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LIFESTYLE MODIFICATIONS, NUTRITION, EXERCISE AND NUTRACEUTICAL INTERVENTIONS IN POLYCYSTIC OVARY SYNDROME: A NARRATIVE REVIEW WITH SYSTEMATIC SEARCH IN THE SOUTH ASIAN CONTEXT

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ABSTRACT

Polycystic Ovary Syndrome (PCOS) affects 8–13% of women of reproductive age globally and up to 22.5% in Indian urban populations, with a pathophysiologically distinct ‘thin-fat’ phenotype. Non-pharmacological strategies are endorsed as first-line therapy by the 2023 International Guideline, yet no systematic synthesis has contextualized this evidence for Indian and South Asian practice, where near-universal vitamin D deficiency, omega-3-deficient diets, and dietary transition from traditional millet-based patterns compound metabolic risk. A narrative review with systematic literature search was conducted in accordance with PRISMA 2020 across five databases (January 2000–December 2024), supplemented by hand-search of three Indian journals. Two reviewers independently screened all records with substantial inter-rater agreement. Risk of bias was assessed using RoB 2.0, Newcastle-Ottawa Scale, and AMSTAR-2. Evidence was graded using the OCEBM hierarchy, with divergences from GRADE certainty ratings explicitly noted. Thirty-six primary and review studies were individually assessed and synthesized (19 RCTs, 7 SR/MAs, 3 cohort/cross-sectional, 3 uncontrolled/open-label, 4 guidelines); an additional 49 unique primary studies were assessed within included SR/MAs. Mediterranean/low-GI diet: Level A; in the Marsh et al. RCT, insulin sensitivity improved approximately threefold versus conventional diet, with menstrual regularity restored in 95% versus 63% of irregular-cycle completers. In the Jakubowicz et al. RCT, caloric front-loading reduced postprandial insulin AUC by 54% and free testosterone by 50%. Myo-inositol: Level A (OCEBM) / low-very low (GRADE). Vitamin D3, omega-3, NAC, berberine: Level B. Curcumin, fenugreek: Level C. Lifestyle modification including exercise is the universal first-line intervention. Myo-inositol provides the strongest nutraceutical evidence despite persistent guideline-OCEBM grading divergence. Curcumin and fenugreek are Indian-context priorities requiring multicentre RCTs. India’s disproportionate PCOS burden and pharmacognostic resources constitute an underutilized research opportunity.

KEYWORDS: polycystic ovary syndrome; myo-inositol; curcumin; fenugreek; Mediterranean diet; glycaemic index; vitamin D; insulin resistance; nutraceuticals; India; PRISMA 2020

1. INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is the most prevalent endocrine disorder in women of reproductive age, with a global prevalence of 8–13% under Rotterdam 2003 diagnostic criteria.^[1,2] This range markedly underestimates burden in South Asian populations: community-based data from Mumbai document prevalence reaching 22.5% in women aged 15–24,^[3] and South Indian adolescent cohorts yield 9.13% under strict Rotterdam criteria.^[4] These figures reflect a pathophysiologically distinct metabolic phenotype. The majority of Indian women with PCOS exhibit the ‘thin-fat’ phenotype — visceral adiposity and insulin resistance coexisting with a lean body mass index (BMI) that appears metabolically normal by European thresholds.^[5] Vitamin D deficiency, reported in 60–90% of Indian adults, compounds metabolic risk from the outset.^[6] The pathophysiological core of PCOS is follicular arrest. Tissue-selective insulin resistance impairs PI3K/Akt metabolic signaling while preserving MAPK/ERK mitogenic activity in ovarian theca cells.^[7] Compensatory hyperinsulinaemia amplifies CYP17A1-mediated androgen synthesis and substantially suppresses hepatic SHBG production.^[7,8] Excess AMH — two to threefold elevated — inhibits CYP19A1 (aromatase) in granulosa cells and blocks FSH-mediated dominant follicle selection.^[9,10] Long-term sequelae include an approximately 2- to 3-fold increased risk of type 2 diabetes.^[11]

Pharmacotherapy addresses downstream targets but rarely corrects the upstream metabolic derangement. Growing evidence supports non-pharmacological strategies as indispensable adjuncts. Despite a substantial international evidence base, no systematic synthesis has contextualized dietary, lifestyle, and nutraceutical interventions for Indian and South Asian clinical practice — a population with disproportionate burden, distinctive metabolic phenotyping, and unique pharmacognostic resources.

