

RARE CLINICAL MANIFESTATIONS OF CONNECTIVE TISSUE DYSPLASIA IN WOMEN WITH GENITAL PROLAPSE

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Abstract. Relevance. *The problem of pelvic organ prolapse remains the focus of attention of gynecologists, despite the long history of the disease, it still does not have a clear solution. The relevance of the problem of pelvic organ prolapse in women has been increasing in recent years, which is largely due to changes in the quality of life of women and the desire to preserve their youth. Every year, the number of studies in which the cause of the disease is found in connective tissue dysplasia (CTD) increases.*

Purpose. *of the study: having studied the features of the clinical manifestations of connective tissue dysplasia syndrome (CTD), to analyze and identify common signs of CTD in women with pelvic organ prolapse.*

Results and discussion. *PG is a heterogeneous disease with various forms of manifestation. In young patients, PG was represented by apical forms – 50.7%: complete and incomplete prolapse of the uterus and vaginal walls of cases, uterine prolapse of the third degree – 15.4% of cases. The body type was noted in asthenic patients suffering from genital prolapse in comparison with healthy women. The tendency of tissue bleeding in the main group, $16.50 \pm 0.37\%$, was higher ($p = 0.016$) than in the control group. Those with varicose veins and hemorrhoids that did not require surgical treatment occurred in $33.00 \pm 0.47\%$ of cases in the main group, in $4.50 \pm 0.21\%$ of cases in the control group ($p = 0.0002$). Pelvic organ prolapse in relatives of patients in the main group was registered in $9.90 \pm 0.30\%$ ($p = 0.031$); women in the control group without signs of prolapse did not indicate the presence of prolapse in close relatives.*

Conclusions. *PG is a multifactorial disease with heterogeneous clinical manifestations. The form of PG is determined by the type of hemodynamics and microcirculation, which are determined by the form of DST. Frequent signs of DST in women with pelvic organ prolapse are asthenic body type, varicose veins and hemorrhoids, the presence of pelvic organ prolapse in close relatives, a tendency to skeletal abnormalities, and elastosis of the skin.*

Keywords: *genital prolapse, pelvic floor muscle incompetence, women, risk factors, predisposition, connective tissue dysplasia.*

Actuality: Today, all experts are unanimous in the opinion that genital prolapse (GP) is a multidisciplinary problem that is of particular interest to doctors of many specialties: gynecologists, urologists, proctologists, as well as functional diagnostics doctors. The prevalence of the disease reaches 11–50% depending on ethnic aspects and customs [1, 2]. The problem of pelvic organ prolapse in women is relevant due to high socialization and the desire of modern women to prolong their youth. Genital prolapse and the discomfort associated with it significantly reduces the quality of life. Despite the long history of this pathology, genital prolapse is still considered a polyetiological disease. Every year there are more and more studies linking genital prolapse with connective tissue dysplasia (CTD). Currently, there is an opinion that connective tissue pathology has a greater negative impact on the vaginal walls and the ligamentous apparatus of the pelvic organs compared to trauma during childbirth (as previously thought) [1, 2]. In this

case, childbirth is considered as a provoking factor. In a number of works G.M. Buchsbaum found that vaginal delivery in parous women did not increase the risk of developing genital prolapse and genitourinary disorders compared with their nulliparous counterparts, confirming a hereditary predisposition [3]. There is evidence of a high content of type III collagen and immature collagen in the ligamentous apparatus of the uterus, which increases the risk of sprain and rupture of the ligaments in women suffering from prolapse. In the collagen structure, it leads to overstretching of the ligaments and, as a consequence, to genital prolapse [4]. There are articles in the literature about the effect of type III collagen, in particular the COL3A1 gene polymorphism, in patients with prolapse [5]. DST is a congenital pathology and is a manifestation of a decrease in the strength of connective tissue [6]. A study found that women with genital prolapse and stress urinary incontinence have altered connective tissue metabolism, which leads to decreased collagen production and may lead to insufficient genitourinary tract support [7]. There is an opinion: the more signs of dysplasia at the multiple organ level, the earlier genital prolapse occurs and the worse the results of surgical treatment, and the risk of relapses increases [8]. Despite the large number of studies related to the search for the cause of prolapse, there is currently no consensus on the etiology of genital prolapse. Connective tissue dysplasia is a genetically determined developmental disorder in which defects of its basic substance and fibers are formed [9]. According to other data, connective tissue dysplasia is a condition in which various congenital visceromotor lesions manifest themselves to varying degrees, have a progressive course and lead to functional disorders [6, 10].

The aim of research: – Having studied the features of clinical manifestations of connective tissue dysplasia syndrome at the systemic, organ, tissue levels, evaluate the contribution of connective tissue dysplasia, features of the course of labor and their impact on connective tissue dysplasia. Conduct an analysis and determine the most common signs of connective tissue dysplasia in women with pelvic organ prolapse.

