



# **Clinical and Prognostic Value of Vascular Wall Elasticity in Pregnant Women with Arterial Hypertension: A Review**

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## **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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**Review Article**

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## **ABSTRACT**

In recent years, the attention of many researchers around the world has been focused on studying the risks associated with the development of the pathological course of pregnancy in women with arterial hypertension (AH). The pathogenesis of gestational complications is complex and is largely associated with endothelial dysfunction, changes in the structure and properties of the vascular wall and a decrease in its elasticity. At the same time, at the present stage, a high prognostic value of the assessment of vascular elasticity in the development of cardiovascular disasters in patients with hypertension in the general population has been proved. In order to predict the risk of gestational complications early, it is promising to study the state of elasticity of the vascular wall, which will optimize the management of pregnancy and improve perinatal

outcomes in pregnant women with hypertension. The literature search was carried out by keywords using the Scopus, Web of Science, Cyber Leninka, RSCI (Russian Science Citation Index) systems.

**Keywords:** *Review; pregnancy; arterial hypertension; endothelial dysfunction; vascular wall elasticity; risk prediction.*

## 1. INTRODUCTION

In modern conditions, arterial hypertension (AH) remains one of the most urgent problems of clinical medicine due to the high risk of developing cardiovascular complications (stroke, myocardial infarction, heart and kidney failure) and mortality. An important area of cardiology is the search for early markers of target organ damage in patients with hypertension-blood vessels, heart, kidneys and brain [1,2]. Hypertension among the pregnant women is an interdisciplinary problem of cardiology and obstetrics, since it leads to an unfavorable course of the gestational process and perinatal pathology. In the world, hypertension complicates 10-20% of pregnancies, in Russia–5-30% [3,4,5]. It should be noted that over the past two decades, the frequency of hypertension among pregnant women has increased by 40-50%. This is due to an increase in the average age of first-time mothers, the prevalence of obesity in women, and the widespread use of assisted reproductive technologies [3,4,6]. According to WHO, in 2014, hypertension and its associated complications ranked second (14%) in the structure of causes of maternal mortality [3,7]. In Russia, according to the Ministry of Health of the Russian Federation, this indicator is in third place, amounting to 18% in 2014, 10.8% in 2015, and 13.1% in 2016 [5]. According to large cohort studies conducted in several countries, perinatal mortality in hypertensive disorders is 9-20%. In addition, in the gestation period up to 24 weeks, perinatal mortality rates exceed 80%, the frequency of pregnancy complications varies from 27 to 71%. In the gestation period of more than 24 weeks, the frequency of serious maternal outcomes is less than 5% [5,6].

Hypertension is a condition in which systolic blood pressure  $\geq 140$  mmHg and/or diastolic blood pressure  $\geq 90$  mmHg are registered in pregnant women. Perinatal mortality in women suffering from hypertension reaches 30-100% [5,6].

According to the National Guidelines for the diagnosis and treatment of cardiovascular

diseases during pregnancy (2018), the following clinical variants of hypertension are distinguished in such patients: chronic hypertension (hypertension that existed before pregnancy): hypertension or symptomatic hypertension; gestational hypertension; hypertension complicated by preeclampsia; preeclampsia/eclampsia.

## 2. METHODS

Chronic hypertension (hypertension) is an increase in blood pressure  $\geq 140/90$  mmHg, determined before pregnancy or up to 20 weeks of its development. Hypertension diagnosed after 20 weeks and not disappeared within 12 weeks after delivery is also classified as pre-existing hypertension, but already retrospectively.

The group of chronic hypertension, in addition to symptomatic hypertension, includes:

- \* Hypertension of the "white coat" – an increase in blood pressure during office measurements (blood pressure  $\geq 140/90$  mmHg), and blood pressure  $< 140/90$  mmHg. with independent (home) measurement or with ADBP (average daily blood pressure  $< 135/85$  mmHg.);
- \* Masked arterial hypertension - blood pressure  $< 140/90$  mmHg at office measurement and blood pressure  $\geq 140/90$  mmHg at independent (home) measurement or with ADBP (average daily blood pressure  $\geq 135/85$  mmHg).

