

# Metrorrhagia iuvenilis and Premenstrual Syndrome as frequent problems of adolescent gynecology with aspects of diet therapy

Grazyna Jarzabek Bielecka<sup>1</sup>, Malgorzata Mizgier<sup>2</sup>, Witold Kedzia<sup>1</sup>

<sup>1</sup>*Division of Developmental Gynecology and Sexology, Department of Perinatology and Gynecology, Poznan University of Medical Sciences, Poland*

<sup>2</sup>*Department of Morphological and Health Sciences, Dietetic Division, Faculty of Physical Culture in Gorzow Wielkopolski, Poznan University of Physical Education, Poland*

## ABSTRACT

Painful menstruation, premenstrual syndrome and metrorrhagia iuvenilis are one of the most common problems related to the sexual cycle in adolescent girls.

Metrorrhagia iuvenilis is acyclic bleeding that occurs in adolescents and lasts from over 10 days even up to 3 months. These bleeds are very abundant and have a tendency to relapse. They cause anemia, and severe cases can be life-threatening.

Premenstrual Syndrome (PMS) is a cluster of somatic, emotional and behavioural symptoms occurring in the luteal phase of the menstrual cycle. The aetiology of PMS remains unknown. According to strict diagnostic criteria, an estimated 2.5–5% of girls and women are affected by PMS. However, some researchers maintain that the symptoms of PMS may be prevalent in as many as 40–80% of girls and women.

This article it has been discussed premenstrual syndrome and metrorrhagia iuvenilis and aspects related to dietotherapy were included.

**Key words:** adolescent gynaecology; iuvenile metrorrhagia; premenstrual syndrome; diet therapy

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## INTRODUCTION

Premenstrual syndrome and metrorrhagia iuvenilis are frequent problems in adolescent gynecology. In the prevention and treatment of both disease entities, it is very important to include diet therapy as a minimally invasive method, which is very important in developmental age.

### Metrorrhagia iuvenilis

Metrorrhagia iuvenilis (heavy menstrual bleeds) is acyclic bleeding that occurs in adolescents and lasts over 10 days, even up to 3 months. These bleeds are very abundant and have a tendency to relapse. They cause anemia, and severe cases can be life-threatening [1–6].

In 2009, at the FIGO congress, the so-called criteria were set. normal menstruation: the frequency of menstruation (from 24 to 38 days), the regularity of menstruation over a period of more than 12 months, the duration of bleeding (from 4.5 to 8.0 days), the volume of blood loss (from 5 mL to 80 mL).

During normal menstruation 90% of wasted blood is in the first three days, and the bleeding in the first two days is the most abundant. Bleeding that does not meet the above conditions is treated as abnormal uterine bleeding (AUB) [7].

Heavy menstrual bleeding (HMB) (above 80 mL) of a cyclic nature concerns women most often in the premenopausal age. The clinical definition set by The National Institute for Health and Care Excellence (NICE) in 2007 is more practical. Defines HMB as excessive loss of menstrual blood, interfering with and interfering with the physical, emotional, social and material quality of a woman's life, which can also be combined with other symptoms. Prevalence according to different authors, it is in the range of 4–9%.

Heavy and prolonged menstrual bleeding (HPMB) is abundant and prolonged menstrual bleeding above 80 mL and lasting more than 8 days, while intermenstrual bleeding (IMB) this is intermenstrual bleeding. Postmenopausal bleeding (PMB) defines postmenopausal bleeding. It is

Corresponding author:

Malgorzata Mizgier

Department of Morphological and Health Sciences, Dietetic Division, Faculty of Physical Culture in Gorzow Wielkopolski, Poznan University of Physical Education, Poland  
e-mail: m.mizgier@awf-gorzow.edu.pl

possible to use the term amenorrhea (absent menstrual bleeding [AMB]) in the absence of menstrual bleeding over a period of more than 90 days.

The causes of abnormal bleeding from the genital tract (eg. from the vagina) can be divided into two groups: structural and non-structural. The structural reasons include: changes in the cervix (eg erosions of the vaginal part of the cervix, cervical cancer, polyps of the cervix), changes in the endometrium (endometrial hyperplasia, uterine polyps, fibroids, adenomyosis, stem cancer). Non-structural causes include: ovulation disorders/lack of ovulation (eg progesterone deficiency, estrogen deficiency, inhibin deficiency, PCOS, hyperprolactinemia), thyroid disease (hypothyroidism), adrenal diseases (Cushing's disease), haematological diseases (eg coagulopathy, thrombocytopenia), diseases of other organs (eg ovarian, adrenal or pituitary tumors, cirrhosis of the liver, some kidney diseases). Other causes include: obesity, injuries, foreign body, stress, medicines used (e.g., antiepileptic, antidepressant, anticoagulants, NSAIDs, hormones).

