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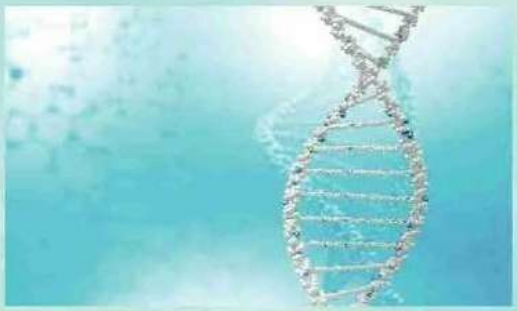

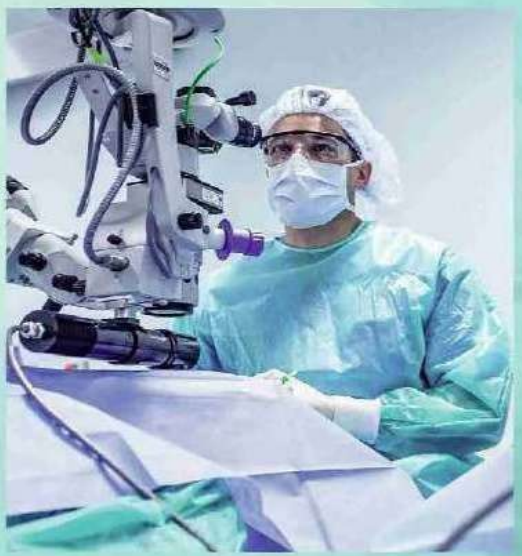

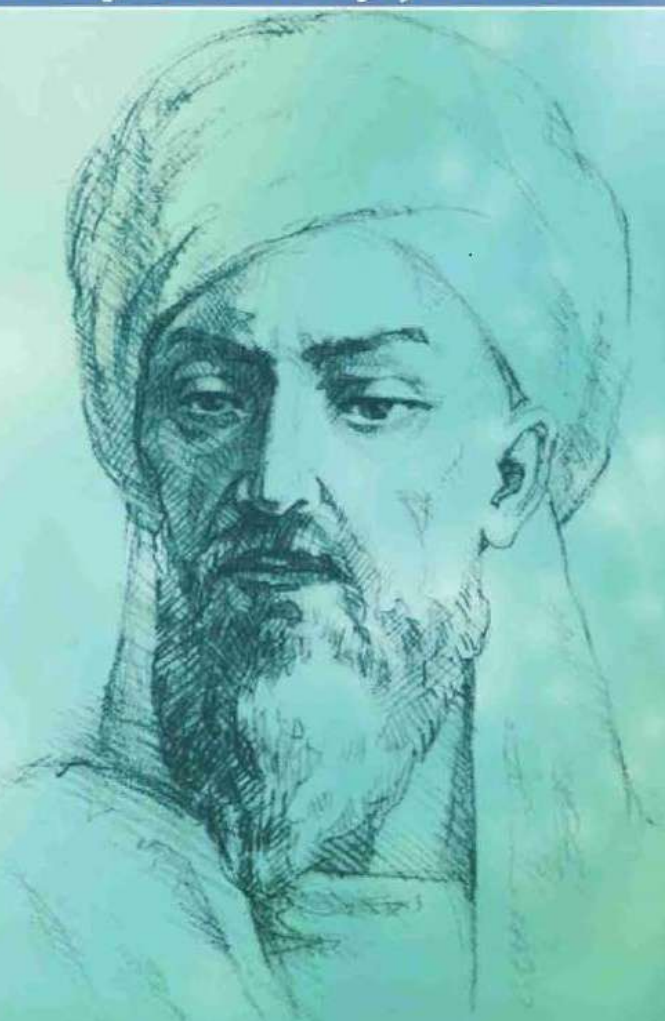

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GENETIC ASPECTS OF GENITAL PROLAPSE IN WOMEN OF REPRODUCTIVE AGE

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✓ ***Resume***

The review article is devoted to the genetic study of predisposition to pelvic organ prolapse. The genetically determined activity of a number of phase II enzymes of the detoxification system is one of the endogenous pathogenetic conditions that contribute to the formation and progression of pelvic organ prolapse.

