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ORIGINAL ARTICLE

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Cardiac Phenotypes of Pregnant Women with Hypertensive Disorders in Different Ethnic Groups

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Abstract

The objective of this study was to conduct a comparative analysis of the features of LV myocardial remodeling in pregnant women with chronic arterial hypertension (CAH) and preeclampsia (PE) on the background of CAH.

Methods and Results: The study cohort included pregnant women (n=547) with hypertensive disorders. All women were divided into two groups: Group 1 included 376 Caucasian patients living in the Republic of Dagestan; Group 2 included 171 patients living in the Republic of Sakha (Yakutia) (indigenous residents [Yakuts and Evenks). Later on, all patients were divided into the following subgroups: Sub1A (n=134), and Sub2A (n=69) – pregnant women with CAH; Sub1B (n=242) and Sub2B (n=102) – pregnant women with PE on the background of CAH. The diagnosis of pregnant women with CAH was made on the basis of existing national and foreign recommendations that an increase in SBP ≥140 mmHg and/or DBP ≥90 mmHg indicates CAH. Different patterns of left ventricular (LV) geometry were defined based on left ventricular mass index (LVMI) and relative wall thickness (RWT), as recommended by the American Society of Echocardiography. The observed/predicted LVM ratio was calculated as 100×(oLVM/pLVM). Participants with an oLVM/pLVM ratio of >128% were categorized as having "inappropriate" LVM (iLVM).

iLVM was found in Subgroups 1B and 2B in the third trimester. The frequency of LV remodeling in pregnant women of Subgroups 1 A and 2A in the second and third trimesters did not differ significantly. In Subgroup 1B, the frequency of concentric left ventricular hypertrophy (cLVH) was higher in the third trimester (42.6%) than in the second trimester (26.9%) (P=0.000). Moreover, in the third trimester, the frequency of cLVH was significantly higher in Subgroup 1B than in Subgroup 2B (42.6% and 29.4%, respectively, P=0.022). At the same time, in the third trimester, the frequency of left ventricular concentric remodeling (LVCR) was significantly higher in Subgroup 2B than in Subgroup 1B (56.9% and 44.2%, respectively, P=0.032). In the second trimester in Subgroup 1B, the frequency of LVCR was higher than in Subgroup 1A (50% and 38.1%, respectively, P=0.026). By the third trimester, the severity of LV remodeling has increased significantly in Subgroup 1B. Thus, in Subgroup 1B, the frequency of c LVH reached 42.6% compared to 31.3% in Subgroup 1A (P=0.03). In Subgroup 2B, in the third trimester, the frequency of LVCR was slightly higher than in Subgroup 2A (56.9% and 43.5%. respectively, P=0.08).

Conclusion: Living conditions predetermine the prevalence of iLVM and LVCR in pregnant northerners with CAH. A more common type of LV remodeling in pregnant women with CAH in conditions of high-altitude hypoxia is also LVCR, which transforms into cLVH by the third trimester in pregnant women with PE on the background of CAH. The study of the type of LV geometry and the appropriateness of LVM allows us to clarify the degree of LV damage in hypertension-related pregnancy. iLVM in pregnant women with CAH appears to be a predictor of the development of PE. The revealed changes in the LV structure—LVCR and cLVH—are more significant in PE on the background of CAH. (**International Journal of Biomedicine. 2022;12(1):38-42.**)

Key Words*:* chronic arterial hypertension • preeclampsia • left ventricular remodeling • inappropriate left ventricular mass

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Abbreviations

BMI, body mass index; **CAH**, chronic arterial hypertension; **DBP**, diastolic BP; **EF**, ejection fraction; **IVST**, interventricular septal thickness; **LVPWT**, left ventricular posterior wall thickness; **LVM**, left ventricular mass; **LVMI**, left ventricular mass index; **LVH**, left ventricular hypertrophy; **LVEDV**, left ventricular end-diastolic volume; **LVESV,** left ventricular end-systolic volume; **LVEDD**, left ventricular end-diastolic dimension; **LVESD**, left ventricular end-systolic dimension; **LVCR**, left ventricular concentric remodeling; **cLVH**, concentric left ventricular hypertrophy; **eLVH**, eccentric left ventricular hypertrophy; **iLVM**, inappropriate LVM; **PE**, preeclampsia; **RWT**, relative wall thickness; **SBP**, systolic BP; **SV**, stroke volume.