In 2009, the FIGO committee recommended the introduction of a new classification of abnormal bleeding from the uterus — The PALM-COEIN Classification System. The name is an acronym from the first letters of causes that can cause bleeding from the uterine cavity:

P — polyp;

A — adenomyosis;

L — fibroids of the uterus;

M — endometrial cancer and proliferation;

C — coagulopathies;

O — ovulation disorders;

E — other causes of disorders;

I — iatrogenic (IUD insert, steroid hormones, anticoagulants, antidepressants);

N — not yet classified [7].

Juvenile bleeding usually occurs shortly after menarche, when the cycles are anovulatory. Juvenile bleeding is functional uterine bleeding and rarely disappears spontaneously. It is assumed that irregular bleeding from the genital tracts in pre-pubescent girls up to 2–3 years from menarche may occur as a physiological phenomenon. Situations with profuse bleeding and secondary anemia are dangerous and require treatment [8–15]. When the cycles are anovulatory, bleeding is not cyclical, and there are no typical premenstrual symptoms associated with premenstrual syndrome, such as fluid retention, breast tenderness, abdominal distension. Juvenile bleedings usually have a sudden onset without any symptoms which predict them [1, 3, 6, 10, 15].

As a result of the lack of ovulation, there is a situation in which unicyclic (often unexpected) exfoliation of the expanded and thickened mucous membrane of the uterine cavity occurs, which stems from the relative hyperestrogen-

ism (deficiency of progesterone, because ovulation does not occur). This results in bleeding. Acyclic bleeding may also be due to insufficient exfoliation of the endometrium (i.e. endometrium). First, there is a slow endometrial hyperplasia for up to 3 months, and then slow functional exfoliation of the endometrium takes place. The exfoliation of the endometrium to its basal layer can last up to a month. Estrogens stimulate the endometrium for growth constantly. In the etiology of profuse bleeding is involved the abnormal process in the endometrium, which controls the supply of arachidonic acid for the production of prostaglandins too. In women and girls with profuse bleeding, endometrium occurs on a much larger scale than in women with normal menstruation, and causes the formation of prostaglandins series 2, which affect the functions of the blood vessels and affects the sensation of pain [5, 11, 15].

In the case of abrupt juvenile hemorrhage, early diagnosis is important to avoid complications that threaten health and life [2, 4, 9, 15]. A gynecologist decides whether the patient's condition is acute and requires immediate hospitalization, or whether it will be possible to monitor it in as an outpatient. During a medical interview, information about family diseases is important. This includes hematological diseases, information about how the patient's development progressed, other diseases, the history of menarche, the course of cycles, and the period during which abnormal bleedings started and their duration. It is important to establish whether the patient takes drugs or dietary supplements, and if so, what kind. Of particular importance is information that excludes or confirms hematological problems, whether the patient is suffering from hemorrhagic diathesis or whether there are bleeds from other places [8, 10, 15].

Excessive menstrual bleeding in girls and women with bleeding disorders occurs with a frequency of 10 to 100%, depending on the particular disorder. In turn, disturbances of thrombosis are also more frequent among girls and women with excessive menstrual bleeding. Research already carried out indicates that coagulation disorders occur in 5–32% of girls and women with heavy menstruation. On the basis of the number of tampons and sanitary towels used, the amount of lost blood can be estimated, as the use of more than 10 sanitary towels or tampons within 24 hours can be a sign of bleeding over 30 mL. During the test, the basic parameters (blood pressure, heart rate, conjunctival assessment, and petechiae evaluation) are measured. In a gynecological examination, it is important to exclude possible pregnancy in juveniles and its consequences of this (an imminent abortion or an ectopic pregnancy). In view of the bleeding and the fact that it is usually their first contact with the gynecologist, girls can be reluctant to undergo an examination with the use of a speculum. In gynecology

of the developmental age, a long narrow speculum is used if necessary, which makes it possible to assess the vagina and cervix. It is worth noting that bleeding can be the result of sexual violence. Moreover, the cause of bleeding may also be injuries experienced while practicing sports. During the examination, the gynecologist must rule out the tearing of the vaginal walls, polyps, foreign bodies, and must check whether the bleeding comes from the uterus. A two-handed study in girls who have not had a sexual relationship yet should be performed via the anus. This may be particularly unpleasant and some authors recommend withdrawing from this practice. An ultrasound examination is performed via the rectum or ultrasound examination is carried out through the abdominal walls, and in the case of patients who have had a sexual relationship, an ultrasound examination is performed. Laboratory tests are recommended: complete blood count, coagulation system, FSH, LH, estradiol, prolactin, thyroid hormones and TSH [1, 5, 9, 10, 15]. On the basis of these, the doctor is able to assess the condition of the patient (exclude anemia, thrombocytopenia, plasma defects) and the hormonal causes of acyclic bleeding. The results of the tests allow decisions to be made as to how to proceed. Bleedings in the case of anovulatory cycles do not always involve excessive blood loss: there are no changes in peripheral blood morphology, and girls may not have additional symptoms at that time. However, patients are always advised to lead a healthy lifestyle, a diet rich in iron ions, and sometimes its supplementation. Advice from a gynecologist, in the absence of patient's knowledge, also has an educational significance [4, 9, 13–15].

