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Risk Factors and Uterine Artery Doppler in the Prediction of Placental Insufficiency in the First Trimester of Pregnancy

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Abstract The analysis of the risk factors dysfunction placenta at the obstetric and extragenital pathology - the role of defects uterine hemodynamics in the first trimester of pregnancy in the Genesis of placental insufficiency abortion, gestational pyelonephritis, arterial hypertension, hypotension of pregnant. By the method of vaginal dopplerography were examined 669 study of pregnant women with pathologies and 40 women with physiologically developing pregnancy, received curves velocity of blood flow in the uterine arteries calculated on the basis of which S/D ratio and pulsatility index (PI) in the left and right a. uterinae. These data together with the anamnesis pregnant used for predicting the placental insufficiency. It is proved that the pathological modulation uterine hemodynamics in the first trimester of pregnancy can be used as objective a prognostic marker of placental insufficiency in pregnant with threatening abortion, vascular dystonia and in pregnant without background obstetric and extragenital pathology.

Keywords: *placental insufficiency, arterial hypertension, arterial hypotension, hemodynamic disturbances, risk factors*

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1. Introduction

«Placental insufficiency» is a clinical syndrome caused by the functional and morphological changes in the placenta with violation of compensatory and adaptive reactions in the system mother-placenta-fetus.

A high frequency of development of placental insufficiency (PlIn) during complicated pregnancy: when miscarriage this disease is diagnosed in the 50-77%, with extragenital pathology - in 25-45% of cases [1].

Various obstetric complications and extra genital diseases (for example, spasm of pre-eclampsia, hypertension), lead to a reduction of blood flow in between chorionic villi space, also contribute to a deterioration in utero-placental perfusion. Slowing blood flow between chorionic villi space is happening and the violation of the outflow of blood and lymph, when increase tone while on long-term threat of abortion, cardiovascular pathology with stagnant syndrome [2].

The concept of the circulatory system as an indicator of adaptive activity of the organism developing for the past few decades, it is subjected to in-depth development, and many of its provisions receive a detailed rationale. Early diagnosis is difficult and requires innovative approaches to its solution.

According to the literature, most studies utero-placental blood flow are held during the second half of pregnancy. The detected violations are often critical that leads to early delivery, increase of perinatal morbidity and mortality.

At the same time it is shown that timely, in the first trimester of pregnancy, rheo- and Doppler study allow us to predict the development of such complications of gestation, as a threat of miscarriage, preeclampsia and IUGR [3,4,5,6,7].

Clarification of the significance of this factor in the early detection and forecasting PlIn defined the purpose of our research.

Objective: To describe the risk factors dysfunction placenta and signal changes in the uterine arteries in the first trimester of pregnancy, but also the analysis of their association with the subsequent risk of placental insufficiency abortion, hypertension, arterial hypotension, chronic pyelonephritis and women without comorbidity.

2. Materials and Methods

To achieve this goal in the period from 2004 to 2011 were examined 669 pregnant, 141 of them gestational process took place against the background of arterial hypertension, the 140 - against the background of arterial hypotension, 115 - when gestational pyelonephritis, 165 - abortion. Placental insufficiency, without background pathology diagnosed 68 pregnant. The control group consisted of 40 pregnant women, who had no extragenital pathology and complications of pregnancy.

The criteria for inclusion in the study were: pregnancy I - III trimester; diagnosis of extragenital pathology, established before pregnancy; threatening abortion, established on the basis of the clinical trial data; localization of the ovum mainly on one of lateral walls of the uterus by ultrasound; informed consent to participate in the study.

Exclusion criteria were: failure to participate in the study; patients with concomitant extragenital pathology; patients with sexually transmitted infections; toxemia and pre-eclampsia; multiple pregnancy, chronic intoxication (nicotine, addiction, alcoholism); malformations in the fetus.

Survey was conducted on the basis of «Maternity hospital», Saransk, Russia.