Key words: women of reproductive age. pelvic organ prolapse, matrix metalloproteinase-9, matrix metalloproteinase-12.

ГЕНЕТИЧЕСКИЕ АСПЕКТЫ ГЕНИТАЛЬНОГО ПРОЛАПСА У ЖЕНЩИН РЕПРОДУКТИВНОГО ВОЗРАСТА

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✓ ***Резюме***

Обзорная статья посвящена к генетическому изучению предрасположенности к пролапсу тазовых органов. Генетически-обусловленная активность ряда ферментов фазы II системы детоксикации является одним из эндогенных патогенетических условий, способствующих формированию и прогрессированию пролапс тазовых органов.

Ключевые слова: женщин репродуктивного возраста, пролапс тазовых органов, матриксная металлопротеиназа-9, матриксная металлопротеиназа-12.

REPRODUKTIV YOSHDAGI AYOLLARDA JINSIY ALOQA PROLAPSINING GENETIK ASPEKTLARI

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✓ ***Rezyume***

Ko'rib chiqilayotgan maqola tos a'zolarining prolapsasiga moyillikni genetik o'rganishga bag'ishlangan. Detoksifikatsiya tizimining bir qator II faza fermentlarining genetik jihatdan aniqlangan faolligi tos a'zolari prolapsasining shakllanishi va rivojlanishiga yordam beradigan endogen patogenetik sharoitlardan biridir.

Kalit so'zlar: reproduktiv yoshdagi ayollar, tos a'zolari prolapsasi, matritsa metalloproteinaza-9, matritsa metalloproteinaza-12.

Relevance

The increase in the incidence of genital prolapse (PG) in recent years, according to most researchers, is rapidly increasing (2016) and ranges from 1.7% to 28% in the structure of gynecological pathology. In women of reproductive age, PG is 50.3%, among patients under 30 years old - 10.1%, from 30 to 45 years old - 40.2% (2019), [1,2,33]. There is still debate about the relative contribution of various factors to the development of GHG. Proven causes of the development of PG are aging, menopause, parity, tissue damage to the soft birth canal during childbirth, heavy physical labor, diseases of the respiratory system, and chronic constipation. PG may be one of the manifestations of non-systemic connective tissue dysplasia (NCTD) [1,2].

In recent years, research has been conducted all over the world to identify the molecular genetic mechanisms of TS diseases related to the complex of systemic and UCTD syndromes. Systemic dysplasia CT includes monogenic diseases determined by mutations in genes that control, among other things, the formation of the primary structure of collagen. And components of the extracellular matrix (ECM). Mutations in the FBLN5, LOXL1, FBLN3, MMP9, COL3A1 genes cause the development of hereditary pathologies associated with CT failure (FBLN5 - lax skin syndrome and age-related macular degeneration, LOXL1 - exfoliant syndrome, FBLN3 - Doyne colloid retinal dystrophy, COL3A1 - Ehlers-Danlos syndrome (pathological mobility in the joints, hyperelasticity of the skin), MMP9 - metaphyseal dysplasia) [1,33]. With these pathologies, there is also often an increased risk of developing PG. However, in the vast majority of women with PG, this disease is multifactorial, that is, caused by a combination of unfavorable factors - clinical, behavioral and genetic. If mutations in genes that determine the structure and composition of collagen, as well as the processes of collagen and elastin remodeling, determine severe hereditary pathologies of TS, then polymorphic variants in these same genes may be associated with a predisposition to these diseases.

In women with PG, a change in the expression level of the corresponding proteins FBLN5, LOXL1, MMP9, COL3A1 [1,33]. Studies of the role of germinal variability in genes that control the synthesis and degradation of vaginal CT components are still scarce, and the results are contradictory [2]. In this regard, the problem of determining genetic risk factors for the development of POP and pelvic floor dysfunction remains relevant and requires further study.

