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Dilemmas concerning the course of pregnancy in patients with anorexia nervosa considering hormonal and somatic parameters

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Abstract

Mental anorexia nervosa is a rare, potentially severe, chronic, and recurrent mental disorder that occurs more often in women than in men, especially during the childbearing years. The disorder is associated with an increased risk of mortality, mainly related to the physical consequences of severe malnutrition and suicide. Malnutrition of the body can cause serious hormonal and somatic problems. Despite significant hormonal disturbances that reduce fertility, a woman with anorexia can become pregnant. A new phenomenon now seen with increasing frequency is pregorexia, an eating disorder associated with pregnancy. It involves the use of dietary restrictions to avoid excessive weight gain during pregnancy. Pregnancy changes the hormonal economy mainly due to the development of the placenta, which secretes many hormones, not just sex hormones. Mental anorexia poses a significant risk to both mother and child if not diagnosed and treated properly. Treatment of anorexia involves simultaneous somatic and psychological treatment. During pregnancy, additional care should be taken to create an optimal environment for the developing foetus. Unfortunately, there is still a lack of research providing guidance in this area. Available studies are mainly case reports or reports focusing on specific clinical situations. It is worth noting that no study to date has attempted a comprehensive assessment of endocrine disruption in pregnant women with anorexia. Recognising the existing knowledge gap on endocrine disorders in pregnant women with anorexia nervosa, a systematic review of the literature was conducted. **(Endokrynol Pol 2024; 75 (3): 279–290)**

Key words: *peripartum disorders; women's mental health; anorexia nervosa; pregorexia nervosa; eating disorders; pregnancy; amenorrhea; oestrogens; bone loss; mental disease; forced treatment*

Introduction

Anorexia nervosa (AN) is a complex psychiatric disorder characterised by severe restriction of food intake, a warped perception of one's mirror image, and a strong fear of gaining weight [1]. Individuals with AN often engage in intense and prolonged exercise, restrictive eating behaviours concerned with their body's negative energy balance, and are obsessed with weight control. In addition, anxiety behaviours and depressed mood are often observed in patients with AN. These behaviours typically lead to significant weight loss, malnutrition, and physiological imbalances in the body. AN is associated with the highest mortality rate of all psychiatric disorders, reaching up to 18% in patients between the ages of 20 and 30 years, according to some authors [2]. It is estimated that the disease affects about 2–3% of the general population [3]. The diagnostic criteria for AN are strictly defined according to classifications of the International Statistical Classification of Diseases (ICD-11) and Diagnostic and Statistical Manual of Mental Disorders (DSM-V).

AN mainly affects young women. Onset usually occurs in adolescence or early adulthood [3]. Psychological and behavioural factors have long been recognised as key domains contributing to the development and persistence of AN symptoms. Emerging newer research has highlighted the significant hormonal changes that occur in individuals with the disorder [4, 5].

AN is a chronic disease with periods of exacerbation and remission. Although the disease usually causes fertility disorders, pregnancy is possible not

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only in women in remission, but also during the active phase of the disease [6]. Pregnancy and the associated organ and hormonal changes are a heavy burden for healthy women, and for women with AN, the burden on the body may prove to be too much. In addition, as a mental illness, it requires close monitoring of mental status and assessment of disease severity, as well as monitoring of the pregnant woman's weight and foetal growth and development. A relatively new phenomenon, gaining in frequency recently, which is worth mentioning, is pregorexia. "Pregorexia" or "pregorexia nervosa" (PN) characterises women who, only during pregnancy, obsessively begin to follow an overly restrictive diet and excessive exercise to control the weight gain naturally associated with normal pregnancy. Pregorexia is not formally ranked in the DSM-V or ICD-11 classifications and is most often classified as an unspecified eating disorder (ED) [7, 8]. PN behaviours are associated with concerns about being overweight, influenced by societal expectations of an "ideal" body during pregnancy and after childbirth [9]. It often affects female celebrities and athletes. Pregnancy introduces significant changes in self-perception, social roles, work schedules and lifestyle, posing a bio-psycho-social challenge for women [10]. This period activates stress coping mechanisms and psychological resilience factors but also poses the risk of revealing biological or psychological vulnerabilities. Weight gain during pregnancy can trigger adaptive reactions ranging from mild discomfort to psychological distress [11]. The co-occurrence of symptoms/anxiety disorders/mood disorders and eating disorders is not uncommon, often rooted in excessive concerns about weight gain, so such symptoms should be given special attention [12]. Monitoring body mass index (BMI) and conducting a thorough interview about feelings of anxiety, as well as diet and exercise, can help detect symptoms of PN. In women with a history of ED, caution should be exercised when monitoring the course of pregnancy, because pregnancy may alleviate and exacerbate weight gain concerns in some and others [13, 14]. The complex relationship between ED and pregnancy is also influenced by fertility problems and anxiety or depression [15]. The symptoms and complications in PN can be very similar to those in pregnancy with AN.