Doppler ultrasound examination of the uterine arteries was performed using an «Aloka - 4000» ultrasound machine equipped with a 4.6-8-MHz transvaginal transducer and a 2.3-4-MHz transabdominal transducer with regard to qualitative hemodynamic performance.

Doppler sonografy estimation of quality indicators of blood flow (sistolic-diastolic ratio and pulsating index) in the uterine arteries side placentation (PP) and intact party (IP) was held

Statistical analysis was performed using the program Exele 2003. Arithmetic mean (M) and standard error of the average arithmetic mean (m) was calculated. Student's criterion was used for the evaluation of critical reliability of differences compared averages. The differences are recognized statistically significant at $P < 0.05$.

3. Results

The retrospective analysis of data age, social status and history in all the surveyed groups found that among pregnant women of the control group was dominated by young women aged 20-29 years (by 65.0%), housewives (60.0%), mainly those in rural areas (by 65.0%).

For women, threatening abortion characteristic was also the age of 20 to 29 years (60.0%), young pregnant women was 24 (14.6%), and patients of late reproductive age (30-39 years) - 18 (10.8%).

Pregnancy on a background of arterial hypertension in 73 (51.8%) women occurred at the age of 20 to 29 years, however, in this group was the prevailing number of women 35 - 39 years - 17 (12,0%) 30 (21.3%) pregnant women under 19 years of age has already been diagnosed with arterial hypertension. In this group there were cases of pregnancy in 4 (2.8%) women aged 40 to 44 years.

In pregnant women with arterial hypotension also dominated patients aged 20 to 29 years – 70.6%, of young pregnant with hypotension was 18 (13.0%), and women above 30 years of age - 23 (16.4%).

In the group of pregnant women suffering from chronic pyelonephritis, prevalent was the age of 20 to 29 years (70.6%). In this group have the least number of pregnancies in the late reproductive age.

When placental insufficiency, developed in women without the «background» of pathology, 26 (38.3%) cases the pregnancy after the age of 30 years, and in this group is the smallest number of young women of up 19 years, only 2 (2.9%).

Thus, by age all examined groups were comparable.

According to our data, among pregnant women by threatening abortion was 36.4% of Housewives, 30.9 percent servants, 17.0% of female students and 16.4% of workers. The same trend continued in the groups of pregnant women with arterial hypertension and hypotension. And in the group of chronic pyelonephritis was 33 (28.8%) of students, employees - 32 (27.8%), workers - 28 (24.3%), Housewives - 22 (19.1%). Placental insufficiency without comorbidity, according to our data, more commonly developed in women of working specialties - 28 (41.2%), and less common among employees (23.5%), students (19.1%) and Housewives (16.2%).

The overwhelming majority (80,0 %) pregnant women surveyed groups were urban women.

The 95,0% of pregnant control group had normal formation of menstrual function with regular normal menstrual flow and normal duration of menstruation.

In the group of pregnant women with threatening abortion in 31 (19.7 %) woman mentioned later onset of menstruation, one quarter of them were irregular menstruation, 27 (16.4%) were oligomenorrhea and 17 (10.3%) - heavy menstrual flow.

When hypertension is on the late menarche indicated only 9 (6.4%) pregnant women, irregular periods - 24 (of 17.1%), shortened menstrual cycle was diagnosed in 10 (7.1%) patients.

In 131 (90.7%) women with arterial hypotension menstruation began to 16 years, but in 35.0% of the menstrual flow was irregular, 2 (1.4%) patients - shortened, 42 (30.0%) - prolonged. 7 (5.0%) women identified violations of the type light.

The normal formation of menstrual function was in 96.5% of pregnant women with chronic pyelonephritis. Violations menstrual cycle in the form of irregular menstruation were 19 (16.5%) patients, 5 (4.3%) women - the duration of menstruation was 2 - 3 days, 6 (5.2%) more than 6 days. Prolonged menstrual cycle said 7 (6.1%) pregnant.

