Chapter

Addressing a Key Metabolic Component of PCOS: Insulin

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Abstract

This chapter addresses insulin - a key metabolic component of polycystic ovary syndrome (PCOS), that manifests as insulin resistance and/or hyperinsulinemia, which are prevalent in 65–95% of women with this complex condition. Insulin, insulin resistance, hyperinsulinemia, markers of insulin, and common health conditions associated with their pathophysiology are reviewed. The chapter also concentrates on nutrition as a viable, effective, evidence-based lifestyle option. Common nutritional approaches and the impact they have are presented. A low-insulin lifestyle approach is discussed as an effective intervention for PCOS management. Finally, this chapter presents research that supports the efficacy of a low-insulin lifestyle. Addressing this key metabolic dysfunction is essential for reducing comorbidities and improving the overall quality of health and quality of life in those with PCOS.

Keywords: polycystic ovary syndrome, insulin resistance, nutrition, lifestyle, low-insulin lifestyle, metabolic dysfunction

1. Introduction

PCOS is the most common metabolic-endocrine disorder, affecting individuals from adolescence through post-menopause [1, 2]. This complex, heterogeneous condition consists of multiple signs and symptoms. Although the etiology has not yet been identified, hyperandrogenemia and insulin resistance (IR) are the primary pathophysiological processes that appear to drive PCOS [3]. This chapter discusses hyperinsulinemia as a key metabolic component of PCOS. This chapter will review the physiological and pathological roles of hyperinsulinemia, along with markers used to assess insulin status. It will also discuss common health conditions associated with dysfunctional insulin activity an overview of dietary lifestyle management options will be provided, with an emphasis on low-insulin lifestyle management. Finally, current scientific evidence supporting the effectiveness of a low-insulin lifestyle approach will be reviewed.

2. Insulin

2.1 Physiology

Insulin is a principal anabolic peptide hormone responsible for the metabolic and mitogenic activity of targeted cells in multiple organs. Its intracellular mechanisms

begin with production in the β-cells of the pancreas from the islets of Langerhans, continuing on to partial clearance by liver hepatocytes, followed by delivery and action on vascular endothelium, the brain, muscle fibers, and adipocytes, and ending with insulin degradation in the kidney [4].

Insulin is a modulator of glucose homeostasis. Generally, it is released after ingesting glucose in a process called glucose-induced insulin stimulation. In human cells, glucose transporter 1 (GLUT1) and GLUT3 are the prominent glucose transporters [5]. Once insulin has been released and circulated through the body, it binds to insulin receptors (InsR) on target cell membranes. The InsR is a heterotetrameric receptor tyrosine kinase that is formed by four subunits composed of two extracellular α-subunits and two transmembrane β-subunits [6]. Insulin binding to InsR results in the phosphorylation of insulin receptor substrate (IRS) and the subsequent activation of two primary signaling pathways: the phosphoinositide3-kinase (PI3K)/protein kinase B (Akt) pathway; responsible for the metabolic effects of insulin, such as increased glucose uptake, glycogen synthesis, and protein synthesis, and the mitogen-activated protein kinase (MAPK) pathway; responsible for proliferative and steroidogenic effects [3, 6]. The PI3K/Akt signaling pathway also regulates the translocation of the insulin-sensitive GLUT4 to the membrane of muscle and fat cells for glucose uptake, aiding in glucose homeostasis [5].

In previous studies of lean and obese women with PCOS, cellular and molecular mechanisms of insulin were highlighted, and glucose uptake in insulin target tissues like adipose and skeletal muscles were evaluated [7–9]. It was concluded that although the receptor affinities of insulin are similar in both women with and without PCOS, decreased insulin binding was recorded at the pancreatic β-cell in adipose tissues, resulting in low glucose uptake and insulin sensitivity in women with PCOS compared to those without PCOS. In women with PCOS, as in the general population, the onset of impaired glucose tolerance (IGT) marks a failure of the pancreatic *β*-cell to maintain a state of insulin sensitivity. It is the decreased insulin sensitivity that plagues a large majority of those with PCOS in the form of IR. Insulin resistance in women with PCOS is a major concern due to the negative health outcomes associated with it.