As mentioned above, it is very important to exclude hematological causes of excessive menstrual bleeding and juvenile bleeding.

### VON WILLEBRAND'S DISEASE

Among women with abundant menstruation, the incidence of VWD is 5–20%, and among teenagers with juvenile bleeding it may be as high as 36% [4]. In girls and women, Von Willebrand's disease (vWD) is often not recognized due to the aforementioned lack of pro-health education.

Von Willebrand's disease is the most common hereditary coagulation problem. It is due to deficiency, dysfunction or lack of von Willebrand factor, which is necessary for platelet adhesion in vascular sites, and for the protection of factor VIII with pre-proteolysis in the bloodstream. Von Willebrand's disease appears through bleeding within the skin and mucous membranes, including uterine bleeding. The incidence of vWD in the general population is 0.6–1.3%, depending on the prevalence of people in a given region with bleeding symptoms, family history and laboratory abnormalities [1–5].

### HAEMOPHILIA

Haemophilia is the most common severe hereditary disorder of coagulation, but as a disease conjugated to the X chromosome, it occurs almost exclusively in men and boys, while women are carriers of it.

In women who are carriers of haemophilia, clinical signs of hemorrhagic diathesis may or may not occur, and the symptomatology of bleeding varies widely, from asymptomatic to severe bleeding [1–5].

### THROMBOCYTOPENIA CONDITIONED IMMUNOLOGICALLY

Primary immune-mediated thrombocytopenia (immune thrombocytopenia, ITP) is an acquired immune disease characterized by isolated thrombocytopenia, defined as the number of platelets in peripheral blood below  $100 \times 10^9/l$  in the absence of an obvious initiating or primary cause. ITP occurs with the frequency of about 1 per 10000 patients, but more often among women between their 30s and 60s [10, 11]. Depending on the intensity of thrombocytopenia, there is a higher risk of abundant periods and other abnormal birth canal bleedings.

The treatment of juvenile metrorrhagia (heavy menstrual bleeds) depends on their etiology, the patient's contraceptive needs, her individual ability to comply with medical recommendations, tolerability of side effects, costs and medical interventions. In the case of girls with adolescent bleeding, estrogen-progesterone therapy, clotting drugs, and iron preparations are individually selected. Sometimes these girls require hospital treatment. Oral progestogens may also be effective, but the choice of therapy is specific to each patient, depending on her age, puberty, ultrasound and laboratory tests. The management of patients with and without coagulation disorders is similar [8–12, 15].

Increased iron loss, caused by e.g. heavy menstruation, also requires proper dietary treatment because it threatens with anemia and anemia occurring in children and adolescents may result in a wide range of serious health consequences such as impaired mental development and physical growth and reduces school performance and work capacity [16, 17]. Adolescent females are particularly vulnerable to iron deficiency because of both high iron losses during menstruation and insufficient dietary iron intake. Based on a study carried out for a representative national Polish sample of adolescents, girls were characterized by a significantly lower intake of all forms of iron (total iron, heme iron, non-heme iron, animal iron, plant iron) compared to male adolescents [18]. The results of Hamułka et al. [19] and Mizgier et al. [20] studies confirm that female individuals commonly have too low iron intakes, which in Poland is confirmed both for pregnant young women and those who are not pregnant.

Dietary restrictions and a vegetarian diet may also lead to limiting the intake of meat and meat products, and ultimately lead to lower iron intake [21].

Iron is present in food products in two forms, as heme iron, which is found in meat, fish and other animal products, and as non-heme iron, which is found in plant as well as animal products. Heme iron is highly bioavailable (25–30% of this form is absorbed), although it represents a minor part of dietary iron. The absorption of non-heme iron is only about 1–10%. The best sources of the both forms of iron in the diet are: offal, dry legume seeds (peas, beans, lentils, chickpeas), poultry, fish, eggs, cereal products (oatmeal, whole grain bread, whole grain pasta), and some vegetables (beets, chard, peas) [20, 22, 23].

