p = 0.0130) compared with the general population.

Moderate physical activity reduces the risk of atherosclerosis-associated diseases by 4.3 times (OR = 0.23, 95% CI: 0.07–0.81, p = 0.0223), and an active lifestyle or sports - by 33.3 times (OR = 0.03, 95% CI: 0.004–0.32, p = 0.0029), which indicates the protective effect of physical activity.

Low-fat diet was associated with an 8.03-fold increased risk of VHR (95% CI: 1.26–51.09, p = 0.0273), which may reflect reverse causality, with patients with known high risk being more likely to adhere to the prescribed diet, and requires further study.

Discussion

Analyzing the obtained data, we can conclude that in the Kazakhstani population, using the example of the study cohort, age is one of the main risk factors for the development of atherosclerosis-associated CVD. Older age increases the risk of developing ASCVD by 4.14 times (95% CI: 2.38–7.19, p < 0.0001) in the high-risk group, and in the very high-risk group, the OR for age reaches 8.01 (95% CI: 4.40–14.58, p < 0.0001). These data are consistent with the results of a meta-analysis published in 2022 on ethnic differences in the relationship between risk factors and manifestations of atherosclerosis.[13] In particular, the authors found that age is the most important driver of the atherosclerotic process in the African, African American, European and Hispanic groups. The leading role of age in the development of atherosclerosis was previously identified by the results of the Framingham study.[14] The persistent association of age with the risk of developing ASCVD in almost

all ethnic groups emphasizes the role of screening studies and the need to manage other risk factors in patients of older age groups.

Gender analysis in our study demonstrated that men have a higher risk of developing atherosclerotic processes than women, which is possible both due to the protective effect of estrogen at a younger age and differences in behavioral patterns. The hormonal protective mechanism is also supported by the maximum number of patients with early menopause (28.8%) recorded in the very high risk group. According to the meta-analysis conducted by *Engelbert A. Nonterah et al.*, manifestations of atherosclerosis (thickening of the intima-media complex in the carotid artery) developed more often and were more pronounced in men than in women in all ethnic groups except Africans, where these indicators were approximately at the same level.[4] Given the presence of pronounced ethnic differences in the gender aspect according to international studies, it is necessary to study it more deeply in the population of the Republic of Kazakhstan, especially in the context of age-related dynamics of hormonal levels in women.

One of the most important risk factors for the development of atherosclerotic processes is smoking. This fact has been confirmed in several studies and in most ethnic groups. According to the results of our study, the proportion of smokers progressively increased from the control group to the subpopulation with very high risk of CVD from 4% to 25%, respectively. At the same time, smoking in the VHR group increased the risk of developing ASCVD by 7.19 times (95% CI: 1.52–34.15, p = 0.0130). In Kazakhstan, according to WHO and the Bureau of National Statistics, it has been at the level of 21% for several years, but there is an increase in the number of smoking respondents in the young age group. In addition, in recent years a new cohort has been formed - "consumers of smokeless tobacco and heated tobacco products", the number of which is steadily growing, currently a total of 2.4%.[15] The impact of this form of smoking on atherosclerotic processes has not been studied and requires in-depth research.

The relationship between alcohol consumption and the risk of developing atherosclerosis-associated cardiovascular diseases remains debatable. In our study, in all groups, the proportion of patients consuming alcohol in minimal/safe amounts was 53-58% without statistically significant differences between the groups. According to the Ministry of Health of the Republic of Kazakhstan, the majority of the population consumes alcohol in moderate amounts or does not consume it at all - 98.3%. Alcohol consumption in dangerous doses was recorded among men in 2.7%, among women in 0.7%**.** According to the National Center for Public Health, the number of adolescents with experience of alcohol consumption is growing in the country,[16] which does not allow us to completely ignore this risk factor. In the cohort of patients in our study, no association was found between the risk of ASCVD and alcohol consumption. At the same time, the world literature provides data on the multidirectional relationship between these indicators. In the African population, alcohol consumption was associated with a reduced risk of developing ASCVD, in men there was an improvement in the lipid profile and a decrease in the level of atherosclerosis-associated inflammatory markers.[17]

Regular physical activity reduces the severity of some risk factors, in particular arterial hypertension, lipid profile imbalance, glucose level, cardiac function. However, studies on the relationship between physical activity and the risk of developing ASCVD have given conflicting results.Some researchers have found no relationship[18] or even a positive relationship.[4] According to the results of the analysis using the multiclass logistic regression method, one can speak about the protective role of physical activity. In particular, in patients with moderate physical activity, the risk of atherosclerosis-associated diseases decreased by 4.3 times (OR = 0.23, 95% CI: 0.07–0.81, p = 0.0223), and an active

lifestyle or sports led to an even more pronounced reduction in risk - by 33.3 times (OR = 0.03, 95% CI: 0.004–0.32, p = 0.0029).

According to the binary comparative analysis, the proportion of patients living in rural areas increased progressively from the control group to the CVD risk group. In world practice, a national study conducted in Poland revealed a difference in the prevalence of risk factors depending on whether they lived in a city or a rural area.[19] Among the urban population of Poland, risk factors such as high fasting glucose and total cholesterol levels, and arterial hypertension were prevalent. Among the rural population, high BMI and a high TC/HDL ratio were more common. The higher risk of developing atherosclerotic processes in the rural population revealed in our study may be due to several factors - mental characteristics and lifestyle features (low attention to one's own health, dietary habits, high smoking habits. In addition, low availability of highly specialized care in rural areas may have a major impact. This issue requires in-depth large-scale country studies in order to subsequently create an optimal screening program and prevention of atherosclerotic diseases.

Limitations. The study has several limitations, including its cross-sectional design, which prevents establishing causality. The sample was limited to Kazakhstani adults, potentially reducing generalizability to other populations. Additionally, self-reported lifestyle factors like diet and physical activity may introduce recall bias.

What's Known? Previous research has identified age, smoking, and dyslipidemia as key risk factors for atherosclerosis globally, with regional variations in risk factor prevalence. Studies in Kazakhstan highlighted high rates of hypertension and metabolic disorders but lacked stratification by cardiovascular risk levels.

What's New? This study provides the first ethnonational analysis of atherosclerosis risk factors in Kazakhstan, revealing rural residence as a significant risk factor and emphasizing the protective role of physical activity. It also highlights gender differences and the impact of early menopause, offering insights for targeted preventive strategies.

Conclusion

Age, smoking and family history of CVD are the main risk factors for the development of ASCVD in the study cohort. Women demonstrate a lower risk of developing atherosclerotic processes compared to men, while the group of patients with early menopause had the highest percentage of women with early menopause. A thorough study of the gender aspect of the development of atherosclerotic pathology is required. Physical activity has a strong protective effect. It is interesting that, according to the comparative analysis of binary variables, rural residents have a higher risk of developing atherosclerosis. This result also requires a detailed and large-scale study, with the definition of the most significant risk factors among the urban and rural population, as well as the influence of the region of residence on the development of ASCVD. The data obtained in this study, as well as the results of future studies, will optimize country preventive strategies for managing risk factors and preventing the growth of ASCVD among the population of the Republic of Kazakhstan.

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