2.2 Pathophysiology

Insulin resistance is defined as an attenuated effect of insulin on blood glucose homeostasis, primarily by less efficient export of glucose from the blood into skeletal muscle, adipose, and liver tissue [10]. Insulin resistance is independent of patients' adiposity, body fat topography, and androgen levels [11, 12]. In PCOS, IR is tissue-selective; skeletal muscles, adipose tissue, and liver lose their sensitivity to insulin, whereas adrenal glands [11, 13], and ovaries remain sensitive [11, 13, 14]. There remains controversy on the direction of cause and effect related to IR and hyperinsulinemia. In diabetic and obesity literature, the dominant paradigm posits that hyperglycemia caused by IR increases β-cell secretion of insulin, resulting in compensatory hyperinsulinemia. On the other side, a framework describes hyperinsulinemia as the primary defect and IR as the protective response of tissues against insulin-induced nutrient overload and metabolic stress [15, 16]. Houston and Templeton presented works to support the view that places IR as the primary defect that causes secondary compensatory hyperinsulinemia, and an alternative framework of hyperinsulinemia as the earlier defect that perpetuates reproductive and metabolic features of PCOS [17]. While debates continue surrounding whether IR or hyperinsulinemia occurs first, the key takeaway for those with PCOS is that there is a dysregulation of insulin causing multiple comorbidities diminishing their quality of health and quality of life.

2.2.1 Hyperinsulinemia

Hyperinsulinemia can both contribute to insulin resistance and arise as a compensatory response to it. It can also develop due to β-cell proliferation or heightened responsiveness of β-cells to nutrient stimulation, potentially driven by chronic overnutrition, triggering increased postprandial insulin secretion [18]. Hyperinsulinemia in the fasted state can arise from inability to regulate basal secretion, resulting in sustained hyperinsulinemia without glucose stimulation [19]. Elevated insulin levels without concurrent IR have been observed in lean PCOS patients. Vrbíková and his colleagues described lean PCOS subjects with higher early-phase glucose-stimulated insulin secretion than controls. They found that lean PCOS subjects had elevated fasting insulin despite normal insulin sensitivity in hyperinsulinemic euglycemic clamps [20]. This point is critical, as later in the chapter, we will discuss a low-insulin lifestyle approach aimed at addressing the harmful effects of elevated insulin levels in individuals with PCOS—shifting the focus from weight management to metabolic health.

3. Insulin markers

As we shift the focus to metabolic health, evaluation and monitoring of physiological events influenced by insulin activity are essential. When evaluating the influence of insulin on those with PCOS, the use of insulin as an assessment marker is not typically supported, but rather markers for IR. When considering monitoring insulin levels, Kahn and colleagues suggested PCOS insulin secretion should always be examined in the context of peripheral insulin sensitivity rather than in isolation [21]. Kahn and colleagues also highlight an important issue: the interpretation of serum insulin levels, both fasting and post-glucose stimulation. The liver plays a central role in maintaining glucose and insulin homeostasis. In insulin-resistant individuals, such as those with PCOS, it becomes challenging to assess not only the pancreas' compensatory capacity but also the influence of hepatic, renal, and peripheral tissue insulin clearance on circulating insulin levels. In light of these challenges, insulin alone has not been clinically accepted as a practical assessment, however, researchers contend that rapid and fast glucose analyses enable them to evaluate IR. For this purpose, homeostatic model evaluation (HOMA), quantitative insulin sensitivity check index (QUICKI), and fasting glucose and insulin levels have been established and utilized in clinical research and metabolic investigations of insulin activity in PCOS [22–25]. Although these measures are commonly used to evaluate IR, it is worth noting that IR is known to precede the development of abnormal blood sugar levels and/or abnormal HbA1c levels for decades [26]. For this reason, early insulin evaluation is critical for early identification and prevention of IR. Liquid chromatography-tandem mass spectrometry (LC-MS/MS) is an appealing approach for the analysis of insulin because this platform has the capacity to distinguish insulin, proinsulin, C-peptide, and many insulin analogs; unlike immunoassays which come with certain limitations [27]. A significant limitation of immunoassays is that it relies on antibodies for detection which can suffer from non-specificity due to antibody cross-reactivity with proinsulin or partially processed forms of proinsulin [28]. LC-MS/MS technology is a proven and increasingly widespread method that should be considered in clinical use for assessment of insulin levels in women with PCOS.

Whether due to IR or hyperinsulinemia, assessing insulin activity is essential, given its wide-ranging impact. Insulin dysregulation plays a significant role in the

cardiometabolic, endocrine, and reproductive manifestations of PCOS. In the following section, we will discuss common comorbidities closely linked to insulin dysregulation of IR.