### Premenstrual Syndrome (PMS)

Premenstrual Syndrome (PMS) is a cluster of somatic, emotional and behavioral symptoms occurring in the luteal phase of the menstrual cycle. Many studies have been conducted, but the etiology of PMS remains unknown. PMS symptoms substantially affect the quality of a woman's life. According to strict diagnostic criteria, an estimated 2.5–5% of girls and women are affected by PMS. However, some researchers maintain that the symptoms of PMS may be prevalent in as many as 40–80% of girls and women. Due to this considerable discrepancy, it is necessary to make the definition of PMS more precise. Patients with PMS experience mood disturbances together with physical and emotional symptoms, which recur in the luteal phase and disappear in the follicular phase of the menstrual cycle [24, 25].

In the last decade, the methods of PMS treatment have undergone significant changes. Although the pathophysiology of the syndrome has not been fully elucidated, effective treatment is possible for most patients. In women with premenstrual syndrome, body composition should be assessed and the appropriate diet and physical activity should be taken into consideration.

The results of the studies conducted confirm the theory of fluid retention in the body as associated with the occurrence of PMS. The theory of fluid retention in the body, which suggests that estrogens induce an increased synthesis of angiotensinogen in the liver, which leads to increased production of aldosterone, which directly affects the retention of sodium and potassium loss. It was also found that in PMS, there is a slight increase in prolactin concentration in the second phase of the sexual cycle, perhaps due to the impaired synthesis or secretion of dopamine and serotonin in the central nervous system. It has been proven that dopamine exerts direct neurotransmission on the kidneys, and serotonin is responsible for excessive sensitivity. The feeling of weight in the lower abdomen and pain in the sacral region are a consequence of retention in the

uterus and venous stasis in the pelvis. Swelling of the central nervous system is the cause of headaches, dizziness, nausea, mental tension, insomnia, anxiety, depression, and increased appetite. At such times, women very often have a craving for something sweet. An increase in body weight of 2 to 4 kg usually disappears in the first days of menstruation [24–27].

The results of Mizgier et al.'s study seem to confirm the fluid retention theory, since statistically significant differences were observed in the two study groups for total body water (TBW) in kilograms. Higher values were reported for PMS women ( $p < 0.005$ ). This statistical significance was confirmed for both the whole study population and for women with  $BMI \geq 25 \text{ kg/m}^2$ . Although the pathophysiology behind PMS has not been fully explained, it is recommended to assess the state of nutrition and body composition which, as the current study shows, are related to premenstrual syndrome prevalence. Since they are modifiable factors, PMS treatment should include a balanced diet and physical activity, which will help to modify not only body mass but also fat mass. Further studies on PMS women should also offer recommendations for lifestyle interventions [24].

The results of the study suggest the importance of proper eating habits and physical activity on the course of menstrual cycles [28]. Physical exertion, e.g. aerobics, but also relaxation or relaxation exercises may be beneficial.

It should be added that conventional methods of treatment of cyclic pain and discomfort over a time period of approximately one month, although numerous and diverse, have disadvantages, including side effects, disruptions of women's functioning. Many of these women also turn to herbal medicine. Clinical evidence supports the efficacy of *Vitex agnus-castus*, but other drugs commonly used by western herbalists to treat menstrual symptoms are not supported by clinical trials. This raises concerns about the effectiveness and safety of these herbs. Treatment options for women must be extended and individualized when current conventional strategies fail, which requires appropriate clinical trials of potentially useful herbal medicines [29].

Some women with PMS want to be treated with acupuncture or acupressure. Limited available evidence suggests that acupuncture and acupressure may improve both the physical and mental symptoms of premenstrual syndrome. There was insufficient evidence to determine whether there is a difference between groups in the frequency of adverse events. There is also no evidence comparing acupuncture or acupressure with currently recommended therapies for PMS, such as selective serotonin reuptake inhibitors (SSRIs). Further research is necessary, using approved measures for PMS, appropriate blindness and appropriate comparative groups reflecting the best practice currently [30].

The basic elements of the diagnosis are: the need to prospectively determine the time of appearance of

symptoms and the occurrence of at least 30% increase in the severity of symptoms in the luteal phase compared to the follicular phase. An additional criterion is the exclusion of mental illness and the condition that women did not use oral contraception and have regular monthly cycles [26–27].

Any woman who notices the severity of symptoms should consult a doctor. It is necessary to exclude other diseases, both internal, neurological and gynecological, which may give similar ailments. Any ailment that contributes to the deterioration of the comfort of life, although it does not cause negative medical effects, should be treated. A typical premenstrual syndrome should be distinguished from monthly complaints, the primary cause of which is not stress, anxiety, depression, emotional disorders, family or professional problems. The study should exclude women with dysmenorrhea, in which local ailments occurring only at the beginning of bleeding, and persistent during its duration, accompanied by abnormalities of the sexual cycle, prevail.