Analysis of the physiological and hormonal changes occurring in the pregnant woman on the one hand, and the changes occurring in the body of the person suffering from AN on the other hand, is crucial to understanding the potential impact of AN on pregnancy [16, 17]. Available recommendations on the management of AN refer to people who are not pregnant, and very few reports attempt to make recommendations on the management of pregnant women with AN [18].

The new ICD-11 and DSM-V disease classifications for anorexia, as in previous versions, retain the term "disorder" rather than "mental illness". According to the definition of "mental disorder", it encompasses a set of 4 interrelated phenomena: psychopathological symptoms, behavioural disorders, functional impairment, and internal pathological stress [19]. In the Polish legal system, AN is also not considered a mental illness [20]. Making a diagnosis of "mental illness" entails the obligation to conduct certain medical, social, and legal rules. The term "disorder" therefore plays a key role in psychiatry and legislation. Failure to define AN as a "mental illness" can lead to abuse and erroneous decisions, for example as to the introduction of coercive treatment. Such decisions can have significant consequences for people with mental disorders, and in the case of a pregnancy with AN, not only for the pregnant woman, but also for the foetus.

The purpose of this article is to review the existing literature on hormonal and somatic changes occurring during pregnancy in women with AN. In the first step, we analyse the changes in the body during physiological pregnancy; in the next step we review the hormonal and somatic changes in women with AN and then try to synthesise these mechanisms. We also discuss the possible clinical implications of this type of eating disorder on the course of pregnancy and the occurrence of possible complications in the mother and child. Finally, we review the Polish legislation and treatment regimens for pregnant women with anorexia in life-threatening cases.

Material and methods

This evaluation is grounded on a search conducted through PubMed and Embase, employing the following terms: ("eating disorder" or "anorexia nervosa" or "pregorexia nervosa" or "mental anorexia" or "anorexia") and ("pregnancy" or "pregnant" or "antenatal" or "perinatal" or "postpartum" or "postnatal" or "infant feeding" or "fertility" or "fetus"). The exploration encompassed articles published in English between January 2000 and March 2023. We excluded case studies and qualitative studies. We scrutinised the titles and abstracts of all studies identified through the search strategy, followed by the complete text of suitable articles. This review encompasses 17 articles.

Physiological changes in pregnancy

The body of a pregnant woman undergoes significant physiological changes to support foetal growth and development [19–22]. These changes include changes in hormone concentrations, increased metabolic demands, and adaptations of various organ systems. They take place primarily through hormonal changes: increases in oestrogen, progesterone, human chorionic gonadotropin (hCG), and prolactin, which play a key

Table 1. *Physiological changes during pregnancy [24]*

Systems	Parameter	Changes
Cardiovascular system	Heart rate	↑ by 20%
	Blood pressure	↓ by 10% until 34 weeks, then ↑ to pre-pregnancy values
	Ejection volume	↑ up to 19 weeks of pregnancy, then plateau
	Minute capacity	By 20%, then ↑ by10% by 28 weeks' gestation
	Peripheral venous vasodilatation	↑ progressively to delivery date
	Peripheral vascular resistance	↓ progressively to term of delivery
	Uterine diaphragm elevation	Heart elevation, apical beat shifted to the side
	Myocardium	Hypertrophy by 12%, ↑ volume by 70–80 mL ↑ capillary vascularisation
Hematopoietic system	Volume	↑ by 50% in the second trimester of pregnancy
	Haematocrit	↓ slight
	Fibrinogen	↑ blood concentrations
	Electrolytes	No change
Respiratory system	Respiratory rate	No change
	Tidal volume	↑ by 30–40%
	Expiratory reserve	↓ gradually
	Vital capacity	No change
	Minute tidal volume	↑ o 40%
Urinary system	Renal flow	↑ by 25–50%
	Glomerular filtration rate	↑ in early pregnancy, then plateau
	Creatinine, urea, uric acid	↓ blood concentrations
	Kidney blood flow	↑ by 50%
	Glomerular filtration rate	↑ by 35%
Gastrointestinal tract	Intestinal passage	↓ movement of intestinal contents, ↓ emptying of stomach, intestines

role in supporting pregnancy. The most important organ changes occurring in the body of a healthy pregnant woman, by system, are shown in Table 1 [23–26].

The cardiovascular system undergoes significant modifications during pregnancy, with an estimated increase in plasma volume of about 45% and an increase in blood cell mass of about 20%. This dynamic change contributes to physiological pregnancy anaemia, accompanied by a decrease in haemoglobin and haematocrit levels. At the same time, there is an absolute increase in the number of leukocytes, which strengthens the body's immune response [27]. Changes in coagulation activity are also observed, mainly through an increase in fibrinogen levels.