4. Comorbidities linked to insulin resistance

4.1 Inflammation, dyslipidemia, hypertension, and cardiovascular disease

Studies have established PCOS as a pro-inflammatory condition marked by chronic low-grade inflammation [29, 30]. Women with PCOS have higher levels of inflammatory markers like C-reactive protein (CRP), leukocytes/white blood cells (WBCs), certain interleukins such as IL-6 and IL-18, and tumor necrosis factor (TNF) [30]. Chronic low-grade inflammation has been associated with obesity, metabolic syndrome, dyslipidemia, hypertension (HTN), endothelial dysfunction, and atherosclerosis, placing those with PCOS at higher risk for long-term metabolic sequelae, such as type 2 diabetes (T2D) and cardiovascular disease (CVD) [31, 32].

Dyslipidemia, the most prevalent metabolic abnormality in PCOS, along with endothelial dysfunction, an early sign of subclinical atherosclerosis, contributes to higher systolic and diastolic BP, making HTN a common clinical concern in these patients [33]. The typical profile of dyslipidemia in PCOS includes decreased HDL cholesterol, increased LDL cholesterol and triglyceride levels [34]. Endothelins are a family of peptides involved in many physiological processes. These processes are linked to several vascular diseases, including as stated above, HTN. Endothelin-1 (ET-1) is a vasoconstrictor peptide that can contribute to vascular structural changes, including thickened artery walls and remodeling and lengthening of small arteries their involvement in PCOS was suggested by the observation that obese and non-obese women with PCOS have higher levels of circulating ET-1 compared with controls [35]. It has been found that hypertensive patients have elevated plasma ET-1 concentrations. Xu and colleagues conducted a meta-analysis that included 450 hypertensive patients and 328 controls and found a potential link between increased ET-1 activity and the development of hypertension. From these findings, Xu and colleagues postulate that it is highly likely that the elevated plasma ET-1 concentrations in hypertensive patients are secondary to HTN and may reflect endothelial cell damage [36].

The causal relationship between aldosterone and IR/hyperinsulinemia remains unclear; Krug and Ehrhart-Bornstein found that hyperinsulinemia is associated with increased aldosterone levels which leads to water retention through complex mechanism impacting sodium and potassium balance potentially contributing to hypertension [37]. Conversely, Colussi and colleagues found that aldosterone itself can worsen insulin resistance, contributing to a cycle of increased aldosterone and HTN [38].

4.2 Obesity

Although there are lean profiles of PCOS, approximately 87.5% of women with PCOS are overweight and 65% are obese [39]. Scientists continue to explore the link between obesity and PCOS, as the exact cause-and-effect relationship remains unclear. While obesity-especially excess visceral and subcutaneous abdominal fat, can worsen PCOS symptoms by increasing insulin resistance, disrupting hormone balance, and contributing to significant metabolic issues, studies have indicated that

it may not be the primary driver of PCOS [15, 30, 40]. The trajectory of weight gain in women with PCOS is a major concern personally and clinically, as phenotypical central obesity-fat around the midsection, worsens IR and PCOS symptoms [29, 41].

4.3 Metabolic syndrome

Polycystic ovary syndrome can be seen as the female-specific form of metabolic syndrome (MetS). Like PCOS the pathophysiology of MetS encompasses several complex mechanisms that are yet to be fully elucidated. Also similar to PCOS, proposed mechanisms, IR, chronic inflammation, and neurohormonal activation are essential players in the progression of MetS and its subsequent transition to CVDs and T2DM [42]. As a syndrome, according to the consensual definition of the International Diabetes Federation, the American Heart Association, and the National Heart, Lung and Blood Institute, MetS is characterized by a clustering of metabolic risk factors, which is defined by the simultaneous occurrence of at least three of the following components: (a) central obesity, (b) dyslipidemia, (c) impaired glucose metabolism, (d) elevated blood pressure (BP), and (e) low levels of high-density lipoprotein cholesterol (HDL-c) [43]. All of the necessary components for Mets are commonly present in PCOS. It is not surprising that the results of a meta-analysis of all studies that assessed the prevalence and risk of MetS in PCOS, regardless of age groups and different methods of confounder control, showed that the odds of MetS among women with PCOS were 2.5-fold higher than in healthy controls [44].