Internal and gynecological examinations are necessary. These aim to identify possible organic changes that may be responsible for ailments and at the same time may have serious health consequences. Similar discomfort is often felt by women after gynecological operations, after childbirth or abortions, and those suffering from other organic diseases of the reproductive organs. In premenstrual syndrome, the doctor may not find any palpable lesions in the genital organ during a pelvic examination. Sometimes the determination of hormonal activity of the ovaries is indicated and helpful in further proceedings. The simplest method is to measure the basic temperature of the body daily, immediately after waking up throughout the menstrual cycle. The doctor may also order the a cyto-hormonic smear to be taken from the vagina, a cervical mucus crystallization test or, in justified cases, determination of the level of sex hormones (ovarian and pituitary) in the blood serum. People with milder symptoms of premenstrual syndrome may try nonpharmacological methods.

If possible, it is good to avoid stress, and more difficult tasks should be planned for the first half of the cycle. Inhalation of essential oils may be helpful, and it is recommended to reduce the consumption of sodium and caffeine. Writing a diary and noting the changes in the mood, and the ways of reacting and physical ailments can help to understand changes in the body and to control behavior. Understanding and acceptance on the part of relatives is of course very important, and a woman has the right to expect various forms of help and tolerance during this period. With a higher severity of premenstrual symptoms, especially in full-blown PMDD, non-pharmacological methods usually fail and should not be used as the sole method of treatment for more than 3 months. After this period, pharmacotherapy should be considered.

As first-line drugs with proven efficacy, antidepressants from the SSRI (serotonergic) group are currently used. It is interesting that studies indicate similar effectiveness of these drugs used both continuously and intermittently only in the second phase of the cycle. Recently, the latter strategy has been preferred. These drugs may cause resolution or outstanding relief of most of the symptoms of PMDD. Other pharmaceuticals are less effective, act on some symptoms or are associated with a higher risk of use. Some efficacy of synthetic analogues of hypothalamic gonadotropin-releasing hormone has been demonstrated, but they are not routinely recommended. These drugs radically change the body's hormonal status, for example, they can overcome ovulation, can have other important side effects, and are also expensive. There are several drugs that are useful in some cases to alleviate individual syndromes of the syndrome. Alprazolam relieves psychical tension, but should be avoided due to the possibility of substitution. Only spironolactone is recommended for diuretics, and can reduce body swelling, while non-steroidal anti-inflammatory drugs, especially for pro-zene and mefenamic acid, can be beneficial especially when pain is an important symptom of the syndrome.

Breast engorgement and tenderness may be ameliorated, through vitamin E administered only in the second half of the cycle, and gammalinolenic acid (e.g. in evening primrose oil). Some studies have demonstrated the benefit of taking calcium carbonate at 1.200 mg per day during three monthly cycles. There is no evidence for the effectiveness of supplementing magnesium, manganese and other micronutrients. The validity of the use of contraceptives was also not confirmed. Several randomized clinical trials were performed in which vitex agnus-castus (monk's pepper) was used to alleviate the symptoms of PMS syndrome. The results indicate a significant improvement in the symptoms of PMS syndrome in 42% to 77% of women taking the drug for 3 months. No side effects were noted. The randomized study also compared the effectiveness of Mastodynon® with pyridoxine. A better therapeutic effect was demonstrated in patients treated with Mastodynon®: in 80% of patients a significant improvement in symptom perception was obtained compared to 21% in the group treated with vitamin B6. The effectiveness of vitex agnus-castus extract in alleviating emotional disorders in the most severe form of PMS, pre-menstrual dysphoric disorder (PMDD) has also been confirmed. Vitex agnus-castus showed efficacy comparable with fluoxetine, one of the most frequently used in PMDD selective serotonin reuptake inhibitors (SSRIs) [27]. Mastodynon's ingredients have been selected so as to have the greatest possible extent to alleviate the various symptoms observed in PMS [26].

It was also shown that aromatherapy with Citrus aurantium flower improved the symptoms of premenstrual tension [31].

The methods of treatment also include the administration of:

- gestagens in the second half of the cycle (17–26 days), e.g. didrogestone (10 mg 1 once 1 tablet) or progesterone (50 mg 1 once 1 tablet),
- contraceptives that stop ovulation when contraception is indicated,
- prolactin inhibitors, when the dominant symptom is mastodynia with abdominal discomfort and edema tendency, e.g. bromocriptine (½–1 tablet), from day 14–28 of the cycle,
- diuretics as a supplement to therapy or exclusive treatment, when the dominant symptom is swelling and weight gain, e.g. hydrochlorothiazide 12.5–25 mg per day,
- a set of vitamins A, B (especially B6), D and E.