When placental insufficiency more often than in other diseases, respondents pointed irregular menstruation - 19 (27.9%).

Analysis of reproductive function showed that among pregnant control group prevailed first pregnant (52.5%). The average number of births in this group is for every woman was 0.25, medical abortions – 0.125, spontaneous abortions – 0.1 (Figure 1; Figure 2).

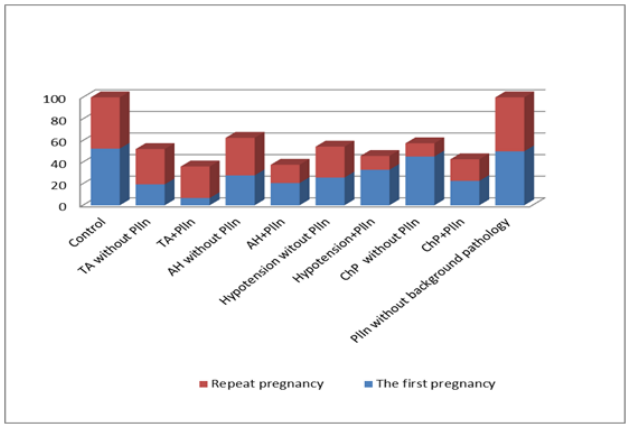

Figure 1. Pregnancies parity (%)

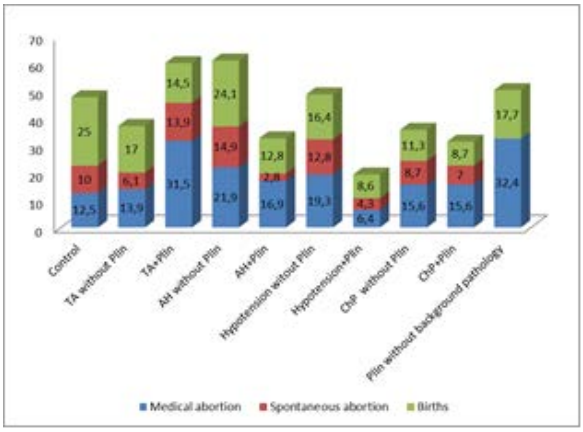

Figure 2. Obstetric history (%)

Among pregnant women by threatening abortion first pregnant was only 43 (26.1%), of which 102 re pregnant, childbirth in history had only 52 (31.5%) women. The average number of medical abortions per woman in this group, was 0,45. In this group more frequently than others, met spontaneous miscarriages. Thus, aggravated obstetric history is a risk factor threatening abortion, that agrees with the data of the majority of authors.

Patients with arterial hypertension first pregnant was also less than half - 68 (48.3%), but in this group was higher number of women with previous childbirth 52 (36.9%). The average number of medical abortions per woman with hypertension was 0.35, and spontaneous abortions – 0.18.

Most pregnant women with arterial hypotension were first pregnant - 82 (58.6%), of which 58 re pregnant, only 17 (12.1%) did not have birth to this pregnancy. However, the average number of honey abortions among them was 0,26, and spontaneous abortions - 0,13.

In the group of women with chronic pyelonephritis prevailed first pregnant - 78 (67.8%). Out of 37 (32.2%) re pregnant preceding childbirth said 23 (20.0%) women. The number of medical abortions in this group amounted to 0.31 and spontaneous abortions – 0.16.

In patients with placental insufficiency this pregnancy was the first half of the cases. Only 12 (17.7%) patients were childbirth in history, as the average number of medical abortions – 0.32. This group was not spontaneous abortions.

According to our data, the patients of the control group ectopia cervix met in 15.0% of cases, coleitis - 12.5%, ovarian cyst – 10.0%, inflammation of the uterus - 7.5 % (Figure 3).

