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Review Article

**THE IMPACT OF KETOGENIC DIET ON HORMONE LEVELS
IN WOMEN WITH POLYCYSTIC OVARY SYNDROME:
A SYSTEMATIC REVIEW**

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Abstract:

Background: There is a complex and multifaceted association between hormone levels in women with Polycystic Ovary Syndrome (PCOS) and the ketogenic diet. **Objectives:** To conduct a thorough evaluation and analysis of the literature on the impact of the ketogenic diet on PCOS-affected women's hormone levels. **Methods:** A comprehensive exploration of relevant databases was conducted to identify studies meeting the inclusion criteria. To locate relevant literature, a comprehensive search of PubMed, Web of Science, SCOPUS, and Science Direct was carried out. The entire procedure made use of the Rayyan QRCI. **Results:** Six trials including 506 women in total were included in our data. The follow-up duration ranged from 45 days and 12 weeks. All of the included studies recorded significant reductions in the mean levels of total testosterone and LH/FSH ratio following the ketogenic diet women among women with PCOS. The ketogenic diet also positively affected menstrual regularity, metabolic parameters, anthropometric parameters, and endocrine parameters. Thus, ketogenic diet is a potential treatment option for PCOS. **Conclusion:** The extent to which these findings may be extensively applied to the PCOS community is limited by the numerous concerns that remain in the accessible literature and require closer examination. However, these findings have important treatment implications, and endocrinologists, gynecologists, and dieticians should carefully plan and modify particular meal recommendations for women with PCOS. Finding the potential for nutritional therapies that can support individualized preventive tactics to safeguard fertility beginning in youth is critical given the long-term effects of PCOS.

Keywords: Ketogenic diet, hormone levels, Polycystic Ovary Syndrome, endocrine disorders, testosterone, hormonal balance, metabolic health, hormone regulation.

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BACKGROUND:

Women who are of reproductive age often suffer from PCOS, a prevalent endocrine condition. Hormonal abnormalities, irregular menstrual periods, and ovarian cysts are its defining features. Since many PCOS-afflicted women have insulin resistance, which can result in elevated blood levels of insulin, insulin is one of the major hormones involved in PCOS [1].

The high-fat, moderate-protein, low-carb ketogenic diet has become more well-known in recent years due to its possible health advantages, which include enhanced insulin sensitivity and weight loss. According to some research, women with PCOS may experience improved hormone levels when following a ketogenic diet [2].

Reducing insulin levels is one of the key ways that the ketogenic diet may impact hormone levels in PCOS-affected women. The ketogenic diet can help control hormone levels by lowering blood sugar and improving insulin sensitivity through carbohydrate restriction [3]. Given that insulin resistance is a typical symptom of PCOS, this may be especially helpful for female patients [4].

The ketogenic diet may have an impact on other hormones linked to PCOS in addition to insulin levels. For instance, research has indicated that the ketogenic diet may assist in lowering testosterone levels, which are typically increased in PCOS-affected women [5]. Symptoms including irregular menstruation periods, hirsutism (excessive hair growth), and acne can all be attributed to high testosterone levels. The ketogenic diet may help with these symptoms and enhance overall hormonal balance by reducing testosterone levels [6].

Furthermore, the ketogenic diet may also have an impact on other hormones such as cortisol and thyroid hormones, which can be dysregulated in women with PCOS. Some research has suggested that the ketogenic diet may help reduce levels of cortisol, a stress

hormone that can contribute to insulin resistance and other hormonal imbalances. Additionally, the

ketogenic diet may support thyroid function, which is important for regulating metabolism and hormone production [5].

It's crucial to remember that while the ketogenic diet might benefit some women with PCOS, there is no one-size-fits-all solution. Some women might discover that the ketogenic diet is not for them, or they might need to adjust it to better fit their needs [7].

Hormonal imbalances are common in PCOS-afflicted women, and these imbalances can result in a number of health issues, including irregular menstrual periods, infertility, and an increased risk of heart disease and diabetes. There is a paucity of thorough research about the ketogenic diet's effects on hormone regulation in women with PCOS, and its impact on hormone levels in this particular population is not well understood.

This study is noteworthy because it attempts to close a gap in the literature by offering a comprehensive analysis of how the ketogenic diet affects hormone levels in PCOS-affected individuals. The management and treatment of PCOS may be significantly impacted by our understanding of the possible effects of the ketogenic diet on hormone control in this group. It may also provide insight into dietary treatments that may be used to improve hormone balance and general health in PCOS-affected women.