Risk factors for the occurrence of PMS symptoms may be vitamin and mineral deficiencies. To synthesize neurotransmitters potentially involved in the pathogenesis of this syndrome, B vitamins and folic acid are needed, among others [32]. Increased amounts of thiamine (vitamin B1), riboflavin (vitamin B2) and pyridoxine (vitamin B6) have a beneficial effect on the alleviation of PMS symptoms. Bertone-Johnson et al. [33] emphasize the importance of vitamin D, which at a dose of  $\geq 2.5 \mu\text{g}$  reduces the risk of premenstrual syndrome. Siuda and Rabe-Jabłońska [34] suggest calcium substitution from ovulation to menstruation, at a dose of 1200 mg/day, with the simultaneous use of tryptophan at a dose of 6 g/day.

In view of the quite diverse positions in the literature regarding the supplementation and dosage of vitamins and microelements, it is safest to use a balanced diet. In this way, overdose is avoided and the effect is reversed to that of a therapeutic one. Selecting the correct, balanced diet is a task for the dietitian. Based on the nutritional interview, he or she has the opportunity to recognize the mistakes made and determine the need and scope of diet modification, which will contribute to reducing the perceived PMS symptoms [32].

### SUMMARY

Adolescent girls often complain of heavy menstrual bleeding, and premenstrual symptoms are also common. Differential diagnosis is extensive and requires vigilance, especially in the area of coagulation disorders. In establishing the diagnosis, the gynecologist's cooperation with the hematologist may be helpful, which may prove invaluable in achieving success.

With reference to the occurrence of above mentioned problems, there is a need for nutritional education among adolescents. Dietary intervention is the most appropriate way to improve knowledge status in young women and

can act as an alternative to conventional treatment. Unfortunately, there are no educational campaigns in Poland related to diet therapy possible in premenstrual syndrome or iron deficiency. Such education should be targeted at broadening knowledge by identifying and promoting various sources of well-absorbed iron. Such a strategy will be beneficial for an individual's health during adolescence and for their future health.

