RESEARCH ARTICLE

Anatomical preconditions for the development of the threat of miscarriage

Dzmitry Valchkevich, Anton Lemesh

The objectives of the study are groups of women with a gestation period of 16 to 34 weeks. The first group consisted of 100 women with the threat of miscarriage. 82% (82 women) of them were under threat of preterm delivery, 15% of them (15 women) were under the threat of abortion and 3% (3 women) were undergoing abortion. The second group included 20 women with normal pregnancy that underwent routine examinations. The aim of the research work is to study the anatomical and physiological features of vascular and fetoplacental systems as predisposing factors for the development of the threat of miscarriage.

The study was carried out with the help of ultrasound, morphometry, statistical method using a PC soft Statistica 10. To study the correlation relationships the Spearman coefficient was used. The results of the study have shown that uterine artery in women with threatened miscarriage are larger in comparison to women with normal pregnancy. First the correlation of morphometric indices of uterine arteries in pregnant women with threat of miscarriage, both among themselves and with the sizes of the foetus, as well as fetometric parameters with thickness of the placenta, and fetal presentation was shown.

It was shown that the anatomical features of the uterine arteries have a direct impact on the development of the foetus. The localization of the placenta in the most blood-supplied part of the uterus is a prerequisite for the normal course of pregnancy, while the attachment of the placenta in the uterine wall, which is characterized by less blood supply, contributes to the development of the threat of miscarriage. Also, the placental thickness as a predisposing factor to miscarriage was shown.

The economic efficiency and importance of the work is extremely high, because knowledge of anatomical prerequisites for the threat of miscarriage will allow in the early stages to identify the risk groups of pregnant women, to include them in the prevention program and thereby reduce the risk of miscarriage. This, in turn, can increase fertility, reduce reproductive losses and have a beneficial effect on the demographic situation.

We are planning to continue research on this topic and aim to establish the anatomical prerequisites for violations of fetal development.

Key Words: *Miscarriage; Uterine artery; Foetus; Fetoplacentar complex; Correlation*

INTRODUCTION

The unfavourable demographic situation is one of the most important social problems. Therefore, increasing the birth rate and reducing reproductive losses are the priorities of all modern reproductive medicine. The problem of miscarriage, which has not only medical, but also socio-economic importance, remains one of the most urgent in modern obstetrics and gynaecology.

According to the classification adopted by WHO (World Health Organization), spontaneous miscarriages are loss of pregnancy up to 22 weeks and premature delivery is childbirth from 22 to 37 full weeks of pregnancy with fetal mass of 500 g. They are subdivided into three groups: 22-27 weeks - very early, 28-33 weeks – early premature birth and 34-37 weeks - premature birth.

Finding out the causes of miscarriage is extremely important from a practical point of view. Knowing the causes and understanding the pathogenesis of miscarriage will allow us to carry out the proper treatment.

Currently, the rate of miscarriage is 10%-25% of all pregnancies, including 5%-10% of preterm birth. Premature infants account for over 50% of stillbirths, 70%-80% of early neonatal mortality, and 60%-70% of infant mortality [1-3]. All this has a very significant impact on state demographic policy and, in particular, on population growth. Many authors point out that miscarriage is one of the most common complications of pregnancy [4,5].

The foundations of reproductive health of women are laid at an early age and depend on genetic characteristics, the presence of pathology of various organs and systems of the body, the action of environmental factors, etc. [7-9].

The main causes of miscarriage, according to WHO are: 1) genetic (violations of the number or structure of chromosomes), 2) endocrine (diabetes, which can lead to polyhydramnios and hormonal disorders in the placenta; thyroid dysfunction, which increases the risk of miscarriage or birth of children with signs of hypotrophy; adrenal pathology increases the probability of premature birth, etc.), 3) immunological (autoimmune, alloimmune), 4) infectious (urogenital infections), 5) thrombophilic (blood clotting disorder), 6) anatomical (isthmic-cervical insufficiency, malformations, uterine tumors, intrauterine synechiae, genital infantilism) [10,11]. Despite the wide prevalence of this problem, any literature does not indicate features of uterine vascularization as a possible cause to the threat of miscarriage.

Hypoxia of foetus can cause stillbirth or neuropsychiatric disorders in the postnatal period. The physiological aging of the placenta, a decreasing in its surface, violations of utero-placental circulation as a result of toxemia, anemia, cardiovascular disease of the mother, etc can lead to hypoxia. Also hypoxia can be caused by the lack of oxygen due to circulatory disorders of the uterus.