Study Aim

The aim of this study is to conduct a systematic review to evaluate the impact of the ketogenic diet on hormone levels in women with PCOS, synthesizing and analyzing the existing evidence to provide insights into the potential effects of ketogenic diet on hormone regulation in this specific population.

Study Objectives:

1. To conduct a thorough evaluation and analysis of the literature on the impact of the

ketogenic diet on PCOS-affected women's hormone levels.

2. To assess the impact of the ketogenic diet on specific hormones implicated in PCOS, such as insulin, testosterone, and estrogen.
3. To identify potential gaps and limitations in the current literature on the relationship between ketogenic diet and hormone regulation in women with PCOS.
4. To provide evidence-based recommendations for future research and clinical practice regarding the use of the ketogenic diet for hormone regulation in women with PCOS.

Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [8] criteria were applied in this systematic review. To find pertinent research published in English, a comprehensive electronic search through online databases including PubMed, Web of Science, SCOPUS, and Science Direct was carried out. Keywords pertaining to the link between ocular problems and endoscopic sinus surgery were included in the search strategy. Independently, two reviewers went through the search results, chose relevant papers, retrieved data, and used the right evaluation instruments to determine the included research's quality.

Eligibility Criteria

Inclusion Criteria:

1. Studies conducted on women diagnosed with PCOS.
2. Studies that investigate the impact of the ketogenic diet on hormone levels in women with PCOS.
3. Cohort studies, case-control investigations, observational studies, randomized controlled trials, and cross-sectional studies.
4. Studies that report quantitative data on hormone levels (Total testosterone and LH/FSH ratio) before and after following a ketogenic diet.
5. Studies with a sample size of at least 10 participants.

Exclusion criteria:

1. Studies not focused on women with PCOS.
2. Studies that do not investigate the impact of ketogenic diet on hormone levels.
3. Animal studies, review articles, case reports, and editorials.
4. Studies with insufficient data on hormone levels.

5. Studies with a sample size of less than 10 participants.

Data Extraction

To guarantee correctness, the search results were validated using Rayyan (QCRI) [9]. Titles and abstracts found in the search results were evaluated for relevancy using both inclusion and exclusion criteria. Papers that satisfied the inclusion requirements were carefully examined by the study team. Discussion was used to settle any disagreements. Key study information, including titles, authors, publication year, study location, participant number, age, follow-up duration, total testosterone before and after the ketogenic diet, LH/FSH ratio before and after the ketogenic diet, and outcomes, will be recorded using a preset data extraction template. An independent document was made to assess the potential for bias.

Data Synthesis Strategy

Using information from relevant studies, summary tables were made to provide a qualitative evaluation of the research findings and its constituent parts. The optimal approach for utilizing the data from the included studies was determined after the data collection for the systematic review.

Risk of Bias Assessment

The Joanna Briggs Institute (JBI) [10] critical assessment criteria for studies reporting prevalence data were applied in order to evaluate the study's quality. There are nine questions in this tool. replies that are negative, ambiguous, or irrelevant are scored zero, whereas replies that are positive are scored one. Less than four, five to seven, and more than eight ratings will be divided into three categories: low, moderate, and exceptional quality, respectively. Academics assessed the work's quality independently, and differences were resolved through debate.

The Cochrane Collaboration Risk of Bias (ROB) tool [11] was used to assess the risk of bias in the included randomized control trials. The results are shown in a table with different color schemes. Red denotes a large bias risk, green denotes a low risk, and yellow denotes an inability to determine the risk due to insufficient information.

RESULTS:

Search results

After 489 duplicates were removed, a total of 991 study papers were found through a systematic search. After 502 studies had their titles and abstracts

evaluated, 466 papers were discarded. Merely four things were not located out of the 36 reports that were required to be retrieved. 32 papers were screened for full-text assessment; 17 were rejected because the study results were wrong, 7 because the population

type was inaccurate, and 2 were abstracts. Six research publications in this systematic review satisfied the requirements for eligibility. An overview of the procedure used to choose the research is illustrated in **Figure 1**.

