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The relationship between impaired uteroplacental blood flow and blood pressure level in pregnant women with chronic and gestational hypertension

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Abstract

Aim. To assess the relationship between impaired uteroplacental blood flow and different levels of blood pressure in pregnant women with chronic and gestational hypertension at different stages of pregnancy with the determination of the optimal systolic blood pressure.

Methods. We conducted a prospective cohort study between 2018 and 2019. The study enrolled pregnant women aged 18 to 45 years: 55 women with chronic and gestational hypertension each, as well as 80 healthy pregnant women as control. The groups were formed by the continuous method, in which all pregnant women with arterial hypertension were included in the study until the required number of subjects was obtained. Follow-up was conducted at different gestation periods (14–16, 20–22, 28–30, 34–36 weeks) until delivery. Independent groups were compared by using the Student's t-test, the Pearson's χ^2 test, the Mann–Whitney U test, the Kruskal–Wallis H test.

Results. Comparison of the groups revealed differences in blood pressure levels at different gestation periods. In chronic hypertension compared with gestational hypertension, there was an increase in the impairment of the uteroplacental blood flow in pregnant women, indicating an unfavorable prognosis. The study of impaired uteroplacental blood flow among pregnant women with various forms of arterial hypertension revealed an increase in pregnant women with chronic arterial hypertension compared with gestational (p=0.04), indicating an unfavorable prognosis. In chronic arterial hypertension, the impairment of uteroplacental blood flow was the least for systolic pressures up to 120 mm Hg (up to 0.9%) at 14–16 and 20–22 weeks of gestation, and for 130–139 mm Hg (from 1.8 to 2.7%) in later pregnancy. In gestational hypertension, the least or no impairment rate of uteroplacental blood flow was determined for blood pressures up to 129 mm Hg at all stages of pregnancy compared with chronic hypertension.

Conclusion. The optimal systolic blood pressure in chronic hypertension reducing the risk of impaired uteroplacental blood flow in pregnant women is <129 mm Hg before 20th week of pregnancy and 130–139 mm Hg in later (20–30 weeks); in gestational hypertension, blood pressure reduction to 129 mm Hg is recommended at all stage of gestation.

Keywords: arterial hypertension, blood pressure, target blood pressure level, pregnancy complications, uteroplacental disorders, gestation, pregnancy stages.

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Background. Arterial hypertension (AH) in pregnant women is recognized as one of the main causes of morbidity and mortality, both on the part of the mother and the fetus. It affects 5%–10% of pregnant women worldwide [1, 2]. The main goal of managing pregnant women with hypertension is to strive to achieve the target blood pressure (BP) levels and thereby prevent the risk of complications in the mother and the fetus. Additionally, maternal mortality worldwide is due to AH in 15%–18% of cases [3, 4], which amounts to 62,000–77,000 lethal outcomes per year [5].

Despite ongoing studies in pregnant women, the leading AH communities cannot agree on target BP levels. Thus, the European Society of Cardiology recommends starting drug therapy in all pregnant

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women with a persistent increase in the systolic BP (SBP) of 150/95 mm Hg or higher and at values higher than 140/90 mm Hg in women with gestational AH (GAH) [1]. According to the international recommendations of most countries in Europe and America, striving for a BP level of 160/105 mm Hg or lower is required [6–8]. According to the recommendations of the Canadian Cardiovascular Society, the target BP level is SBP of 130–155 mm Hg and diastolic BP of 80–105 mm Hg [9].

The Russian recommendations suggest a BP level of 150/95 mm Hg and higher as criteria for prescribing antihypertensive therapy in case of chronic hypertension (CAH) without target organ damage and that of 140/90 mm Hg or higher in the presence of lesions of target organs, as well as GAH and preeclampsia [10]. According to the Ministry of Health of the Republic of Kazakhstan protocol in 2017, BP that is lower than 140/90 mm Hg is recommended as the target BP level for CAH and GAH, BP of 140/90 mm Hg and higher is recognized as the criterion for the initiation of antihypertensive therapy in CAH, and BP of 150/100 mm Hg and higher is recognized as the criterion with GAH [11].