This review aims to:

- (i) synthesize evidence on dietary patterns, lifestyle modification, and nutraceuticals in PCOS, graded by the OCEBM hierarchy;
- (ii) contextualize findings for Indian women; and
- (iii) identify priority targets for future Indian multicentre RCTs. The review does not address pharmacological agents, surgical interventions, or assisted reproductive technologies.

1.1. PICO Framework

Population: women aged 15–45 with confirmed PCOS (Rotterdam 2003, NIH 1990, or AES criteria),

with attention to Indian and South Asian cohorts. Intervention: dietary patterns (Mediterranean, low-GI, ketogenic, time-restricted eating), structured exercise (aerobic, resistance, HIIT), and nutraceuticals (myo-inositol, vitamin D3, omega-3, NAC, berberine, curcumin, fenugreek, CoQ10, resveratrol, zinc, magnesium). Comparison: placebo, standard care, healthy diet control, or active comparator. Outcomes: primary — ovulatory function, hormonal parameters (testosterone, LH, SHBG, AMH); secondary — HOMA-IR, lipid profile, CRP, body weight, menstrual regularity, quality of life.

2. METHODS

2.1. Study Design and Reporting

This narrative review with systematic literature search was conducted and reported in accordance with PRISMA 2020.^[12] We use the designation ‘narrative review with systematic literature search’ rather than ‘systematic review’ because, while the search strategy, screening, and risk-of-bias assessment followed systematic review methodology, a narrative synthesis approach was used and the protocol was not prospectively registered in PROSPERO. This is acknowledged as a methodological limitation. The completed PRISMA 2020 checklist is available as Additional file 2.

2.2. Information Sources and Search Strategy

Five databases were searched: PubMed/MEDLINE, Scopus, Web of Science, Cochrane CENTRAL, and Embase (January 2000–December 2024). Google Scholar supplemented grey literature retrieval. Three Indian journals were hand-searched: JHRS, IJEM, and JOGI.^[13] Reference lists of included articles were screened.

The Boolean search string was: (“polycystic ovary syndrome” OR “PCOS” OR “PCOD”) AND (“diet” OR “nutrition” OR “nutraceutical” OR “myo-inositol” OR “vitamin D” OR “omega-3” OR “berberine” OR “curcumin” OR “fenugreek” OR “lifestyle” OR “exercise” OR “physical activity”) AND (“insulin resistance” OR “hyperandrogenism” OR “anovulation” OR “metabolic”). MeSH terms were applied in PubMed.

2.3. Eligibility Criteria

2.3.1. Inclusion. Human studies; women with confirmed PCOS (Rotterdam 2003, NIH 1990, or AES criteria); peer-reviewed English-language publications; RCTs, SR/MAs, cohort studies, case-control studies, and clinical guidelines; interventions comprising dietary modification, physical activity,

or nutraceuticals; reporting ovulatory, hormonal, or metabolic outcomes; published January 2000–December 2024; minimum sample size ≥20.

2.3.2. *Exclusion.* Animal and in vitro studies; case reports <20 participants; non-peer-reviewed editorials; inadequate outcome reporting; duplicate publications (most comprehensive retained).

2.4. Study Selection and Data Extraction

All records were imported into Zotero. Automated deduplication removed 1,310 duplicates. Two reviewers independently screened titles and abstracts using a standardized eligibility form; disagreements were resolved by consensus discussion, with adjudication by a third reviewer where consensus could not be reached. Inter-rater agreement was substantial (formal Cohen's κ was not calculated; the screening log and agreement calculations are available from the corresponding author). Full texts of 540 potentially eligible studies were independently evaluated; 504 were excluded. Data were extracted into a standardized spreadsheet capturing study design, country, sample size, diagnostic criteria, interventions, comparators, outcomes, follow-up duration, and risk of bias.