In addition, there is an adaptation of the respiratory system through a 40% increase in lung ventilation and minute respiratory capacity. Although the pregnant woman's respiratory rate remains unchanged, gas exchange capacity increases. This results in a decrease in partial pressure of carbon dioxide (pCO_2) (28–32 mm Hg), providing optimal oxygenation for both mother and foetus.

Changes observed in the urinary system in pregnant women are mainly due to increased progesterone levels. Increased hypotonia of the smooth muscle of the ureters, relaxation of the bladder muscles, and dilatation of the urinary tract are observed. Adaptations of the urinary tract to pregnancy can cause an increased risk of urinary retention and increased susceptibility to infection.

Reduced gastrointestinal muscle tone is responsible for reflux and heartburn, which are typical symptoms that often occur in the second half of pregnancy [28]. In addition, pregnant women experience an increase in saliva secretion with decreased pH, which can cause an increased risk of tooth decay and bleeding gums.

In a healthy pregnancy, there is a steady increase in the concentration of oestrogen and progesterone. High concentrations of these hormones are responsible for transforming the glandular tissue of the breast and preparing the nipple for lactation. A significant increase in oestrogen concentrations is observed, with a 50-fold increase in oestradiol (E2) and oestrone (E1) and an approximately 1000-fold increase in estriol (E3) levels [21].

It is also observed to increase the concentration of prolactin, which stimulates breast development and milk production. hCG is produced by chorion cells from the very early stages of pregnancy. It reaches its maximum concentration at around 12–14 weeks and then decreases slightly until the end of pregnancy. The hormone helps support the corpus luteum and thus the production of progesterone, which sustains the foetal egg in utero [28, 29].

In the pregnant woman's liver, there is an intensified production of sex hormone-binding globulin (SHBG). The main role of SHBG is to bind free testosterone, so that lower levels of free testosterone are observed in pregnant women compared to non-pregnant women [20].

It is noteworthy that androgen production sums up to a moderate increase throughout pregnancy. Foetal dehydroepiandrosterone (DHEA) is mainly produced by the foetal adrenal glands. DHEA that is not bound by SHBG is used by the foetal-placental unit as a substrate for oestrogen synthesis. This contributes to an overall decrease in dehydroepiandrosterone sulphate (DHEAS).

From the very beginning, a gradual increase in cortisol levels is observed throughout pregnancy. At the end of pregnancy, it is about twice as high as at the beginning.

Increased concentrations of aldosterone are also observed (about an 8–10-fold increase), but despite this increase, healthy pregnant women show only slight symptoms of hyperaldosteronism [30].

Progesterone becomes a protective factor, acting as a competitive inhibitor of mineralocorticoids in the distal renal tubules, preventing hypokalaemia and hypernatraemia. Iodine clearance and ^{11}I uptake increase, leading to relative iodine deficiency. Total

Table 2. *Changes in hormone concentrations during pregnancy*

Place of synthesis	Hormone	Changes during pregnancy	Peak concentration
Corpus luteum/placenta	Progesterone	↑ until termination of pregnancy	190 ng/mL — before delivery
	17-OH progesterone	Peak 5 weeks of pregnancy then ↓ concentration	6 ng/mL — 5th week of gestation
Foetus ÷ Placenta	Estriol (E3)	↑ until termination of pregnancy	15–17 ng/mL — before delivery
	Oestradiol (E2)	↑ until termination of pregnancy	12–15 ng/mL — before delivery
	Oestrone (E1)	↑ until termination of pregnancy	5–7 ng/mL — before delivery
	Oestetrol (E4)	↑ until termination of pregnancy	1.2 ng/mL — before delivery
	Testosterone **á???**	↑ until termination of pregnancy	2000 pg/mL — before delivery > 10 × — before pregnancy
	DHEA	↓ concentrations	< 5 ng/mL — before delivery
	Androstenedione	↑ concentrations insignificant	2.6 ng/mL — pre-birth
Anterior pituitary lobe	hGH	Gradually ↑ due to placental GH	20–40 ng/mL — in 36th week of gestation
	LH/FSH	↓ concentrations	0.1–1.0 mIU/mL
	ACTH	No change	6.0–63 pg/mL
	TSH	↓ concentrations in the first trimester, then constants	0.4–4.01 mU/l
	PRL	↑ until the end of pregnancy	200 ng/mL — before delivery
Adrenals	Cortisol	↑ until termination of pregnancy	300 ng/mL — before delivery
	Aldosterone	Plateau until 34 weeks of pregnancy, ↑ until termination of pregnancy	100 ng/mL- before delivery
	DOC	↑ until termination of pregnancy	1200 pg/mL — before delivery
Thyroid	T_4	↑ concentrations in 1st trimester, then constants	150 ng/mL
	fT_4	Unchanged	30 pg/mL
	T_3	↑ concentrations in 1st trimester, then constants	2 ng/mL
	fT_3	Unchanged	4 pg/mL

E1 — oestrone; E2 — oestradiol; E3 — oestriol; E4 — oestetrol; DHEA — dehydroepiandrosterone; hGH — human growth hormone; LH — lutropine; FSH — follicle stimulating hormone; LH — luteinising hormone; ACTH — adrenocorticotropic hormone; TSH — thyroid-stimulating hormone; PRL — prolactin; DOC — deoxycorticosterone; T4 — thyroxine; fT4 — free thyroxine; T3 — triiodothyronine; fT3 — free triiodothyronine

thyroxine concentrations increase due to increased oestrogen and elevated thyroxine-binding globulin (TBG) levels. However, free thyroxine (fT4) and free triiodothyronine (fT3) concentrations remain within the normal range [22].