Introduction

Hypertensive conditions complicate up to 10% of pregnancies worldwide and are a leading cause of maternal, fetal, and neonatal morbidity and mortality.[1] The frequency of adverse outcomes in these women has doubled over the past 10–20 years.[2,3] There is evidence of the relationship between chronic arterial hypertension (CAH), which existed before pregnancy, and the risk of developing severe hypertension and preeclampsia.[4]

Chronic arterial hypertension (CAH), defined by clinical practice guidelines as SBP (≥140 mmHg) and or DBP ((≥90 mmHg) before pregnancy or up to 20 weeks, complicates or use of antihypertensive medication before pregnancy. Preeclampsia (PE), a pregnancy-specific disorder characterized by hypertension (≥140/90 mmHg) and proteinuria (≥300 mg in 24-hour urine), occurs de novo or may be superimposed on CAH.

Human health can be affected by various factors, including environmental, social, climatic, demographic, and economic factors.[5,6] The Republic of Dagestan, one of the largest republics of the North Caucasus, is located on the northeastern slope of the Great Caucasus Range and in the southwest of the Caspian Lowland. In the structure of general morbidity and mortality of the population, the pathology of the cardiovascular system occupies the leading place.[7] Most Dagestan people are residents of the mountainous and high-mountainous parts. It creates an unsolvable problem of ensuring the population's access to medical care, increasing complications of pregnancy and childbirth.[9] The Republic of Sakha (Yakutia) occupies one-fifth of Russia. Yakutia is one of the coldest regions in the world. Extreme climatic factors of Yakutia have a depleting effect on the functional reserves of the human body. The tension of the adaptive mechanisms often manifests itself in the form of an increase in blood pressure.[9,10]

Cardiac remodeling during pregnancy is considered a physiological adaptation to an increased volumetric load and increased body needs.[11]

Hypertrophy is understood as an increase in heart mass above normal value with an increase in hemodynamic load: afterload (pressure load), or preload (volume load), or both at the same time.

Left ventricular hypertrophy (LVH) is defined as increased left ventricular mass in response to volume overload and/or pressure overload.[12] Pressure overload typically leads to concentric LVH, volume overload (anemia and hypervolemic states) – to eccentric LVH. According to the concept of "hypertensive" LV remodeling, concentric hypertrophy in CAH is regarded as an adaptive response to normalize tension in the heart wall.[13] There is also a possibility of developing eccentric LVH.[14]

The impact of LV remodeling patterns, especially concentric LVH, on the risk of developing PE has not been definitively resolved. It is necessary to study the predictive value of cardiac "phenotypes" of pregnant women with CAH, considering ethnic characteristics to individualize treatment and reduce the risk of developing severe forms of the disease.

The objective of this study was to conduct a comparative analysis of the features of LV myocardial remodeling in pregnant women with CAH and PE on the background of CAH.

Materials and Methods

The study cohort included pregnant women (n=547) with hypertensive disorders. All women were divided into two groups: Group 1 included 376 Caucasian patients living in the Republic of Dagestan; Group 2 included 171 patients living in the Republic of Sakha (Yakutia) (indigenous residents [Yakuts and Evenks]).

Later on, all patients were divided into the following subgroups: Sub1A (n=134), and Sub2A (n=69) – pregnant women with CAH; Sub1B (n=242) and Sub2B (n=102) – pregnant women with PE on the background of CAD. Control group 1 (CG1) consisted of healthy pregnant women (n=34) living in the Republic of Dagestan. Control group 2 (CG2) consisted of healthy pregnant women (n=40) living in the Republic of Dagestan.

Inclusion criteria: single-child progressing pregnancy, the presence of CAH confirmed before pregnancy, the woman's informed consent for participation in research.

The diagnosis of pregnant women with CAH was made based on existing national and foreign recommendations that an increase in SBP ≥140 mmHg and/or DBP ≥90 mmHg indicates CAH. The program of a patient's examination included a survey on a special questionnaire, anthropometric examination using a standard technique, office blood pressure (BP) measurement, echocardiography.

BMI was calculated as weight in kilograms divided by squared height in meters (kg/m^2). A BMI of less than 18.5 kg/m² is considered underweight; normal weight – a BMI of 18.5 kg/m² to 24.9 kg/m²; overweight – a BMI of 25 kg/m² to 29.9 kg/m²; obesity – BMI of≥30 kg/m².

Office BP was measured using a mercury sphygmomanometer, according to Korotkov's method. BP was measured three times, and the means of these measurements were used in the analyses.