The presented review of the world literature made it possible to substantiate the feasibility of searching for specific molecular genetic factors that form the structure of hereditary predisposition to pelvic floor dysfunction in women.

Despite the growing prevalence of pelvic floor dysfunction in women, there is currently no consensus on its etiology and pathogenesis. However, there is no doubt that this is a multifactorial pathology with a hereditary predisposition, the development of which is determined by the interaction of multiple additive genetic factors (mutations and/or polymorphic alleles) and environmental factors. It has been shown that carriage of a polymorphic variant is associated with the development of pelvic organ prolapse in women rs1800012 of the COL1A1 gene, the rs1800255-A/A genotype of the COL3A1 gene and the polymorphic variant of the rs2228480 ESR1 gene, although these data are contradictory and still need verification in independent samples. Systematic accumulation of data and their reproduction in different populations and ethnic groups are necessary for further generalization of all known information about the pathogenetic and functional significance of each gene variant.

Pelvic floor dysfunction is understood as a complex of dysfunctions of the ligamentous apparatus and pelvic floor muscles that hold the pelvic organs in a normal position and ensure the retention of urine and feces [1,3]. Although these disorders do not lead to death, they have an extremely negative impact on the quality of life of patients [1,4].

The most common types of pelvic floor dysfunction in women are various types of urinary and fecal incontinence, chronic cystourethritis, pelvic organ prolapse (POP) and sexual dysfunction. About a quarter of women have one of the clinically significant pelvic disorders, and in most cases there is a combination of them [2,6,8].

UI in the structure of pelvic floor dysfunctions in Russian women is 33.6–36.8% [1,9]. In women of reproductive age, stress-related UI predominates; in women over 50 years old, a mixed type of UI predominates. POP, which occurs as a result of dysfunction of the pelvic floor muscles, plays a significant role in the development of UI [10]. PTO in the structure of gynecological pathology in Russia is 28–38.9% [11,12], in European countries – 30.8% [13], in the countries of the Middle East – 19.9–

49.6% [14], in countries of North and East Africa – 46–56% [15]. In recent years, there has been an increase in the incidence of POP worldwide [16,17].

However, despite the growing prevalence of pelvic floor dysfunction in women, there is currently no consensus on its etiology and pathogenesis. There is no doubt that this is a multifactorial pathology, the development of which is determined by genetic and environmental factors.

Environmental factors contributing to the development of pelvic floor dysfunction in women have been studied quite well. These include traumatic and long labor, estrogen deficiency conditions, diseases accompanied by increased intra-abdominal pressure (bronchitis, bronchial asthma, constipation, etc.), disruption of microcirculation of blood and lymph in the pelvis, obesity, sedentary lifestyle [18,20].

One of the main reasons is considered to be aging of the body [20]. Pelvic floor dysfunction in women develops mainly in the late reproductive and perimenopausal periods of life, and the incidence of the disease progressively increases with increasing age [1,22]. The prevalence of pelvic floor dysfunction among women over 80 years of age is 5 times higher than that among patients aged 20–39 years [2].

As for genetic factors, back in the early twentieth century. Familial cases of POP were known to exist. This circumstance served as the basis for conducting large-scale studies aimed at elucidating the role of hereditary factors in the development of pelvic floor dysfunction in women using classical methods of genetic analysis: clinical-genealogical, population-statistical and twin. The generalized results of these studies convincingly demonstrated that in families of probands (patients), pelvic floor dysfunction occurs 3–5 times more often than would be expected based on the frequency of this pathology in the population. It has been shown that for healthy first-degree relatives of the proband (mothers, sisters, daughters), the risk of developing a similar pathology is increased by 5 times compared to the general population risk [2].

Formal genetic analysis performed on the material of the Swedish and Danish twin registries showed that the relative contribution of hereditary and environmental factors to the predisposition to PTO is 43 and 57%, respectively [2].