### REFERENCES

1. Sanchez J, Andrabi S, Bercaw JL, et al. Quantifying the PBAC in a pediatric and adolescent gynecology population. *Pediatr Hematol Oncol*. 2012; 29(5): 479–484, doi: [10.3109/08880018.2012.699165](https://doi.org/10.3109/08880018.2012.699165), indexed in Pubmed: [22866673](https://pubmed.ncbi.nlm.nih.gov/22866673/).
2. Friberg B, Ornö AK, Lindgren A, et al. Bleeding disorders among young women: a population-based prevalence study. *Acta Obstet Gynecol Scand*. 2006; 85(2): 200–206, indexed in Pubmed: [16532915](https://pubmed.ncbi.nlm.nih.gov/16532915/).
3. Frishman GN. Evaluation and treatment of menorrhagia in an adolescent population. *J Minim Invasive Gynecol*. 2008; 15(6): 682–688, doi: [10.1016/j.jmig.2008.08.014](https://doi.org/10.1016/j.jmig.2008.08.014), indexed in Pubmed: [18971130](https://pubmed.ncbi.nlm.nih.gov/18971130/).
4. Sokkary N, Dietrich JE. Management of heavy menstrual bleeding in adolescents. *Curr Opin Obstet Gynecol*. 2012; 24(5): 275–280, doi: [10.1097/GCO.0b013e3283562bcb](https://doi.org/10.1097/GCO.0b013e3283562bcb), indexed in Pubmed: [22729091](https://pubmed.ncbi.nlm.nih.gov/22729091/).
5. James AH. Bleeding disorders in adolescents. *Obstet Gynecol Clin North Am*. 2009; 36(1): 153–162, doi: [10.1016/j.ogc.2008.12.002](https://doi.org/10.1016/j.ogc.2008.12.002), indexed in Pubmed: [19344853](https://pubmed.ncbi.nlm.nih.gov/19344853/).
6. Chi C, Pollard D, Tuddenham EGD, et al. Menorrhagia in adolescents with inherited bleeding disorders. *J Pediatr Adolesc Gynecol*. 2010; 23(4): 215–222, doi: [10.1016/j.jpag.2009.11.008](https://doi.org/10.1016/j.jpag.2009.11.008), indexed in Pubmed: [20471874](https://pubmed.ncbi.nlm.nih.gov/20471874/).
7. National Institute for Health and Care Excellence. Heavy menstrual bleeding. NICE Guideline. 2007.
8. Wang W, Bourgeois T, Klima J, et al. Iron deficiency and fatigue in adolescent females with heavy menstrual bleeding. *Haemophilia*. 2013; 19(2): 225–230, doi: [10.1111/hae.12046](https://doi.org/10.1111/hae.12046), indexed in Pubmed: [23106971](https://pubmed.ncbi.nlm.nih.gov/23106971/).
9. James AH, Hoots K. The optimal mode of delivery for the haemophilia carrier expecting an affected infant is caesarean delivery. *Haemophilia*. 2010; 16(3): 420–424, doi: [10.1111/j.1365-2516.2009.02142.x](https://doi.org/10.1111/j.1365-2516.2009.02142.x), indexed in Pubmed: [20028425](https://pubmed.ncbi.nlm.nih.gov/20028425/).
10. Provan D, Stasi R, Newland AC, et al. International consensus report on the investigation and management of primary immune thrombocytopenia. *Blood*. 2010; 115(2): 168–186, doi: [10.1182/blood-2009-06-225565](https://doi.org/10.1182/blood-2009-06-225565), indexed in Pubmed: [19846889](https://pubmed.ncbi.nlm.nih.gov/19846889/).
11. Sarpatwari A, Bennett D, Logie JW, et al. Thromboembolic events among adult patients with primary immune thrombocytopenia in the United Kingdom General Practice Research Database. *Haematologica*. 2010; 95(7): 1167–1175, doi: [10.3324/haematol.2009.018390](https://doi.org/10.3324/haematol.2009.018390), indexed in Pubmed: [20145266](https://pubmed.ncbi.nlm.nih.gov/20145266/).
12. Levens ED, Scheinberg P, DeCherney AH. Severe menorrhagia associated with thrombocytopenia. *Obstet Gynecol*. 2007; 110(4): 913–917, doi: [10.1097/01.AOG.0000279138.64895.2b](https://doi.org/10.1097/01.AOG.0000279138.64895.2b), indexed in Pubmed: [17906028](https://pubmed.ncbi.nlm.nih.gov/17906028/).
13. Jarząbek-Bielecka G, Warchol-Biedermann K, Sowińska E, et al. Precocious puberty. *Ginekol Pol*. 2011; 82(4): 281–286.
14. Jarząbek-Bielecka G, Mizgier M. Eating disorders as a problem in adolescent gynecology. *Now Lek*. 2009; 78(3–4): 234–236.
15. O'Brien B, Mason J, Kimble R. Bleeding Disorders in Adolescents with Heavy Menstrual Bleeding: The Queensland Statewide Paediatric and Adolescent Gynaecology Service. *J Pediatr Adolesc Gynecol*. 2019; 32(2): 122–127, doi: [10.1016/j.jpag.2018.11.005](https://doi.org/10.1016/j.jpag.2018.11.005), indexed in Pubmed: [30472382](https://pubmed.ncbi.nlm.nih.gov/30472382/).
16. Tesfaye M, Yemane T, Adisu W, et al. Anemia and iron deficiency among school adolescents: burden, severity, and determinant factors in southwest Ethiopia. *Adolesc Health Med Ther*. 2015; 6: 189–196, doi: [10.2147/AHMT.S94865](https://doi.org/10.2147/AHMT.S94865), indexed in Pubmed: [26719736](https://pubmed.ncbi.nlm.nih.gov/26719736/).
17. Jain M, Chandra S. Correlation between hematological and cognitive profile of anemic and non anemic school age girls. *Curr Pediatr Res*. 2012; 16: 145–149.
18. Skolmowska D, Głąbska D. Analysis of Heme and Non-Heme Iron Intake and Iron Dietary Sources in Adolescent Menstruating Females in a National Polish Sample. *Nutrients*. 2019; 11(5), doi: [10.3390/nu11051049](https://doi.org/10.3390/nu11051049), indexed in Pubmed: [31083370](https://pubmed.ncbi.nlm.nih.gov/31083370/).