Data on the target BP levels for GAH and the criteria for antihypertensive therapy initiation are currently extremely scarce and contradictory. The lack of consensus on target BP levels entails a divergence of opinions on the criteria for starting antihypertensive therapy. Drug selection, therapy regimen, and antihypertensive drug dosage largely depend on the correct determination of the target BP levels. Most researchers hold to the same opinion that in any type of AH, BP should not be reduced to values less than 130/80 mm Hg, which leads to impaired uteroplacental blood flow (UPBF) [12–14].

Until now, there is no differentiated approach and definition of clear criteria for the target BP level for pregnant women with CAH and GAH, especially considering the timing of pregnancy, the study of which was performed in the main databases of the Cochrane Library, PubMed, and MEDLINE.

Impaired UPBF is one of the most frequent complications in pregnant women with AH. The risk frequency of impaired UPBF in pregnant women with AH reaches 70%–100% [15, 16]. Complications in AH, regardless of its type, are more common in the physiological course of pregnancy; however, these complications should be noted as more common in CAH compared with GAH [17].

Frequent impaired UPBF in pregnant women with CAH compared to GAH is confirmed by comparing the disorder of blood flow in the uterine arteries. Thus, an in-depth study in pregnant women with CAH revealed impaired blood flow in one uterine artery in 32.7% and 21.4% in patients with GAH. In CAH, bilaterally impaired blood flow in the uterine arteries and fetal hypoxia were more common compared to GAH [16].

In her research, O.V. Tretyakova confirms that impaired UPBF is directly proportional to AH severity [18]. Long-term impaired UPBF further leads to the development of intrauterine growth retardation [19]. Pregnant women with AH and intrauterine growth retardation had impaired UPBF in 79.5% of cases, and its incidence is directly proportional to the severity of fetal growth retardation. Thus, the incidence of impaired UPBF was 62.5% with a delay in the intrauterine fetal development of degree I, 83.3% with degree II, and 100% with degree III [20].

This study aimed to assess the relationship between impaired UPBF and different BP levels in pregnant women with CAH and GAH at different terms of pregnancy with the determination of the optimal SBP level.

Materials and methods. A prospective cohort study on the case follow-up of 110 pregnant women with AH was performed at the perinatal centers No. 1 and No. 3 in Nur-Sultan (Kazakhstan) in 2018–2019. These pregnant women made up the main group, which included 55 female patients with CAH and 55 patients with GAH. The groups were formed by a continuous method, in which all pregnant women with AH were included in the study until the required number of participants was obtained.

The inclusion criteria were the age of pregnant women from 18 to 45 years, the presence of AH verified as CAH or GAH.

Exclusion criteria are the following:

– a pregnancy that is induced by assisted reproductive technologies;

– symptomatic AH confirmed before or during pregnancy;

– concomitant somatic diseases that independently increased the risk of unfavorable outcomes of pregnancy and childbirth (cardiac defects, myocardial diseases, systemic connective tissue diseases, neurological pathology, injuries, etc.).

All pregnant women with AH received antihypertensive therapy according to the severity and level of BP.

This study was conducted as part of the thesis research, approved by the local ethics committee (protocol No. 4 dated 12/20/2018), and was approved for the publication of the work results (protocol No. 14 dated 04/20/2021).

A control group was formed to compare the pregnancy course and childbirth outcomes in

female patients with AH. It consisted of 80 healthy pregnant women who did not have somatic diseases that affect the hemodynamic changes.

The average age of female patients was 30.28 ± 5.46 years in the main group (pregnant women with AH) and 31.6 ± 5.68 years in the control group ($p = 0.67$). No significant differences were found in the parity of childbirth in the main and control groups ($p = 0.42$).

