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JOURNAL	World Science
p-ISSN	2413-1032
e-ISSN	2414-6404
PUBLISHER	RS Global Sp. z O.O., Poland
ARTICLE TITLE	CLINICAL ASPECTS IN WOMEN WITH MENSTRUAL DYSFUNCTION IN PUBERTY
AUTHOR(S)	Kovalyshyn O. A.
ARTICLE INFO	Kovalyshyn O. A. (2020) Clinical Aspects in Women with Menstrual Dysfunction in Puberty. World Science. 9(61). doi: 10.31435/rsglobal_ws/30122020/7336
DOI	https://doi.org/10.31435/rsglobal_ws/30122020/7336
RECEIVED	16 October 2020
ACCEPTED	04 December 2020
PUBLISHED	09 December 2020
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CLINICAL ASPECTS IN WOMEN WITH MENSTRUAL DYSFUNCTION IN PUBERTY

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DOI: https://doi.org/10.31435/rsglobal_ws/30122020/7336

ARTICLE INFO

Received: 16 October 2020

Accepted: 04 December 2020

Published: 09 December 2020

KEYWORDS

puberty, menarche, oligomenorrhea, pubertal bleeding, luteal phase insufficiency, pregnancy.

ABSTRACT

The reproductive system is exposed to various adverse factors and harmful effects at all stages of functioning of an organism. Against the background of declining levels of women's reproductive health in recent years, there has been a clear tendency towards an increase in the number of patients with pathology of puberty. The low level of somatic and reproductive health before pregnancy causes a high incidence of complicated labors, which leads to a deterioration in the development of subsequent generations.

The purpose of the study. To provide clinical characteristics of women who had menstrual dysfunction in puberty, which were based on the study of clinical and anamnestic data, laboratory and instrumental research methods, analysis of risk factors, clinical course, treatment effectiveness and dispensary observation.

Materials and methods. According to the nature of the disfunctions, the main group of women (n = 210) who had menstrual disorders in puberty was divided into 3 subgroups (n = 70): the first - women with primary oligomenorrhea and timely average menarche, the second - with late menarche, the third - with pubertal bleeding. The control group included women (n = 70) with the correct rhythm of menstruation in puberty.

Results. The clinical prospective study analyzed the social status of women with reproductive dysfunction in puberty, the frequency and structure of existing concomitant somatic diseases, the duration of the menstrual cycle, the nature of diseases of the female genital organs; the assessment of the comprehensive treatment of revealed disorders, which allowed to obtain a favorable reproductive prognosis. The majority of surveyed women (53.3%) planned a pregnancy, which occurred in 75.9% from among of planning ones.

Conclusions. The conduction of clinical and anamnestic analysis of the reproductive function of women with menstrual dysfunction in puberty will increase the effectiveness of the treatment of identified disorders and will allow developing algorithms for management of such women during planning and during pregnancy.

Citation: Kovalyshyn O. A. (2020) Clinical Aspects in Women with Menstrual Dysfunction in Puberty. *World Science*. 9(61). doi: 10.31435/rsglobal_ws/30122020/7336

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A woman's reproductive system is the most dynamic biological object, which is extremely sensitive to adverse external and internal factors by the emergence of new adaptive reactions, which acquire the properties of the pathological process under certain conditions [1]. At the same time, many issues of the pathogenesis of fertility disorders have not been completely studied and remain controversial. The formation of reproductive health is a long and complex process. A woman's health and its integral component - reproductive health - are largely determined by the conditions of her development in the womb, in the neonatal period, childhood and adolescence [2].

The urgency of the problem depends on many components:

- demographic crisis of society;
- low level of formation of reproductive attitudes, reproductive behavior;
- medical factors;
- environmental factors and social components [3].

There are a wide range of medical factors: high frequency of infertility, miscarriage; high level of chronic pathology in married couples, increase in the incidence of chronic sexually transmitted

infections; persistence a significant frequency of abortions, which today remains one of the main methods of birth control and family planning and a factor of irreversible harm to a woman's health; inflammatory diseases of the female genital organs; increase in the overall incidence of girls (in particular, diseases of the genitourinary system and menstrual disorders); complications of childbirth, perinatal pathology and secondary infertility [3].