Gestational hypertension is a condition induced by pregnancy and manifested by a blood pressure level  $\geq 140/90$  mmHg after 20 weeks. Within 12 weeks after delivery in patients with gestational hypertension, blood pressure returns to normal levels. If blood pressure remains elevated 12 weeks after delivery, then you should think about hypertension or symptomatic hypertension.

Hypertension complicated by ET (embryo transfer) is characterized by the following criteria:

1. The appearance of proteinuria for the first time after 20 weeks ( $\geq 0.3$  g of protein per day) or the progression of the level of previously available protein in the urine;
2. Increasing increase in blood pressure and /or instability of hypertension (with constant monitoring of blood pressure up to 20 weeks of pregnancy);
3. The appearance after 20 weeks of signs of multiple organ failure.

Preeclampsia is a multisystemic pathological condition that develops in the second half of pregnancy (after the 20th week), characterized by arterial hypertension in combination with proteinuria ( $\geq 0.3$  g / l per day), often edema, and signs of multiple organ / polysystemic dysfunction / insufficiency.

Eclampsia is an attack of seizures or a series of convulsive seizures on the background of preeclampsia in the absence of other causes. In 30% of cases, eclampsia develops suddenly without prior preeclampsia.

Among all hypertensive conditions, 30-51% of cases are due to hypertension [8].

In this regard, attention has significantly increased to the study of the risks of developing a pathological course of pregnancy (preeclampsia, placental insufficiency, fetal growth retardation, premature birth) in hypertension [9,10,11]. In turn, it was noted that the pathogenesis of obstetric and perinatal complications in women with hypertension is associated with endothelial dysfunction, leading to a violation of placentation and maladaptation of regulatory mechanisms [11,12].

### 3. RESULTS

In the modern literature, it is shown that endothelial dysfunction is accompanied by an increase of stiffness of the vascular wall [2, 13, 14, 15]. This direction is being actively studied on the example of patients with essential hypertension. To date, it has been proven that increased arterial wall stiffness is associated with an increased risk of cardiovascular mortality in patients with hypertension [2,13,16]. Thus, the HARVEST study (Hypertension and Ambulatory Recording VEnetia SStudy) showed that the stiffness of the vascular wall can be increased already at an early stage of the development of hypertension. The relationship between an

increase in the level of systolic and pulse pressure and a decrease in the elasticity of the walls of large arteries, even in patients with "white coat" hypertension, has been proved [17].

The rigidity of the arterial wall affects the ability of large vessels to smooth out the pulsation caused by cardiac output and turn the shock pressure in the ascending aorta into a stable blood flow in the peripheral vessels. An increase in the rigidity of the arterial wall in hypertension contributes to a violation of the damping function of the arteries, acceleration of the reflected wave, an increase in systolic and pulse pressure, a decrease of diastolic pressure and the risk of myocardial ischemia [16,18,19 20].

In the last decade, foreign and domestic researchers have been studying the processes of remodeling of elastic-type vessels and its clinical significance. According to the European Guidelines for the treatment of Arterial Hypertension ESH/ESC 2018, aortic stiffness has an independent prognostic significance for cardiovascular disasters in patients with hypertension [2].

There are currently few data on the study of the state of the arterial wall elasticity in pregnant women with hypertension in both domestic and foreign literature. There are a number of studies on the effect of violations of the daily blood pressure profile on the course of pregnancy and the condition of the fetus in patients with hypertension. It was found that the greatest prognostic value is the average blood pressure indications and night time blood pressure dip – (NCBI) [21,22,23]. It is noted that the feature of the daily blood pressure profile in pregnant women with hypertension is the predominance of the type of daily curve with an insufficient nighttime decrease in blood pressure-non-dipper ( $0 < \text{NCBI} < 10\%$ ), as well as with nighttime blood pressure exceeding daily values-night-picker ( $\text{NCBI} < 0$ ) [21, 22, 24, 25]. According to other data, hypertensive pregnant women are characterized by systolic hypertension in the morning and in emotional states, as well as the optimal degree of nocturnal blood pressure reduction (10-20%) – the dipper type [26,27,28]. At the same time, 20-30% of normotensive women with a physiological course of pregnancy have a non-dipper profile, which may complicate the diagnosis of hypertension [29].