An "individual record of a pregnant woman" was developed for the qualitative information collection and data stratification. This record included the passport part, anthropometric data at the time of dispensary registration of the woman, anamnesis data on concomitant diseases, course and outcomes of previous pregnancies and childbirth, results of instrumental (electrocardiography and echocardiography), and laboratory (general blood test and clinical urine analysis, glucose, creatinine, total cholesterol, and low-density lipoproteins) research methods. Data on the current pregnancy course were also recorded, including the timing of the increased BP, the level of BP at certain periods of gestation and after childbirth, hospitalization during the current pregnancy for AH and other diseases, and UPBF assessment, as well as regimens and doses of prescribed antihypertensive drugs. In addition to the anamnesis and course of pregnancy, birth outcomes and data on newborns were entered into the record.

The main method for BP monitoring includes office measurement, which was performed in the perinatal center using the Omron HEM-FL31-E apparatus in compliance with the ESC 2018 recommendations [1]. The comparative analysis included indicators of average office BP in the gestational periods of 14–16, 20–22, 28–30, and 34–36 weeks of gestation.

The Statistical Package for the Social Sciences version 20.0 software was used for statistical data processing. The mean values were expressed as mean values with standard deviation (M ± m) or median (Me) and interquartile range after testing for normal distribution. The criterion for statistical significance of the results was considered $p < 0.05$. The comparison of two independent groups, depending on the type of distribution, was performed using the Student's t, Pearson χ^2, and Mann-Whitney tests. The Kruskal-Wallis test for two or more group comparisons.

Results and discussions. Stage I of our study included the comparison of the complication incidence during pregnancy and childbirth in the group of pregnant women with AH and the control group. Comparative analysis of pregnancy and childbirth outcomes between the main group of pregnant women with AH and the control group was performed for the following complications:

– mild and severe preeclampsia;
– prenatal amniotic fluid discharge;
– atonic bleeding;
– poor uterine contraction strength;
– premature birth;
– impaired UPBF (degree IA, IB, II);
– fetal distress;
– small for gestational age fetus;
– newborn Apgar score of 6 points or less immediately after birth.

Despite the control and treatment of AH, such obstetric complications as preeclampsia ($p = 0.001$), poor uterine contraction strength ($p = 0.04$), and impaired UPBF ($p = 0.001$) were significantly more frequent in the main group than in the control group. Comparative analysis of labor outcomes revealed that complications, such as a small for gestational age fetus ($p = 0.001$) and a low Apgar score ($p = 0.001$) were statistically significantly more frequent in the main group than in the control group. The most significant difference between the main and control groups was found in impaired UPBF ($p = 0.001$).

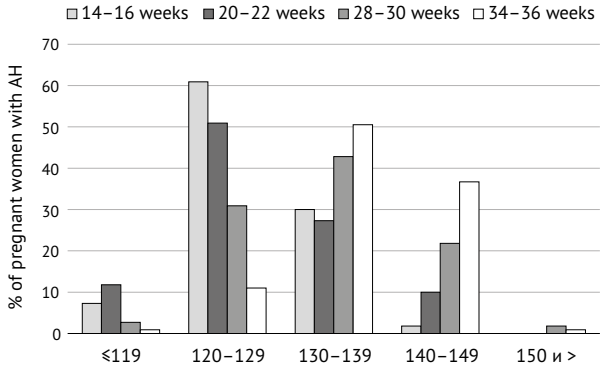
The data presented indicate the existing differences in the outcomes of pregnancy and childbirth in the compared groups.

The complication incidence during pregnancy and childbirth in pregnant women with various types of AH, such as CAH and GAH, was compared. An increased incidence of UPBF disorders was found in the CAH compared to the GAH group ($p = 0.04$), whereas no statistically significant differences between CAH and GAH for other complications of pregnancy [21]. The presented data indicate tendencies in the risks of developing complications of pregnancy, mainly in CAH, but without statistically significant differences.