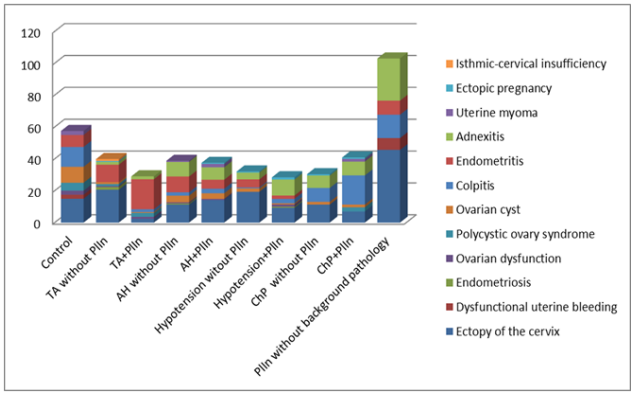

Figure 3. Gynecological morbidity (%)

55 (33.3%) females with threatening abortion gynecological medical history was often burdened with pelvic inflammatory diseases, cervical ectopy in 38 (23.0%) of the cases in isolated cases in this subgroup met ovarian dysfunction, PCO, ovarian cyst, ectopic pregnancy, ICI.

In the group of pregnant women with hypertension are also the most frequent gynecological diseases were inflammation of the uterus and ovaries - 46 (32.6%) patients and cervical ectopy in 36 (25.5%). Cyst ovarian history called 11 (7.8%) pregnant.

In arterial hypotonia ectopy of the cervix of the uterus was observed in 40 (28,6%) cases, adnexitis - 20 (14.3%), inflammation of the uterus - 10 (7.1%).

Pregnant women with chronic pyelonephritis often pointed out coleitis in history- 31 (27,0%), 21 (18.3%) the woman in this group - the cervical ectopy 19 (16.5%) - on adnexitis.

In the group with placental insufficiency ectopy of the cervix of the uterus was observed in 31 (45.6%) pregnant, inflammation of the uterus and appendages 24 (35.3%), obesity - in 10 (14.7%), the DUB - 5 (7.4%).

Among women of the control group 5 (12.5%) of the pregnant women had a history of anemia and obesity and 2 (5.0) thyroid patology (Figure 4).

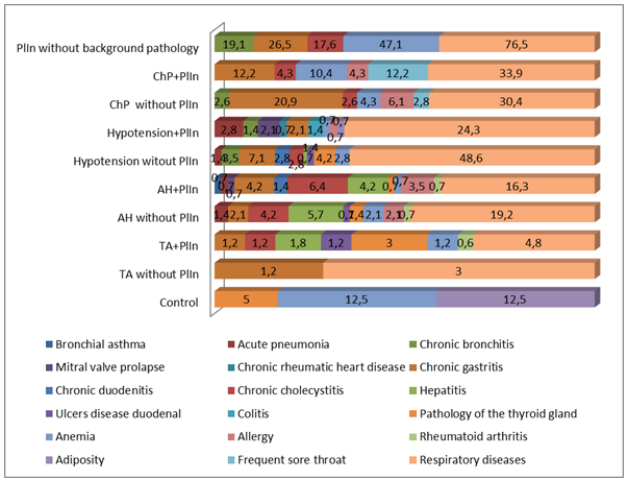

Figure 4. Extragenital incidence (%)

11 (6.67%) pregnant women with threatening abortion was noted pathology of the gastrointestinal tract, 5 (3.0%) - a disease of the thyroid gland. Pay attention to a low level of respiratory diseases in this group. Pointed to them only 13 (7.8%) pregnant women with threatening abortion.

When hypertension is also the most frequent comorbidity were diseases of the digestive tract. They met at 41 (29.1%) pregnant. One woman noted bronchial asthma in history, 3 - severe pneumonia. In pregnant women of this group of allergic reactions pointed 8 (5.6%) patients. Respiratory diseases in history have transferred 50 (35.5 %) women.