Among environmental factors and social components, the leading role is played by declining living standards, increasing stress loads, deteriorating nutritional quality, bad habits, underestimation of marriage, insufficient and ineffective use of contraceptives, early onset of sexual activity and related problems, decreasing role of the family in socialization of adolescents and youth [4]. Accordingly, not only the development of informative methods for assessing the state of the reproductive system, but also the restoration of women's reproductive function are important and are becoming increasingly relevant due to the high level of gynecological morbidity in adolescence, which is dominated by menstrual disorders [5]. The formation of regular menstrual cycle occurs within 6-24 months after menarche. In puberty, all chains of the reproductive system actively adapt to cyclical functioning, and by the age of 17 a close relationship is established between the parameters of the ovarian reserve and hormonal levels [6].

The purpose of the study. To provide clinical characteristics of women who had menstrual dysfunction in puberty, which were based on the study of clinical and anamnestic data, laboratory and instrumental research methods, analysis of risk factors, clinical course, treatment effectiveness and dispensary observation.

Materials and methods.

Clinical prospective study was conducted a survey on 280 women of reproductive age. The main group included 210 women who had menstrual dysfunctions in puberty. According to the nature of disorders of the main group, there are 3 subgroups: the first group is women with primary oligomenorrhea and timely average menarche (n = 70); the second one is with late menarche (n = 70); the third one is a subgroup with pubertal bleeding (n = 70). The control group consisted of 70 women with the correct rhythm of menstruation in puberty.

A retrospective clinical and anamnestic analysis in the main group of examined women was conducted to study the risk factors for menstrual dysfunction in puberty, the presence of somatic and gynecological diseases, the scope of therapeutic measures and their effectiveness. There were analyzed the data of outpatient cards and medical records of the examined women. A retrospective analysis of the control group was carried out through questionnaires.

The criteria for inclusion in the main group were women of reproductive age who had menstrual dysfunctions in puberty:

- primary amenorrhea - the absence of independent menstruation from menarche from 45 days to 6 months with timely average population menarche;
- late age of menarche from 15 years;
- heavy menstruation in puberty in the form of pubertal bleeding

Exclusion criteria from the main group were overweight, hyperandrogenism (confirmed clinically and hormonally), the use of hormone therapy during the study, somatic and endocrine pathology, congenital anomalies and chromosomal disorders, surgical treatment of ovarian cysts in adolescence, benign (leiomyoma) and malignant neoplasms.

Data on each woman was entered into a specially designed card. Anamnesis was collected according to the generally accepted scheme. In the first part of the card there was a fixation of retrospective data on hereditary history, parental health, pregnancy and labor, birth weight, infectious diseases, clinical and laboratory data, results of examination and treatment in puberty. Particular attention was paid to the period of formation of menstrual function, age of menarche, duration and regularity of the menstrual cycle, duration and amount of bleeding, gynecological disease. Analysis of the nature of menstrual dysfunctions in puberty, the methods of diagnosis, treatment and dispensary observation and their effectiveness in women of the main group were carried out according to extracts from the case histories and outpatient cards. The second part included data on social status, anamnesis, reproductive function, somatic diseases of women and the results of a prospective survey. Reproductive function, the number of pregnancies and their results also were specified while analyzing.

Transvaginal ultrasound examination was performed on 11-14 days (late proliferative phase) and on 20-22 days (middle secretory phase) of the menstrual cycle, the measurements were carried out in real time with an intracavitary transducer with a frequency of 5-9 MHz. They examined the uterine size, endometrial thickness, the volume of ovarian follicle number and diameter.