4.4 Diabetes and gestational diabetes

Impaired glucose tolerance, pre-diabetes, diabetes, and gestational diabetes (GDM) are all common metabolic conditions in PCOS. Insulin levels are higher in women with PCOS, which raises their risk of these conditions [45]. Increased insulin levels in early pregnancy (before gestation week 16) are strong predictive factors for GDM by gestational weeks 32–34 [46]. Insulin resistance is a hallmark feature of PCOS. Epidemiological studies have established a strong link between PCOS and an elevated risk of type 2 diabetes, IGT, and GDM. A meta-analysis found that women with PCOS are approximately three times more likely to develop these conditions [47–49].

4.5 Infertility

Reproductive physiology is a complex and delicate interplay of the hypothalamic-pituitary-ovarian (HPO) axis. Interactions that disturb the balance of these elements cause metabolic and reproductive disorders, as seen in PCOS. Women with PCOS are at an increased risk of infertility due to hormonal imbalances related to irregular ovulation or anovulation, which can make it difficult to conceive. Starting from the hypothalamus, gonadotropin-releasing hormone (GnRH) triggers the release of the gonadotropins, follicle-stimulating hormone (FSH) and luteinizing hormone (LH). These gonadotropins exert their action on the ovaries to stimulate follicular growth and ovulation [50]. In PCOS, hyperinsulinemia and hyperandrogenemia play major roles in disruptions to this process by inhibiting follicle growth and, ultimately, ovulation [51, 52]. Additionally, elevated insulin levels are toxic to early placental growth leading to increased risk of miscarriage [53]. While PCOS is a chronic condition, it's often treatable, and many women with PCOS can still become pregnant with treatment.

4.6 MASLD

Metabolic dysfunction-associated steatotic liver (MASLD) previously known as Nonalcoholic fatty liver disease, or NAFLD, is a chronic condition in which fat accumulation occurs in the liver, and is histologically identical to alcoholic liver disease, in patients with no or minimal alcohol consumption [54]. MASLD is a significant contributor to adverse health outcomes due to its potential progression to end-stage liver disease. Insulin resistance plays a key role in the development of this condition, with numerous studies demonstrating a strong association between the two conditions. The prevalence of MASLD is elevated in individuals with obesity, type 2 diabetes, and dyslipidemia—conditions that are also commonly seen in PCOS [55]. Research indicates that MASLD is the hepatic manifestation of metabolic syndrome and that it is highly prevalent among women with PCOS [56, 57].

4.7 Mental health disorders

It is well known that PCOS is associated with a high prevalence of depression and anxiety [58]. No specific mechanism of etiology has been identified, but there are multiple factors that are suggested to play a role. Hyperandrogenemia manifesting as increased body and facial hair, male pattern balding and cystic acne can impact self-esteem and body image. Overweight and obesity, which are present in 65–87% of those with PCOS can also impact self-esteem and body image leading to decreased quality of life [39]. As previously mentioned, visceral adiposity, in particular, contributes significantly to the low-grade inflammatory state of PCOS by producing the cytokines, tumor necrosis factor alfa (TNF-α), Interlukin-6 (IL-6), and interlukin-18 (IL-18), chemokines, and other adipokines, which may also contribute to increased association of mental disorders present in PCOS [30]. Additionally, inhibitory neurotransmitters such as serotonin (5-HT), dopamine (DA), gamma-aminobutyric acid (GABA), and acetylcholine (Ach) are diminished in PCOS [59]. Although there are data to support neuroendocrine involvement in PCOS, there is a lack of neuroimaging studies investigating those processes. Saydam and Yildiz (2021), published a mini review discussing the relevance of central nervous system imaging modalities in understanding the neuroendocrine pathophysiology of PCOS as well as their relevance to understanding its comorbidities. Twelve neuroimaging studies were identified between 2011 and 2020 (Three investigated structural differences and nine investigated functional disturbances). Structural differences via magnetic resonance imaging (MRI) and Functional disturbances via functional magnetic resonance imaging (fMRI) and positron emission tomography and computed tomography (PET CT) provided insight into clinical implications of IR in women with PCOS. Insulin resistance implications included: (a) decreased global and regional brain volumes, (b) altered white matter microstructure, (c) diminished reward response in corticolimbic areas, (d) brain glucose hypometabolism, (e) greater μ-opioid receptor availability in reward related regions, and (f) increased activation during memorial and emotional tasks. Clinical implications due to the presence of IR manifested as: (a) increased non-homeostatic eating, (b) diminished appetitive responses, (c) cognitive dysfunction, and d) mood disorders [60].