The fetoplacental system is one of the main systems responsible for the formation of conditions necessary for the development of the foetus [12]. Complications of pregnancy, as well as extra-genital diseases of the mother often lead to a variety of changes in the placenta, significantly violating its function which negatively affects the state of the foetus causing the development of hypoxia and delay in its growth. A very important diagnostic criterion is the thickness of the placenta. Both too thin and too thick placenta can be indicators of various pathologies. The only way to determine the thickness of the placenta is ultrasound.

The unfavourable demographic situation is one of the most important social problems in the world. Therefore, increasing the birth rate and

Department of Normal Anatomy, Grodno State Medical University, Grodno, Belarus

Correspondence: Dzmitry Valchkevich, Department of Normal Anatomy, Grodno State Medical University, Grodno 230006, Belarus, Tel: +37529-7814545, E-mail: donn7@tut.by

reducing reproductive losses are the priorities of all modern reproductive medicine. Based on the information above, we can conclude that the problem of miscarriage is quite to the present day and requires further study.

The aim of the research work is to study the anatomical and physiological features of vascular and fetoplacental systems as predisposing factors for the development of the threat of miscarriage.

MATERIALS AND METHODS

Two groups of women with a gestation period of 16 to 34 weeks were the subject of the study. The first group included 100 people under the threat of miscarriage. 82% (82 women) were diagnosed with threat of preterm delivery, 15% (15 women) – with threatening abortion and 3% (3 women) – with the started abortion. Started abortion is the second stage of the process of child birth. The second group included 20 women with normal pregnancy that underwent routine examination.

The study was carried out with the help of ultrasound method, morphometry: the measurement of the diameter of the uterine arteries, the measurement of bi-parietal size (the distance between the most distant points of the parietal bones), abdominal circumference (along the line of the liver, stomach and umbilical vein) and thigh diameter of the of the foetus), statistical method with the help of PC soft Statistica 10. When studying the correlation relationships the Spearman coefficient was used.

RESULTS AND DISCUSSION

The collection of material was held during one year in the Department of Pathology of Pregnancy in "Clinical Emergency Hospital of Grodno". During this period there were 2655 pregnant in the clinic, 451 of them (17%) were diagnosed with threatened miscarriage, 762 (28.7%)- with the threat of premature birth. Among other diagnoses were: Gestosis- 191 pregnant women (7.2%), placental disorders- 87 (3.3%). Other diagnoses were noted even rarer.

Thus, almost every second woman comes to the Department of Pathology of Pregnancy with the threat of miscarriage, which indicates a sufficiently high incidence of this pathology. This fact dictates the requirements of fundamental and applied medicine for a more detailed study of the causes leading to the threat of miscarriage with the aim of adjust preventive and therapeutic measures [13].

The morphology of the uterine artery in miscarriage

According to our hypothesis, the anatomical features of the uterine artery can affect the degree of blood supply to the uterus of a pregnant woman, and this, in turn, can cause normal or pathological development of pregnancy. Our study showed that the uterine arteries always arouse from the internal iliac artery in all women from the both study groups (experimental and control). The diameter of the right uterine artery in patients with threatened miscarriage was 4.96 ± 0.7 mm. The left artery was slightly thinner (4.87 ± 0.6 mm). In nulliparous pregnant women both right (5.43 mm) and left (5.14 mm) uterine arteries were larger than in multiparous (5.18 mm and 5.13 mm respectively).

We want to note the interesting result that in pregnant women from the control group the uterine arteries were significantly smaller ($p<0.0005$) in diameter (3.75 ± 0.4 mm- right one and 3.92 ± 0.36 mm- left one) compared with vessels in women of the experimental group (4.93 ± 0.7 mm- right one, 4.80 ± 0.8 mm- left one).

It was found that in patients with the threat of miscarriage the uterine arteries were the thinnest in women with the diagnosis of threatened abortion (4.85 ± 0.56 mm- right and 4.71 ± 0.52 mm- left), and were the largest in women with abortion (5.2 ± 0.1 mm and 5.2 ± 0.4 mm, respectively).

The results showed the interdependence of the diameter of both uterine arteries in women with the threat of miscarriage. The correlation coefficient was 0.82 ($p<0.05$). This suggests that the larger the right artery, the thicker the left one, and Vice versa.