Due to its structural similarity, hCG mirrors the action of thyrotropic hormone (TSH), exerting a thyrotropic effect in early pregnancy [31]. This may result in transient biochemical hyperthyroidism, a phenomenon associated with the stimulatory effects of hCG [32].

Anorexia nervosa in pregnancy

Pregnancy involves significant physiological changes, which means that recommendations created for pregnant women cannot be literally applied to AN during pregnancy. Conversely, treatment and dietary recommendations created for non-pregnant women with AN cannot be literally translated in the case of pregnancy.

Although there are guidelines from numerous scientific societies regarding expected weight gain in pregnancy, they are of little use in women with anorexia. Weight stabilisation, which would be reassuring in non-pregnant women with AN, will reflect measurable weight loss in the case of pregnancy. In obstetric care, the recommended weight gain in pregnancy is based on a calculated pre-pregnancy body mass index (BMI). For a BMI below 18.5 kg/m^2, a gain of 12.5–18 kg with 0.5 kg/week in the second and third trimesters and 0.5–2 kg in the first trimester is recommended. For a pre-pregnancy BMI between 18.5 kg/m^2 and 24.9 kg/m^2, the suggested total weight gain is 11.5–16 kg [33]. However, there is no specific guidance on the recommended weight gain for people with extremely low pre-pregnancy BMI (≤ 15 kg/m^2). Those with extremely low BMI require personalised management. In addition, it is important to keep in mind that monitoring weight gain by BMI becomes increasingly flawed as gestational age advances due to altered body fluid volume and variable placental and foetal weight.

Diagnosis and monitoring of ED in pregnant women based on routine measures alone is inadequate due to the potential overlap of pathological eating behaviours [34]. Many common changes in food preferences, eating patterns, food aversions or cravings, and appetite fluctuations have been described by both pregnant women and those with eating disorders [34, 35]. It is necessary to take a careful history to avoid pathologising adaptive responses to pregnancy. A comprehensive anamnesis focusing on specific eating habits and a psychiatric examination assessing the degree of distorted perception of one's own body is essential.

Hormonal changes in anorexia nervosa

The hypothalamic–pituitary–adrenal (HPG) axis is a key hormonal pathway responsible for regulating reproductive function [35, 36]. Low body weight in individuals with AN, malnutrition, and excessive exercise disrupt normal hypothalamic function, leading to decreased secretion of gonadotropin-releasing hormone (GnRH), followed by decreased production of luteinising hormone (LH) and folliculotropic hormone (FSH) [37, 38]. HPG axis dysfunction results in reduced oestrogen levels in women and reduced testosterone levels in men [39]. Consequently, symptoms of hypogonadism-hypogonadotropic hypogonadism are observed, i.e. lack of menstruation in women, and reduced libido and sexual dysfunction in men [40].

Typical of AN, chronic malnutrition and psychological stress lead to dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis [41]. Their corticotropin-releasing hormone (CRH) levels show persistently elevated levels, contributing to increased ACTH synthesis and increased cortisol production. This dysregulation is also characterised by altered diurnal rhythms of cortisol secretion as well as elevated basal cortisol levels and blunted cortisol reactivity to stress stimuli [42, 43]. These abnormalities contribute to the persistence of chronically elevated cortisol levels, further perpetuating the pathophysiology of the disorder. Elevated cortisol levels, in turn, disrupt the pulsatile release of FSH and LH, affecting menstrual regularity and bone health while contributing to neuronal dysfunction and depressive symptoms [42, 43].