In this regard, in order to assess the adaptive processes of the cardiovascular system in

pregnant women with hypertension, an important direction is to study the elasticity of the vascular wall.

In pregnant women with hypertension, vascular remodeling occurs against the background of increased activity of the sympathetic part of the autonomic nervous system, which leads to increased stiffness and a decrease in the lumen of the arteries to maintain stable blood flow in the tissues [30].

To assess the stiffness of the arteries in patients with hypertension, there are a number of parameters: the speed of the carotid-femoral pulse wave (PWV), Pulse Wave Velocity is the "gold standard" for measuring aortic stiffness (it is directly related to the stiffness of the vascular wall and is inversely proportional to its elasticity); ankle-brachial index, ankle-brachial pressure index (a marker of peripheral vascular damage, used to diagnose atherosclerosis in patients with asymptomatic peripheral artery damage, is a predictor of cardiovascular events); cardio-ankle vascular index, cardio-ankle vascular index (used to assess the severity of coronary atherosclerosis); pulse wave augmentation index, Alx (characterizes the magnitude of the reflected wave from the pools of the lower half of the body, highly correlates with the indicators of central aortic pressure augmentation and reflects the degree of increase in the pulse wave in the aorta); arterial stiffness index, arterial stiffness index (reflects the stiffness of peripheral arteries and the risk of CHD); outpatient arterial stiffness index, ambulatory arterial stiffness index (has a high prognostic significance for fatal strokes, cardiovascular complications and a positive correlation with PWV, augmentation index, central and peripheral pulse blood pressure); flow-induced vasodilation (used to assess endothelial regulation of vascular tone) [2,14,16,18,31,32].

In the European Guidelines for the treatment of arterial hypertension ESH/ESC 2018, to identify the risk of target organ damage in hypertension, the list of mandatory studies includes an assessment of the speed of the carotid-femoral pulse wave and the ankle-shoulder index [2].

European experts have found that the determination of PWV is the simplest, non-invasive and reproducible method for assessing arterial stiffness [2,20]. A number of studies have also shown that the measurement of PWV reduces the probability of underestimating the

risk of cardiovascular events in patients with hypertension according to the classical scales (SCORE and the Framingham scale) [2, 16]. Alternative parameters of arterial rigidity cannot be used as independent, they correlate with each other and the degree of risk of cardiovascular complications, are time-consuming and are currently being actively studied [2,16,33].

According to the European Guidelines for the treatment of Arterial hypertension ESH/ESC 2018, the recommended tests for assessing the risk of cardiovascular disasters are the determination of the rigidity of the vascular wall and central pulse pressure, especially in cases where no signs of damage to target organs were detected during a standard examination [2].

Various methods for assessing the elasticity of the vascular wall in patients with essential hypertension have been developed. Previously, "invasive arteriography techniques (radiopaque arteriography) "were used to study the state of the vascular wall. Currently, a wide range of non – invasive methods is presented-direct imaging (ultrasound and MRI) and indirect (plethysmography, sphygmography, oscillometry) [34].

A highly informative and safe method for determining outpatient blood pressure for the mother and fetus is ABPM (24-hour blood pressure monitoring) - a method of applanation tonometry that registers a pulse wave on the brachial artery, allows you to study the rigidity of the vascular wall, central aortic blood pressure (CAP), daily fluctuations in peripheral pressure and differentiate hypertensive disorders during pregnancy [34,35].