The next stage of the study was the comparison of the relationship between the disorder of UPBF depending on the levels of BP in CAH and GAH and the gestational age. Therefore, impaired UPBF was studied at various levels of SBP (≤119 mm Hg, 120–129 mm Hg, 130–139 mm Hg, 140–149 mm Hg, and ≥150 mm Hg) and gestational age (14–16; 20–22; and 34–36 weeks).

Figure 1 presents the frequency of distribution of pregnant women with AH (including those with CAH and GAH) at different pregnancy terms and revealed that at the gestational age of 14–16 weeks, in 60.9% of cases ($n = 67$), the level of 120–129 mm Hg was determined, with a smaller number of cases with 140–149 mm Hg ($n = 2$).

As the gestational age increased, the distribution of BP levels changed, so that at terms of 28–



30 and 34–36 weeks, and increased BP was noted among pregnant women with AH with a level of 130–139 mm Hg., namely 42.8% (n = 47) and 50.5% (n = 55), respectively. Additionally, an increased number of pregnant women with AH was noted, whose SBP incidence of 140–149 mm Hg increased up to 21.8% (n = 24) at a term of 28–30 weeks of gestation and up to 36.7% (n = 40) at 34–36 weeks.

Thus, as the gestational age increases, a redistribution of SBP levels toward its increases. However, despite the tendency of increasing SBP, the level of 150 mm Hg and higher was registered in a small number of cases. The group comparison (control, CAH, and GAH) revealed differences in the level of pressure at different terms of gestation ($\chi^2 = 85.704$, df = 2, $p < 0.001$).

Recommendations for the choice of values are presented on the use of target BP levels in AH. AH has been revealed to increase the risk of complications of pregnancy and childbirth in pregnant women with AH [1], which is also confirmed by our study results. Concurrently, differences were also revealed depending on the type of AH (CAH and GAH). In the range of all analyzed complications (preeclampsia, prenatal discharge of amniotic fluid, atonic bleeding, poor uterine contraction strength, premature labor, fetal distress, fetus small for gestational age, and low Apgar score), statistically, significant differences were revealed between CAH and GAH in the development of UPBF disorders [21]. Revealing the relationship between the development of impaired UPBF and the level of BP in the studied groups of CAH and GAH could improve our understanding and make significant assistance for further management of these patients. The relationship between impaired UPBF and BP levels considered SBP at various pregnancy stages.

Figure 2 presents the frequency of distribution of pregnant women compared with the general group of pregnant women with AH and CAH and with pregnant women with CAH and with impaired UPBF. Thus, at a term of 14–16 weeks, in 21.8% (n = 24) and 19% (n = 21) of cases among the group of pregnant women with CAH, the SBP was determined at the level of 120–129 mm Hg and 130–139 mm Hg, respectively. The level of 150 mmHg and higher was not recorded at a given gestational age, including in pregnant women with impaired UPBF. At 14–16 weeks of gestation, impaired UPBF in CAH was detected in 12.8% (n = 14, out of 50 pregnant women with CAH), and generally, this cohort had SBP levels of 120–129 and 130–139 mm Hg, namely in 5.5% of cases each (n = 6).

At a term of 20–22 weeks of gestation in CAH, the SBP levels were also 120–129 and 130–139 mm Hg and amounted to 18.2% (n = 20) of cases. In CAH with impaired UPBF, in 8.2% of female patients with a given gestational age, the SBP level was also 120–129 and 130–139 mm Hg, respectively, namely 7.3% (n = 8) and 0.9% (n = 1), while at low (≤119 mm Hg) and high (>140 mm Hg) BP levels, no cases with impaired UPBF were registered.

At a follow-up period of 28–30 weeks of gestation, the SBP level was also predominantly at the level of 120–129 and 130–139 mm Hg, amounting to 23.6% (n = 26) and 20% (n = 22), respectively. The lowest incidence of impaired UPBF was revealed at a level of 130–149 mm Hg. The incidence of CAH with impaired UPBF at this term increased to 12.7% and decreased at SBP values above 130–149 mm Hg.