In the group with arterial hypotension in 13 (9.3%) patients had respiratory pathology, 26 (18.6 per cent) diseases of the digestive tract and 102 (72.9%) pregnant women had respiratory diseases in history.

38 (33.1%) pregnant women with chronic pyelonephritis was marked by chronic gastritis. In this group met anemia - 17 (14.7%), frequent sore throats -

(15.0%) and allergic reactions - 12 (10.4%). Respiratory diseases were 74 (64.3%).

In the group with placental insufficiency 13 (19.1%) pregnant pointed to a history of chronic bronchitis, 30 (44.1%) - on diseases of digestive tract, 32 (47.1%) anaemia, 52 (76,5%) - on respiratory diseases.

During dopplerography of blood flow in a. uterine for the normally developing pregnancy in periods of 6 - 12 weeks was revealed asymmetry indices vascular resistance (Table 1). So S/D ratio was lower side placentation 17.9% ($P < 0.05$), and PI (13.4%) ($P < 0.01$).

Table 1. Indexes vascular resistance in a. uterina during pregnancy 6 - 12 weeks in normal and study of pathology (M ± m)

Group	S/D ratio		PI	
	PP	IP	PP	IP
Physiological pregnancy	3,21±0,05	3,91±0,17[1]	1,29±0,05	1,49±0,07[3]
Threatening abortion	2,24±0,23[2]	3,08±0,24[2,ё3]	0,88±0,09[2]	0,73±0,17[2]
Arterial hypertension	6,50±0,18[2]	5,40±0,16[1, 2]	2,29±0,17[2]	1,75±0,18[3]
Arterial hypotension	3,73±0,12[2]	6,06±0,34[1, 2]	1,96±0,19[2]	2,26±0,14[2]
Chronic pyelonephritis	3,43±0,18	4,00±0,28[3]	1,35±0,17	1,50±0,14
Placental insufficiency without extragenital pathology	3,23±0,14	3,28±0,25[4]	1,25±0,16	1,30±0,13

[1] - P < 0,05 between the opposing a. uterina
[2] - P < 0,05 between the similar indices in normal and study of pathology
[3] - P < 0,01 between the opposing a. uterina
[4] - P < 0,01 between the similar indices in normal and study of pathology

The formation of a dysfunction of the placenta in pregnant women with threatening abortion happened with a more pronounced bilateral difference indicator S/D, which was 27.3% ($P < 0.01$) lower side placentation than the intact side. Relative to the control group, the value of S/D in these women declined by 1.3 - 1.4 times ($P < 0.05$). In this group of pregnant attention PI lower than normal: 1.4 times on PP and 2 times on IP ($P < 0.05$). Moreover, absent bilateral differences in PI.

In pregnant women with arterial hypertension hemodynamic disturbances manifested as the increase in peripheral resistance on PP 2.0 times ($P < 0.05$), and the IP 1.4 times ($P < 0.05$) regarding patients with physiological pregnancy, as well as higher IVR on the side of the emerging placenta.

When pregnancy is against the background of arterial hypotonia pathology of uterine circulation was to improve vascular resistance, compared with the norm, mainly on the side opposite to implantation. Hemodynamic asymmetry was decrease of S/D PP by 38.4% ($P < 0.05$), in the case of symmetric metric PI on both sides of the uterus.

In pregnant women with chronic pyelonephritis in pregnancy 6-12 weeks were absent abnormal blood flow modulation, and S/D and PI did not differ significantly from those in the control group.

Placental insufficiency developed those somatically healthy women who in 6-12 weeks has not been registered the difference bilateral indexes vascular resistance the uterine arteries.

Studies have shown that in the genesis of placental insufficiency in pregnant women, threatening abortion may lie vascular malformations, as indicated by the decrease of the IVR and the threat of termination of pregnancy in these cases is a consequence of the pathological process.