Psychological health in PCOS has been neglected as a condition that requires evaluation in the same manner as all the other comorbidities present in PCOS. The Recommendations from the 2023 International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome suggest healthcare

professionals should be aware of the high prevalence of moderate to severe depressive symptoms, depression and anxiety in adults and adolescents with PCOS and should screen for these conditions in all adults and adolescents with PCOS, using regionally validated screening tools [61].

The high prevalence of comorbidities present in PCOS indicates that this condition should be considered a general health problem related to insulin dysregulation rather than primarily a reproductive condition. Whether cause or consequence, there is a critical need to address both hyperinsulinemia and IR in PCOS, where it is worth noting again that 65–95% of those with PCOS suffer from this condition, which includes lean, overweight and obese individuals. The current era of anti-obesity therapy offers pharmacologic tools to improve metabolic, reproductive, and other clinical outcomes in a subset of patients who are overweight or obese, primarily through weight reduction [62]. However, shifting the focus from weight-related issues to the metabolic effects of insulin—as the primary pathophysiological factor influencing individual PCOS phenotypes—is essential for improving the management of all patients with PCOS. As we consider interventions that are inclusive of all PCOS phenotypes, the next section will focus on nutrition and the role it plays in lifestyle management.

5. Nutrition as a viable intervention

Nutrition plays a critical role in the management of PCOS, yet typical dietary recommendations often focus primarily on weight loss without addressing the root problem: elevated insulin levels and IR [63, 64]. Patients are often told to simply "eat less and exercise more," but this approach overlooks how certain foods uniquely affect hormonal regulation, especially insulin [65, 66]. Rather than focusing on calorie reduction, nutritional strategies for PCOS should aim to reduce insulin levels and improve metabolic flexibility. A more effective approach begins with understanding how different foods impact insulin levels, not just calories or macronutrient ratios. This approach is called a low-insulin lifestyle [67].

Lifestyle change is well accepted as a first-line treatment, but those with PCOS often find their efforts frustrating and unsuccessful. While they may attempt calorie restriction, portion control, or increased physical activity, these strategies do not always lead to meaningful improvements, especially when insulin resistance is unaddressed. The issue is often not a result of a lack of willpower or effort, but that traditional weight loss recommendations fail to appreciate the central role that insulin plays in driving PCOS symptoms. Addressing insulin directly, rather than focusing solely on weight, offers a more effective and targeted strategy for improving outcomes.

6. Why insulin should be the primary focus in PCOS

Chronically elevated insulin is one of the key drivers of nearly every symptom associated with PCOS [68, 69]. It contributes to increased androgen production, irregular ovulation, weight gain, acne, and hirsutism. Elevated insulin also suppresses sex hormone-binding globulin (SHBG), increasing the amount of free testosterone circulating in the body. Lowering insulin can help reverse these effects, restoring ovulation, improving skin, reducing cravings, and improving mood and energy. Whether a woman is lean or overweight, focusing on lowering insulin levels is the most effective way to improve both metabolic and reproductive outcomes [70, 71].

7. Dietary approaches and their impact on insulin

7.1 Low fat

Low-fat diets were long considered the gold standard for heart health and weight loss. In PCOS, they are sometimes recommended with the goal of reducing overall calorie intake. However, studies have not found diets low in fat to be successful for long-term weight loss, most likely because these diets often lead to increased consumption of sugar, starch, and processed low-fat products that can spike insulin levels [72]. For individuals with PCOS, this can be counterproductive. Dietary fat plays an important role in hormone production, skin and hair health, and satiety [73]. When fat is removed from the diet, it often leads to increased hunger, cravings, and nutrient deficiencies that can worsen PCOS symptoms.

Rather than avoiding fat, the focus should shift to choosing the right types of fats. Those with PCOS should be encouraged to include plenty of healthy fats from whole food sources like avocados, nuts, seeds, olive oil, coconut, and fatty fish. These fats help increase satiety, promote hormonal balance, and support long-term metabolic health without triggering excessive insulin release.