At the late gestational age of 34–36 weeks, the CAH was distributed by SBP levels with the maximum in 21.1% of cases (n = 23) with a level of 130–139 mm Hg, and the smallest one at the lowest and highest SBP levels, in 0.9% of cases each (n = 1). Impaired UPBF in CAH occurred more often at SBP values of 140–149 mm Hg (7.3%, n = 8).

In cases of impaired UPBF in pregnant women with CAH, adhering to BP values below 130 mm Hg up to week 20 of gestation is recommended. Following these recommendations could positively influence the prognosis of the management of such female patients. This will focus on such a target SBP level, with an acceptable SBP decrease of <130 mm Hg and a higher SBP value up to 140 mm Hg at later stages of pregnancy (up to week 30).

Figure 3 presents the distribution frequency of pregnant women compared with the general group of pregnant women with AH and GAH, as well as those with GAH, with impaired UPBF. At 14–16 weeks, SBP was maintained at 120–129 and 130–139 mm Hg in 39.1% (n = 43) and 10.9% (n = 12) of cases, respectively, among the group of pregnant women with GAH. The SBP levels of 119 and lower, as well as 150 mm Hg and higher, at a given

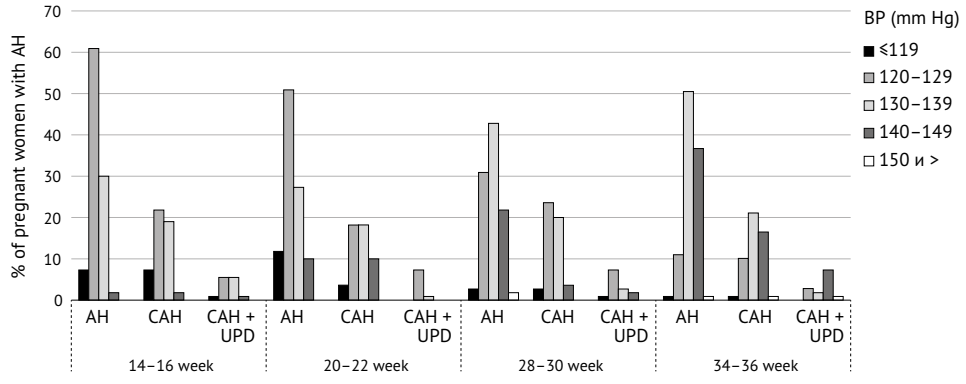


Fig. 2. Distribution of pregnant women with arterial hypertension (AH) and chronic arterial hypertension (CAH), depending on the terms of pregnancy; BP: blood pressure; UPD: uteroplacental disorders.

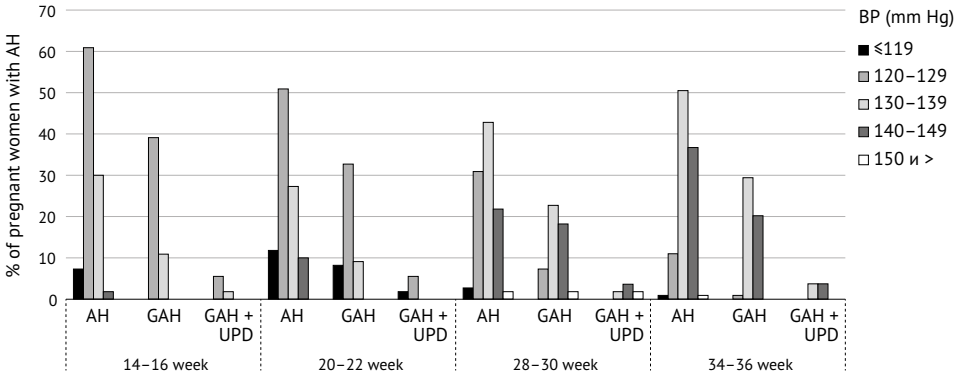


Fig. 3. Distribution of pregnant women with arterial hypertension (AH) and gestational arterial hypertension (GAH), depending on the terms of pregnancy; BP: blood pressure; UPD: uteroplacental disorders.

gestational age was not registered, including the impaired UPBF. At 14–16 weeks of gestation, impaired UPBF with GAH was detected in 7.3% of female patients (n = 8, out of 50 pregnant women with GAH), and generally, the SBP was determined at the level of 120–129 and 130–139 mm Hg, namely in 5.5% (n = 6) and 1.8% cases (n = 2), respectively, in this cohort.