It has been established that in the general structure of PTO, familial forms (2 or more cases among 1st degree relatives) account for 28% and that in such families the disease is inherited in an autosomal dominant manner with high penetrance [33].

Thus, genetic and epidemiological studies have substantiated the feasibility of searching for specific molecular genetic factors that form the structure of hereditary predisposition to pelvic floor dysfunction in women.

There is ample evidence that pelvic floor dysfunction in women is the result of connective tissue dysplasia (CTD) and that pathological changes in connective tissue, more than childbirth and obstetric trauma to the pelvic floor, contribute to the development of this pathology. Moreover, there is an opinion that without DST, significant changes in the pelvic floor after childbirth do not occur. The main role is given to genetic factors that determine the pathology of connective tissue. Pregnancy and childbirth are considered precipitating factors [1,2,6,8]. This is confirmed by observations that in some patients with Marfan, Ehlers–Danlos and osteogenesis imperfecta syndromes, which are classified as monogenic collagenopathies, POP may be one of the manifestations of the syndrome [3]. In addition, POP is often combined with joint hypermobility, varicose veins of the lower extremities, low bone mineral density, hemorrhoids, stretch marks and hernias. It is possible that the etiology of these forms of pathology is due to a partial share of common genetic factors [3].

The International Database of Disease Genes (HuGENavigator) contains about 30 publications related to the search for genetic factors associated with pelvic floor dysfunction in women. Most studies are devoted to the study of genes that control the processes of synthesis and degradation of connective tissue, in particular the genes for collagen (COL1A1, COL3A1), matrix metalloproteinases-1, -3, -9 (MMP1, MMP3, MMP9) and laminin (LAMC1) [4].

As early as 1966, a hypothesis was put forward about the role of impaired collagen metabolism in the development of POP, based on data on a 25% reduced content of total collagen in the vaginal epithelial tissue in women with POP compared to healthy women [4].

As you know, collagen is a fibrillar protein that forms the basis of connective tissue and ensures its strength. The collagen molecule consists of three α-chains twisted into one regular helix, stabilized by hydrogen bonds between the side groups of its constituent amino acids [48]. The amino acid composition of collagen is characterized by a high content of glycine residues (33%), proline (10%) and hydroxyproline (10%).

Types I and III collagens are most important for supporting the pelvic organs. To a greater extent, the binding apparatus is represented by type I collagen, which imparts strength to the ligaments due to the length and thickness of the fibers, and to a lesser extent by type III collagen, an increase in the amount of which is associated with a decrease in the mechanical strength of the connective tissue [33].

In order to clarify the role of the COL1A1 gene polymorphism in the development of PTO, its polymorphic variant rs1800012, located in the binding site of the Sp1 transcription factor, was studied. Replacing the nucleotide guanine (G) with thymine (T) in the structure of the COL1A1 gene leads to a disruption of the normal ratio of amino acids in the collagen molecule, as a result of which its mechanical properties deteriorate. It is known that the rs1800012 polymorphic variant of the COL1A1 gene is associated with a decrease in bone mineral density and osteoporosis, especially in postmenopausal women [1].

However, studies of the role of the rs1800012 polymorphic variant of the COL1A1 gene in the development of POP turned out to be very controversial. Thus, a meta-analysis performed in 2014 by R.M. Ward et al. did not confirm the connection between the rs1800012 polymorphism of the COL1A1 gene and PTO. The authors showed that the development of PTO is associated not with this polymorphic variant, but with carriage of the rs1800255-A/A genotype of the COL3A1 gene, which increases the likelihood of developing PTO by 4.79 times. According to the authors, the nucleotide substitution 2092G>A (rs1800255) leads to the replacement of alanine with threonine (Ala698Thr), which can affect the strength of collagen fibers [5].

Another meta-analysis performed in 2015 by Cartwright et al. did not confirm the association of rs1800255-A/A of the COL3A1 gene with the development of POP, but confirmed the presence of a correlation of the rs1800012 polymorphic variant of the COL1A1 gene with the risk of developing POP [2].

