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FEATURES OF THE COURSE OF GESTATION IN WOMEN WITH MITRAL VALVE PROLAPSE AGAINST THE BACKGROUND OF UNDIFFERENTIATED CONNECTIVE TISSUE DYSPLASIA

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ABSTRACT

The article is devoted to the problems associated with connective tissue dysplasia (CTD), predominantly undifferentiated forms of the disease (nDST). The topic's relevance is due to the high prevalence of this pathological condition. The generalized nature of connective tissue damage with the involvement of the reproductive system in the pathological process significantly affects the course of pregnancy and Birth. Complications that may be associated with pregnancy, childbirth, and the postpartum period in women with nDST and which cause a high need for surgical aids: amnio-, episio- and perineotomy, and cesarean section are presented. Particular attention is paid to magnesium, which plays one of the determining roles in the complex biosynthesis of the extracellular matrix in the formation of connective tissue and the morphofunctional state of fibroblasts. The methods used to detect connective tissue metabolism disorders (determination of the level of oxyproline and fibronectin in blood serum, pyrinx D and glucosaminoglycans in urine, etc.) are described. Given the lack of reliable diagnostic (biochemical and genetic) criteria for nDST, special attention is paid to the need for an integrated approach to assessing the condition of patients using anamnesis data, the results of clinical, instrumental, and laboratory examinations.



KEYWORDS

Connective tissue dysplasia, hemostasis, complications of pregnancy and childbirth, magnesium deficiency, endothelial dysfunction, markers of collagen breakdown, genital prolapse.

INTRODUCTION

In recent years, much attention has been paid to the problem of connective tissue dysplasia, which is associated with the high prevalence of its manifestations in the population from 26 to 80% [2]. Mitral valve prolapse (MVP) is a minor abnormality in the development of the heart, considered one of the common abnormalities of the valvular apparatus of the heart and the most common visceral marker of connective tissue dysplasia [2]. MVP occurs in 60.8% of the population, 17–38% of women of reproductive age, and 8% to 32.9% of pregnant women [4, 5]. The combination of mitral valve prolapse and undifferentiated connective tissue dysplasia (NCSTD) increases the incidence of complications of the gestational period, both in the somatic state of a woman's health and in the course of pregnancy [1, 3, 4]. In this regard, it is worth paying attention to the study of the features of reproductive and somatic health, the course of pregnancy and childbirth, and perinatal outcomes in women against the background of the incompetence of connective tissue structures.

The study aimed to examine the features of the gestational course in women with mitral valve prolapse

against the background of undifferentiated connective tissue dysplasia.

METHODS

In 2023–2024, we followed 190 pregnant women with voluntary informed consent per WHO international ethical requirements. The observation group consisted of 124 pregnant women with mitral valve prolapse against the background of undifferentiated connective tissue dysplasia of mild severity, the comparison group consisted of 66 practically healthy pregnant women.

The criteria for inclusion in the observation group were the presence of mitral valve prolapse and mild undifferentiated connective tissue dysplasia.

Exclusion criteria: differentiated forms of connective tissue dysplasia; endocrine diseases; chronic somatic pathology at the stage of decompensation; congenital or acquired heart defects; operated heart defects; infectious diseases; pregnancy after the use of assisted reproductive technologies; history of infertility and/or miscarriage; multiple pregnancies. The groups were formed according to the principle of continuous selection for the period: 2021–2024 using random and



typological sampling – by the method of balanced groups identically in terms of age, parity of pregnancies, social, educational and family status. The age range of the examined patients ranged from 17 to 41 years. In the observation group, the mean age was 28.6 ± 4.6 years, in the comparison group 27.7 ± 5.2 years ($p > 0.05$).

Women of both groups were observed in the dynamics of gestation under the procedure for providing care in the profile "obstetrics and gynecology (except for the use of assisted reproductive technologies)", approved by the order of the Ministry of Health of the Republic of Uzbekistan No. 572n dated 01.11.2021.

The diagnosis of MVP and the stage of heart failure was made in conjunction with cardiologists by the International Classification of Diseases, tenth revision: I34.1 Mitral valve prolapse.

RESULTS

MVP was diagnosed before pregnancy in 108 (87.1%) and during the present pregnancy in 16 (12.9%) women in the observation group. Mitral valve regurgitation of the 1st degree has been established in all pregnant women. Anterior leaflet MVP was diagnosed in 70.2% of cases. Of these, 95.4% of the 1st degree and 4.6% of the 2nd degree. MVP of the posterior leaflet was detected in 29.8% of cases. Myxomatous degeneration of the mitral valve leaflets of the 1st degree was only in 8.9%.

Chronic heart failure of the first degree of severity occurred in 12 (9.7%) women in the observation group.