At 20–22 weeks of gestation with GAH, the SBP was also at the level of 120–129 and 130–139 mm Hg, namely in 32.7% (n = 36) and 9.1% cases (n = 10), respectively. With GAH, impaired UPBF was registered in 7.3% of cases at a given gestational age, with an SBP level of 120–129 mm Hg, UPBF disorders were detected in 5.5% (n = 6) female patients. No cases of impaired UPBF were revealed at a level of >130 mm Hg, but it should be noted that at a gestational age of 20 weeks or more, GAH is diagnosed with an increase in BP, therefore, not such high BP figures are more often detected with this type of AH.

As the gestational age increases, the SBP increases. At a term of 28–30 weeks of gestation, 22.7% (n = 25) and 18.2% (n = 20) of female patients had a level of 130–139 and 140–149 mm Hg, respectively. Impaired UPBF in pregnant women with GAH at a given gestational age was determined as a maximum at an SBP level of 140–149 mm Hg in 3.6% (n = 4), and a similar situation was registered at 34–36 weeks. GAH at a term of 34–36 weeks of gestation was determined to a greater extent at SBP levels of 130–139 mm Hg (29.4%) and 140–149 mm Hg (20.2%). With GAH at a given gestational age, impaired UPBF were detected in 7.4% of cases (n = 8) and 3.7%, each with SBP levels of 130–139 and 140–149 mm Hg, respectively (n = 4).

Therefore, the presented data revealed that SBP levels of 130–139 and 140–149 mm Hg are noted more often with GAH. Impaired UPBF is also related to a greater extent to these SBP levels, which necessitates the achievement of lower target SBP values in pregnant women with GAH, regardless of the timing of pregnancy. The optimal SBP level is <120 mm Hg for pregnant women with GAH, which can be concluded based on the relationship

between the incidence of UPBF disorders and SBP levels.

Thus, at 28–30 weeks, the optimal SBP level was 130–139 mm Hg for pregnant women with CAH, where the frequency of impaired UPBF was 13.6%. The decreased SBP level below 119 mm Hg and 120–129 mm Hg increased the impaired UPBF to 33.3% and 30.8% of cases. When the SBP level increased to 140–149 mm Hg in pregnant women with CAH, an increased impaired UPBF of up to 50% was noted.

A similar situation is noted in pregnant women with CAH at 34–36 weeks. With a decreased SBP to 120–129 mm Hg, the frequency of impaired UPBF was 23.3%, whereas with an increase in SBP to 140–149 mm Hg, the frequency of impaired UPBF was 44.4%. The smallest number of impaired UPBF at a given term of pregnancy in female patients with CAH (8.7%) was recorded at an SBP level of 130–139 mm Hg.

The frequency of UPBF abnormalities in pregnant women with GAH revealed that at terms of 14–16 and 20–22 weeks of gestation, the optimal SBP level was <119 mm Hg, while at 28–30 and 24–36 weeks, the lowest number of impaired UPBF was noted at an SBP level of 120–129 mm Hg.

The obtained results revealed that the target BP levels for pregnant women with CAH and GAH should be different. Adhering to BP values below 129 mm Hg in the early stages of pregnancy (up to 20 weeks) is recommended, as well as below 130–139 mm Hg in the later stages (20–30 weeks) to prevent impaired placental circulation in pregnant women with CAH. However, in pregnant women with GAH, in the first half of gestation, BP is optimally below 119 mm Hg and up to 120–129 mm Hg in the second half of gestation. Consequently, the obtained data implemented a differentiated approach in the choice of regimens for prescribing antihypertensive drugs for pregnant women and improve perinatal outcomes in female patients with gestational toxicosis and placental insufficiency.