In women with normal pregnancy there was a broad correlation of uterine blood vessels. For example, the diameter of the right uterine artery increases with gestation term ($R=0.61$, $p<0.05$), and also influences the thickness of the placenta ($R=0.98$, $p<0.05$) and one of the main dimensions of the foetus- the diameter of the thigh ($R=0.45$, $p<0.05$). The thickness of the placenta is directly proportional to the size of the foetus ($R=0.7$). In addition, the size of the foetus depends on the size of the lumen of the right uterine artery ($R=0.5$).

It was noted, the left uterine artery was in correlation only with placental thickness ($R=0.98$, $p<0.05$).

Dopplerography allows the registration of blood flow in different parts of the vascular bed, to carry out a quantitative assessment of its parameters and to assess the functional state of the emerging placental and extraembryonic blood flow. The dopplerometric method has a high diagnostic and prognostic value in complicating pregnancy, as it allows to establish the initial manifestations of the threat of miscarriage and uteroplacental insufficiency [14-16].

Quantitative parameters of blood flow in uterine arteries (peak systolic velocity, PSV) were studied. PSV in women with normal pregnancy was 42.5 ± 11.3 cm/s (right) and 42.3 ± 9.0 cm/s (left). These rates were higher at the risk of miscarriage. They were 52.7 ± 10.2 cm/s on the right side and 54.2 ± 10.7 cm/s on the left one. The study showed that the peak systolic velocity of blood flow in the uterine arteries does not depend on their diameters. In addition, there is a weak tendency to inverse correlation of blood flow velocity from placenta location ($R= -0.28$, $p<0.05$).

Anatomical characteristics of the fetoplacental system in normal pregnancy and the threat of miscarriage

The placenta is located where the fertilized egg is attached to the wall of the uterus [17,18]. The posterior wall of the uterus and the place that is closest to its bottom are best supplied with blood [6]. It is therefore considered that these regions of the uterus are the most favourable for the attachment of child seats. There are many variants for placenta attachment, and they depend only on the individual characteristics of the organism of the expectant mother.

The results of study found that in women with the threat of miscarriage, the placenta is most often attached to the anterior wall of the uterus (15% of cases) or its posterior wall (15% of cases). In 10 women placenta was attached to the anterior-upper-left corner of the uterus and in the same amount of pregnant – to the anterior-upper-right one. Other variants of attachment were observed in fewer cases. It should be noted that women with threatening preterm labour were more likely to have placenta localization on the posterior wall of the uterus closer to the bottom (in 15% of cases), and in pregnant women with threatening abortion – in the upper part of the anterior wall (in 40% of cases). In the majority of women from the control group (in 55% of cases, in 11 people) placenta was located on the posterior wall of the uterus in its upper part.

It is also worth noting the fact that the location of the placenta in women with the threat of miscarriage is more variable than in pregnant women from the control group.

The size of the placenta is characterized by its thickness, area and volume. However, standard ultrasound investigation can only accurately determine the thickness of the placenta [19]. It is obvious that for the study of its compensatory capabilities it is of great value to determine its area and volume, but the calculation of these indicators using modern ultrasound diagnostic equipment is associated with a time-consuming procedure of stereo- and planimetry, which cannot be widely used in clinical practice. In addition, the results of these measurements have very large errors, which undoubtedly affect the interpretation of clinical data.

The thickness of the placenta varies in its different parts. Therefore, for its correct definition and most importantly for high reproducibility of the results, we used common methodological approaches for determining of this parameter. The most optimal site for measuring the thickness of the placenta is the place of origination of the umbilical cord. The study of placental thickness was carried out in this place.

The results of our study showed that the thickness of the placenta was significantly less (p<0.0005) in pregnant women with miscarriage and was in average 27.5 ± 5.4 mm, while in women with normal pregnancy it was 34.6 ± 3.2 mm. It should be noted that the most extensive placenta was observed in pregnant women with threat of premature birth (29.4 ± 3.4 mm). The placenta was almost 10 mm thinner in women with threat of spontaneous abortion (20.4 ± 4.2 mm), and the thinnest placenta was noted in women with a diagnosis of spontaneous abortion (19.3 ± 4.5 mm).

After establishing the important morphological features of the placenta, we tried to find out its correlation relationship. Thus, it was found that in women with normal pregnancy placental thickness depends on the diameter of both the right uterine artery (R=0.98, p<0.05) and the left one (R=0.98, p<0.05). It was shown that the placental thickness significantly has a direct effect only on the diameter of foetus's thigh (R=0.83, p<0.05). At the same time, there is an inverse relationship of the circumference of the fetal abdomen to the thickness of the placenta (R= -0.67, p<0.05). No correlation between the thickness of the placenta and the bi-parietal size of the foetus in women with the normal pregnancy has been established. It should also be noted that in women without pathology the thickness of the placenta depends on its location in the uterus (R=0.98, p<0.05). The thinnest placenta was located on the anterior wall of the uterus (32.8 ± 5.4 mm).