In domestic studies, the association of PTO with the polymorphic variant of the COL3A1 genes (rs1800255) was also not confirmed, however, in a meta-analysis, when the author added his own data, the association of PTO with the rs1800255-A/A genotype of the COL3A1 gene was reliably confirmed [3].

Both foreign and domestic studies have shown that with POP there is increased activity of matrix metalloproteinases (MMPs) in the vaginal walls and uterosacral ligaments. It is known that the activity of matrix MMPs is regulated by tissue metalloproteinase inhibitors (TIMPs), which can block the destruction of the extracellular matrix [1,3]. In patients with POP, a decrease in the expression level of the TIMP-1 and TIMP-2 genes and a simultaneous increase in the activity of matrix MMPs were revealed [1,5]. In addition, an association of PTO with the insertion of guanine at position -1607/-1608 of the promoter region of the MMP1 gene (rs1799750) and the insertion of adenine at position -1612/-1617 of the promoter region of the MMP3 gene (rs3025058) was revealed [5].

A certain contribution to the structure of predisposition to PTO is made by the LAMC1 gene, which encodes the adhesive glycoprotein laminin, which is an important component of basement membranes [3]. There is evidence that the polymorphic variant of the LAMC1 gene (rs 10911193-T) is associated with the development of familial PTO [61], and polymorphic variants of the LAMC1 gene (rs1413390, rs20563 and rs20558) are associated with sporadic PTO [2].

The formation of collagen chains is also influenced by the proteoglycan lumican (LUM gene) and the protein fibromodulin (FMOD gene). Animal experiments revealed that deletions of these genes lead to symptoms reminiscent of Ehlers–Danlos disease and other hereditary diseases of human connective tissue [63]. In a biopsy of paraurethral tissue from all women with POP included in the study, PCR revealed a decrease in the expression of the FMOD gene compared to the control [1].

When studying the role of polymorphism of the estrogen receptor (ESR1 and ESR2) and progesterone receptor (PGR) genes in the development of POP, associations of this pathology with variants rs2228480 (ESR1), rs484389 (PGR) and the ESR2 gene haplotype were identified [2,27].

According to domestic studies, polymorphism of the ESR1 receptor gene occurs in 75.0% of patients with POP and minor forms of CTD, as well as in 53% of patients who do not have indirect signs of CTD. The same work showed that in all recurrent forms of POP, polymorphic genotypes COL3A1 and ESR1 are present [1,26].

As is known, one of the key components of the ligamentous apparatus of the pelvic organs is elastic fiber, which determines the extensibility and elasticity of connective tissue [6,25]. The synthesis and assembly of elastic fibers are critical for restoring pelvic organ support after vaginal delivery, and

disruption of elastogenesis plays a major role in the development of POP [1, 24]. In women suffering from POP, there is a decrease in elastin content in the vaginal walls and ligaments, as well as a decrease in the width of elastic fibers, which leads to weakening of the apparatus that supports the pelvic organs [2,17].

Fibulin-5 (FBLN5) protein and lysyl oxidase-like protein 1 (LOXL1) play an important role in the synthesis and assembly of elastic fibers, and disorders in the genes encoding these proteins cause the development of diseases associated with connective tissue defects [7,17]. Over the past decade, a sufficient number of studies have accumulated that have proven the important role of fibulin-5 in the development of PTO [18,31]. Thus, in an animal experiment involving vaginal stretching, simulating childbirth in Fbln5-/- mice, a rapid progression of POP was noted, which was subsequently never eliminated [1, 14,29]. It was shown that in more than 90% of mice knockout for this gene, PTO developed in the sixth month of life, even in the absence of vaginal birth, and other manifestations of elastinopathy were observed even in the early stages of development, while the formation of PTO was accompanied by increased activity of MMP9 in the vaginal walls [7,16] .

LOXL1 is also known as an important genetic factor in the development of exfoliation syndrome and glaucoma [3,12,29].

