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## DEBATABLE ISSUES OF PATHOLOGICAL COURSE OF PREGNANCY AND CHILDBIRTH IN CONNECTIVE TISSUE DYSPLASIA

**Submission Date:** January 31, 2024, **Accepted Date:** February 05, 2024,

**Published Date:** February 10, 2024

**Crossref doi:** <https://doi.org/10.37547/ajsshr/Volume04Issue02-04>

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### ABSTRACT

The main function of CT is to provide structural support to other tissues. Cartilage and bone are the main types of connective tissue, other types include areolar connective tissue, which holds organs together, and dense connective tissue, which forms ligaments and tendons. We examined 47 pregnant women with uCDT and 15 healthy pregnant women without uCDT aged 24-30 years. The threat of termination of pregnancy occurred in 50% of women with uCDT, and the threat of preterm birth was observed 6 times more often than in healthy pregnant women. Thus, pregnant women with signs of various forms of uCDT belong to high-risk groups of obstetric and perinatal pathology, and therefore they need close monitoring during pregnancy, childbirth and the postpartum period, and it is also necessary to examine newborns who have a high probability of inheriting this disease.

### KEYWORDS

Undifferentiated connective tissue dysplasia (uCTD), tumor necrosis factor (TNF-), connective tissue (CT), interleukin-1 (IL-1).

## INTRODUCTION

The main function of CT is to provide structural support to other tissues. Cartilage and bone are the main types of connective tissue, other types include areolar connective tissue, which holds organs together, and dense connective tissue, which forms ligaments and tendons. Undifferentiated connective tissue dysplasia (uCTD) is a heterogeneous group of diseases that, in turn, can lead to various chronic diseases. uCTD often corresponds to abnormal structural and functional changes in CT. This leads to disturbances in the morphology and function of organs [11]. The clinical and morphological manifestations of uCTD are extremely diverse. They may include skeletal changes associated with cartilage disorders, disproportionately long limbs, arachnodactyly, chest deformities, spinal scoliosis, flat feet, pathology of tooth development, occlusion, cysts, joint pathology (tendency to dislocation), hyperelasticity, thinning, a tendency to traumatize the skin, varicose veins and external signs of accelerated aging - early formation of wrinkles, deformation of the oval of the face, including gravitational ptosis (sagging soft tissues of the face) [8,9]. Lesions of the cardiovascular system are very diverse: mitral valve prolapse (the most common of all cardiac anomalies in CTD is usually detected by echocardiography), venous insufficiency, varicose veins, and hemostasis pathologies [7].

Diagnosis of uCTD is based on these symptoms and additional findings (e.g., anthropometry, external respiration, reduced heart size, decreased blood pressure, plethysmography, specific characteristics of ECG and ultrasound phleboscanning) [10]. According to the analysis of these phenotypic markers of uCTD, its prevalence may be relatively high in the general population (e.g., 8.5% in a sample of 400 people [9]). Although it is often stated that the etiology of DST has a genetic component, an exhaustive analysis of the relative roles of environmental factors (nutrition, environmental conditions, movement hygiene, psycho-emotional background) and genetic factors has not been carried out. The term "dysplasia" refers to the abnormal growth/development of a tissue or organ. The diagnosis of CDT is made based on a thorough analysis of symptoms and the results of clinical trials. However, the diagnosis of DST in practice is rarely accompanied by any specific histological confirmations. Accordingly, dysplasia detected at the clinical level may correspond to numerous changes in tissue structure.

In the case of connective tissue, dysplasia (i.e., "abnormal growth") can occur due to: 1) abnormal collagen synthesis or assembly; 2) synthesis of abnormal collagen; 3) excessive collagen degradation; 4) disorders of the structure of collagen fibers due to insufficient cross-linking; 5) similar anomalies related

to elastin fibers; 6) tissue destruction through autoimmune reactions [5,7]. According to Y. Chia, mitral valve prolapses accounts for 60.8% of congenital heart diseases in pregnant women [3]. Clinical polymorphism of mitral valve prolapse is often combined with other signs of connective tissue dysplasia: asthenic physique, pathological joint mobility, myopia, flat feet, as well as prolapse of other heart valves, patent foramen ovale, nephroptosis, biliary dyskinesia, varicose veins, and increased bleeding. It is known that in patients with mitral valve prolapse, additional pathways are found 3 times more often than in the general population [2].

