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Features of Pregnancy in Women with Undifferentiated Connective Tissue Dysplasia in the Samarkand Region

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Abstract **Background.** Undifferentiated connective tissue dysplasia (UCTD) is a genetically determined systemic disorder characterized by impaired collagen synthesis and structural organization, affecting the morphofunctional integrity of the uterus, placenta, and vascular wall. In obstetric practice, UCTD is associated with an increased risk of adverse pregnancy outcomes, including miscarriage, premature birth, placental insufficiency, and hemorrhagic complications. Due to the high prevalence of UCTD among women of reproductive age and the absence of unified diagnostic criteria, further investigation of its clinical impact on pregnancy remains relevant. The aim of the present study was to determine the prevalence of UCTD among pregnant women in the Samarkand region and to assess its clinical and obstetric significance. **Materials and Methods.** A combined retrospective and prospective study was conducted between 2023 and 2025 at Family Polyclinic No. 3 and the Gynecology Department of the Maternity Complex of the Multidisciplinary Clinic of Samarkand State Medical University. Among 3,482 admitted pregnant women, 739 (21.2%) demonstrated clinical signs of UCTD. A prospective cohort of 213 pregnant women was formed, including 93 patients with UCTD and 120 age- and gestation-matched controls. Diagnostic criteria included anamnestic data, Beighton score assessment, clinical phenotypic markers, biochemical indicators of collagen metabolism, and instrumental examinations. Statistical analysis was performed using SPSS software. Differences were evaluated using χ^2-test and Student's t-test, with $p < 0.05$ considered statistically significant. **Results.** UCTD was diagnosed in 21.2% of pregnant women. The highest prevalence was observed in women under 25 years (27.5%). Patients with UCTD demonstrated significantly higher rates of obstetric complications, including isthmic-cervical insufficiency (21.5% vs. 1.7%, $p < 0.001$), threatened miscarriage (32.3% vs. 15.0%, $p < 0.01$), premature rupture of membranes (16.1% vs. 2.5%, $p < 0.001$), premature birth (26.9% vs. 3.3%, $p < 0.001$), and postpartum hemorrhage (32.3% vs. 5.0%, $p < 0.001$). Somatic manifestations such as varicose veins (40.9% vs. 10%, $p < 0.001$) and heart valve prolapse (29% vs. 1.7%, $p < 0.001$) were significantly more frequent in the UCTD group. **Conclusion.** Pregnancy in women with UCTD is associated with a significantly increased risk of obstetric and somatic complications. The systemic nature of connective tissue insufficiency contributes to impaired cervical competence, vascular fragility, and functional disorders. Early identification and individualized monitoring strategies are essential to reduce adverse perinatal outcomes in this high-risk population.

Keywords Connective tissue dysplasia, Pregnancy complications, Cervical insufficiency, Premature birth, Joint hypermobility

1. Introduction

Currently, special attention in obstetrics is paid to the problem of managing pregnancy against the background of undifferenciated connective tissue dysplasia (UCTD), which is considered as a systemic disorder affecting the structures that ensure the morphofunctional integrity of the uterus, placenta, and vascular wall [1,2]. Connective tissue diseases are among the significant causes of complicated pregnancies and adverse perinatal outcomes, including premature birth and placental dysfunction. According to the definition by T.I. Kadurina [3], UCTD is a genetically determined disorder of connective tissue development in the embryonic and postnatal periods due to mutations in genes encoding the synthesis and spatial organisation of collagen, elastin and other proteins, leading to homeostasis disorders at the tissue, organ and organism levels [4,5,6,7].

The relevance of studying UCTD is due to its high prevalence in the population, which, according to various authors, ranges from 13% to 85.4% [8,9]. Such significant fluctuations in prevalence rates are associated with the lack of uniform diagnostic criteria and different approaches to the identification of phenotypic markers of the disease. The problem is particularly significant because UCTD mainly affects young people, including women of reproductive age [10,11,12]. Therapeutic approaches to the management of pregnant women with UCTD should be based on pathogenetic principles, taking into account the individual characteristics of the patient. Promising areas include the development of

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personalised medicine and the introduction of new methods of diagnosis and treatment, which served as the theoretical basis for this study.

The aim of the study was to determine the incidence of undifferentiated connective tissue dysplasia in pregnant women of the Samarkand region and to study the characteristics of its clinical course.

2. Material and Methods

The study was conducted at Family Polyclinic No. 3 and the Gynaecology Department of the Maternity Complex of the Multidisciplinary Clinic of Samarkand State Medical University between 2023 and 2025. An retrospective analysis of pregnant women admitted to the maternity complex showed that out of 3,482 patients, 739 had signs of UCTD, which is 21.2%. The diagnostic criteria for UCTD included anamnestic data (frequency of spontaneous miscarriages, premature births, family history), clinical signs (asthenic body type, increased joint mobility on the Beighton scale, varicose veins, symphysiopathy, valve prolapse, skin manifestations in the form of striae and atrophic scars).