Mathematical and statistical processing of the obtained data was performed with the use of statistical software package Microsoft Office Excel 2007, "Statistica 6.0". Statistical significance of the differences was assessed with the use of Student's parametric t-test for independent samples ($M \pm \sigma$). Differences in all cases were evaluated as statistically significant at $p < 0.05$. The strength of the correlation between the studied traits was determined by Spearman's correlation criterion.

Results of the study and their discussion. The average age of women of the main group was 22.42 ± 0.21 years, in the control one was 22.34 ± 0.31 years (from 19 to 32 years). In each of the subgroups of the main group, female students of educational institutions were less than in the control group ($p < 0.05$). Employees in groups and subgroups were distributed equally often. The number of non-working women in the main group exceeded the control group ($p < 0.05$) (table 1).

Table 1. Social status of women in the surveyed groups.

Group		Female students		Employees		Unemployed	
		Abs	%	Abs	%	Abs	%
Control (n=70)		47	67,1	22	31,4	1	1,4
Main (n=210)		109	51,9 $p < 0,05$	80	38,1	21	10,0 $p < 0,05$
Subgroup	1 (n=70)	33	47,1 $p_1 < 0,05$	31	44,3	6	8,6
	2 (n=70)	34	48,6 $p_1 < 0,05$	27	38,6	9	12,8 $p_1 < 0,05$
	3 (n=70)	42	60,0	22	31,4	6	8,6

Note: p – the degree of reliability of differences between the indicators of the control and main groups;
 p_1 – control group and subgroups of the main group.

The frequency of somatic diseases in women in the main group is higher than in the control group ($p < 0.001$) (table 2). Diseases of the endocrine system are represented by diffuse (endemic) goiter, which is associated with iodine deficiency; women of the main group were observed 4 times more often in comparison with the control group. Diseases of the digestive system, represented by chronic gastritis, in women of the main group were detected 1.6 times more often than in the control group, and were statistically significant in women with late age of menarche in comparison with women with pubertal bleeding ($p < 0.05$). One in five women of the third subgroup has been diagnosed with chronic tonsillitis.

Table 2. The frequency and structure of somatic diseases in women of the surveyed groups

Group		DISEASES										TOTAL	
		urinary system		digestive organs		respiratory system		circulatory system		endocrine system			
		Abs	%	Abs	%	Abs	%	Abs	%	Abs	%	Abs	%
Control (n=70)		4	5,7	3	4,3	4	5,7	2	2,9	1	1,4	14	20,0
Main (n=210)		23	11,0	15	7,1	29	13,8	19	9,0	12	5,7	98	46,6 $p < 0,001$
Subgroup	1 (n=70)	9	12,9	6	8,6	9	12,9	9	12,9	4	5,7	37	53,0 $p_1 < 0,001$
	2 (n=70)	8	11,4	8	11,4	6	8,6	2	2,9	3	4,3	27	38,6 $p_1 < 0,05$
	3 (n=70)	6	8,6	1	1,4 $p_4 < 0,05$	14	20,0	8	11,4	5	7,1	34	48,5 $p_1 < 0,01$

Note: p – the degree of reliability of differences between the indicators of the control and main groups;
 p_1 – control group and subgroups of the main group; between subgroups 2 and 3 – p_4 .

The average body mass index (BMI) in women in the main group was 20.25 ± 0.21 kg / m², in the control group - 21.05 ± 0.41 kg / m² ($p > 0.05$). In women with late menarche, BMI was 19.97 ± 0.32 kg / m² and was lower in comparison with the control group ($p < 0.05$). In women with primary oligomenorrhea and pubertal bleeding, the ITM was 20.44 ± 0.36 kg / m² and 20.28 ± 0.44 kg / m², respectively, and did not have significant differences with the control group.

The duration of the menstrual cycle in women who had menstrual dysfunction during puberty was longer than in the control group, but corresponded to the duration of the normal menstrual cycle (Table 3). In women with pubertal bleeding, menstruation lasted longer in comparison with women with primary oligomenorrhea and the control group ($p < 0.001$). In 7 (10%) women with pubertal bleeding, menstruation was severe, no intermenstrual bleeding was observed.