The diagnosis of undifferentiated connective tissue dysplasia in the observation group was made before the onset of real pregnancy in 35 (28.2%) women, in real pregnancy – in 89 (71.8%) pregnant women. All patients were diagnosed with a mild degree of undifferentiated connective tissue dysplasia.

It draws attention to the fact that each group of pregnant women accounted for an average of 4.8 somatic diseases, which is 3 times higher than the comparison group. In the structure of extragenital morbidity, diseases of the circulatory system were in the first place in the observation group ($p < 0.001$). Among them, rhythm and conduction disorders ($p < 0.001$), minor cardiac anomalies ($p < 0.001$), neurocirculatory dystonia ($p < 0.001$) were in the lead, mainly of the hypotonic type [6]. Thus, pregnant women with MVP are 1.7 times more likely to have cardiovascular diseases. In terms of the frequency of occurrence, the second place was taken by previous infectious diseases, which are significantly more common in women in the observation group ($p < 0.001$). Women were significantly more likely to suffer from influenza and childhood infections, especially chickenpox. The third place was occupied by blood diseases significantly different from the comparison group in the observation group ($p < 0.001$). Every third pregnant woman with MVP was diagnosed with iron

deficiency anemia ($p < 0.001$). Thrombocytopenia was diagnosed only in pregnant women in the observation group. It should be noted that diseases of the skin and musculoskeletal system were detected only in the women of the observation group ($p < 0.001$).

Prior to the onset of real pregnancy, complaints about the underlying disease bothered mainly women in the observation group, the main of which were palpitations and heart failures, pain in the heart area of an aching and stabbing nature, shortness of breath during physical exertion, headaches, dizziness. It should be noted that 38 pregnant women with MVP (30.6%) did not complain in the dynamics of gestation. Attention is drawn to the fact that the clinical manifestations of palpitations and interruptions in the work of the heart, pain in the heart area, disorders of thermoregulation and heat transfer, asthenia, vascular syndrome tended to increase by the second trimester and decrease by the time of delivery. Respiratory syndrome, on the other hand, tended to increase depending on the gestational age due to increasing complaints of shortness of breath and poor tolerance to stuffy rooms. Thus, for women with MVP due to NCSTD in the first and third trimesters of pregnancy, the most common complaints are from the cardiovascular system, which may be due to physiological stress.

When assessing gynecological morbidity, it was revealed that there were 1.3 gynecological diseases for

each patient of the observation group, and 0.6 for each patient of the comparison group, which is 2 times more often. Among gynecological diseases, women in the observation group were significantly more likely to suffer from chronic pelvic inflammatory diseases ($p < 0.001$) in combination with endocervicitis ($p < 0.01$), and cervical diseases ($p < 0.05$). Bacterial vaginosis was also significantly more common in the observation group compared to the comparison group ($p < 0.05$). Thus, women in the observation group were 5 times more likely to have a history of gynecological diseases than practically healthy pregnant women. Clinical examination revealed that almost every pregnant woman had a history of sexually transmitted infections. It should be noted that 34 (27.4 ± 4.0 per 100 examined) pregnant women in the observation group suffered from ureaplasma infection, 28 (22.6 ± 3.8) suffered from candidiasis, and 16 (12.9 ± 3.0) suffered from chlamydial infection ($p > 0.05$). It should be noted that during the examination for perinatally significant infections in the 1st trimester, it was revealed that women in the observation group were more often carriers of cytomegalovirus infection 20.2 ± 3.6 per 100 examined ($p < 0.05$) and herpes simplex virus type II 21.8 ± 3.7 ($p < 0.001$).

The analysis of menstrual function revealed that women in the observation group were significantly more likely to observe various disorders compared to practically healthy women ($p < 0.01$). In the observation

group, 23 (18.5±3.5%) patients had significantly more algodysmenorrhea compared to the comparison group – 3 (4.5±2.6%) ($p<0.01$), as well as hypermenorrhea, respectively, 16 (12.9±1.3) and 4 (6.1±2.9) ($p<0.05$).

Women in the observation group were taken for dispensary observation for pregnancy in the antenatal clinic at an average period of 8.1±0.3 weeks of pregnancy and in the comparison group at 9.7±0.4 ($p>0.05$) in antenatal clinics at the place of medical care or district hospitals. It should be noted that in the antenatal clinic specialized in the management of women with cardiovascular diseases at the Republican Clinical Diagnostic Center of the Udmurt Republic, every third (31.5%) woman with NCST was observed. The number of visits by a pregnant woman to the antenatal clinic did not differ in the groups ($p>0.05$).