Echocardiography was carried out according to the recommendations of the American Society of Echocardiography[15] in M- and B-modes. The following parameters were measured and calculated: IVST, LVPWT, LVEDD, LVESD, EF, LVEDV, LVESV, SV, EF. LVM was calculated using the formula of R. Devereux and Reichek.[16] LVMI was calculated as LVM indexed to height$^{2.7}$, and LVH was defined as LVMI ≥ 45 g/m$^{2.7}$ [17] RWT was calculated as 2 times PWT divided by the LV diastolic diameter. Normal RWT was defined as RWT ≤0.42, and increased RWT was defined as RWT>0.42.[17] Patterns of the left ventricular structure were defined as follows: normal (normal LVMI and RWT≤0.42); concentric remodeling (normal LVMI and RWT>0.42); eccentric hypertrophy (LVH and RWT≤0.42); and concentric hypertrophy (LVH and RWT>0.42).[17]

Predicted LVM was calculated using the following formula: pLVM=55.37+[(6.64×height(m$^{2.7}$)+(0.64×SW (g-m/beat)]–(18.07×gender), where SW (stroke work) in gram-meters/beat [g-m/beat]) was computed as follows: cuff SBP×stroke volume×0.0144; female gender coefficient = 2.[18]

The observed/predicted LVM ratio was calculated as 100×(oLVM/pLVM). Participants with an oLVM/pLVM ratio of >128% were categorized as having "inappropriate" LVM (iLVM).[19]

Statistical analysis was performed using the statistical software package SPSS version 19.0 (Armonk, NY: IBM Corp.). The normality of the distribution of continuous variables was tested by the one-sample Kolmogorov-Smirnov test. Baseline characteristics were summarized as frequencies and percentages for categorical variables and as mean (M) and standard error of the mean (SEM) for continuous variables. The Student unpaired t-test was used to compare average values for data with normal distribution. Mann-Whitney U test was used to compare means of 2 groups of variables not normally distributed. Group comparisons with respect to categorical variables are performed using chi-square test. A probability value of $P \le 0.05$ was considered statistically significant.

Results and Discussion

The average age of pregnant women in Croups 1 and 2 did not differ – 33.4±4.6 years and 34.6±5.2 years, respectively (Table 1). The BMI of pregnant women in Group 2 was slightly higher than in Group 1. The average height of pregnant women in Group 2 was slightly lower than in Group 1. The number of pregnant women with BMI > 30 kg/m^2 in Groups 1 and 2 did not differ, as well as the number of births.

Table 1.

Main characteristics of pregnant women with CAH

Variable	Group 1 (n=376)	Group 2 (n=171)	*P*-value
Age, yrs	34.6±5.2	33.4±4.6	0.85
BMI, kg/m^2	25.1±6.1	26.7±4.8	0.84
Height, cm	165.4±5.8	156.68±6.2	0.27
Parity (number of births)	2.4±1.1	2.2±1.2	0.86
BMI >30 kg/m^2	27(7.2%)	14 (8.2%)	0.68

The oLVM/pLVM values in pregnant women of Group 1 are presented in Table 2. In the second and third trimesters, in Subgroup 1B, the oLVM/pLVM ratio was significantly higher than in Control group 1 and Subgroup 1A ($P<0.05$). iLVM was found in Subgroup 1B in the third trimester.

Table 2.

oLVM/pLVM ratio (%) in pregnant women of Group 1 according to stages of pregnancy

Trimester	Subgroup 1A (n=134) [1]	Subgroup 1B (n=242) [2]	CG1 (n=34)[3]	Statistics
2nd trimester	114.8±2.6	124.8±4.3	100.4±4.5	P_{1-2}=0.047 P_{1-3}=0.006 P_{2-3}=0.00
3rd trimester	118.7±4.3	130.5±3.8	107.3±3.6	P_{1-2}=0.04 P_{1-3}=0.04 P_{2-3}=0.00

The oLVM/pLVM values in pregnant women of Group 2 are presented in Table 3. In the second trimester and the third trimester, in Subgroup 2B, the oLVM/pLVM ratio was significantly higher than in Control group 2 and Subgroup 2A ($P<0.05$). iLVM was found in Subgroup 2B in the third trimester.

Table 3.

oLVM/pLVM ratio (%) in pregnant women of Group 2 according to stages of pregnancy

Trimester	Subgroup 2A (n=69) [1]	Subgroup 2B (n=102) [2]	CG2 (n=40) [3]	Statistics
2nd trimester	116.2±2.2	126.7±4.6	107.3±3.8	P_{1-2}=0.02 P_{1-3}=0.04 P_{2-3}=0.001
3rd trimester	122.7±2.2	135.3±4.2	110.4±3.8	P_{1-2}=0.00 P_{1-3}=0.006 P_{2-3}=0.00

In the meta-analysis performed by De Haas et al.,[20] forty-eight studies were included, with publication dates ranging from 1977 to 2016. The authors found that during normotensive pregnancy, most cardiac geometric indices change from the second trimester onwards (LVM and RWT increase by 20% and 10%, respectively, that consistent with concentric rather than eccentric remodeling). A more remarkable change in LVM (95% increase from reference) and RWT (56% increase from reference data) occurs during hypertensive pregnancy.

The introduction of the oLVM/pLVM ratio, which allows us to differentiate the risk group for severe hypertension and PE with an indicator ">128%," showing the presence of iLVM, regardless of the LVH type, seems optimal when examining women with CAH. Patterns of the left ventricular structure in pregnant women with hypertensive disorders in various ethnic populations are presented in Table 4.