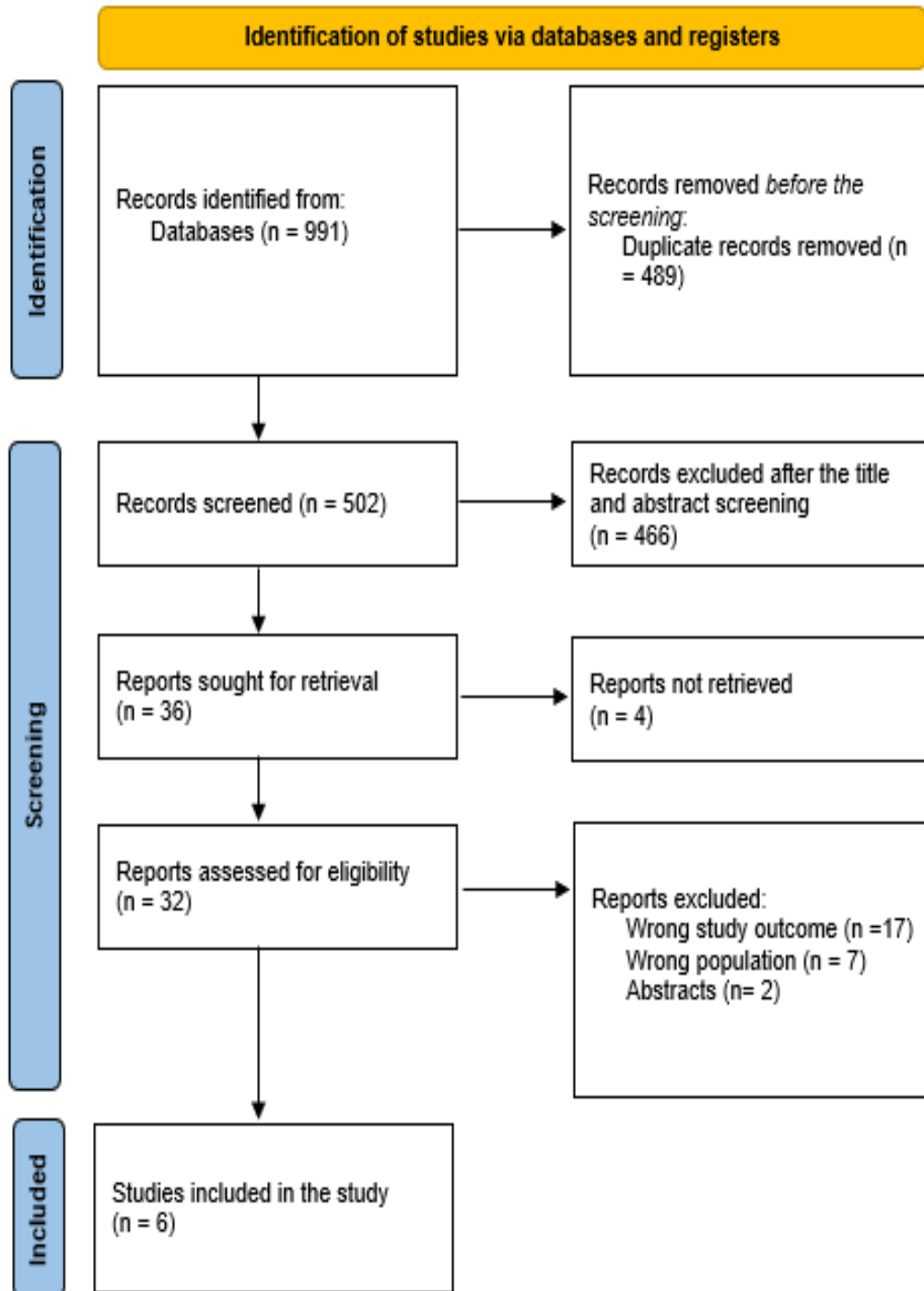


Figure (1): Study decision is summed up in a PRISMA diagram.

Sociodemographic features of the comprised studies

The research publications' sociodemographic information is displayed in **Table 1**. Six trials including 506 women in total were included in our data. Four studies were randomized control trials (RCTs) [14-17], one was a case-control study [12], and one was a prospective cohort [13]. Three studies were conducted in Pakistan [12, 15, 16], two in Italy [13, 14], and one in China [17]. The earliest study was conducted in 2020 [14] and the latest in 2024 [12].

Clinical outcomes

The clinical features are displayed in **Table (2)**. The follow-up duration ranged from 45 days [13, 15] and 12 weeks [12, 14, 16, 17]. All of the included studies

recorded significant reductions in the mean levels of total testosterone and LH/FSH ratio following the ketogenic diet women among women with PCOS. The ketogenic diet also positively affected menstrual regularity [12, 17], metabolic parameters [12, 15], anthropometric parameters [15, 16], and endocrine parameters [15]. Thus, ketogenic diet is a potential treatment option for PCOS.