7.2 Low carbohydrate and ketogenic diets

Low carbohydrate and ketogenic diets are also often recommended for individuals with PCOS. These dietary approaches have been shown to improve metabolic and cardiovascular biomarkers compared to low fat diets [72, 74]. However, low-carb does not always mean low insulin. Certain proteins, such as whey and casein, can still cause a major insulin spike, even though these products are free of carbs. This is because they are highly concentrated in branched chain amino acids (BCAAs), which are potent insulin-spiking amino acids. These BCAAs not only lead to a significant insulin spike, but they also increase insulin-like growth factor one (IGF-1), which is associated with worsened PCOS symptoms such as acne and hirsutism, in addition to other health concerns [12–16, 75–79]. Since whey protein powder is now added to everything from protein bars to pancakes, it could potentially be causing more problems than people realize [80–83].

The ketogenic diet is a very low-carb, high-fat diet, drastically limits fruit and vegetables, which can impact gut health, nutrient intake, and long-term sustainability. Since low-carb and ketogenic diets require consistent carbohydrate tracking, they can often lead to burnout, which is why they are usually difficult to sustain. They can also lead to food obsession and binge eating as people struggle to track macronutrient intake, which could potentially do more harm than good mentally, especially for those already navigating hormonal issues.

7.3 Mediterranean

The Mediterranean diet is often recommended for its heart health benefits and anti-inflammatory approach. It emphasizes fruits, vegetables, whole grains, legumes, olive oil, nuts, seeds, and fish. Some studies have shown that the Mediterranean diet can improve menstrual regularity and reduce inflammation in PCOS. However, the inclusion of whole grains and legumes, foods high in starch, while perhaps beneficial for the general population, can potentially lead to excessive insulin stimulation in those with severe IR [84, 85]. Additionally, while a Mediterranean diet approach may benefit individuals with mild IR or those

transitioning off a standard Western diet, it may not go far enough for individuals with hyperinsulinemia or severe PCOS symptoms. Instead, a focus on healthy fats, non-starchy vegetables, whole fruits, nuts, seeds, and fish without the grains and legumes may be an approach that provides all the benefits of a Mediterranean approach, without excess starch [86, 87].

7.4 Paleo

The Paleo diet emphasizes whole, unprocessed foods and excludes grains, legumes, dairy, and refined sugars. It can be naturally lower in insulin spiking foods and has gained popularity among those with PCOS for its emphasis on protein, vegetables, nuts, and healthy fats. However, depending on how it is implemented, Paleo can be high in sugar and starch if excessive amounts of starchy tubers, honey, or maple syrup are consumed, as well as modern processed starches such as tapioca and cassava which are often added to paleo processed foods.

Additionally, the exclusion of all dairy may limit options that could be included thoughtfully in an insulin-lowering approach. Fermented dairy products, like full-fat Greek yogurt and aged cheeses, contain little to no whey, which is the portion of dairy most responsible for insulin spikes. Fermentation also alters the structure of the proteins, from BCAAs to branched chain keto acids (BCKA), reducing their insulinogenic impact [88, 89]. When included in limited amounts, they can provide beneficial nutrients like calcium and probiotics, without significantly affecting insulin levels [90].

7.5 Plant-based

Plant-based diets, including vegetarian and vegan, are often recommended to improve overall metabolic health. These diets are rich in fiber, antioxidants, and anti-inflammatory foods. However, many plant-based diets are high in starches like grains, beans, and potatoes, which can be problematic for individuals with IR [84, 85, 91]. It's possible to follow an insulin-friendly, plant-based diet, but it requires focusing on non-starchy plant-based proteins, such as edamame, tofu, tempeh, lupini beans, and hemp seeds. These protein options can help ensure you get enough protein without the starch. For those who follow a vegetarian diet, including eggs and fermented dairy products provide additional protein options.

8. What is a low-insulin lifestyle

Unlike traditional dietary recommendations, a low-insulin lifestyle specifically focuses on limiting foods that cause excessive insulin secretion. It focuses on the insulin response to certain foods rather than carbohydrate or calorie content [86, 92–95].

This lifestyle is ideal for individuals with PCOS because it targets hyperinsulinemia directly. Since up to 95% of patients with PCOS have chronically elevated insulin levels, limiting foods that are known to elicit excessive insulin response is ideal for lowering insulin levels, reversing IR, and improving metabolic and reproductive health. Instead of chasing weight loss, this approach helps facilitate weight loss by improving appetite regulation and improving energy levels.