Most often, mitral valve prolapse is asymptomatic, has a favorable prognosis, but is sometimes associated with cardiac arrhythmias, heart failure, thromboembolism, infective endocarditis, and sudden death. The peculiarities of the hemodynamics of the gestational period, namely an increase in the volume of circulating blood, cardiac output, increase the load on the cardiovascular system and can provoke the development of these complications. In some cases, it is during pregnancy that signs of heart failure and paroxysmal cardiac arrhythmias manifest themselves in women with mitral valve prolapse [6]. The greatest threat is posed by patients with hemodynamically significant mitral regurgitation and myxomatous degeneration of the valve leaflets, which are the

source of blood clots and the cause of thromboembolic complications [12].

In recent years, the problem of the course of pregnancy and childbirth in women with uCDT, which is a genetically determined disorder of its development in the embryonic and postnatal periods, has been actively discussed. As a result of various mutations in the genes encoding the structure of collagen and elastin, defects in fibrous structures and the main substance of uCDT are formed, followed by the development of various morphofunctional disorders of a systemic and local nature [6].

The morphological basis of uCDT is a decrease in the content of certain types of collagen or a violation of the ratio between them, which leads to a decrease in the strength of the connective tissue of many organs and systems. The external manifestation of uCDT is the so-called "dysembryogenesis stigmas", which can manifest themselves as both obvious deformities and subtle signs. Up to 35% of healthy people have some degree of uCDT, and 70% of them are women [3]. The variety of mutagenic effects on the development of this pathology determines a wide range of its clinical variants - from well-known gene differentiated syndromes (Marfan, Ehlers-Danlos) - to numerous hereditary undifferentiated (nonsyndromic) uCDT. uCDTs are thought to be "phenotypic" copies of known syndromes [8]. The generalized nature of connective tissue damage affects the pathological development

of the organs of the reproductive system, which further provokes the manifestation of a number of obstetric problems [12]. In contrast to syndromic forms, uCDT is manifested mainly by mild heterogeneous symptoms and syndromes, united under the general name of "dysembryogenesis stigmas" [1,3]. The peculiarities of the course of pregnancy and childbirth in women with uCDT have not been sufficiently studied and are the subject of close attention of researchers. Pregnancy pathology occurs significantly more often in women with uCDT than in healthy women - 85.5% versus 53.3%, there are indications in the literature of a higher incidence of the threat of early and late termination of pregnancy in women with uCDT. There is also a higher incidence of preeclampsia and eclampsia in women with uCDT [7,8].

## METHODS

Methods of investigation: We examined 47 pregnant women with uCDT and 15 healthy pregnant women without uCDT aged 24-30 years. The threat of termination of pregnancy occurred in 50% of women with uCDT, and the threat of preterm birth was observed 6 times more often than in healthy pregnant women. The main cause of recurrent miscarriage in this group of patients was isthmio-cervical insufficiency. At the same time, according to our data, the threat of termination of pregnancy at a period of up to 20 weeks occurred in almost 1/3 of cases, the threat of premature birth - in 17.2%, pregnancy ended in premature birth in

4.6% of cases. Analysis of the course of the gestational process in pregnant women with uCDT revealed that one of the most common complications was early gestosis, which occurred in 48.6% of cases. At the same time, there was a direct significant correlation between the severity of the clinical picture and the incidence of early gestosis. According to our data, the most common complication of the second half of pregnancy in women with uCDT was preeclampsia (49.8%), and the course of childbirth in these patients was characterized by frequent complications. It is known that preeclampsia occupies the 2nd-3rd place in the structure of causes of maternal mortality and is one of the main causes of premature birth and perinatal fetal death. One in five children born to a mother with preeclampsia has some degree of abnormality in physical and psycho-emotional development. Also, placental dysfunction was very common in uCDT - in 37.5% of cases. At the same time, there was a violation of uteroplacental and fetal hemodynamics, transport, trophic, endocrine, metabolic functions of the placenta, which led to fetal malformations (12.1%).