Pregnant without comorbidity and patients with dystonia formation of placental insufficiency occurs against disadaptation uterine hemodynamics, and when the dysfunction of the placenta, emerging on the background of chronic pyelonephritis, impaired blood flow in the uterine arteries are secondary, and, apparently, formed after 12 weeks of pregnancy.

4. Discussion

The retrospective analysis found that women in the Republic of Mordovia placental insufficiency developed in 38.8% of cases in pregnant women with threatening abortion, 37.6%, with arterial hypertension, or 45.7%, with arterial hypotension, and in 42.6% for women with chronic pyelonephritis.

Assessment of risk factors has allowed to reveal, that the PlIn more commonly developed aged 20 to 29 years, while young age often was a risk factor for abortion, arterial hypotension, and, especially alarming is the fact of increasing the frequency of placental insufficiency in pregnant women with young arterial hypertension. Although I.G. Fedotov et al. [8] indicate the presence of progressive arterial hypertension at 17-25% of teenagers, and the development of endothelial dysfunction take place every second teenager with hypertension (55.3% of cases). This may also explain the high frequency of gestational complications in women with arterial hypertension. N.S. Tarasova et al. [9], C.E. Hayward et al. [10] have identified the morphological basis PlIn in young women, in particular, decreased activity of the syncytiotrophoblast and narrowing of the utero-placental arteries in the basal membrane of placentae. However, in our study, young age was not a risk factor PlIn in chronic pyelonephritis and somatically healthy women. The results showed that the PlIn has developed 41.5% of young women, which is slightly below the data contained S.P. Sinchihin et al. [11] for up to 76% and T.G. Zakharova et al. [12] more than 50%.

Later reproductive years (after 30 years) became the reason of increasing the frequency of PlIn with abortion, hypertension and somatically healthy patients. In General, placental insufficiency developed in 31.7% of pregnant women participating in the study, which is more than 2 times higher than the values given W. Cerensambuu et al. [13].

Of the factors influencing on perinatal outcomes, in the literature there are indications of the influence of the professional activity of women. Social status does not have significant influence on the formation of dysfunction of the placenta, which contradicts the results obtained previously [14], which showed a significant increase in the frequency of this complication in the low socio-household level pregnant.

There is a certain experience on the impact of the environment on health and reproductive behavior of women, as well as the influence of the kind of work [15]. Our results showed that the pregnancy is complicated by placental insufficiency in 1,8 times more common in urban counterparts.

Menstrual irregularities late menarche, accompanied by heavy menstrual flow, became a frequent cause of abnormal formation of the placenta in pregnant women with threatening abortion, that is not contrary to the literary data [16]. Irregular menstrual periods have also been identified patients with arterial hypotension.

Only among patients with threatening abortion and dysfunction of the placenta number first pregnant was more than 4 times more than re pregnant, and less than half of them had previous generations in history. In patients with study extragenital pathology in the case of hypertension, chronic pyelonephritis and «pure» form PlIn has not been noted significant differences between the first and re pregnants. And in the group of pregnant women with arterial hypotension PlIn developed 2.5 times more frequently during the first pregnancy. In all groups, number of previous births are not the same as the number re pregnants. Consequently, the majority of patients had intrauterine intervention to this pregnancy. However, in groups with extragenital pathology was also high rate of medical abortions and spontaneous abortions. In women with hypertension who placental insufficiency has not been formed, the number of medical abortion was 1.5 times more spontaneous in 5 times more, than in the group with PlIn. In arterial hypotension, was noted at the same trend, but in chronic pyelonephritis, these figures did not differ in both subgroups. Among patients without somatic pathology number of medical abortions was higher than in the control group in 3 times, but there was not any indication on spontaneous termination of pregnancy in history.

Thus, obstetric history, coupled intrauterine interventions before this pregnancy is not likely to be considered a factor in the development of placental insufficiency in dystonia and chronic pyelonephritis, then how it affects the formation of placental disorders in threatening abortion and in patients without somatic pathology.