In Loxl1-/- mice, along with PTO in the postpartum period, increased sagging and redundancy of the skin, pulmonary emphysema and vascular pathologies are also observed. These disorders are accompanied by the accumulation of tropoelastin, which indicates a disruption of the elastogenesis process [31]. It has been shown that Loxl1 knockout mice develop severe forms of PTO after the first litter [2,12,23,32].

Interesting data were obtained when studying the role of mutations in the mitofusin type 2 gene (Mfn2) in the etiology of PTO. The function of this gene is believed to be associated with cellular senescence, cell proliferation and apoptosis by affecting mitochondrial synthesis. The expression of mRNA, proteins of mitafusin-2 and procollagens types I and III (1A1/1A2/3A1) was measured in fibroblasts of the uterosacral ligaments of postmenopausal women suffering from POP (main group) and healthy women (control group). As it turned out, in the main group the level of expression of the Mfn2 gene was significantly higher, and procollagen types I and III were lower than in the control group, and this condition clearly correlated with the duration of postmenopause. The author explains the results obtained by fibroblast apoptosis, which he associates with high expression of mitafusin-2 [2,21,31].

In addition, it has been shown that weakening of the pelvic organ support apparatus is accompanied by increased apoptosis in the uterosacral ligaments due to oxidative stress [84]. In this regard, genes of the second phase of the detoxification system (NAT2, GSTT1, GSTM1, GSTP1) were considered as candidate genes involved in the development of POP. As a result, it was revealed that the alleles rs1695-G (Ile105Val) of the GSTP1 gene (glutathione S-transferase pi 1) and rs1136410-C (Val762Ala) of the PARP1 gene (poly(ADP-ribose) polymerase 1), involved in DNA repair, have a protective effect effect [2,11,22].

As a result of 2 genome-wide studies, it was found that chromosome regions 4q21 (rs1455311), 8q24 (rs1036819), 9q22 (rs430794), 15q11 (rs8027714), 20p13 (rs1810636), 21q22 (rs2236479) and 9q21 are associated with an increased risk of developing PTO in relatives Nnits 1 -th degree of relationship (mothers, daughters and sisters) of patients suffering from POP [1,10,20].

Another genome-wide study found that PPO in African-American women is associated with a polymorphic variant of the CPE gene (carboxypeptidase E, rs28573326), and in Spanish women - with AL132709.5 (rs1950626). In the total sample, significant effects were found for DPP6 (dipeptidyl peptidase like 6, rs11243354) and near-gene variants of the genes PGBD5 (piggyBac transposable element derived 5, rs740494), SHC3 (SHC (Src homology 2 domain containing) transforming protein 3, rs2209875) [18,28] .

As a result of exome sequencing of biological samples obtained from women with POP, two missense mutations were identified in the sensory polyneuropathy gene (WNK1): c.2668G>A (p.G890R) and c.6761C>T (p.P2254L). Validation of these data by the Sanger method revealed eight additional variants in the WNK1 gene associated with POP [8,9]. The WNK1 gene (WNK lysine deficient protein kinase 1) encodes a protein that is a key regulator of blood pressure, controlling the transport of sodium and chloride ions. Mutations in this gene are associated with pseudohypoaldosteronism type II and hereditary sensory neuropathy type II. It should be noted that WNK kinases activate the canonical Wnt/ß-catenin signaling pathway, the role of which in the genesis of PTO was previously proven [1,2,3,4,5,8,30].

Two genome-wide studies identified associations of six single nucleotide polymorphisms (SNPs) on chromosome 9q21 associated with susceptibility to the development of severe forms of prolapse in Caucasian families [6,7,13,15]. In the work of Russian authors, the correlation of these SNPs on chromosome 9q21 with the development of severe forms of PTO in Caucasian families was verified using an independent sample. In addition, a connection was found between the risk of developing POP and a group of genes responsible for bone mineral density (WLS, SP7, MEPE, C6ORF10, CCDC170, SPTBN1). According to the authors, it is advisable to study this group of genes in the future as "causal" genes for the development of PTO [5,33].