Materials and methods: The study involved 135 women, among whom 2 groups were divided. The main group included 91 patients with clinical signs of pelvic prolapse; the control group included 44 women in whom the absence of prolapse was objectively proven. The examination was carried out in maternity complex No. 3 - in the gynecological department of Samarkand.

Inclusion criteria in the main group: the presence of established genital prolapse; age over 45 years; availability of informed voluntary consent. Criteria for inclusion in the control group: absence of genital prolapse; age over 45 years; availability of informed voluntary consent.

Non-inclusion criteria: age less than 45 years, male gender. Nationality, the presence of somatic pathology, and bad habits were not taken into account. All women signed informed consent to participate in the study.

Research methodology: In this study, questionnaires and general clinical methods were used: indicators of a general blood test were determined on a Coulter LH 500 automatic hematology analyzer (Beckman Coulter, USA), a general urinalysis - on a urine analyzer, and coagulograms of a biochemical blood test. All women were offered a survey that included questions about the course of pregnancy, childbirth, the weight of the children born, the presence of complications during pregnancy and childbirth, as well as data according to the criteria presented below. To determine the presence of signs of dysplasia, we used the authors' criteria [11] for the severity of connective dysplasia in points (Table 1). According to these criteria, signs

of connective dysplasia are divided into 3 groups: small, large signs and severe manifestations. Minor signs are scored 1 point, major signs – 2 points, severe signs – 3 points. The sum of points awarded for each sign determines the severity of connective tissue dysplasia. Mild severity (mild connective tissue dysplasia) corresponds to 9 points or less, moderate severity (moderate connective tissue dysplasia) – 10–16 points, severe severity (severe connective tissue dysplasia) – 17 or more points.

Statistic analyze. Statistical analysis of the results included calculation of the average value of indicators (M), arithmetic mean error (m) and standard deviation (σ). In order to evaluate data that had a normal distribution, parametric methods were used (Student's test), and for data that had a different distribution of indicators, non-parametric methods (Fisher's test) were used in the analysis.

In this study, the following designations were used: n – numerical value of the variable (number of women); σ – standard deviation; σ^2 – dispersion; t -value – Student's test; p – statistical significance; F -ratio – Fisher criterion; P – percentage relative to the total number of studies; $\pm p$ – percentage error, calculated by the formula: χ^2 criterion – a non-parametric criterion for the significance of the difference between the compared samples (analogous to the Student's test), only for samples that do not have a normal distribution. Most often, it shows reliability in 100% of cases where the Student's t -test is reliable. OR (odds ratio) - odds ratio - a characteristic used in mathematical statistics to quantitatively describe the closeness of the relationship between characteristics in a statistical population. The database was created and initially processed in Excel 2007. In this work, multivariate statistics methods were used, correlation coefficients were calculated; To develop a prognostic algorithm for the development of pelvic organ prolapse, discriminant analysis was performed. Multivariate statistical analysis was performed in standard Excel 2007 software packages.

Results: The study shows a high frequency of asthenic body type in patients of the main group ($16.70 \pm 0.38\%$) compared to the control group ($2.30 \pm 0.15\%$; $p = 0.016$). The tendency to increased tissue bleeding in the main group of women with genital prolapse ($16.50 \pm 0.37\%$) was higher ($p = 0.016$) than in the control group. Scoliosis, kyphosis, kyphoscoliosis were detected in $14.30 \pm 0.35\%$ in the main group, and in $2.30 \pm 0.15\%$ in the control group ($p = 0.032$). Signs of skin elastosis were noted in $25.3 \pm 0.44\%$ of patients suffering from genital prolapse; this pathology was not registered in healthy women ($p = 0.0002$). Signs of varicose veins and hemorrhoids that do not require surgical treatment occurred in $33.00 \pm 0.47\%$ in the main group, and in $4.50 \pm 0.21\%$ in the control group ($p = 0.0002$). Prolapse of the pelvic organs and hernias in mothers and offspring of women in the main group were registered in $9.90 \pm 0.30\%$; women in the control group did not indicate the presence of prolapse and hernias in close female relatives ($p = 0.031$). Hernias (umbilical, femoral, linea alba) in patients with genital prolapse were noted in $12.10 \pm 0.33\%$, while in healthy women this concomitant pathology was not detected ($p = 0.016$). Surgeries for varicose veins of the lower extremities and hemorrhoids were performed in $9.9 \pm 0.30\%$ of patients in the main group; in the control group there was no history of such operations ($p = 0.031$). According to the data obtained (Table 2), the sum of points when determining the severity of connective dysplasia in the study groups varied significantly: in the main group the average value was 3.94 ± 0.02 points, in the control group – 1.02 ± 0.01 points ($p = 0.002$). At the same time, the number of patients with a score > 2 in the group suffering from prolapse was $86.82 \pm 0.05\%$ ($p < 0.05$), and in healthy women – $20.46 \pm 0.15\%$ (Table 3).