A total of 213 pregnant women were monitored, formed prospective group and divided into two groups depending on the presence of signs of UCTD: group I - 93 patients diagnosed with UCTD; group II - 120 practically healthy pregnant women without clinical and laboratory signs of UCTD, matched by age and gestation period to the main group. Patients in both groups were comparable in terms of key socio-demographic indicators (level of education, social status, marital status). Most of the subjects were in their second trimester of pregnancy (18–24 weeks), which corresponded to the timing of standard screening examinations.

The laboratory and instrumental part of the diagnosis included the determination of biochemical markers of collagen metabolism (hydroxyproline, glycosaminoglycans, hyaluronic acid, hyaluronidase activity), as well as indicators of mineral metabolism (Mg^{2+}, Ca^{2+}, P). A mandatory step was the exclusion of differentiated hereditary collagenopathies, such as Marfan syndrome, Ehlers-Danlos syndrome, imperfect osteogenesis, and others. When analysing the age composition of the examined patients, it was found that the average age of women in group I (with UDCT) was 28.1±0.5 years, in group II – 27.6±0.4 years, with no statistically significant differences between the groups ($p>0.05$). The age range of patients in the main group was from 18 to 39 years, and in the control group, from 19 to 38 years, which indicates the comparability of the groups in terms of this indicator. The gestational age at the time of inclusion in the study was 18.9 ± 0.6 weeks in group I and 19.4±0.5 weeks in group II, also with no statistically significant differences ($p>0.05$). Thus, the groups were comparable in terms of age and gestational age.

3. Results of Our Own Research

When assessing obstetric history, it was found that the average number of pregnancies in patients with UCTD was 1.8±0.1, which was comparable to the control group – 1.7±0.1 ($p>0.05$). The number of births in group I was significantly lower (1.0±0.1) than in group II (1.3±0.1; $p<0.05$), reflecting the reproductive function characteristics of women with signs of connective tissue dysplasia.

Particular attention was drawn to the rate of spontaneous miscarriages: in group I, it was 0.82±0.1, which was more than twice as high as the corresponding rate in the control group – 0.43±0.05 ($p<0.001$). This fact indicates the significant role of UCTD in the formation of adverse outcomes in the early stages of pregnancy. The body mass index before pregnancy in both groups did not differ significantly and was 21.4±0.3 kg/m ²in the main group and 22.0±0.3 kg/m ²in the control group ($p>0.05$). Thus, the compared groups were homogeneous in terms of age, gestational age, body mass index, and socio-demographic characteristics. Differences were identified in obstetric history indicators. Patients with UCTD had significantly fewer births and more spontaneous miscarriages, indicating significant reproductive risks in this category of women.

An analysis of the medical records of pregnant women admitted to the maternity complex in 2024 showed (Table 1) that out of 3,482 patients, signs of UCTD were detected in 739 women, which accounted for 21.2%. Thus, one in five pregnant women admitted had clinical or laboratory-instrumental signs of CD. The obtained CD frequency rate is consistent with the literature data, according to which the prevalence of this pathology in women of reproductive age ranges from 20 to 30%. This confirms the high significance of connective tissue dysplasia as a background condition that can affect the course of pregnancy and its outcomes.

The obstetrical score (OS) was calculated as an integral indicator reflecting the cumulative risk of obstetric complications in the study groups. The score was derived based on the presence of clinically significant pregnancy-related complications and was used for comparative risk assessment between groups.

Table 1. Prevalence of UCTD among pregnant women

Indicator	Absolute number	%
Total number of pregnant women admitted	3 482	100
With signs of UCTD	739	21,2

An analysis of the distribution of UCTD by age revealed that the highest incidence was among women under 25 years of age. Among 812 pregnant women in this group, signs of UCTD were recorded in 223, accounting for 27.5%. In the 25–29 age group, UCTD was diagnosed in 262 out of 1,210 women (21.6%). In patients aged 30–34, connective tissue dysplasia was noted in 185 out of 987 cases, corresponding to 18.7%. The lowest frequency was recorded in women aged 35 and older - 69 cases out of 473, or 14.6%.

Thus, the frequency of UCTD detection tended to decrease with increasing maternal age: from 27.5% in women younger than 25 years to 14.6% in the age category ≥35 years.

This may be due to both the peculiarities of the formation of phenotypic manifestations at a young age and the effect of 'natural selection' of patients with the most severe course of the pathology in the early stages of reproduction.

