Influence Of Excess Body Weight And Deficiency Of Vitamin D On The Clinical Course Of Uterine Myoma

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ABSTRACT

Uterine fibroids is the most common benign gynecological disease, the pathogenesis of which is not fully explored. We examined 152 women in the II clinic of the Tashkent Medical Academy. The saturation of the body with vitamin D (25(OH)D) and its relationship with concomitant obesity in patients with uterine fibroids and healthy women were studied. In less than half of women with symptomatic myoma, deficiency and severe deficiency of vitamin D prevails with concomitant obesity of varying degrees. Studying the relationship between vitamin D deficiency and excess body weight in this pathology makes it possible to predict the development of the disease, the nature of the course and the risk of possible complications.

Key words: uterine fibroids, vitamin D (prohormone D), risk factors, body mass index (BMI), obesity.

1. INTRODUCTION

Leiomyomas are benign clonal tumors in women [11]. Myoma uterus diagnosed in 30-35% of women of reproductive age, usually in late reproductive age [16], and in 1/3 of patients it becomes symptomatic [1, 18 , 20], and by the age of 50 - 80% of women [17 , 1 8].

The authors describe risk factors for the development of fibroids (age before menopause, black race, obesity), reproductive (infertility, earlier menarche, use of oral contraception under 16 years of age, etc.) and environmental (diet, reduced insolation, leading to vitamin D deficiency, environmental toxins environment) factors that are the subject of current research [12 , 1 3]. Given the high prevalence of the disease in the population, at the present stage, the study of risk factors in the development of the disease is one of the topical, but, unfortunately, not fully studied issues in gynecology and is still a subject of discussion. According to many researchers, obesity is a significant potentiating endocrine factor of the disease and occurs in women with fibroids higher in 25-70% of cases [2].

Several studies show that vitamin D deficiency is a risk factor for the development of uterine fibroids [8,9,12,19,21,23] . The protective role of vitamin D on the growth of fibroids has been demonstrated during in vitro [10] and in vivo [8] studies, as well as retrospective clinical studies [3], which indicate the existence of a clear protective effect of vitamin D on the growth of fibroids , which is based on lie inhibition of cell proliferation, stimulation of apoptosis and other pharmacodynamic effects . The next logical step would be to demonstrate the inhibitory effect of vitamin D in humans, which would require clinical research. The authors argue that vitamin D deficiency is associated with fibroids and that supplementation helps nodule shrinkage and disease regression [14,25].

The aim of the study is to identify the level of vitamin D supply and the degree of obesity, and their relationship with the clinical course in women with uterine fibroids.

2. NMATERIALS AND METHODS

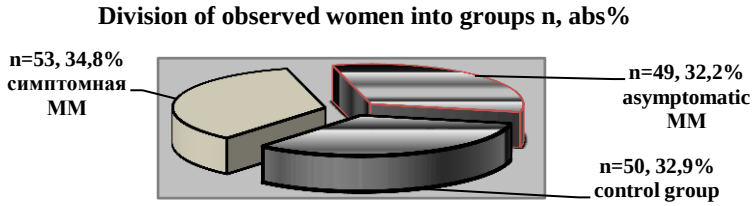
The design of a cohort prospective controlled study was used. The study was based on clinical and laboratory examination of 152 women who were admitted to the 2nd clinic of the Tashkent Medical Academy . The surveyed women were divided into 2 groups: the control group consisted of 50 healthy women and the main group of 102 women with uterine myoma. Main group patients were subdivided into two subgroups - 53 women with symptomatic iomoy and 49 women - asymptomatic . [15] .

During the observation period, all women underwent identification of risk factors according to a modified scale recommended by the guidelines, general clinical examination, ultrasound of the uterus and appendages with duplex scanning of the uterine artery, morphological studies of aspirates from the uterus. The marker of the body saturation with vitamin D - 25 (OH) D was determined by the method of ELISA quantitative determination - chemiluminescence analysis on microparticles (CMIA) [7]. Mathematical processing and statistical analysis of the results obtained were carried out using the program "Statistika 6.0".