19. Hamułka J, Wawrzyniak A, Piątkowska D, et al. Evaluation of iron, vitamin B12 and folate intake in the selected group of women at childbearing age. *Rocz Panstw Zakl Hig.* 2011; 62: 263–270.
20. Mizgier M, Jarzabek-Bielecka G, Marcinkowska E, et al. Interwencja dietetyczna czy suplementacja witaminowo-mineralna podczas ciąży? *Pielęgniarstwo Polskie.* 2016; 62(4): 546–551, doi: [10.20883/pielpol.2016.57](https://doi.org/10.20883/pielpol.2016.57).
21. Mizgier M, Jarzabek-Bielecka G, Jakubek E, et al. Zachowania zdrowotne dziewcząt w wieku prokreacyjnym a profilaktyka otyłości, zaburzeń płodności i powikłań położniczych – doniesienie wstępne. *Pielęgniarstwo Polskie.* 2016; 62(4): 524–528, doi: [10.20883/pielpol.2016.53](https://doi.org/10.20883/pielpol.2016.53).
22. Gulec S, Anderson GJ, Collins JF. Mechanistic and regulatory aspects of intestinal iron absorption. *Am J Physiol Gastrointest Liver Physiol.* 2014; 307(4): G397–G409, doi: [10.1152/ajpgi.00348.2013](https://doi.org/10.1152/ajpgi.00348.2013), indexed in Pubmed: [24994858](https://pubmed.ncbi.nlm.nih.gov/24994858/).
23. Beck KL, Conlon CA, Kruger R, et al. Dietary determinants of and possible solutions to iron deficiency for young women living in industrialized countries: a review. *Nutrients.* 2014; 6(9): 3747–3776, doi: [10.3390/nu6093747](https://doi.org/10.3390/nu6093747), indexed in Pubmed: [25244367](https://pubmed.ncbi.nlm.nih.gov/25244367/).
24. Mizgier M, Jarzabek-Bielecka G, Jakubek E, et al. The relationship between body mass index, body composition and premenstrual syndrome prevalence in girls. *Ginekol Pol.* 2019; 90(5): 256–261, doi: [10.5603/GP.2019.0048](https://doi.org/10.5603/GP.2019.0048), indexed in Pubmed: [31165464](https://pubmed.ncbi.nlm.nih.gov/31165464/).
25. Dzygadło B, Łepecka-Klusek C, Pilewski B. Use of bioelectrical impedance analysis in prevention and treatment of overweight and obesity. *Probl Hig Epidemiol.* 2012; 93(2): 274–280.
26. Stanowisko Zespołu Ekspertów Polskiego Towarzystwa Ginekologicznego w sprawie zastosowania leku Mastodynon w ginekologii. *Ginekol Pol.* 2013; 84: 157–159.
27. Green LJ, O'Brien PMS, Panay N, et al. on behalf of the Royal College of Obstetricians and Gynaecologists. Management of premenstrual syndrome. *BJOG.* 2017; 124: e73–e105.
28. Negi P, Mishra A, Lakhera P. Menstrual abnormalities and their association with lifestyle pattern in adolescent girls of Garhwal, India. *J Family Med Prim Care.* 2018; 7(4): 804–808, doi: [10.4103/jfmpc.jfmpc\\_159\\_17](https://doi.org/10.4103/jfmpc.jfmpc_159_17), indexed in Pubmed: [30234057](https://pubmed.ncbi.nlm.nih.gov/30234057/).
29. Fisher C, Adams J, Frawley J, et al. Is there a role for Western herbal medicine in treating cyclic perimenstrual pain and discomfort? *Aust N Z J Obstet Gynaecol.* 2018; 59(1): 154–156, doi: [10.1111/ajo.12883](https://doi.org/10.1111/ajo.12883).
30. Arslantaş H, Abacigil F, Çınaklı Ş. Relationship between premenstrual syndrome and basic personality traits: a cross-sectional study. *Sao Paulo Med J.* 2018; 136(4): 339–345, doi: [10.1590/1516-3180.2018.0061240418](https://doi.org/10.1590/1516-3180.2018.0061240418), indexed in Pubmed: [30110077](https://pubmed.ncbi.nlm.nih.gov/30110077/).
31. Heydari N, Abootalebi M, Jamalimoghadam N, et al. Investigation of the effect of aromatherapy with Citrus aurantium blossom essential oil on premenstrual syndrome in university students: A clinical trial study. *Complement Ther Clin Pract.* 2018; 32: 1–5, doi: [10.1016/j.ctcp.2018.04.006](https://doi.org/10.1016/j.ctcp.2018.04.006), indexed in Pubmed: [30057033](https://pubmed.ncbi.nlm.nih.gov/30057033/).
32. Pałucka K, Łepecka-Klusek C, Pilewska-Kozak AB, et al. Stadnicka G; Premenstrual syndrome – myth or reality. *Journal of Education, Health and Sport.* 2016; 6(6): 478–490.
33. Bertone-Johnson ER, Hankinson SE, Willett WC, et al. Adiposity and the development of premenstrual syndrome. *J Womens Health (Larchmt).* 2010; 19(11): 1955–1962, doi: [10.1089/jwh.2010.2128](https://doi.org/10.1089/jwh.2010.2128), indexed in Pubmed: [20874240](https://pubmed.ncbi.nlm.nih.gov/20874240/).
34. Siuda I, Rabe-Jabłońska J. Premenstrual syndrome and premenstrual dysphoric disorder – diagnosis and treatment. *Psychiatr Psychol Klin.* 2007; 7(1): 29–35.