Chronic inflammatory diseases of the small pelvis in all groups of the surveyed pregnant, but most pointedly their influence on formation of dysfunctions of the placenta was abortion. And the highest among all surveyed pregnant frequency cervical ectopy was lowest in pregnant women with placental insufficiency in groups with TA and the ChP.

Among extragenital diseases surveyed pregnant often pointed to the pathology of the gastrointestinal tract. However, there were no differences in the amount and forms of the disease in groups with PlIn and without PlIn.

Anemia had a significant influence on the formation of DP only in the group with chronic pyelonephritis (24.5%), as well as in patients without the study of somatic pathology (47.1%). However, these data do not exclude latent iron deficiency. Formed deficiency of iron in the period of active placentation can be an additional risk factor for the development of placental insufficiency even before the development of anemia [17].

The frequent presence of angina in history indicated only patients with PlIn formed against the ChP. And catarrhal diseases in history most rarely seen in the group, threatening abortion, and often in chronic pyelonephritis and «pure» form of placental insufficiency.

Revealed by the results of our study of risk factors for development of placental insufficiency are not specific. These include:

1. age up to 19 years - abortion and dystonia;
2. age over 30 years at TA, AH and somatically healthy pregnant women;
3. accommodation in the city - in all the surveyed groups;
4. later menarche - abortion;
5. violations menstrual cycle, abortion, and when the arterial hypotonia;
6. polimenorrhea - when TA;
7. AOA - abortion, women without somatic pathology.
8. gynecological diseases of inflammatory nature - in all groups;
9. ectopia cervix in all groups, except TA;
10. anaemia in chronic pyelonephritis and the «pure» PlIn
11. frequent sore throats - in chronic pyelonephritis
12. colds - in all groups, except for the TA.

Thus, our results allow assert that the leading factor in forming metabolic and trophic dysfunctions of the placenta are hemodynamic disorders in the breeding link utero-feto-placental complex that with the initial stages of gestation impede the flow in the placenta of the products of metabolism, providing prenatal development of the embryo. As a consequence, in the body of the mother (and then in the body of the foetus) begin to form adaptive responses aimed at correcting deviations arising metabolic homeostasis - compensatory acceleration of systemic blood flow to the mother, induced fetal tachycardia, increased activity of the enzyme systems of the placenta and other.

As early studies showed [3], diagnostics occurring disorders in hemodynamics in the emerging utero-placental system in the initial stages of pregnancy is possible by our method vaginal bipolar rheography [18] the difference of velocity of blood flow in the uterine arteries side placentation and intact side of the uterus, as defined in the dynamics. The expediency of application of such a methodology has been confirmed in studies of other authors [19].

It is essential that the diagnostic value of this method is not reduced from the existing background pathologies in pregnant, and performance of the values of S/D and PI in a. uterinae with the development of a gestational process in 6-12 weeks pregnant at risk of developing PlIn may indicate the emergence of disadaptation and serve as a prognostic sign of the pathological course of pregnancy and the development of placental insufficiency.

5. Conclusion

This study sets uterine artery Doppler indicators in physiological and complicated pregnancy which is recommended for clinical use in the Republic of Mordovia. It also recommends that the interpretation in relation with the age of the mother, her social status, parity and extragenital pathology.

Acknowledgement

All authors have contributed significantly, and that all authors are in agreement with the content of the manuscript.

Declaration of Interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

List of Abbreviations

AH	arterial hypertension
AOA	aggravated obstetric anamnesis
ChP	chronic pyelonephritis
DP	dysfunction of placenta
DUB	dysfunctional uterine bleeding
GIT	gastrointestinal tract
ICI	isthmic-cervical insufficiency
IP	intact party
IVR	indexes vascular resistance
PlIn	placental insufficiency
PCO	polycystic ovaries
PP	party placentation
TA	threatening abortion

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