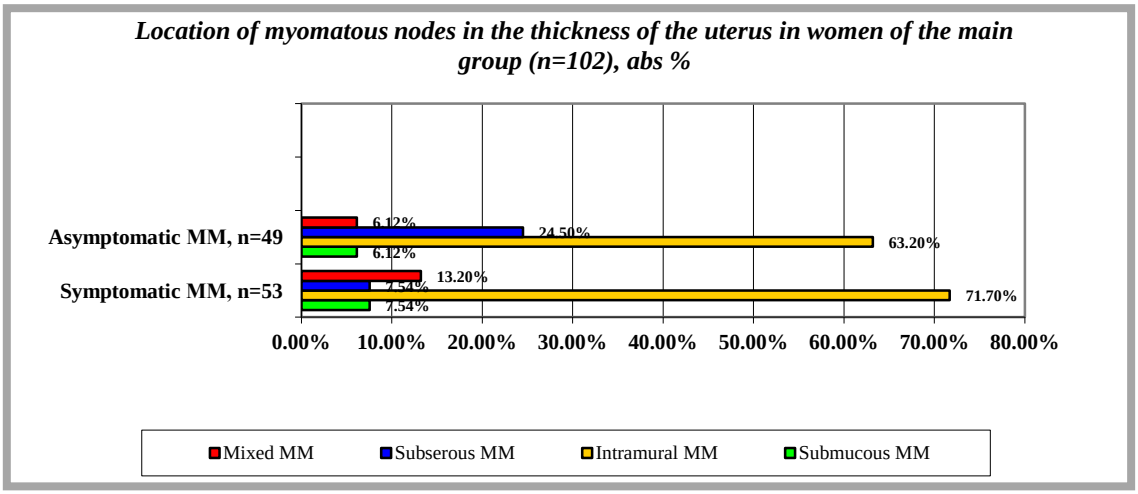
3. RESULTS

The age of the surveyed women in the main group was 19-55 years, the average age in the first subgroup was 44.35 ± 0.83 (n = 53) and in the second subgroup 42.6 ± 0.7 years (n = 49), which corresponds to the authors' data [6 , 1 6 , 22] that fibroids are more often

diagnosed in the late reproductive period. Whereas in the control group (n = 50), the average age was 40.12 ± 0.7 years (p <0.01).



Ultrasound study on the myoma node localization in the thickness of the uterus in both groups the main group prevailed intramural node (71.7% and 63.2%, respectively groups. Mixed fibroids in women with symptomatic fibroids were 2 times more likely than women with asymptomatic myoma (13.2% and 6.12%, respectively). The median uterine volume calculated according to Brunn's formula (1981) in the subgroup with symptomatic MM was 237.54 mm ^{3}, asymptomatic MM - 103.45 mm ^{3} and in the control group - 52.1 m m ^{3}.

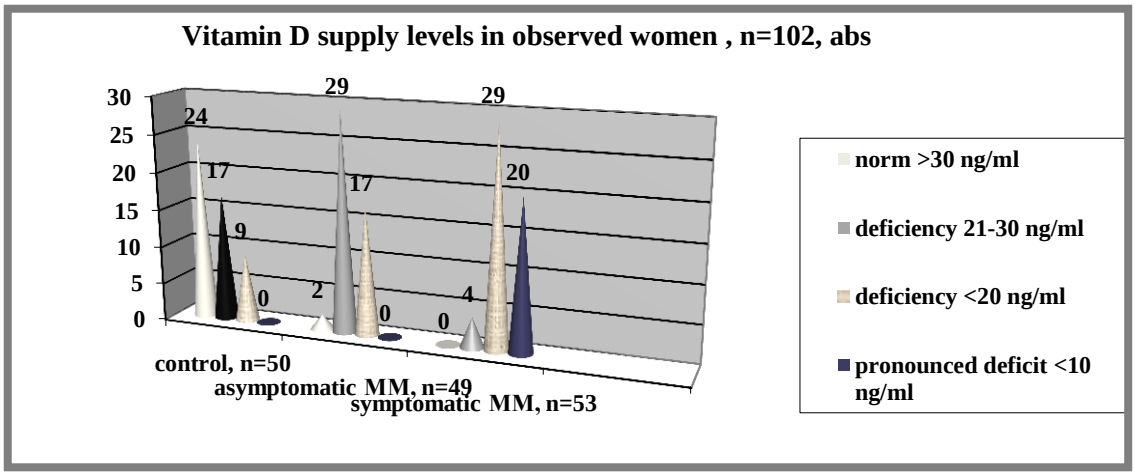


By analysis of risk factors prevalent factors such as overweight BMI (29.7 ± 11.83 and 28.1 ± 0.08 kg / m ^{2}, respectively subgroups and the control group of 23.3 ± 0.01 kg/ m ^{2}, p <0.01), burdened obstetric and gynecological history. According to WHO (2012), vitamin D levels are affected by dietary intake of vitamin D and factors affecting its absorption metabolism, as well as obesity. Researchers have described the relationship between excess BMI and vitamin D deficiency [9 , 24] . Our analysis to identify excess BMI showed that in 47.2% of women with symptomatic MM, obesity of I , II , III degrees was calculated (28.3%, 11.3% and 7.5%, respectively) [15] .