The frequency of LV remodeling in pregnant women of Subgroups 1 A and 2A in the second and third trimesters did not differ significantly. In Subgroup 1B, the frequency of cLVH was higher in the third trimester (42.6%) than in the second trimester (26.9%) (*P*=0.000). Moreover, in the third trimester, the frequency of cLVH was significantly higher in Subgroup 1B than in Subgroup 2B (42.6% and 29.4%, respectively, *P*=0.022). At the same time, in the third trimester, the frequency of LVCR was significantly higher in Subgroup 2B than in Subgroup 1B (56.9% and 44.2%, respectively, *P*=0.032). It is important to note that in the second trimester in Subgroup 1B, the frequency of LVCR was higher than in Subgroup 1A: 50% and 38.1%, respectively, *P*=0.026). By the third trimester, the severity of LV remodeling has increased significantly in Subgroup 1B. Thus, in Subgroup 1B, the frequency of c LVH reached 42.6% compared to 31.3% in Subgroup 1A (*P*=0.03). In Subgroup 2B, in the third trimester, the frequency of LVCR was slightly higher than in Subgroup 2A (56.9% and 43.5%, respectively, *P*=0.08).

Table 4.
Patterns of the left ventricular structure in pregnant women with hypertensive disorders in various ethnic groups

Group		n	2nd trimester				3rd trimester			
			Normal geometry	CRLV	eLVH	cLVH	Normal geometry	CRLV	eLVH	cLVH
Subgroup 2A	abs	69	13	31	5	20	13	30	0	26
	%		18.8	44.9	7.2	29.0	18.8	43.5	0.0	37.7
Subgroup 1A	abs	134	33	51	9	41	23	62	7	42
	%		24.6	38.1	6.7	30.6	17.2	46.3	5.2	31.3
P-value			NS	NS	NS	NS	NS	NS	NS	NS
Subgroup 2B	abs	102	20	49	0	33	14	58	0	30
	%		19.6	48.0	0.0	32.4	13.7	56.9	0.0	29.4
Subgroup 1B	abs	242	56	121	0	65	32	107	0	103
	%		23.1	50.0	0.0	26.9	13.2	44.2	0.0	42.6
P-value			NS	NS	-	NS	NS	0.032	-	0.022
CG2	abs	40	31	4	5	0	26	0	14	0
	%		77.5	10.0	12.5	0.0	65.0	0.0	35.0	0.0
CG1	abs	34	28	0	6	0	26	0	8	0
	%		82.4	0.0	17.6	0.0	76.5	0.0	23.5	0.0

It should be noted that the incidence of cLVH in both ethnic samples was higher than that of other authors in foreign sources.[14] probably due to late seeking medical care and delayed hypertensive therapy. This fact is probably due to the high frequency of delayed hypotensive therapy in our samples.

Variants of LV geometric types in Control groups 1 and 2 did not practically differ. Conclusions about the adverse effect of abnormal LV geometry on the prognosis of arterial hypertension and hypertension-related pregnancy prevail in cLVH.[21-24]

According to Mureddu et al.,[25] iLVM is associated with concentric geometry, high peripheral resistance, and depressed wall mechanics. Several studies have shown that the deviation of LVM from the value appropriate for stroke work, body size, and sex correlates with measures of myocardial function better than LVM.[25-29] iLVM in the indigenous women of the Yakutia population indicated a better informative value of this parameter than the type of LV geometry in assessing the nature of adaptation of the heart muscle to stress. These differences might be related to the anthropometric measurement between the Caucasian and Mongoloid populations.[30,31]

The indigenous women of Yakutia are characterized by typical features inherent in the northern adaptive type – a short body length with a relatively high body density, a stocky physique with well-developed musculoskeletal mass, increased waist and hip circumference.[5] Such characteristics represent the result of adaptation to the harsh climatic and geographical conditions of living in the North.[32] These living conditions predetermine the prevalence of iLVM and LVCR in pregnant northerners with CAH.

The peculiarities in LV remodeling of pregnant women living in different regions of the Republic of Dagestan consist in adaptation to hypoxia conditions of women living in the mountainous areas.[33] A more common type of LV remodeling in pregnant women with CAH in conditions of high-altitude hypoxia is also LVCR, which transforms into cLVH by the third trimester in pregnant women with PE on the background of CAH.

Conclusion

The study of the type of LV geometry and the appropriateness of LVM allows us to clarify the degree of LV damage in hypertension-related pregnancy. iLVM in pregnant women with CAH appears to be a predictor of the development of PE. The revealed changes in the LV structure—LVCR and cLVH—are more significant in PE on the background of CAH.

Competing Interests

The authors declare that they have no competing interests.

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