Table 2. Frequency of occurrence of the main clinical manifestations of UCTD in pregnant women (n=739)

Clinical signs	Abs.	%
Joint hypermobility (Beighton score ≥5)	514	69,6
Varicose veins	321	43,4
Symphysiopathy/pelvic pain	214	28,9
Heart valve prolapse (according to echocardiography)	132	17,9
Asthenic body type	415	56,2
Striae, atrophic skin scars	198	26,8
Tendency to bleed, haematomas	147	19,9

An analysis of the structure of clinical manifestations of UCTD in 739 pregnant women showed (Table 2) that the most common symptom was joint hypermobility, detected in 514 patients (69.6%), which reflects the key role of this sign in the diagnosis of connective tissue insufficiency. The second most common symptom was asthenic body type, recorded in 415 women (56.2%), which corresponds to data on the high prevalence of morphophenotypic manifestations of CSD among pregnant women. Varicose veins were diagnosed in 321 patients (43.4%), which emphasises the frequent involvement of the vascular system in the clinical manifestations of the pathology. Among obstetric and orthopaedic symptoms, symphysiopathy (pelvic pain) was significant, occurring in 214 women (28.9%). Heart valve prolapse was detected in 132 patients (17.9%) according to echocardiography data, confirming the high frequency of combination of UCTD with functional disorders of the cardiovascular system. Skin manifestations, such as striae and atrophic scars, were observed in 198 women (26.8%). In 147 pregnant women (19.9%), a tendency to bleeding and haematomas was noted, which is also a typical manifestation of connective tissue dysplasia and reflects vascular-haemostatic disorders.

Pregnancy in women with undifferentiated connective tissue dysplasia is accompanied by a number of features caused by systemic disorders of the structure and functions of connective tissue components. The polymorphism of clinical manifestations of UCTD creates an unfavourable background, against which the likelihood of complications during the gestational period increases. The most significant of these are the threat of miscarriage, premature birth, placental insufficiency, bleeding, and obstetric pathology associated with impaired biomechanical properties of the uterus and pelvic ligaments. An important aspect is the combination of obstetric complications with extra-systemic manifestations of DST: joint hypermobility, heart valve prolapse, varicose veins, a tendency to bleed, and an asthenic physique. These clinical signs, manifesting themselves with varying degrees of severity, can not only reduce the quality of life of the pregnant woman, but also act as predictors of an unfavourable course of gestation.

Analysis of the frequency and structure of pregnancy complications against the background of UCTD, as well as their relationship with the severity of clinical manifestations of the disease, allows for a deeper understanding of the pathogenesis and identification of key areas for prevention and management of this category of patients.

Table 3. Comparative characteristics of obstetric complications in patients in the study groups

Indicator	I-gr (n=93)		II-gr (n=120)		χ^2	P	OS
	abs.	%	abs.	%			
Isthmic-cervical insufficiency	20	21,5	2	1,7	22,26	<0,001	16,16
Threatened miscarriage	30	32,3	18	15,0	8,94	<0,01	2,70
Premature rupture of membranes	15	16,1	3	2,5	12,58	<0,001	7,50
Premature birth	25	26,9	4	3,3	24,70	<0,001	10,66
Weak labour	18	19,4	10	8,3	5,57	<0,05	2,64
Foetal position abnormalities	10	10,8	8	6,7	1,13	>0,2	1,69
Caesarean section	28	30,1	16	13,3	8,99	<0,01	2,80
Postpartum haemorrhage	30	32,3	6	5,0	27,72	<0,001	9,05

Note: P – significance of differences between indicators in groups I and II

Table 4. Comparative characteristics of somatic manifestations of UCTD in patients in the study groups

Indicator	I-gr (n=93)		II-gr (n=120)		χ^2	P	OS
	abs.	%	abs.	%			
Varicose veins	38	40,9	12	10	27,78	<0,001	6,22
Valve prolapse	27	29	1	1,7	33,36	<0,001	24,14
Orthostatic hypotension/syncope	10	10,8	7	5,8	1,73	>0,1	1,94
Arrhythmia/extrasystole	12	12,9	9	7,5	1,72	>0,1	1,83

Note: P – significance of differences between indicators in groups I and II

The data presented (Table 3) demonstrate that the course of pregnancy in patients with UCTD is accompanied by a significantly higher frequency of obstetric complications compared to women in the control group. Thus, isthmic-cervical insufficiency was recorded in 21.5% of patients in group I, which is 12.6 times more often than in group II (1.7%; χ^2=22.26; P<0.001; OS=16.16). This indicator reflects the weakness of the connective tissue structures of the cervix, characteristic of dysplastic disorders.