Table 3. Characteristics of the menstrual cycle in women of the surveyed groups

Group		Duration of the menstrual cycle (days)	Duration of menstruation (days)	Profusion of menstruation
Control (n=70)		28,1±0,2	4,9±0,1	moderate
Main (n=210)		29,2±0,3 p<0,05	5,2±0,1 p<0,05	-
Subgroup	1 (n=70)	29,5±0,4 p ₁ <0,01	4,9±0,1	moderate
	2 (n=70)	29,9±0,7 p ₁ <0,01	5,3±0,1 p ₁ , p ₂ <0,05	moderate
	3 (n=70)	28,0±0,3 p ₃ <0,01, p ₄ <0,05	5,6±0,1 p ₁ , p ₃ <0,001	moderate, 10% severe

Note: p – the degree of reliability of differences between the indicators of the control and main groups; p₁ – the degree of reliability of differences in the indicators of the control group and subgroups of the main group; between subgroups: p₂ – 1 and 2, p₃ – 1 and 3, p₄ – 2 and 3.

Benign breast dysplasia was diagnosed in 13 (6.2%) women of the main group, in women with pubertal bleeding - 3.6 times less often with primary oligomenorrhea in the anamnesis (2 women (2.9%) vs. 7 (10.0%), respectively) and 2 times than with late menarche age (4 women (5.7%)).

Diseases of the female genital organs in women with menstrual dysfunction in puberty were detected more often in the control group (p <0.001). Cervical ectopia prevailed in the structure of diseases (p <0.05), no statistically significant differences were found between subgroups (table 4).

Inflammatory diseases of the female pelvic organs in women of the surveyed groups and between the subgroups had no significant differences.

41 (19.5%) women who had menstrual dysfunction in puberty, the menstrual cycle did not return to normal, including: with primary oligomenorrhea in 15 (21.4%), with late menarche in 14 (20.0%) and with pubertal bleeding in 12 (17.1%). Oligomenorrhea was periodically observed in women 1 and 2 subgroups, women from the third subgroup suffered from severe menstruation.

Table 4. Frequency and structure of female genital diseases in women of the examined groups

Group	Ectopia of the cervix		Inflammatory diseases of the female genital organs		Female infertility		Menstrual dysfunction		Non-inflammatory lesions of the ovary		Total		
	Abs	%	Abs	%	Abs	%	Abs	%	Abs	%	Abs	%	
Control (n=70)	9	12,9	5	7,1	-	-	-	-	-	-	14	20,0	
Main (n=210)	58	27,6 p<0,05	11	5,2	24	11,4	41	19,5	19	9,0	153	72,9 p<0,001	
Subgroup	1 (n=70)	21	30,0 p ₁ <0,05	4	5,7	10	14,3	15	21,4	9	12,9	59	84,3 p ₁ <0,001
	2 (n=70)	22	31,4 p ₁ <0,05	2	2,9	7	10,0	14	20,0	7	10,0	52	74,3 p ₁ <0,001
	3 (n=70)	15	21,4	5	7,1	7	10,0	12	17,1	3	4,3	42	60,0 p ₁ <0,001

Note: p – the degree of reliability of differences between the indicators of the control and main groups; p₁ – control group and subgroups of the main group.

Female infertility was detected in 24 (11.4%) women of the main group; differences between subgroups were not significant. The absence of ovulation was detected in 10 women with primary oligomenorrhea, 7 with late menarche and 7 with pubertal bleeding. Scleropolycystic ovary disease (PCOS) was formed in 15 (7.1%) women. The treatment was carried out in a comprehensive manner, taking into account somatic diseases. Ovulation induction was performed in 7 patients with PCOS who were observed due to infertility. Pregnancy occurred in 7 cases, ovulation was ineffective in 1 case, which is why the patient underwent cauterization of the ovaries and she became pregnant while the natural menstrual cycle.