CONCLUSIONS

1. An increased incidence of pregnancy and childbirth complications was largely registered in pregnant women with AH.

2. The incidence of impaired uteroplacental blood flow was higher in pregnant women with AH.

3. Depending on the type of AH, differences were revealed in the impaired uteroplacental blood flow, which was more often detected in pregnant women with CAH (25.5%) compared with GAH (14.5%, $p = 0.04$).

4. Adhering to BP values below 129 mm Hg in the early stages of pregnancy (up to week 20) is recommended to prevent impaired uteroplacental blood flow in pregnant women with CAH. At a later date (20–30 weeks), BP up to 130–139 mm Hg is permissible.

5. For pregnant women with GAH in the first half of pregnancy, the recommended target BP level is below 119 mm Hg. While in the second half of pregnancy, it rises to 120–129 mm Hg.

Author contributions. M.D.M. collected and generalized the research material, and wrote some sections; A.S.K. was the work supervisor, and wrote the main sections; N.A.L. generalized the research materials obtained, performed stylistic processing of the article content; V.R.V. performed general management of work, edited the text; A.S.I. collected and generalized the material; R.G.N. collected the information, interpreted, and performed mathematical processing of the research results; A.M.M. performed mathematical processing of the research results and generalized the material.

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REFERENCES

1. Regitz-Zagrosek V., Roos-Hesselink J.W., Bauersachs J., Blomström-Lundqvist C., Cifkova R., De Bonis M., Iung B., Johnson M.R., Kintscher U., Kranke P., Marthe Lang I., Morais J., Pieper P.G., Presbitero P., Price S., Giuseppe M.C.R., Seeland U., Simoncini T., Swan L., Warnes C.A. ESC Scientific Document Group, 2018. ESC guidelines for the management of cardiovascular diseases during pregnancy: the task force for the management of cardiovascular diseases during pregnancy of the European Society of Cardiology (ESC). *Eur. Heart J.* 2018; 39 (34): 3165–3241. DOI: 10.1093/eurheartj/ehy340.

2. Webster K., Fishburn S., Maresh M., Findlay S.C., Chappell L.C. Diagnosis and management of hypertension in pregnancy: summary of updated NICE guidance. *BMJ.* 2019; 366: 15119. DOI: 10.1136/bmj.15119.

3. Duley L. The global impact of pre-eclampsia and eclampsia. *Semin. Perinatol*. 2009; 33: 130–137. DOI: 10.1053/j.semperi.2009.02.010.

4. Steegers E.A., von Dadelszen P., Duvekot J.J., Pijnenborg R. Pre-eclampsia. *Lancet*. 2010; 376: 631–644. DOI: 10.1016/S0140-6736(10)60279-6.

5. Abalos E., Cuesta C., Carroli G., Qureshi Z., Widmer M., Vogel J.P., Souza J.P.; WHO Multicountry Survey on Maternal and Newborn Health Research Network. Pre-eclampsia, eclampsia and adverse maternal and perinatal outcomes: a secondary analysis of the World Health Organization Multicountry Survey on Maternal and Newborn Health. *BJOG*. 2014; 121 (Suppl. 1): 14–24. DOI: 10.1111/1471-0528.12629.

6. ACOG practice bulletin No. 202: gestational hypertension and preeclampsia. *Obstet. Gynecol*. 2019; 133: e1–e25. DOI: 10.1097/AOG.0000000000003018.

7. Butalia S., Audibert F., Côté A.-M., Firoz T., Logan A.G., Magee L.A., Mundle W., Rey E., Rabi D.M., Daskalopoulou S.S., Nerenberg K.A., Hypertension Canada. Hypertension Canada's 2018 guidelines for the manage-

ment of hypertension in pregnancy. *Can. J. Cardiol*. 2018; 34 (5): 526–531. DOI: 10.1016/j.cjca.2018.02.021.