Conclusion

Summarizing the analysis of world literature, it should be noted that classical genetic and epidemiological studies have provided evidence that pelvic floor dysfunction in women is a pathology with a hereditary predisposition, the development of which is determined by the interaction of multiple additive genetic factors (mutations and/or polymorphic alleles) and environmental factors .

Follow-up studies aimed at testing candidate genes for susceptibility to pelvic floor dysfunction in women are certainly of scientific value, but only a few scientific facts are convincing. In particular, carriage of the rs1800012 polymorphic variant of the COL1A1 gene, the rs1800255-A/A genotype of the COL3A1 gene and the rs2228480 ESR1 gene polymorphism are associated with the development of pelvic organ prolapse in women, although these data are contradictory and still require verification in independent samples. The task of applied genetics in relation to pelvic floor dysfunction in women today is the systematic accumulation of data, their reproduction in different populations and ethnic groups, and the synthesis of all known information about the pathogenetic and functional significance of each gene variant.

LIST OF REFERENS:

1. Anterior colporrhaphy compared with collagen-coated transvaginal mesh for anterior vaginal wall prolapsed: a randomized controlled trial / M. Rudnicki, E. Laurikainen, R. Pogosean, et al.. // British Journal of Gynecology. 2014;121(1):102-110.
2. Apokina A. N. Predicting the effectiveness of surgical correction of pelvic organ prolapse : abstract dis. … dr. ph. and med. science: 31.08.01 / Apokina Anna Nikolaevna. - M., 2012;11.
3. Bacterial colonization of the reproductive tract of women with genital prolapse / Y. L. Naboka, A. N. Rymashevskiy, M. I. Kogan et al. // Medical Advice. 2014;19:53-55.
4. Barski D. Systematic review and classification of complications after anterior, posterior, apical, and total vaginal mesh implantation for prolapse repair // Surgical Technologies International. 2014;24:217-224.
5. Khamdamova M. T. Anthropometric characteristics of the physical status of women in the first and second period of middle age // A new day in medicine. Tashkent, 2020;1(29):98-100.
6. Khamdamova M.T. Age-related and individual variability of the shape and size of the uterus according to morphological and ultrasound studies // News of dermatovenereology and reproductive health. - Tashkent, 2020;1-2(80-88):49-52.
7. Khamdamova M. T. Anthropometric characteristics of the physical status of women in the first and second period of middle age // Новый день в медицине. Бухара, 2020;1(29):98-100.
8. Collins, C. W. AUA SUFU adult urodynamics guideline: a clinical review / C. W. Collins, J. C. Winters // Urologic Clinics of North America. 2014;41(3):353-362.
9. Dallenbach P. To mesh or not to mesh: a review of pelvic organ reconstructive surgery // International Journal of Women's Health. 2015;7:331-343.
10. Khamdamova M.T., Khasanova M.T. Various mechanisms of pathogenesis of endometrial hyperplasia in postmenopausal women (literature review) // New day in medicine. Bukhara. 2023;8(58):103-107.
11. Khamdamova M.T. Reproductive Health of Women Using Copper-Containing Intrauterine Contraception // Eurasian Medical Research Periodical Volume 28 January 2024;39-45. ISSN: 2795-7624 .www.geniusjournals.org
12. Khamdamov I.B. Advantages Of Laparoscopic Hernioplasty in Obesity Women of Fertile Age // Eurasian Medical Research Periodical Volume 28 January 2024;33-38. ISSN: 2795-7624 .www.geniusjournals.org