In addition to the HPG and HPA axes, malnutrition affects the concentrations of several peripheral hormones involved in appetite regulation, energy balance, and metabolism. The concentration of ghrelin, known as the "hunger hormone", is elevated in people with AN [44, 45]. Elevated ghrelin levels contribute to the increased appetite and food-seeking behaviour observed in the early stages of the disorder. In contrast, levels of leptin, a hormone produced by adipose tissue, are reduced in AN [46]. Low leptin levels signal a state of energy deficiency, triggering adaptive physiological responses to conserve energy and maintain body homeostasis [47, 48]. Besides, leptin has important functions in the regulation of glucose metabolism, immunomodulation, and reproductive processes. In pregnancy, it plays a role in regulating foetal growth [49]. In women with anorexia nervosa, significantly reduced leptin levels can affect impaired trophoblast development and function, potentially having a negative impact on later pregnancy outcomes mediated by

Table 3. *Endocrine disorders in mental anorexia nervosa [35–56]*

Site of synthesis	Hormone	AN (hormone concentration)	Function
Hypothalamus	CRH	↑	↑ ACTH synthesis
Pituitary	ACTH	↑	↑ synthesis of cortisol
Adrenals	Cortisol	↑	• ↓ pulsatile release of FSH and LH (absence of menstruation) • ↓ osteoblasts activity, ↑ osteoclast activity (osteopenia), • neuronal dysfunction (depression)
	DHEAS	No consensus	Anxiolytic effect*
Hypothalamus	TRH	↓ or no change	↑ TSH synthesis
Pituitary	TSH	↓ or no change	↑ synthesis of T3, T4
Thyroid	T_4	↓ or no change	↑ metabolism
	T_3	↓	↑ metabolism, antidepressant effect
	$r_1 3$	↑	Metabolically inactive
Hypothalamus	GnRH	↓	↑ synthesis of FH, LH
Pituitary	FSH, LH	↓	Folliculogenesis, ↑ oestradiol synthesis
Adnexa	E_2, T	↓	Bone mineralization, anxiolytic effects*
Pituitary	GH	↑ hormone resistance	↑ gluconeogenesis ↑ lipolysis, ↑ osteoblastogenesis, ↓ osteoclastogenesis
Liver	IGF-1	↓	↑ osteoblastogenesis, ↓ osteoclastogenesis, ↑ bone growth
Hypothalamus	ADH	↓ or unchanged	↑ renal water reabsorption
Hypothalamus	Oxytocin	↓	Anxiolytic effect*, ↑ osteoblastogenesis, ↓ osteoclastogenesis
Gastrointestinal tract	Ghrelin	↑	↑ orexigenic effect, ↓ LH, ↓FSH, ↑ACTH, ↑GH
	NPY	↓ or unchanged	↑ anorexigenic effect
Adipose tissue	Leptin	↓	↑ kisspeptin signalling to GnRH neurons, ↑ orexigenic effect
Liver	FGF-21	↑	↓ GH action

CRH — corticotropin-releasing hormone; ACTH — adrenocorticotropic hormone; DHEAS — dehydroepiandrosterone sulphate; FSH — follicle stimulating hormone; LH — luteinizing hormone; TRH — thyroxin-releasing hormone; GnRH — gonadotropin-releasing hormone; E2 — oestradiol, T — testosterone; T4 — thyroxine; T3 — triiodothyronine; rT3 — reverse triiodothyronine; GH — growth hormone; IGF-1 — insulin growth factor 1; ADH —antidiuretic hormone, **NPY-**, FGF-21 — fibroblast growth factor. *affects nerve impulse transmission in the central nervous system (CNS) (↓ anxiety, ↓ anxiety, ↓ emotional tension, sedative and sleeping effects)

the placenta [50]. An increased prevalence of insulin resistance and altered glucose metabolism have also been reported in individuals with AN [51–54].

The concentration of thyroid-releasing hormone (TRH) in the hypothalamus is reduced or shows no change in anorexics, affecting TSH synthesis. There is a decrease in TSH and thyroid hormones and, as a result, a slowing of metabolism in all cells of the body. The antidepressant effect of T3, which when lowered does not elicit sufficient protection, also appears to be important in AN [38].

Bone health is subject to significant modulation in individuals with AN due to elevated cortisol levels, increased growth hormone resistance, reduced insulin-growth factor 1 (IGF-1) levels, and reduced oxytocin levels. This constellation of these hormones leads to an eminently increased tendency to osteoporosis. In addition, elevated levels of fibroblast growth factor 21 (FGF-21) can negatively affect the action of growth hormone (GH), contributing to the energy imbalance and metabolic processes observed in AN [55]. In addition, reduced oxytocin levels reduce emotional responses [56].

The known major endocrine disorders recognised in AN are shown in Table 3.

Effects of anorexia nervosa on maternal health

Due to common hypothalamic–pituitary dysfunction in women with AN, they often experience reduced levels of oestrogen and progesterone. This often manifests as irregular menstrual cycles, scanty periods (infrequent menstruation), or no menstruation (amenorrhoea) and ultimately leads to reduced fertility and difficulty getting pregnant [36]. Restoring hormonal balance and regulating the menstrual cycle contributes to improved reproductive health [57].