Risk of bias

Two studies were non-randomized designs and assessed using the JBI tool [12, 13]; both were at moderate risk of bias. Four studies were RCTs and we evaluated them using Cochrane presented in **Figures (2 & 3)** [14-17]. **Table (1): The sociodemographic attributes of the participating populations.**

Study	Study design	Country	Participants	Mean age
Naveed et al., 2024 [12]	Case-control	Pakistan	320	28.1±4.2
Cincione et al., 2021 [13]	Prospective cohort	Italy	17	28.5 ± 5.38
Paoli et al., 2020 [14]	RCT	Italy	24	18-45
Masood et al., 2023 [15]	RCT	Pakistan	80	18-45
Khalid et al., 2023 [16]	RCT	Pakistan	47	18-45
Li et al., 2021 [17]	RCT	China	18	31.13 ± 3.64

Table (2): Clinical features and results of the included research.

Study	Follow-up (weeks)	Total testosterone before diet (ng/dL)	Total testosterone after diet (ng/dL)	LH/FSH ratio before diet	LH/FSH ratio after diet	Main outcomes	JBI
Naveed et al., 2024 [12]	12	80±15	60±10	NM	NM	The enhancements seen in menstrual regularity and metabolic parameters bolster KD's possible use as a therapeutic intervention in PCOS management.	Moderate
Cincione et al., 2021 [13]	45 (days)	39.08 ± 20.88	31.74 ± 16.82	2.72 ± 1.30	1.4 ± 0.96	The outcome of PCOS is improved by the ketogenic diet.	Moderate
Paoli et al., 2020 [14]	12	47.43±6.08	40.71±5.77	2.00 ± 0.3	1.15 ± 0.2	Ketogenic diet as a potential treatment option for PCOS, should be used in conjunction with a more well-balanced diet, but always paying special attention to the quantity of carbohydrates.	NA
Masood et al., 2023 [15]	45 (days)	39.89±17.38	29.68±13.89	2.7±2.3	1.09±1.3	After a ketogenic diet, anthropometric, metabolic, and endocrine indicators showed a more significant improvement in overweight or obese PCOS women.	NA
Khalid et al., 2023 [16]	12	NM	NM	2.03 ± 0.12	1.22 ± 0.106	In overweight individuals, a ketogenic Mediterranean diet plus phytoextracts showed a significant reduction in BMI.	NA
Li et al., 2021 [17]	12	NM	NM	1.58 ± 0.76	0.86 ± 0.32	The ketogenic diet enhanced menstrual cycle, lowered blood glucose and body weight, enhanced liver function, and corrected fatty liver in obese women with PCOS and liver dysfunction in comparison to usual pharmacological treatment.	NA

*NM=Not-mentioned

*NA=Not-applicable

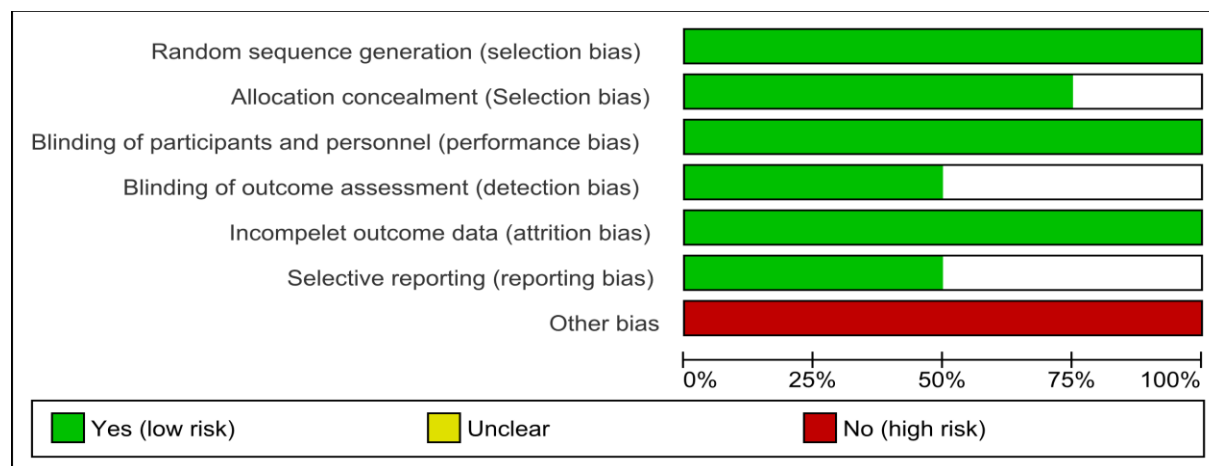


Figure 2: Bias risk graph.