A low-insulin lifestyle emphasizes lean meats, poultry, eggs, and fatty fish, which supply protein without the excessive insulin-spiking effects of whey or casein [67]. Non-starchy plant-based proteins, such as edamame, tofu, tempeh, hemp seeds, and

lupini beans, offer alternatives for those following vegetarian or plant-based diets. Non-starchy vegetables, like leafy greens, cruciferous vegetables, peppers, carrots, tomatoes, and cucumbers, are the foundation of this approach due to their minimal insulin impact and high nutrient density. Whole fruits are included as well; while they contain natural sugars, the fiber content slows absorption and the fructose component does not directly trigger insulin secretion. Healthy fats from sources like avocados, olives, coconut, nuts, and seeds, along with olive, avocado, or coconut oil, are a critical part of this approach. These fats support hormone production, promote satiety, and help stabilize blood sugar without stimulating insulin. Fermented dairy products, such as full-fat Greek yogurt and aged cheese, may be included in limited amounts (e.g., up to 1 serving per day total).

While certain foods are considered "healthy" by conventional standards (e.g., whole grains, beans and legumes, and sweet potatoes), they may still drive chronic insulin elevation [84, 85]. Below are the three most critical food categories that are limited or avoided on a low-insulin lifestyle due to their strong insulin-stimulating effects:

8.1 Starches

Starches are long chains of glucose molecules. Once consumed, the body quickly breaks these chains down into glucose, which is rapidly absorbed into the bloodstream. This rise in blood glucose stimulates a sharp rise in insulin [91, 96]. Starches include foods like bread, pasta, rice, potatoes, oats, corn, and grain-based flours as well as starchy vegetables, such as sweet potatoes. While many nutrition guidelines recommend starches as a core part of a balanced diet, these foods are often counterproductive for someone trying to lower insulin levels.

In addition, modern starches differ from ancient forms in several important ways. Over thousands of years, agricultural practices have selectively bred grains, corn, and potatoes to be larger and sweeter, optimizing them for their starch content while reducing their fiber content. As a result, today's starches are not only more insulin-spiking, but they also lack the natural buffering effect that higher fiber content was meant to provide [97–99].

The way we cook starches worsens this effect. Most starchy foods are boiled, baked, mashed, or otherwise cooked in ways that increase their *gelatinization* [96]. Gelatinization is a process in which starch granules absorb water and swell, making them easier to digest. While this improves taste and texture, it also makes the starch much more accessible to digestive enzymes, which means it is broken down and absorbed even faster, leading to a more rapid and pronounced insulin spike.

Even so-called "whole grain" products are often finely milled or processed, removing much of the intact fiber structure that would otherwise slow digestion. And while starchy vegetables like sweet potatoes or corn do offer some vitamins and minerals, it's important to recognize that all of the essential nutrients found in these foods can also be found in non-starchy vegetables and fruits. The difference is that non-starchy produce offers these benefits without the same degree of insulin stimulation [85].

8.2 Added sugars

It's well known that sugar is one of the most potent stimulators of insulin. This includes not only table sugar but also honey, maple syrup, agave, coconut sugar, and even so-called "natural" sweeteners like fruit juice or date syrup. These sugars are rapidly absorbed and drive a sharp insulin response, even in small amounts.

Chronically elevated insulin drives frequent hunger and intense cravings, especially for sugary, processed foods. The more sugar consumed, the more insulin is released, creating a cycle that's hard to break [66]. Unfortunately, many foods marketed as healthy still contain hidden sugars, keeping insulin levels elevated throughout the day. A low-insulin lifestyle removes or strictly limits added sugars, helping to break this cycle. It encourages whole foods and allows for occasional use of non-insulinogenic sweeteners like erythritol, allulose, monk fruit extract, or stevia.

8.3 Dairy

Milk is a food designed by nature to promote rapid growth [100, 101]. It naturally contains both insulin and insulin-like growth factor 1 (IGF-1), two powerful growth promoting hormones. These play an important role in milk's biological purpose: to help newborn mammals grow quickly during their earliest stage of life. While this is beneficial for infants, chronically elevated insulin and IGF-1 can be problematic in adults, especially those with PCOS [77, 102].