Table 4. *Somatic complications in mental anorexia nervosa*

Systems	Complications
Central nervous system	Cortical atrophy, white matter atrophy, enlargement of fluid spaces, persistent neuropsychological deficits, apathy, difficulty concentrating, depression, epileptic seizures
Cardiovascular system	Bradycardia, arrhythmias, drops in blood pressure, cyanosis
Skeletal system	Osteopenia, osteoporosis, susceptibility to bone fractures
Muscular system	Muscle weakness, muscle cramps and pain, muscle atrophy
Haematopoietic system	Anaemia, pancytopaenia, neutropaenia with lymphocytosis, thrombocytopaenia, bone marrow hypoplasia
Gastrointestinal system	Abdominal pain, vomiting, bloating, constipation, prolonged gastric emptying, abnormal gastrointestinal transit, abnormal liver indices, superior mesenteric artery syndrome
Urinary tract	Hunger oedema, nephropathy, decreased glomerular filtration rate, nephrolithiasis
Metabolic abnormalities	Electrolyte disturbances, hypophosphatemia, hyperphosphatemia, hypoglycaemia, dehydration, hypercholesterolaemia, impaired body temperature regulation, metabolic disturbances due to large food intake (so-called refeeding syndrome)
Systemic changes	Low body weight, emaciation, cachexia
Skin	Lanugo skin, dry skin and brittleness of nails, acrimony, hair loss
Reproductive system	Amenorrhea, infertility stunted **psychoomatic [Psychosomatic?]** development

A long-term complication of oestrogen deficiency in AN and amenorrhoea is accelerated bone mass loss and increased risk of osteoporosis [58]. Inadequate bone mineral density can jeopardise maternal skeletal health and, indirectly, abnormal foetal bone calcification. Close monitoring of bone health markers and appropriate prevention of bone loss, such as calcium and vitamin D supplementation, are essential to reduce this risk [59]. During pregnancy in these patients, special care should be taken to supplement vitamin D levels; also, remember that calcium requirements are higher [60].

In the central cerebral system, atrophy in the form of cortical atrophy occurs, and clinically features of neuropsychological deficits are observed, most often in the form of attention and memory deficits [61]. On the cardiovascular side, significant drops in blood pressure and increased bradycardia are encountered [62]. In the musculoskeletal system, features of atrophy in the form of osteopaenia and osteoporosis as well as muscle weakness and atrophy are also observed. All this contributes to a significant increase in the risk of fractures [63]. The haematopoietic system is damaged, which can lead to anaemia and pancytopaenia, caused mainly by deficiencies of iron, folic acid, and other B vitamins. Patients may report increased gastrointestinal symptoms such as abdominal pain, heartburn, and nausea, which can also be aggravated by disease-related stress and sub-depressive or depressive states. [63]. This fact further adds to the complexity of the problem, as inadequate food intake is compounded by impaired food absorption. Metabolic abnormalities, including electrolyte disturbances and hypophosphatemia, pose additional risks [64] to both the cardiovascular and skeletal systems. All these phenomena occurring in AN compel us to emphasise the importance of comprehensive treatment of these complications.

Pregnant women with AN are at higher risk for obstetric complications than women without the disorder. Complications can include a higher risk of early pregnancy loss, risk of bleeding, abnormal placental implantation, and associated gestational hypertension and pre-eclampsia. Due to a weaker immune system, there is an increased risk of infection, including systemic infections and vaginal and genital infections. As a result of impaired secretion of pancreatic hormones, there is a greater tendency for pregnant women with anorexia to develop gestational diabetes. There is an increased risk of preterm labour and an increased number of caesarean sections [65]. These risks can be attributed, at least in part, to hormonal imbalances, nutrient deficiencies, and excessive stress on the body resulting from the physiological course of pregnancy in a woman with AN (Tab. 5).

Effects of anorexia nervosa on foetal development

In addition to the traditional role of the placenta to transfer nutrients and oxygen between the mother and foetus, it should be remembered that the placenta is the site of synthesis and modification of many hormones, not just steroid hormones. Low concentrations of oestrogen and progesterone in women with AN may interfere with the normal implantation of the chorionic villi in the early stages of pregnancy and be the cause of abnormal function of the placenta in its later stages. The clinical effect of impaired placentation can be all

Table 5. *Adverse consequences of anorexia in pregnancy* [70-72]

Pregnant	Foetus*
Miscarriages	Low birth weight
Premature births	Low Apgar score
Anaemia	More frequent birth defects
Hypertension	Smaller head circumference
Bleeding from the genital tract	Breathing problems
Surgical termination of pregnancy	Delayed development
Forced hospitalisations	Impaired appetite, eating disorders
Forced parenteral nutrition	Higher infant mortality rate
Problems with breastfeeding	Depression
Postpartum depression	Growth and developmental disorders
	Cognitive process disorders

*As a result of nutritional deficiencies, teratogenic and embryotoxic effects of diuretics and laxatives

Table 6. *Additional tests and procedures (in addition to the tests resulting from regional recommendations) that should be performed during pregnancy in a woman with anorexia* [73]