The threat of pregnancy termination occurred in every third patient with UCTD (32.3%), which is significantly more often than in women without signs of dysplasia (15.0%; χ^2=8.94; P<0.01; OR=2.70). This indicates a decrease in the compensatory capacity of the uteroplacental complex. Premature rupture of the membranes was observed in 16.1% of pregnant women in group I and only in 2.5% in group II (χ^2=12.58; P<0.001; OR=7.50), which is probably associated with a violation of the collagen structure of the membranes and their mechanical strength. Premature births occurred in 26.9% of women with UCTD, which was more than eight times higher than the frequency of this complication in the control group (3.3%; χ^2=24.70; P<0.001; OS=10.66).

A comparative assessment of somatic manifestations revealed (Table 4) that patients with UCTD significantly more often had disorders caused by dysplastic changes in connective tissue compared to women in the control group. Varicose veins were diagnosed in 40.9% of patients in group I, while in group II this figure was only 10% (χ^2=27.78; P<0.001; OS=6.22). This reflects the weakness of the venous wall and decreased vascular tone characteristic of dysplastic disorders. Orthostatic hypotension and syncopal states occurred in 10.8% of pregnant women in group I versus 5.8% in group II (χ^2=1.73; P>0.1; OS=1.94). The differences are not statistically significant, but the trend indicates a disturbance in autonomic regulation and a decrease in vascular tone in women with UCTD. Heart rhythm disturbances and extrasystole were observed in 12.9% of patients in group I compared to 7.5% in group II (χ^2=1.72; P>0.1; OS=1.83). Although the differences did not reach statistical significance, their presence confirms the tendency of patients with UCTD to develop cardiac manifestations.

Analysis of functional disorders in pregnant women with UCTD showed a higher frequency of a number of pathological conditions compared to the control group. Pelvic pain and symphysiopathy were recorded in 26.9% of patients in group I, which is significantly higher than in women without signs of UCTD (3.3%; χ^2=24.70; P<0.001; OS=10.66). This complication is associated with the insufficiency of the ligamentous apparatus and pronounced weakness of the connective tissue structures of the pelvis. Stretch marks and atrophic skin scars were found in 32.3% of women with UCTD versus 8.3% in group II (χ^2=19.66; P<0.001; OR=5.24), confirming a decrease in the elasticity and strength of collagen fibres in this category of patients. Constipation and gastrointestinal dyskinesia were observed in 19.4% of pregnant women in group I and in 10% in group II (χ^2=3.79; P>0.05; SD=2.16). Despite the absence of statistically significant differences, the identified trend reflects the involvement of connective tissue in the regulation of gastrointestinal motility. Functional oedema was found in 26.9% of patients with UCTD and in 16.7% of women in the control group (χ^2=3.28; P>0.05; SD=1.84). This indicates a tendency towards fluid retention and vascular disorders, although statistical significance was not achieved.

A comparative analysis of clinical and anamnestic indicators revealed both similarities and significant differences between women with UCTD and patients in the control group. The duration of menstruation in women in group I was 28.40±0.12 days and was significantly higher than in group II (28.00±0.08 days; P<0.01). Despite the small difference, this difference may indicate menstrual cycle instability in patients with dysplasia. The duration of the menstrual cycle did not differ significantly (6.08±0.09 days vs. 6.00±0.07 days; P>0.2), indicating that the basic parameters of the reproductive rhythm were preserved.

Prenatal ultrasound data showed significantly smaller sizes in women with UCTD (head circumference was 286.48±0.76 mm versus 293.63±0.64 mm (P<0.001), and weight was 2016.77±16.78 g versus 2158.67±14.45 g (P<0.001)). These results confirm a tendency towards intrauterine growth retardation. The most pronounced differences concerned the Beighton index, which reflects the degree of joint hypermobility: in women with UCTD, it was 5.55±0.18, while in the control group it was 1.38±0.10 (P<0.001). This confirms the systemic insufficiency of connective tissue as a key phenotypic feature of dysplasia.

4. Conclusions

Thus, the analysis showed that pregnancy in women with undifferentiated connective tissue dysplasia occurs against a background of a significantly higher frequency of obstetric complications. The most frequently recorded complications were isthmic-cervical insufficiency, threatened miscarriage, premature birth, premature rupture of the membranes, and postpartum haemorrhage. These complications have a direct pathogenetic link to connective tissue insufficiency. Somatic manifestations in patients with UCTD were characterised by a high frequency of varicose veins and heart valve prolapse, confirming the systemic nature of dysplastic disorders. In addition, functional disorders were noted, the most pronounced of which were symphysiopathy and dermatological manifestations (stretch marks and atrophic skin scars). The combination of the data obtained indicates that the clinical manifestations of UCTD in pregnant women have a pronounced obstetric and perinatal significance, determining a high risk of adverse pregnancy outcomes and the need for a differentiated approach to monitoring, prevention, and correction of complications in this category of patients.

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