The analysis of morphoanthropometric data revealed that the average height and body weight of pregnant women in the observation group did not differ from the average height of pregnant women in the comparison group ($p>0.05$). The average weight gain in the patients of the observation group of 17.8±6.4 kg was higher than that of the comparison group – 11.5±6.9 kg, but no significant differences were revealed ($p>0.05$).

Pelvimetry of pregnant women with MVP against the background of NCST revealed an anatomically narrow pelvis 4.5 times more often (69.4±4.1 out of 100

examined) than in practically healthy pregnant women (28.8±5.6). When assessing the forms of pelvic constriction, it should be noted that in pregnant women with MVP against the background of NCST, the first rank is occupied by the transversely narrowed pelvis, the second by the flat pelvis, and the third by the generally uniformly narrowed pelvis. At the same time, in practically healthy pregnant women, the generally uniformly narrowed pelvis is in the lead, followed by a flat and transversely narrowed pelvis. In terms of the degree of pelvic narrowing, the groups were comparable.

Analysis of the course of pregnancy revealed that in the observation group, 93 (75.0±3.9 per 100 examined) various pregnancy complications were diagnosed significantly more often in the first trimester than in the comparison group – 31 (47.0±6.1 per 100) ($p<0.001$). It should be noted that toxicosis in the first half of pregnancy was significantly more common in pregnant women with MVP against the background of NCST ($p<0.01$), as well as diseases of the urinary system and acute respiratory diseases ($p<0.05$). Thus, pregnant women with MVP in combination with NCST in the first trimester of pregnancy are 3 times more likely to have obstetric and somatic complications compared to healthy pregnant women. In the second trimester, among the obstetric complications in women with MVP on the background of NCST, disorders of uterofetal-placental circulation and fetal growth



retardation appeared as signs of formed placental insufficiency. Among the extragenital pathology in the second trimester about practically healthy pregnant women, women with MVP against the background of NCST were 4 times more likely to have somatic pathology. Blood diseases were detected significantly more often 46.8 ± 4.5 per 100 examined ($p < 0.01$), including anemia and thrombocytopenia ($p < 0.05$), as well as diseases of the urinary system ($p < 0.01$). In the third trimester, pregnant women with MVP against the background of NCST were significantly more likely to have chronic intrauterine fetal hypoxia (11.3 ± 2.8) ($p < 0.01$), fetal growth retardation (11.3 ± 2.8) ($p < 0.01$), impaired uterofetal-placental circulation (12.9 ± 3.0) ($p < 0.01$) and chronic placental insufficiency (12.9 ± 3.0) ($p < 0.001$). The threat of preterm birth and preeclampsia were also significantly more common in pregnant women with MVP on the background of NCST, respectively ($p < 0.05$) and ($p < 0.001$).

Thus, the mutual influence and aggravation of pregnancy and MVP, especially in the setting of NCST, led to a higher incidence of pregnancy complications. He draws attention to the fact that every tenth of them was treated in an inpatient setting 2-3 times.

According to the data of the study, in the anamnesis of pregnant women in the observation group, 42 ($17.6 \pm 2.5\%$) pathological births were 4 times more often than in the comparison group – 3 (4.5 ± 2.6 ; $p < 0.001$). Most women gave birth at term on average,

at an average of 38.5 ± 1.4 weeks of pregnancy in the observation group and at 38.3 ± 1.2 weeks in the comparison group ($p > 0.05$). In the observation group, 115 (92.7%) pregnant women had an urgent birth and, accordingly, 64 (97.0%) in the comparison group. The incidence of preterm birth was higher in the observation group, but no significant differences were found ($p > 0.05$). It should be noted that in all cases of the women we examined, premature birth occurred at gestational age from 32 to 35 weeks, in the observation group at the mean gestation period – 33.8 ± 0.5 weeks, and in the comparison group – 34.5 ± 0.5 weeks of pregnancy ($p > 0.05$).

Labor in puerperas in the observation group was longer ($p < 0.01$). This may be due to the high incidence of abnormalities in labor, particularly in labor weakness. The anhydrous interval was 7.8 ± 1.2 hours in pregnant women in the observation group and 6.1 ± 0.9 hours in pregnant women in the comparison group ($p > 0.05$). Timely rupture of amniotic fluid was observed in 69 ($55.6 \pm 4.5\%$) women in the observation group and 42 ($63.7 \pm 5.9\%$) in the comparison group. Premature effusion was 2 times more frequent in 25 ($20.2 \pm 3.6\%$) and 8 ($12.1 \pm 4.0\%$), respectively. Early effusion was diagnosed in 30 ($24.2 \pm 3.8\%$) women in the observation group and 16 ($24.2 \pm 5.3\%$) in the comparison group. Thus, the most common complication of childbirth in patients was untimely discharge of amniotic fluid. According to our data, 83



(66.9±4.2) women in the observation group and 59 (89.4±3.8) in the comparison group had normal births. The results of the analysis of the course of labor showed that pregnant women with MVP against the background of NCST significantly more often had such complications of labor as abnormalities of labor in the form of its weakness ($p<0.01$), and hypotonic bleeding ($p<0.05$).