The main indicator of the elasticity of the vascular wall is pulse wave velocity (PWV) [2,30,34]. The clinical significance of PWV in pregnant women with hypertensive disorders is debatable.

#### 4. DISCUSSION

It was previously shown that in women with hypertension in the second trimester of pregnancy, the PWV index does not change compared to healthy pregnant women, which could be due to the vasodilating effect of hormones and vasodilating factors [26,36].

Further studies of vascular elasticity were conducted in pregnant women with preeclampsia

(II-III trimester). In some studies, an increase in PWV and the augmentation index was shown in comparison with normotensive pregnant women [35], in others, an increase in PWV with an unchanged augmentation index [37], and in a number of studies, these parameters did not differ from physiological pregnancy [38]. There is also information in the literature where only an increase in the augmentation index was detected in women with preeclampsia, while other stiffness parameters were not studied [39]. In addition, there are research results according to which a high level of PWV is a predictor of preeclampsia in early pregnancy. Thus, according to Phan K, Schiller I, Dendukuri N et al (2021), it was shown that in pregnant women with preeclampsia, the PWV index increased from 14-17 weeks and at 22-25 weeks was 1.2 m/s higher compared to the value of this parameter in pregnant women without preeclampsia. The same study showed an increase in the augmentation index from 18-21 weeks in pregnant women with subsequent development of preeclampsia, whereas in women without preeclampsia, this indicator increased at 30-33 weeks of gestation [27].

In other studies, an increase in PWV and the augmentation index was demonstrated in patients with preeclampsia developed during full-term pregnancy with the preservation of elevated levels of these parameters and in the postpartum period, which may indicate persistent changes in the vascular wall. The same authors examined women with a history of preeclampsia. Data were obtained on high values of the augmentation index, PWV, the time of propagation of the reflected wave and the index of arterial rigidity in the second trimester, which may indicate more rigid vessels compared to pregnant women without a history of preeclampsia [35].

In recent years, when examining women with hypertension in the II and III trimesters of pregnancy, an increase in PWV and elastic modulus of elasticity along the arteries of the muscular and elastic type was revealed in comparison with pregnant women who do not suffer from hypertension. At the same time, the highest deviations were found in patients with hypertension complicated by preeclampsia [11,30,40].

According to modern concepts, CAP and vascular wall rigidity are considered as independent markers of the development of cardiovascular complications [2]. The level of

CAP in comparison with peripheral blood pressure is regulated by the elastic properties of large vessels, structural and functional elements of medium-caliber arteries and resistive vessels, and is the most informative indicator that determines the state of the arterial wall [11, 22].

Despite the available evidence base of the clinical and prognostic value of CAP in patients with cardiovascular risk, there is very little work on the study of this parameter in pregnant women with hypertension in both foreign and domestic literature. Thus, in studies conducted in the II-III trimester of pregnancy, it was noted that in women with hypertension, the values of central systolic blood pressure, central diastolic blood pressure, central mean hemodynamic pressure and central pulse blood pressure are higher than in physiological pregnancy. At the same time, the highest levels of central systolic blood pressure and central diastolic blood pressure were found in pregnant women with hypertension complicated by preeclampsia [11]. There is also evidence that in patients with hypertension throughout pregnancy, the indicators of central systolic blood pressure and central pulse blood pressure are lower than the values of peripheral systolic blood pressure and peripheral pulse blood pressure, which may indicate a decrease in the elasticity of the main vessels in cardiovascular diseases [11,41].