It should be noted that in 14 (6.7%) women of the main group was detected lutein phase deficiency (NLF): 1 subgroup - 10 cases (14.3%), 2 and 3 subgroups - 2 cases (2.9%). This might have been the cause of primary infertility due to insufficiently prepared endometrial blastocysts for implantation [6]. Women of 1 (n = 8) and 3 (n = 2) subgroups received progestogen treatment in the second phase of the menstrual cycle.

In case of hypoestrogenic condition, women of 1 and 2 subgroups were recommended cyclic hormonal medication, containing 17 β -estradiol and dydrogesterone (2 cases each).

Follicle persistence was found in 5 (7.1%) women with pubertal bleeding who had severe menstruation during their reproductive years. The women received medical treatment with hemostatic drugs. Hysteroscopy and separate scraping of the mucous membrane of the body and cervix were performed in two cases. The result of histological examination of the obtained material is polypoid endometrial hyperplasia. They were recommended estrogen-gestagens in low-dose COCP during 6 months, ultrasound scanning and dynamic monitoring.

Non-inflammatory lesions of the ovary are represented by ovarian cyst, which were diagnosed in 19 (9.0%) women of the main group, but not detected in the control group. Women who had primary oligomenorrhea, were diagnosed an ovarian cyst 3 times more often in comparison with women with pubertal bleeding.

Hormonal treatment with estrogen-progestogens as part of low-dose COCP was carried out in 10 (52.6%) women with ovarian cysts. They were recommended dynamic observation and ultrasound control. Laparoscopic cystectomy was revealed in 9 (47.3%) women. Indications: rupture of the ovarian cyst with severe pain and intra-abdominal bleeding. Histological examination of the obtained material is hemorrhagic cyst of the corpus luteum. To regulate the menstrual cycle and prevent recurrence of ovarian cysts, the patients were recommended low-dose of monophasic COCP before planned pregnancy.

Among 210 women who had menstrual dysfunctions in puberty, 112 (53.3%) planned pregnancy, including: 46 with primary oligomenorrhea (65.7%), 34 with late menarche (48.6%), 32 with pubertal bleeding (45.7%). Before planning pregnancy, 58 (51.8%) women took low-dose monophasic COCP, in 18 (39.1%), 21 (61.7%) and 19 (59.4%) subgroups, respectively.

During the observation period, pregnancy occurred in 85 (75.9%) women from the total number of those who were planning pregnancy, including: 31 (67.4%), 29 (85.3%) and 25 (78.1%) women in subgroups, respectively. 6 (7.1%) women had a spontaneous abortion in the early gestation period. Pregnancy did not occur in 27 (24.1%) women during the follow-up, 17 (15.2%) had no ovulation, 10 (8.9%) had insufficient luteal phase.

Conclusions. 1. Women, who had menstrual dysfunction in puberty, has characteristics of anamnesis and reproductive clinics, which are formed during the formation of the reproductive system and are most affected by various factors, starting from the age of menarche.

2. Somatic diseases were observed 2.3 times more often in the main group in comparison with the control group. The structure of diseases of the female genital organs in the main group was dominated by cervical ectopia (mostly in the subgroup of women with late menarche - 31.4%), women with oligomenorrhea suffered from menstrual dysfunction (21.4%), female infertility (14.3%) and non-inflammatory lesions of the ovaries (12.9%), and women with pubertal bleeding were detected the highest percentage of inflammatory diseases of the female genital organs - 7.1%.

3. 19.5% of women who had menstrual disorders in puberty, the menstrual cycle had not returned to normal, including: primary oligomenorrhea in 21.4%, late menarche in 20.0% and pubertal bleeding in 17.1%. In addition, women of third subgroup were periodically suffering from severe menstruation.

4. 75.9% of women who were planning pregnancy became pregnant during the observation period.

5. Clinical and anamnestic analysis of reproductive function of women with menstrual disorders in puberty has prognostic value, which will increase the effectiveness of treatment of identified disorders according to the main criterion - normalization of menstrual function, as well as to develop algorithms for such women during planning and pregnancy.

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