8. Brown M.A., Magee L.A., Kenny L.C., Karumanchi S.A., McCarthy F., Saito S., Hall D.R., Warren C., Adoyi G., Ishaku S. The hypertensive disorders of pregnancy: ISSHP classification, diagnosis & management recommendations for international practice. *Pregnancy Hypertens*. 2018; 13: 291–310. DOI: 10.1016/j.preghy.2018.05.004.

9. Magee L.A., Pels A., Helewa M., Rey E., von Dadelszen P. Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy. *Pregnancy Hypertens*. 2014; 4 (2): 105–145. DOI: 10.1016/j.preghy.2014.01.003.

10. Diagnosis and treatment of cardiovascular diseases during pregnancy 2018. National guidelines. *Russian journal of cardiology.* 2018; 155 (3): 91–134. (In Russ.) DOI: 10.15829/1560-4071-2018-3-91-134.

11. Clinical protocol of the Ministry of Health of the Republic of Kazakhstan *"Arterial hypertension in pregnant women"*. 2017. https://diseases.medelement.com/disease/артериальная-гипертензия-у-беременных-2017/15691 (access date: 04.08.2021). (In Russ.)

12. Tkacheva O.N., Shifman E.M., Runikhina N.K., Polyanchikova O.L., Khodzhaeva Z.S., Lyashko E.S., Chukhareva N.A. Clinical protocol. Diagnostics and treatment of arterial hypertension in pregnant women. *Akusherstvo i ginekologiya.* 2012; (4-2-S): 10–14. (In Russ.)

13. Von Dadelszen P., Magee L.A. Fall in mean arterial pressure and fetal growth restriction in pregnancy hypertension: an updated metaregression analysis. *J. Obstet. Gynaecol. Can*. 2002; 24 (12): 941–945. DOI: 10.1016/s1701-2163(16)30592-8.

14. Malik R., Kumar V. Hypertension in pregnancy. *Adv. Exp. Med. Biol*. 2017; 956: 375–393. DOI: 10.1007/5584_2016_150.

15. Gupta S., Gupta V., Gupta S., Tayal B.B. Hemodynamic changes in uteroplacental vasculature in pregnancy-induced hypertension and its effect on pregnancy outcome. *National J. Physiol. Pharm. Pharmacol*. 2021; 11 (3): 269–273.

16. Ayala D.E., Hermida R.C. Ambulatory blood pressure monitoring for the early identification of hypertension in pregnancy. *Chronobiol. Int*. 2013; 30: 233–259. DOI: 10.3109/07420528.2012.714687.

17. Simpson L.L. Maternal medical disease: risk of antepartum fetal death. *Semin. Perinatol*. 2002; 26 (1): 42–50. DOI: 10.1053/sper.2002.29838.

18. Tret'yakova O.V. Fetoplacental insufficiency in hypertensive disorders during pregnancy. *Vestnik of the KRSU*. 2008; 8 (4): 134–136. (In Russ.)

19. Gamzayeva S.E. Influence hypertensive mechanism of formation of the uteroplacental-fetal blood flow. *Fundamentalnye issledovaniya.* 2013; (9-1): 14–18. (In Russ.)

20. Strizhakov A.N., Ignatko I.V., Timokhina E.V., Kardanova M.A. *Kriticheskoe sostoyanie ploda: diagnosticheskie kriterii, akusherskaya taktika, perinatal'nye iskhody.* (Critical state of the fetus: diagnostic criteria, obstetric tactics, perinatal outcomes.) M.: GEOTAR-Media. 2018; 176 p. (In Russ.)

21. Medubayeva M.D., Latypova N.A., Kerimkulova A.S., Markabaeva A.M., Kiselova N.I. Peculiarities of pregnancy course and delivery outcomes in women with various forms of arterial hypertension. *Georgian medical news*. 2020; (3): 26–32. (In Russ.)