Additional tests anorectic pregnant women
Determination of sodium, potassium, magnesium, phosphate, chloride, iron, vitamin D
Periodic assessment of blood glucose and HbA_{1c} concentration
Assessment of liver function: transaminases: AST, ALT and GGTP aminotransferase
Assessment of bone marrow function (including complete blood count, white blood cell count, neutrophil count, platelets, and haemoglobin)
Assessment of inflammatory markers CRP
Assessment of cardiac function (electrocardiogram and echocardiogram, measurement of blood pressure and pulse in the lying and standing position, and body temperature
Widening the diagnosis depending on the complications occurring in the course of pregnancy

HbA_{1c} — glycated haemoglobin; ALT — alanine aminotransferase; AST — aspartate aminotransferase; GGTP — gamma-glutamyl transpeptidase; CRP — C-reactive protein

pregnancy complications from the hypertensive spectrum [66], and it can negatively affect foetal growth and development. Poor maternal weight gain, nutrient deficiencies, and impaired placental function can result in intrauterine growth restriction (IUGR) or low birth weight [67]. These factors are involved in so-called foetal programming and may contribute to long-term health consequences for the child, including increased risk of metabolic disorders, cardiovascular disease, and neurodevelopmental delays [68]. Disturbed hormonal profiles in AN can affect neurodevelopmental processes in the foetus, potentially leading to cognitive impairment, behavioural problems, and psychiatric disorders in the offspring [69, 70]. The exact mechanisms underlying these effects require further study.

Another complication that realistically threatens pregnant women with AN is preterm labour (including iatrogenic preterm delivery) and lower birth weight [71]. This is mainly due to reduced tissue strength, immune dysfunction, and increased risk of infection.

All these factors can affect the immediate and long-term health outcomes of the newborn. In addition, it has been noted that infants born to mothers with AN may experience difficulties in adapting to the ectopic environment. They may exhibit feeding difficulties, problems with body temperature regulation, and increased susceptibility to infections [72]. The increased risk of developing ED and mental illness in the offspring requires further study.

Management and interventions for pregnant women with anorexia nervosa

Pregnancy in a woman with AN carries high risk. Multidisciplinary and comprehensive care involving cooperation between obstetricians, psychiatrists, nutritionists, and other health professionals for pregnant women suffering from AN is extremely important. Table 4 summarises the parameters that must be monitored. In addition to regular monitoring of nutrient

Table 7. *Life-threatening parameters in a pregnant woman with mental anorexia nervosa that are absolute indications for hospitalisation without the patient's consent* [73]

Parameters	Results
Body weight	BMI < 16–15 kg/m² or a decrease in body mass of more than 25% of the normal weight
Cardiovascular system	Heart rate < 50/min during the day and/or < 40/min at night
	Systolic blood pressure < 90 mm Hg
	Orthostatic changes in heart rate and pressure: increase of > 20 beats/min and/or decrease of > 10 mm Hg
	Arrhythmia
Electrolyte disturbances	Mainly hypokalaemia
Body temperature	< 36.5°C
Neurological disorders	Muscle pain, paraesthesia, hemiparesis, visual disturbances
Infections	↑ CRP, leukocytosis, fever, cough, rapid pulse

BMI — body mass index; CRP — C-reactive protein

levels, liver function, bone marrow function, inflammatory markers, and cardiac function, the role of regular assessment of body weight, blood pressure, body temperature, and vital signs is emphasised.

The most important factors in caring for a pregnant woman with AN appear to be nutritional rehabilitation and ensuring adequate weight gain. Close monitoring of the mother's nutritional status must include monitoring the intake of specific nutrients. Nutritional counselling should be conducted, and individualised meal plans should be prepared. Criteria for admission to nutritional rehabilitation usually include weight loss. During pregnancy, admission may also be based on insufficient weight gain or low gestational weight. A maternal BMI of less than 18 kg/m² (with a pre-pregnancy BMI of 18 kg/m² or less) should raise concerns about nutritional support. Additionally, suboptimal foetal growth, or significant changes in blood parameters or physiological markers should prompt consideration of nutritional support. Malnutrition during pregnancy can lead to inappropriately low heart rates, conduction abnormalities, and hypoglycaemia, all of which require admission to restore nutrition [73]. Table 7, outlining life-threatening parameters in pregnant women with anorexia nervosa, highlights the absolute indications for hospitalisation without patient consent.

Non-pregnant patients with AN are often deficient in iron, folic acid, zinc, and vitamin A, so these levels should be monitored if pregnancy occurs [74]. In addition to the routinely used iodine and folic acid in pregnant women, patients with AN may additionally require routine thiamine supplementation. Supplementation with iodine and vitamin D at higher than standard doses as well as vitamin B12 D and electrolytes should also be considered [75]. These patients are at much higher risk for osteoporosis because they begin pregnancy with compromised calcium reserves in their bones [76]. Increased intake of calcium-rich foods should be recommended to improve calcium absorption. Vitamin A requirements increase slightly during pregnancy, but care should be taken to avoid excessive intake [75]. If vitamin A deficiency is suspected, supplementation with beta-carotene rather than retinol is preferred during pregnancy [77].