We have not found the relationship between the thickness of the placenta and the diameter of uterine arteries in the women with threat of miscarriage (if not to take into account the low significant correlation with the diameter of the left artery, R=0.24, p<0.05). However, the influence of placental thickness on fetal size was observed: abdominal circumference (R=0.80, p<0.05), femoral diameter (R=0.80, p<0.05), and here the dependence with bi-parietal size (R=0.79, p<0.05) was established, which was not observed in the women with normal pregnancy.

Some fetometric indicators are also interdependent. Thus, the bi-parietal size of the foetus depends on the size of the abdominal circumference (R=0.86; p<0.005) and the thigh diameter (R=0.91; p<0.005).

Features of biochemical blood analysis in women with the threat of miscarriage. Our study showed that the main blood parameters (AST (aspartate transaminase), ALT (alanine transaminase), total protein, creatinine, urea, total bilirubin) of pregnant women with the threat of miscarriage are within the norm. There is an increased level of ESR (28.5 ± 14.4 mm/h). We decided to direct our attention to the correlation relationship of these indicators. According to our study, the relationship between ALT and AST (R=0.88; p<0.05) was established in women with gestation term up to 20 weeks. In women with a gestation term of 20 to 30 weeks, the following correlations were found: total protein and bilirubin (R=0.4; p<0.05), total protein and AST (R=0.55; p<0.05), creatinine and urea (R=0.72; p<0.05), bilirubin and AST (R=0.5; p<0.55), bilirubin and ALT (R=0.5; p<0.05), AST and ALT (R=0.7; P<0.05). In women with gestation term more than 30 weeks relationship between total protein and AST (R=0.5; p<0.05), urea and creatinine (R=0.73; p<0.05), bilirubin and AST (R=0.6; p<0.05), bilirubin and ALT (R=0.8; p<0.05), AST and ALT (R=0.7; p<0.05) was found.

CONCLUSION

The study showed the presence of anatomical features of both the vascular bed of a pregnant woman and the entire fetoplacental complex. Thus, it was found that there was no asymmetry in the structure of uterine arteries in pregnant women. Uterine arteries in women under the threat of miscarriage are larger than in women with normal pregnancy. The interdependence of the diameters of the both, right and left, uterine arteries was noted in pregnant women with the threat of miscarriage. There is a correlation only of the right uterine artery in normal pregnancy.

The results of our study showed that the diameter of the right uterine artery depends on the term of pregnancy in women without pathology, and the diameter of the left uterine artery in women with the threat of miscarriage. In addition, the results of our study showed the presence of significantly correlated morphometric parameters of uterine arteries with the size of the foetus, fetometric parameters with thickness of the placenta. It was found that the anatomical features of the uterine arteries have a direct impact on the development of the foetus.

It can be concluded that the placenta in women with normal pregnancy is more often located on the most blood supplied posterior wall of the uterus, in its upper part, while in pregnant women with miscarriage, the location of the placenta is more variable. The placenta was thinner in women with miscarriage and has the smallest thickness at the beginning of the spontaneous abortion.

In women with pregnancy without complications, the dependence of the placental thickness on the diameter of the arteries supplying the uterus, as well as its influence on such fetal sizes as the abdominal circumference and the diameter of the thigh was established. With the threat of miscarriage, the correlation between the uterine arteries and the thickness of the placenta is lost, but the latter is directly related to the development of the foetus and its size. Since the placenta is thinner in people with the threat of miscarriage, the foetus will be less developed and it will have smaller size in women with this pathology compared to foetuses belonging to women with normal pregnancies.

In women under the threat of miscarriage, a direct correlation between the six most frequently determined and informative laboratory blood parameters was established. The highest correlation coefficients were observed between blood transaminases in pregnancy with the miscarriage up to 20 weeks and this can be used as an additional criterion for the diagnosis of these conditions. During later stages (after 30 weeks), it is necessary to pay attention to the "liver diagnostic panel", as there is a high correlation between bilirubin and ALT, which is an organ-specific enzyme of the liver.

With this, it should be noted that the aims of the study have been achieved and the tasks have been accomplished. We are planning to continue research on this topic, in order to establish the anatomical prerequisites of miscarriage, to establish the impact of the psycho-emotional status of women on the course and prognosis of pregnancy.

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