Women with symptomatic myoma of the main group (n = 53) applied to various clinics: the symptom of bleeding and anemia prevailed to a greater extent in 83.01% (n = 44), of which 16.9% underwent blood transfusion due to severe anemia; a symptom of rapid growth - 9.43% (n = 5), a symptom of infertility in 5.6% (n = 3) and a symptom of pelvic pain (n = 2) 3.77%.

The status of vitamin D in the studied women showed that the values in the group of women with fibroids ranged from 4 to 36 ng / ml and averaged 16.7 ± 1.8 ng / ml, which turned out to be significantly lower than in healthy women (p < 0.001) . It is important to note that,

according to the researchers, the determination of the initial serum level of prohormone 25 (OH) D by laboratory methods is the most acceptable, reliable and clinically significant for assessing the saturation of vitamin D in the human body [5]. When assessing the content of vitamin D in the blood in the structure of the main group in women with symptomatic MM, the average was 11.84 ± 0.46 ng / ml and in asymptomatic - 21.54 ± 0.04, while in the control group 29, 83 ± 1.13 ng / ml (p <0.001). At the same time, a pronounced deficiency of prohormone D was detected in the subgroup of symptomatic MM 6.62 ± 0.9 ng / ml in 37.7% of women with an obvious clinical manifestation of menorrhagia (in 100%) and a recurrent course of the disease, and in the subgroup of asymptomatic myoma in 1 / 3 patients (36.7%) have a vitamin D deficiency 16.7 ± 1.6 [4] . The prohormone values in the control group differed significantly (p <0.001).



When comparing vitamin D indices between the subgroups of the main group, the statistical differences were significant, which indicated the presence of a relationship between the level of vitamin D saturation in women with MM and clinical manifestations of the disease and the size of the uterus. The distribution of women according to the degree of vitamin D provision, based on its content in the blood [15], showed a significant difference between the subgroups of the main group and healthy ones.

No.	Groups	Symptomatic MM , n = 53		Asymptomatic MM , n = 49		Control group , n = 50	
	Criteria	n, abs	(ng / ml)	n, abs	(ng / ml)	n, abs	(ng / ml)
1	Norm	**0**	-	**2 (4.08%)**	**34 ± 1.2 ''**	**24 (48%)**	**40.4 ± 1.7**
2	Failure	**4 (7.54%)**	**20.8 ± 1.9 *****	**29 (59.2%)**	**23.6 ± 1.4 ''**	**17 (34%)**	**24.4 ± 1.7**
3	Deficit	**29 (54.7%)**	**14.02 ± 0.2 *****	**17 (34.7%)**	**16.8 ± 1.6 ''**	**9 (18%)**	**14.2 ± 0.9**
4	Severe deficiency	**20 (37.7%)**	**6.62 ± 0.9 *****	**0**	-	**0**	-

Note: * p <0.001 in relation to the first subgroup; - ' p <0.001 with respect to the second subgroup.

Table 1. Values of vitamin D levels in women in the study groups.

In the main group of women with asymptomatic MM, normal values of vitamin D were only 4.08% of cases, insufficiency - in more than half (59.2%) and deficiency - in 1/3 of women, in the subgroup of symptomatic fibroids, normal values were not found in women, deficit - 54.7% and pronounced deficit - 37.7%, which is 2.88 times more than in the group of asymptomatic myoma and 5.4 times more than in the control group. It is noteworthy that, despite the absence of the disease, 52% of healthy women had an insufficient level and deficiency of vitamin D in the blood, in a country with sufficient insolation. Correlation analysis showed a direct weak positive relationship in the control group between the content of vitamin D in the blood and BMI ($r = 0.345$, $p < 0.001$), that is, normal values of vitamin D corresponded to a normal level of BMI; while the correlation between these indicators in the main group, especially in the subgroup of symptomatic myoma, was a direct mean positive ($r = 0.482$, $p < 0.001$).