13. Lifetime risk of stress urinar incontinence or pelvic organ prolapse surgery [Text] / J. M. Wu, C. A. Matthews, M. M. Conover et al. // Obstetrics and Gynecology. 2014;123(6):1201-1206.
14. Longterm follow-up after native tissue repair for pelvic organ prolapse [Text] / S. H. Oversand, A. C. Staff, A. E. Spydslaug [et al.]. // International Urogynecology Journal. 2014;25(1):81-89.
15. Lucioni, A. The surgical technique and early postoperative complications of the Gynecare Prolift pelvicfl oor repair system / A. Lucioni // The Canadian Journal of Urology. 2008;15:4004-4008.
16. Madhu C. How to use the ntification (POP-Q) system [Text] / C. Madhu, S. Swift, S. Moloney-Geany // Neurourology and urodynamics. 2018;37(6):S39-S43.
17. Khamdamova M. T. Somatometric characteristics of women of the first and second period of adulthood using different contraceptives with different body types // The american journal of medical sciences and pharmaceutical research 2020;8(2):69-76.
18. Khamdamova M.T., Zhaloldinova M.M., Khamdamov I.B. The state of nitric oxide in blood serum in patients with cutaneous leishmaniasis // New day in medicine. Bukhara, 2023;5(55):638-643.
19. Khamdamova M.T., Zhaloldinova M.M., Khamdamov I.B. The value of ceruloplasmin and copper in blood serum in women wearing copper-containing intrauterine device // New day in medicine. Bukhara, 2023;6(56):2-7.
20. Khamdamova M. T. Bleeding when wearing intrauterine contraceptives and their relationship with the nitric oxide system // American journal of pediatric medicine and health sciences Volume 01, Issue 07, 2023;58-62 ISSN (E): 2993-2149.
21. Pahwa A. K. Physical examination of the female internal and external genitalia with and without pelvic organ prolapse: A review // Clinical Anatomy. 2015;28(3):305-313.
22. Patient reported outcome measures in women undergoing surgery for urinary incontinence and pelvic organ prolapse in Denmark 2006-2011 / R. Guldberg, U. S. Kesmodel, J. K. Hansen [et al.]. // International Urogynecology Journal. 2013;24(7):1127-1134.
23. Khamdamov I.B. Improving tactical approaches in the treatment of hernias of the anterior abdominal wall in women of fertile age // New day in medicine. Bukhara, 2022;10(48):338-342.
24. Khamdamov I.B. Morphofunctional features of the abdominal press in women of reproductive age // New day in medicine. Bukhara, 2022;3(41):223-227.
25. Khamdamova M.T. Ultrasound features of three-dimensional echography in assessing the condition of the endometrium and uterine cavity in women of the first period of middle age using intrauterine contraceptives // Biology va tibbyot muammolari. - Samarkand, 2020;2(118):127-131.
26. Khamdamova M. T. Ultrasound assessment of changes in the endometrium of the uterus in women of the first and second period of middle age when using intrauterine and oral contraceptives // Биомедицина ва амалиёт журнали. – Ташкент, 2020;2(8):79-85.
27. E. A. Deviatova, K. A. Tsaturova, Z. I. Esmurzieva [et al.]. Perineum Design // Obstetrics and Gynecology: news, opinion, education. 2015;3:70-79.
28. Pontiroli A. E. Female sexual dysfunction and diabetes: a systematic review and meta-analysis [Text] / A. E. Pontiroli, D. Cortelazzi, A. Morabito // Journal of Sexual Medicine. 2013;10(4):1044-1051.
29. Urinary incontinence after surgery for pelvic organ prolapse / E. J. M. Lensen, M. I. Withagen, K. B. Kluivers et al. // Neurourology and Urodynamics. 2013;32(5):455-459.
30. Khamdamov I.B. Experimental determination of the extensibility of the anterior abdominal wall tissues at different times of pregnancy using various approaches to hernioplasty // Academicia: An International Multidisciplinary Research Journal April 2022;12(4):193-201. SJIF 2022 = 8.252
31. Khamdamov I.B. Improving tactical approaches in the treatment of hernias of the anterior abdominal wall in women of fertile age // New day in medicine. Bukhara, 2022;10(48):338-342.
32. Khamdamov I.B. Morphofunctional features of the abdominal press in women of reproductive age // New day in medicine. Bukhara, 2022;3(41):223-227.
33. Women's experiences of receiving care for pelvic organ prolapse: a qualitative study / P. Abhyankar, I. Uny, K. Semple et al. // BMC Women’s Health. 2019;19(1):45.

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