Recently, there have been data on the value of arterial stiffness indicators in pregnant women with hypertension. In studies conducted in the second trimester of pregnancy, it was shown that in women with hypertension, the augmentation index  $aix_{75}$  (measured for a heart rate of 75 beats/min to exclude the influence of heart rate on this indicator), the index of arterial rigidity, the maximum rate of increase in blood pressure are increased, especially with the development of preeclampsia, while the time of propagation of the reflected wave and pulse pressure amplification do not differ from normotensive women [10,42]. In other studies, conducted in the third trimester of pregnancy in patients with hypertension, the daily profile of CAP and arterial stiffness indicators were studied. It was shown that the CAP rhythm corresponds to the profile of peripheral blood pressure and also decreases during sleep. The augmentation index at night, on the contrary, increases, since it is inversely dependent on the heart rate, which decreases when a person sleeps, as well as when the body is horizontal. The indicator of the time of propagation of the reflected wave was also

higher at night, since it inversely depends on the level of blood pressure [9,22]. A significant correlation was obtained between the time of propagation of the reflected wave and the augmentation indices, as well as between the augmentation indices in the brachial artery and the aorta [22]. A weak correlation is shown between the time of propagation of the reflected wave and the arterial stiffness index [22], which does not coincide with the opinion of some scientists, according to which these indicators are well correlated with each other [43].

When analyzing the current literature, few data were obtained on the significance of the state of vascular wall elasticity in the prognosis of gestational and perinatal complications in pregnant women with hypertension. In some studies, the prognostic value of the CAP and the difference between central and peripheral blood pressure on the course and outcome of pregnancy were studied. Therefore, when performing ABPM in the second trimester, the predictors of the development of fetal growth retardation in pregnant women with hypertension are a decrease in the elasticity of the vascular wall and a decrease in the difference between the central nervous system and peripheral blood pressure. The prognostic significance of the risk of fetal growth retardation is the difference between central and peripheral systolic blood pressure equal to  $8.3 \pm 0.9$  mm Hg; the difference between central and peripheral pulse blood pressure equal to  $9.8 \pm 1.0$  mm Hg; the level of central systolic blood pressure  $\geq 118$  mm Hg; peripheral diastolic blood pressure  $\geq 82$  mm Hg; peripheral mean hemodynamic pressure  $\geq 99$  mm Hg. In the studies of the same authors, a direct relationship was revealed between the complications of childbirth (premature birth, untimely discharge of amniotic fluid, a long anhydrous period, anomalies of labor activity) and an increase in central systolic blood pressure in the II-III trimesters  $\geq 118$  mm Hg [22].

There are studies that show that hypertension in pregnant women is a high-risk factor for the development of preeclampsia. Thus, in the first trimester, high values of the augmentation index and PWV were detected in women with hypertension compared to normotensive pregnant women [9].

In other studies, it was noted that when performing ABPM at the time of 16-22 weeks in patients with hypertension, the average daily aortic systolic blood pressure and the arterial

stiffness index can serve as independent indicators for predicting preeclampsia. Thus, the highest diagnostic significance of the risk of developing preeclampsia against the background of hypertension is the level of average daily aortic systolic blood pressure above 115 mmHg (sensitivity-85%, specificity-88%, prognostic value of a positive result-79%, prognostic value of a negative result-91%, overall accuracy-86%) [10].

The works of foreign authors have shown a positive significant correlation ( $p < 0.001$ ,  $r = 0.835$ ) between the increased body mass index and the parameters of aortic stiffness (aortic systolic blood pressure and brachial artery rigidity index) in pregnant women with hypertension, which can serve as a marker of a high risk of complications of the gestational process [44].

## 5. CONCLUSION

Therefore, until now, the question of the clinical and prognostic significance of the state of vascular wall elasticity in pregnant women with hypertension remains unresolved. Most of the studies were conducted in the second half of pregnancy, individual parameters of vascular rigidity were studied, the indicators with the greatest practical significance were not determined.

At the same time, the practical significance of assessing the elasticity of the vascular wall is to improve the stratification of the risk of gestational complications in pregnant women with hypertension. Assessment of the parameters of vascular wall rigidity and CAP in early gestation in women with hypertension will allow forming a high-risk group for the development of preeclampsia, placental insufficiency and premature birth, optimize pregnancy management and improve perinatal outcomes. Detection of target organ damage in hypertension among pregnant women will allow us to select a group of women for follow-up care after childbirth by a cardiologist.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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