In addition to the hormones naturally present in milk, dairy proteins, particularly whey, are highly insulinogenic [80, 82]. This means they stimulate a significant insulin response, even when there's very little carbohydrate or sugar involved. In fact, whey protein is one of the most insulin-stimulating components of the human diet. Clinical studies have shown that whey triggers a strong insulin release independent of its effect on blood glucose [80]. Considering the widespread use of whey protein among food products, often marketed as "high protein," this may have unintended consequences. It is a potentially hidden contributor to chronic hyperinsulinemia in susceptible individuals.

For individuals with PCOS, this is especially concerning. High insulin levels are already a key driver of hormonal imbalance, and regular consumption of insulin-stimulating dairy products can further worsen the cycle. Elevated insulin promotes increased androgen production, disrupts ovulation, and contributes to acne, hirsutism, and irregular menstrual cycles.

Dairy also increases circulating levels of IGF-1, a hormone that shares structural similarities with insulin and stimulates cell growth and hormone production [77, 103]. In women with PCOS, who are already prone to elevated androgens and acne, increased IGF-1 can worsen these symptoms. Numerous studies have linked dairy consumption with higher IGF-1 levels and an increased risk of acne and symptoms of hormonal imbalance [95, 104–106].

However, not all dairy products affect the body in the same way. Fermented dairy products like full-fat Greek yogurt and aged cheeses undergo a bacterial fermentation process that alters the protein structure and reduces their insulin stimulating properties [88–90]. Because of this, a low-insulin lifestyle allows for limited consumption of full fat Greek yogurt and aged cheese.

Importantly, there is no nutrient in dairy that cannot be obtained elsewhere. Calcium, potassium, vitamin D, and protein can all be found in other whole foods like leafy greens, chia seeds, almonds, and fortified non-dairy milks as well as fermented dairy products.

9. Scientific evidence supporting a low-insulin lifestyle

Multiple clinical trials have evaluated a low-insulin lifestyle as an intervention for PCOS and found consistent improvements in insulin sensitivity, menstrual function, and weight reduction [86, 92–94].

Studies using this approach have reported up to a 52% reduction in fasting insulin, with improvements in both HOMA-IR and QUICKI scores observed in just 8 weeks. Across three prospective clinical trials, including one randomized controlled trial comparing the approach to standard care plus metformin, participants lost an average of 12 to 19 pounds in 8 weeks without pharmacologic intervention. These trials also documented increases in fat oxidation, indicating improved metabolic flexibility and an improved ability to utilize fatty acids for energy. Despite their short duration, the studies showed significant reductions in hemoglobin A1c, as well as marked improvements in triglyceride levels and free testosterone, key markers of cardiometabolic and reproductive health in PCOS. Together, these results highlight the rapid and multisystem benefits of reducing insulin through targeted nutritional intervention.

In addition to biomarker improvements, participants experienced reductions in acne, mood stabilization, more consistent energy, and fewer cravings. A case series also documented spontaneous pregnancies in individuals who had previously experienced infertility [92]. Couples conceived on average 86 days of starting a low-insulin lifestyle approach.

Most recently, a systematic review and meta-analysis further supported these findings, concluding that low insulin dietary strategies are effective for improving metabolic parameters and reproductive outcomes in PCOS [95].

10. Conclusion

This chapter has provided a brief overview of the physiology and pathophysiology of insulin, as well as common markers used in the evaluation of insulin status within PCOS. Metabolic dysfunctions characterized in the various comorbidities that exist in PCOS were presented. These comorbidities stress the need to consider PCOS as metabolic disorder and not primarily a reproductive condition. Given its prevalence and the impact it has on health and quality of life in lean, overweight and obese individuals with this condition; a narrative shift is necessary. Rather than centering care around weight management, the focus must shift toward improving metabolic health and addressing the root driver: elevated insulin levels. Early screening for hyperinsulinemia is critical, as it allows for timely intervention before more severe symptoms and complications develop. A low-insulin lifestyle offers a targeted, evidence-based, and sustainable approach that addresses hyperinsulinemia directly. Multiple prospective trials have demonstrated its ability to significantly improve weight, insulin sensitivity, and hormonal balance, without the need for medications. This lifestyle approach has the potential to be a meaningful part of the solution for improving the health and quality of life for individuals with PCOS.

Conflict of interest disclosure

Ali Chappell is the Founder and CEO of Lilli Health, a digital health company focused on providing education for individuals with insulin resistance and PCOS.

DOI: http://dx.doi.org/10.5772/intechopen.1010981

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