Discussion: A high frequency of asthenic body type was noted in patients suffering from genital prolapse ($16.70 \pm 0.38\%$) compared to healthy women ($2.30 \pm 0.15\%$; $p = 0.016$). According to a study among women with stress urinary incontinence and pelvic organ prolapse who were scheduled for surgery, there was greater similarity among monozygotic twins compared to dizygotic twins, indicating a genetic predisposition to the pathology [12]. Our study noted a high hereditary predisposition in women suffering from pelvic organ prolapse. Prolapse of the pelvic organs among close female relatives in women of the main group was registered in $9.90 \pm 0.30\%$; in the control group there were no genital prolapses or hernias in close relatives ($p = 0.031$).

Table 1. The average value of the sum of points according to the criteria for the presence of signs of connective tissue dysplasia in the examined women.

Indicator	Main group (n = 91)	Control group (n = 44)	t-value	p	F-ratio σ^2
Overall balls, M \pm σ	3,94 \pm 2,36*	1,02 \pm 1,38	7,58*	0,00*	2,89*

Note: * $p < 0.05$ – differences are statistically significant compared to the control group.

Table 2. Sum of points according to the criteria for the presence of signs of connective tissue dysplasia in the examined women

Balls	Mail proup (n = 91)			Control group (n = 44)			t-value	χ^2	OR ($\pm 95\%$)
	n	P, %	$\pm p$	n	P, %	$\pm p$			
0	6	6,59	2,60	20	45,45	7,51	-4,89*	26,36 *	0,09 (0,03– 0,26)
1	6	6,59	2,60	15	34,09	7,15	-3,62*	15,00 *	0,09 (0,03– 0,26)
2	15	16,48	3,89	3	6,82	3,80	1,78	1,63	0,14 (0,04– 0,42)
3	15	16,48	3,89	2	4,55	3,14	2,39*	2,83*	2,70 (0,68– 12,50)
4	16	17,58	3,99	3	6,82	3,80	1,97*	2,02	4,15 (0,84– 27,56)
5	11	12,09	3,42	0	0,00	0,00	3,54*	4,29*	2,92 (0,74– 10,93)
6	7	7,69	2,79	1	2,27	2,25	1,51	0,74	
7	7	7,69	2,79	0	0,00	0,00	2,75*	2,18	3,58(0,42– 81,26)
8	7	7,69	2,79	0	0,00	0,00	2,75*	2,18	
9	1	1,10	1,09	0	0,00	0,00	1,01	0,005	

Note: * $p < 0.05$ – differences are statistically significant compared to the control group; OR – odds ratio.

According to a study carried out in 2019, a complicated obstetric history, a family history of pelvic organ prolapse and menopause (more than 10 years) influence the development of pelvic organ prolapse. The study included 736 women, including 500 women who had undergone surgery

for pelvic organ prolapse and 236 women without signs of prolapse [13]. Signs of skin elastosis in our study were noted in $25.3 \pm 0.44\%$ of women suffering from genital prolapse; this pathology was not recorded in healthy women ($p = 0.0002$) revealed the relationship between pelvic organ prolapse and the presence of stretch marks in women. More than half of the examined women with prolapse (54.7%) indicated the presence of stretch marks on the body, while only 25.0% of women without genital prolapse reported the presence of stretch marks. This analysis confirmed that striae are a significant risk factor for the development of clinical genital prolapse [14]. Another study compared the prevalence of signs of connective tissue dysplasia in patients with genital prolapse ($n = 110$) and women in the control group ($n = 100$). Patients with genital prolapse reported a higher prevalence of varicose veins, rectal prolapse and joint hypermobility, and were more likely to have family members with genital prolapse compared to the control group [15]. In our study, signs of varicose veins and hemorrhoids that did not require surgical treatment were 8 times more common in the main group of patients than in the control group: $33.00 \pm 0.47\%$ versus $4.50 \pm 0.21\%$ ($p = 0.0002$). A history of operations for varicose veins of the lower extremities and hemorrhoids was established in $9.9 \pm 0.30\%$ of patients in the main group; in the control group, there was no history of such operations ($p = 0.031$). We confirmed the high correlation between the criteria of connective dysplasia and genital prolapse. The goals set in this study were fully achieved. In the future, it is planned to study the influence of individual genes on the development of pelvic organ prolapse.

Thus. As a result of the study, we can conclude that in women with pelvic organ prolapse, the generally accepted signs of connective tissue dysplasia were much more common than in healthy women. According to the results of our study, the tendency to increased tissue bleeding, skin elastosis, the presence of concomitant varicose veins and hemorrhoids, and hernias of other localizations were the most common accompanying symptoms of pelvic organ prolapse in women. The presence of prolapse in close relatives, in our opinion, is one of the most prognostically significant signs.

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