In this regard, women with MVP were significantly more likely to undergo amniotomy (42.7±4.4 compared to the comparison group 25.8±5.4 ($p<0.05$), induction of labor using prepil gel, 8.9±2.6 and 1.5±1.4 ($p<0.05$), induction of labor (20.2±3.6 and 6.1±2.9 ($p<0.01$), respectively. It draws attention to the fact that women in the observation group more often required induction and stimulation of labor due to labor abnormalities, which had a significant difference to the comparison group ($p<0.001$).

Blood loss during childbirth did not differ in the groups and amounted to an average of 347.7±42.1 ml in the observation group and 329.0±27.5 ml ($p>0.05$) in the comparison group. Hypotonic bleeding in the third stage of labor was present only in 3 (2.4%) women in the observation group, for which therapeutic measures were taken.

The prevalence of birth canal injuries in puerpera in the observation group was more common in 51 (41.1±4.4 per 100) women, compared to 14 (21.2±5.0 per 100)

women ($p<0.01$). Birth injuries are associated with the failure of the mechanical properties of the connective tissue fibers of the birth canal and abnormalities of labor activity [2, 6]. Cervical rupture and labia fissures ($p<0.01$) were significantly more common in women in labor with MVP on the background of NCST compared to the comparison group. Various complications have led to a higher need for operational aids. Operative delivery was performed in 31 (25.0±3.9 per 100) women in the observation group and 13 (19.7±4.9 per 100) women in the comparison group ($p>0.05$). The main indications for cesarean section were: the presence of an untenable scar on the uterus, maca cervical dystocia, and fetal growth retardation. In the postpartum period, women in the observation group had a higher incidence of pregnancy complications such as uterine subinvolution and hypogalactia ($p<0.05$). In 3 (1.3±0.7 per 100) parturient women in the observation group, perineal sutures were inadequate after episiotomy.

The results obtained confirmed the opinion of some authors that pregnant women with MVP, especially against the background of NCST, have a significantly higher incidence of complicated pregnancy and childbirth compared to healthy women, and the tactics of delivery in this category of women are determined individually, taking into account the general condition of the patient, complications of pregnancy and the obstetric situation.



The average weight of babies born in patients suffering from MVP was 3085.7 ± 554.2 grams, but there were no significant differences from the comparison group – 3644.6 ± 587.1 grams ($p > 0.05$). In the Apgar assessment of newborns at the first and fifth minutes, lower scores were also found in the group of children of mothers with MVP than in the children of mothers of the comparison group ($p < 0.001$). The condition of puerperal infants with MVP against the background of NCSTD at birth was worse than that of infants of healthy women and 5 minutes after birth did not reach the indicators of the comparison group, which indicates the presence of the most pronounced pathological changes of a hypoxic nature in newborns of this group.

Intrauterine growth retardation occupies an important place in the structure of neonatal pathology. It draws attention to the fact that premature babies were born 4.5 times more often in the observation group. In the observation group, the number of children with grade I hypotrophy was 4.6 times more common in 9 (7.3 ± 2.3 per 100 examined) than in the comparison group (3.0 ± 2.1), and only this subgroup included newborns with grade II hypotrophy. The rate of perinatal morbidity in newborns born to women with MVP for NCSTD is higher than in the comparison group. The course of pregnancy in patients with MVP in combination with NCSTD against the background of chronic hypoxia and metabolic disorders in the

placenta led to a significantly more frequent perinatal lesion of the central nervous system and conjugation jaundice in children relative to the comparison group ($p < 0.001$), respiratory distress syndrome ($p < 0.01$), and intrauterine infection ($p < 0.001$). It should be noted that only in the observation group, small heart anomalies were diagnosed in 15 (12.1 ± 2.9) newborns in the form of an open foramen ovale, a false chord in the left ventricle, and an atrial septal defect.

CONCLUSION

Thus, the presence of extragenital disease – MVP during pregnancy, the progression of circulatory disorders due to the interaction of pregnancy and MVP, along a complicated gestational period, were of particular importance in the prognosis of adverse outcomes of pregnancy and childbirth in patients with MVP against the background of NCSTD. The presented data convincingly show that patients with MVP, especially against the background of NCSTD, have a higher incidence of pre- and postnatal pathology. The health status of newborns from mothers with MVP was determined by fetal suffering due to placental insufficiency and several obstetric complications, depending on the presence of NCSTD in the mother, the course of pregnancy, the weight of the newborn, and the timing and method of delivery.

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