	Random sequence generation (selection bias)	Allocation concealment (Selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Khalid et al., 2023	+		+	+	+	+	!
Li et al., 2021	+	+	+		+		!
Masood et al., 2023	+	+	+	+	+		!
Paoli et al., 2020	+	+	+		+	+	!

Figure (3): Bias risk summary.

DISCUSSION:

Using information from 506 individuals, this thorough analysis evaluated the evidence of a connection between reproductive hormone levels and the ketogenic diet in PCOS-affected women. Following the ketogenic diet, we observed a substantial decrease in the mean levels of both total testosterone and the LH/FSH ratio in PCOS-affected women. Menstrual regularity [12, 17], metabolic parameters [12, 15], anthropometric parameters [15, 16], and endocrine parameters [15] were all positively impacted by the ketogenic diet. Consequently, one possible PCOS treatment option is the ketogenic diet. A possible connection between a ketogenic diet and higher levels of reproductive hormones in PCOS-affected women was revealed by Khalid et al. in their systematic review and meta-analysis [18].

A variety of environmental (acquired obesity) and genetic (insulin resistance, insulin secretory deviations, hyperandrogenemia, polycystic ovarian morphology) variables combine to cause PCOS, a

complex condition. The disorder's complex pathophysiology attests to the condition's diverse nature and heterogeneous expression [19]. An aberration in the gonadotropin-releasing hormone (GnRH) secretory pattern, which upsets the hypothalamic-pituitary-ovarian or adrenal axis and results in a relative increase in the ratio of LH to FSH, is closely linked to the pathophysiology of PCOS. In healthy women, the LH to FSH ratio normally falls between 1 and 2, but in those with PCOS, it may even approach 2 or 3 [20].

While a relative FSH deficiency further hinders follicular growth, an excess of serum LH increases the generation of androgen in the ovaries. Therefore, in women with PCOS, ovulation is absent due to an elevated LH/FSH ratio. The LH/FSH ratio was shown to be greatly lowered by a ketogenic diet in this study [13-17]. The mechanism by which the ketogenic diet's carbohydrate limits were able to have this impact is hypothesized to be indicative of enhanced insulin sensitivity leading to endocrine re-normalization [21].

In addition to lowering the LH/FSH ratio, our research revealed that women with PCOS who followed a ketogenic diet had lower levels of total testosterone [12-15]. In PCOS, hyperandrogenism is linked to elevated circulating testosterone levels as a result of enhanced steroidogenesis from ovarian theca cell proliferation brought on by an unbalanced LH/FSH ratio [22]. Hyperandrogenism has a major role in the development and incidence of PCOS-related issues such as obesity, type 2 diabetes mellitus, hypertension, atherosclerosis, cardiac hypertrophy, coronary heart disease, and renal diseases [23].

The first line of treatment for PCOS recommendations is changing one's lifestyle. This entails eating a different diet and getting more exercise, both of which have been shown to be useful in reaching WL and changing body composition [13]. A meta-analysis by **Xing et al.** supports earlier findings that PCOS can be effectively managed with a low-calorie, high-nutrient diet [24]. Less than 20 grams of carbohydrates per day was reported in the majority of the trials that were included in the analysis. This type of diet lowers calories and carbs while increasing insulin sensitivity. Customized protein intake is required for lean mass maintenance during the course of ketogenic diet therapy in order to maintain effects over time [25]. The lipid supply is rich in mono- and polyunsaturated fatty acids, which are well-known for their anti-inflammatory and insulin-sensitizing qualities [26]. Further research is required to confirm the therapy's long-term advantages and determine whether less restricted, more sustainable eating behaviors may lead to desired long-term outcomes.

CONCLUSION:

The extent to which these findings may be extensively applied to the PCOS community is limited by the numerous concerns that remain in the accessible literature and require closer examination. However, these findings have important treatment implications, and endocrinologists, gynecologists, and dieticians should carefully plan and modify particular meal recommendations for women with PCOS. Finding the potential for nutritional therapies that can support individualized preventive tactics to safeguard fertility beginning in youth is critical given the long-term effects of PCOS.

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