When analyzing the odds ratio (OR) of MM in women with deficiency and/or deficiency of vitamin D, it was revealed: in women with insufficiency and/or deficiency of vitamin D, the chances of developing MM is OR = 16.13, which proves that the factor of prohormone deficiency is strong a provoking factor for the development of the disease in these women (Table 2).

Odds ratio (OR)	Study women with MM	Study women without MM
Vitamin D deficiency/ deficiency	100	74
Vitamin D norm	2	24
Total	102	98

100/2 = 50 74/24 = 3.1

50/3.1 = 16.13 (OR) positive strong factor

Table 2. Odds ratio (OR) of developing MM in women with vitamin D deficiency/deficiency .

When analyzing the odds ratio (OR) of MM in women with obesity, it was revealed that in obese women the chances of developing MM are OR = 7.38, which proves that excess weight is a factor promoter for the development of severe clinical symptoms of the disease in these women, reducing the quality life of women of this cohort (Table 3).

Odds ratio (OR)	Study women with MM	Study women without MM
Women with excess BMI and obesity	78	thirty
Women without obesity	24	68
Total	102	98

78/24 = 3.25 30/68 = 0.44

3.25 / 0.44 = 7.38 (OR) positive strong factor

Table 3. Odds ratio (OR) of developing MM in women with excess BMI and obesity.

4. DISCUSSION

Our results showed that lower values of vitamin D in patients with fibroids with concomitant excess BMI and obesity can affect the nature of the course of the disease and the incidence of

complications. Patients with severe deficiency of vitamin D in the subgroup symptomatic uterine myoma (<10 ng/ml) had a bright clinical manifestations of the disease: menorrhagia, leading to anemizatsii women in this category, the rapid growth myoma node amid critical deficiency of vitamin D and obesity, accompanying with pelvic pain, infertility m. In women with symptomatic myoma, the level of vitamin D was significantly lower in the group compared with the group with asymptomatic myoma.

5. CONCLUSION

A positive correlation between blood vitamin D and elevated BMI is especially noted in the subgroup of symptomatic myoma. Next studies to detail the mechanisms of the effect of vitamin D and the modifying factors - obesity on for uterine fibroids may in the future, find wide application in the field of health care and become the basis of modern personalized medicine, since it makes it possible to predict the development of the disease, the nature of the course and the risk of possible complications.

CONFLICT OF INTERESTS AND CONTRIBUTION OF AUTHORS

The authors declare the absence of obvious and potential conflicts of interest related to the publication of this article and report on the contribution of each author.

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6. REFERENCES:

[1] L.V. Adamyan M Yoma uterus: diagnosis, treatment and rehabilitation. Clinical practice guidelines for the management of patients (draft). Moscow, 2015. Pp. 8-11.

[2] Badmaeva S.Zh., Tskhai V.B., Grigoryan E.S., Polstyanaya G.N. M Yoma uterus: modern aspects of the etiology and pathogenesis (review). Mother and child in Kuzbass. No. 1 (76) 2019. Pages. 4-9.

[3] Buyanova SN, Shchukina NA, Babunashvili EL .. Biological role, therapeutic potential of phytoflavonoids, vitamin D in the treatment of patients with uterine fibroids and other promising pharmacological directions. 2018 pp. 71-86. https : // orcid . org / 0000-0002-1358-6640.

[4] Irnazarova D.Kh. Vitamin D supply for women with uterine fibroids. Medical journal. ISSN 0025-830 the X . 2020, no. 1, pp. 45-54.

[5] Povoroznyuk V.V., Pludovski P., Balatskaya N.I. and other Vitamin D deficiency and deficiency: epidemiology, diagnosis, prevention and treatment. - Kiev, 2015 .-- 262 p.

[6] Radzinsky V.E., Arkhipova M.P. Uterine myoma: Problems and perspectives of the beginning of the century Medical Council, 2014. Pp. 30-32.

[7] Yuldasheva D.Yu., Kayumova D.T., Irnazarova D.Kh., Kamilova I.A. Treatment algorithm for uterine fibroids. M etodicheskie recommendations. Tashkent, 2020. Page 30.

[8] Ayman Al-Hendy, Marwa Badr. Can vitamin D reduce the risk of uterine fibroids? Women's Health July (2014) 10 (4), 353–358. DOI: 10.2217 / whe.14.24.