Hypokalaemia, common in women with anorexia nervosa, requires more than just oral potassium

Table 8. *The procedure of forced treatment in the case of life-threatening pregnancy with anorexia in Poland* [85, 86]

Forced treatment in the case of life-threatening pregnancy with anorexia in Poland
Consent of the Guardianship Court having jurisdiction over the patient's domicile
The application is submitted by the family, the attending physician in the ward, or the consulting psychiatrist
The application should be submitted within 48 hours of admission to the hospital
Treatment of anorexia without the patient's consent – procedure: • admission to the hospital • restraint or immobilisation in a situation of significant agitation or aggression • forced administration of medication • forced feeding (gastric probe, parenteral nutrition) • behavioural methods to force weight gain (including isolation from family, deprivation of personal items, or cutting off from amenities offered by the hospital)

Abnormal eating behaviour is undertaken by one in five expecting women, and 1.5–5.0% develop pregorexia. If a pregnant woman's weight is less than 85% of the recommended weight for her age and height and expected weight gain during pregnancy, gestational anorexia can be diagnosed.

Figure 1. *Insufficient body weight in a pregnant woman*

Lack of menstruation is common among women with AN.
Women with AN are twice as likely to have an unplanned pregnancy because ovulation can occur in the absence of menstruation.

Unplanned pregnancy increases the likelihood that a woman is unaware of her pregnancy, delays prenatal care, engages in unsafe behaviours and does not receive adequate nutrition, increasing the risk to both mother and foetus. Contraception should be discussed with all patients with AN.

Figure 2. *Contraception in a woman with anorexia nervosa (AN)*

supplementation. First and foremost, the risk of vomiting must be minimised. This can be especially difficult when nausea and hyperemesis gravidarum overlap. If hypokalaemia persists longer, magnesium deficiency should be ruled out, which would indicate the need for magnesium supplementation. If the medical history is not too long and the patient experienced rapid weight loss immediately before pregnancy, consider multivitamin supplementation with ingredients analogous to recommendations for pregnant women after bariatric surgery: folic acid, iodide, iron, calcium, thiamine, zinc, selenium, copper, magnesium, biotin, riboflavin B2, niacin B3, pyridoxine B6, vitamin C, vitamin D, vitamin A, vitamin E, vitamin K, and vitamin B12 [77]. In chronic AN, well established compensatory mechanisms can lead to unpredictably low levels of vitamins and minerals in the blood. Therefore, an individualised approach should be taken, their concentrations monitored, and supplementation guided.

In addition to optimal treatment of somatic and hormonal complications of AN in pregnant women, the role of psychiatric treatment and psychological therapy should be emphasised [78, 79]. The decision as to the use of pharmacological treatment during pregnancy requires consideration of the classic risks to the mother and foetus, including the possibility of placental transfer of the drug or its metabolites. When conducting pharmacological treatment, one should follow the principles of using the lowest effective doses possible and avoiding the use of multidrug therapy [80]. Unfortunately, most psychiatric drugs lack evidence of safety in pregnancy. This leads to inconsistent findings regarding the risk of short-term complications in the foetus and newborn and long-term complications in children and adolescents [81]. Clinicians must support informed decision-making by the patient. The patient and her relatives should be interviewed before deciding whether to include drug treatment. It should be emphasised that the risks of drug treatment should be weighed against the risks of untreated disease, which, especially in the case of AN, can adversely affect pregnancy and infant outcomes [82]. Psychological support, therapy, and counselling should be an integral part of the treatment plan. Cognitive-behavioural therapy (CBT), family therapy, and support groups can be very helpful in promoting recovery and preventing relapse [83, 84].

In the Polish legal system, there is a specific procedure for compulsory treatment in cases of life-threatening AN. It involves obtaining the approval of the guardianship court for such treatment. The application to the court can be submitted by the patient's family, attending physician, or consulting psychiatrist. Coercive treatment without the patient's consent can include hospitalisation, restraint in cases of significant agitation, forced administration of medication, and forced feeding by methods such as gastric probes or parenteral nutrition. Behavioural methods to encourage weight gain, including isolation and deprivation of personal belongings, may also be used. This approach is designed to protect health and well-being. In the case of pregnant women in the most critical situations, the matter becomes more complicated, because not only the mother, but also the yet-to-be-born child must be kept in mind [85].

Conclusions

Unlike mood, anxiety, and psychotic disorders, limited guidelines and research are available on the management of AN during pregnancy. Health guidelines make little mention of the assessment and treatment of EDs during pregnancy. Available recommendations say little about the somatic complications that pregnancy adds to the already difficult medical situation of women with AN. The urgent need for research should be underscored due to the increasing prevalence of restrictive EDs in pregnancy.

Author contributions

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