However, this assumption cannot be considered indisputable. The main clinical manifestation of placental dysfunction in pregnant women with uCDT was fetal distress. Microscopy of the placenta in puerperas with uCDT showed various forms of impaired placental maturation. Another, no less important complication for obstetrics - untimely



discharge of amniotic fluid - was observed in 40.0% of cases in women with uCDT. The incidence of premature and early rupture of amniotic fluid in our pregnant women with uCDT ranged from 37.4% to 41.7% of cases. The microscopic picture of fetal membranes in uCDT was characterized by thickening of the compact layer of the amnion of varying degrees of severity due to the proliferation of collagen fibers in it. Of the features of the course of labor associated with uCDT, a relationship with a rapid and rapid course of labor was revealed, and in severe cases of uCDT, the frequency of rapid and rapid labor in primiparous women reached 47%, and in mild signs of uCDT was about 14%. Recently, a new concept of the development of labor weakness (DLW) has been put forward, in which its causal factor may belong to the uCDT. The data of the literature review indicate a fairly high incidence of ECS, which is 2-10% in parturient women with its primary development and 2.5% in its secondary development. In women over 30 years of age, ECS is 2 times more common than in women aged 20-25 years. ECS leads to a protracted course or complete cessation of labor, the appearance of signs of fetal distress, which leads to prompt delivery. In the structure of emergency caesarean section, ECS ranks 2-3rd, reaching 37% [9,10]. It is known that during pregnancy there are significant changes in the structure of muscle tissue and collagen fibers of the cervix. The volume of muscle tissue increases by more than 2 times due to the growth of the vascular link with the simultaneous destruction of

collagen fibers. In the course of many studies, it was found that in 15-20% of women such changes were not observed, which made it possible to attribute such patients to the risk group for the development of abnormalities in labor [14]. Another discussed cause of DRD is the pathology of immune status. As is known, endogenous prostaglandins and endothelial growth factors play an important role in the nature of labor [13]. It has been established that the main role in the development of labor belongs to the fetus. At the junction of maternal and fetal tissues in the uterus, there is a release of the main modulators of myometrial contractile activity - prostaglandins of fetal and maternal origin. As a result, another mechanism of childbirth is triggered - immunological rejection of the fetus [10]. Cytokines such as interleukin-1 (IL-1), IL-6, IL-8 and tumor necrosis factor (TNF-) are of great importance in the mechanism of labor [11]. The study of the peculiarities of the course of pregnancy and childbirth in 47 patients with small and large signs of uCDT made it possible to establish that abnormalities of labor in the first stage of labor occurred in 75.3% of parturient women against 23.7% in the control group without uCDT. Caesarean section in the study group was performed in 15% of pregnant women and only in 3% of patients in the control group. Hypotonic bleeding in the third stage of labor occurred in 7.8% of mothers with uCDT and was absent in the control group. Pubic joint divergence was diagnosed in 8.3% of women with uCDT and was not detected in the control group. Signs

of prolapse of the internal genitals, confirmed by clinical and ultrasound data, were found in 45% of patients in the main group, in the control group this pathology was not revealed. Birth injuries of newborns from mothers with uCDT were diagnosed in 38% of cases versus 3.9% in the control group. This study showed that patients with generalized manifestations (involvement of three or more organs in the connective tissue defect) of uCDT, even in the absence of severe forms of this pathology, are at high risk for the formation of obstetric and neonatal pathology [4].

## CONCLUSION

Thus, pregnant women with signs of various forms of uCDT belong to high-risk groups of obstetric and perinatal pathology, and therefore they need close monitoring during pregnancy, childbirth and the postpartum period, and it is also necessary to examine newborns who have a high probability of inheriting this disease. The high incidence of complications during pregnancy, childbirth and the postpartum period in patients with uCDT determines the relevance of this problem in obstetrics and the thoroughness of examination of this category of women. However, ambiguous and sometimes contradictory data on the association and incidence of these complications with uCDT require further research to determine a set of diagnostic and preventive measures.

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