[9] Baird DD, Hill MC, Schectman JM, et al. Vitamin D and the risk of uterine fibroids. Epidemiology, 2014; 24: 447-53. doi: 10.1097 / EDE.0b013e31828acca0.
[10] Blauer M., Rovio PH, Ylikomi T., Heinonen PK Vitamin D inhibits myometrial and leiomyoma cell proliferation in vitro. Fertil Steril 2009; 91: 1919-25.
[11] Brakta S., Diamond JS, Al-Hendy A., et al. Role of vitamin D in uterine fibroid biology. Fertil. Steril. 2015; 104 (3): 698-706.
[12] Dora Pavone, Sara Clemenza, Flavia Sorbi, Massimiliano Fambrini, Felice Petraglia. Epidemiology and Risk Factors of Uterine Fibroids. Best Practice & Research Clinical Cyesiologyand Gynaecology 46 (2018) 3-11. https://doi.org/10.1016/j.bpobgyn.2017.09.004 .
[13] Geum Seon Sohn, SiHyun Cho, Yong Man Kim, Chi-Heum Cho, Mee-Ran Kim, Sa Ra Lee. Current medical treatment of uterine fibroids. Cyesiologyand Gynecology Science 2018; 61 (2): 192-201. https://doi.org/10.5468/ogs.2018.61.2.192 .
[14] Hajhashemi M., Ansari M., Haghollahi F., Eslami B. The effect of vitamin D supplementation on the size of uterine leiomyoma in women with vitamin D deficiency. Caspian J Intern Med 2019; 10 (2): 125-131. Doi: 10.22088 / cjim.10.2.125.
[15] Irnazarova DH, Yuldasheva D.Yu., Najmutdinova DK, Kayumova DT, Sadikova DR, Atahodjayeva FA, Ahmedova G. Vitamin D status in women with uterine fibroids (uf) of the uzbek population. JOURNAL OF CRITICAL REVIEWS. ISSN- 2394-5125 VOL 7, ISSUE 17, June 2020. p . 2240-2250. http://www.jcreview.com/?mno=96009
[16] Irnazarova D.Kh. Innovative technologies in the diagnostics of uterine fibroids. R e-Health Journal Scientific and practical journal. ISSN 2181-0443. Andijan 2020, issue: 4. Pages. 29.
[17] John L. Wu, James H. Segars. Is vitamin D the answer for prevention of uterine fibroids? Fertility and Sterility, Vol. 104 No. 3 / September 2015. P. 559-560. http://dx.doi.org/10.1016/j.fertnstert.2015.06.034 .
[18] Maria Syl D. De La Cruz, Edward M. Buchanan. Uterine Fibroids: Diagnosis and Treatment. American Family Physician . 2017; 95 (2): 100-107.
[19] Mohamed Ali, Ayman Al-Hendy, Qiwei Yang. Vitamin D, a promising natural compound with anti-uterine fibroid characteristics. Fertility and Sterility, Vol. 111 N. 2 / February 2019. Https://doi.org/10.1016/j.fertnstert.2018.11.004 .
[20] Mohanambal M. Munusamy, Wills G. Sheelaa, Vijaya P. lakshmi. Clinical presentation and prevalence of uterine fibroids: a 3-year study in 3-decade rural South Indian women. Int J Reprod Contracept Obstet Gynecol. 2017 Dec; 6 (12): 5596-5601. DOI: http://dx.doi.org/10.18203/2320-1770.ijrcog20175288]
[21] Paffoni A., Somigliana E., Vigano P., et al. Vitamin D status in women with uterine leiomyomas. J Clin Endocrinol. Metab. 2013; 98 (8): E1374-8.
[22] Ren Jinhe . Color Doppler Ultrasound in Uterine Arterial Embolization. Open Med. 2017; 12: 489-493. https://doi.org/10.1515/med-2017-0069 .
[23] Sabry M., Halder SK, Allah AS, et al. Serum vitamin D3 level inversely correlates with uterine fibroid volume in different ethnic groups: a cross-sectional observational study. Int J Womens Health 2013; 5: 93-100.
[24] Scientific Advisory Committee on Nutrition. Vitamin D and Health, 2016. P 11-12. https://www.gov.uk/government/groups/scientific-advisory-committee-on-nutrition.

[25] Xess S., Sahu J. International Journal of Reproduction, Contraception, Cyesiologyand Gynecology . 2020 Apr; 9 (4): 1477-1481. DOI: http://dx.doi.org/10.18203/2320-1770.ijrcog20201208 .