2.5. Risk of Bias Assessment

Quality was assessed using Cochrane RoB 2.0 for RCTs (five domains), NOS (≥7/9 = high quality) for observational studies, and AMSTAR-2 for systematic

reviews. Assessments were independent with consensus resolution. Results are summarized in Table 4.

2.6. Evidence Grading

Evidence was graded using the OCEBM hierarchy: Level A — consistent evidence from multiple RCTs and/or SR/MAs; Level B — at least one well-designed RCT or consistent cohort data; Level C — small, uncontrolled, or single-centre studies. OCEBM levels assess evidence *design*, whereas GRADE ratings used by the 2023 guideline [1] assess confidence in *effect estimates* incorporating risk of bias, imprecision, indirectness, inconsistency, and publication bias. Divergences are stated explicitly.

2.7. Synthesis of Results

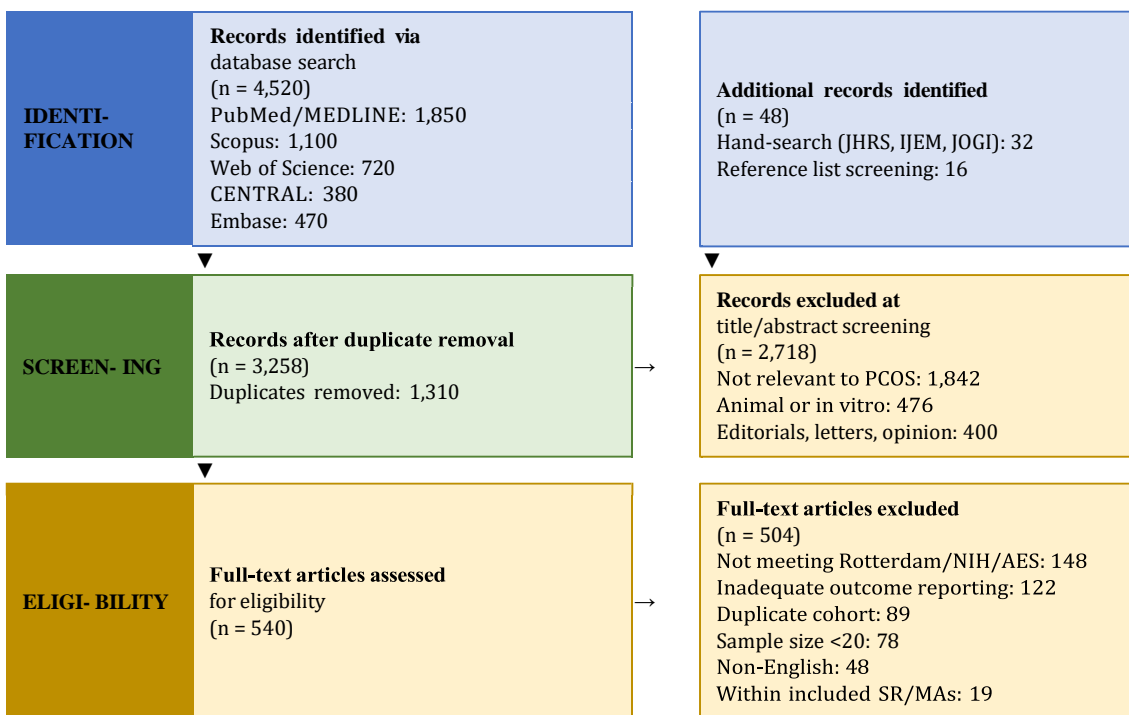
A narrative synthesis was adopted. Meta-analytic pooling was not performed because included interventions spanned heterogeneous categories precluding meaningful statistical combination. Where quantitative data were available, effect sizes are reported descriptively.

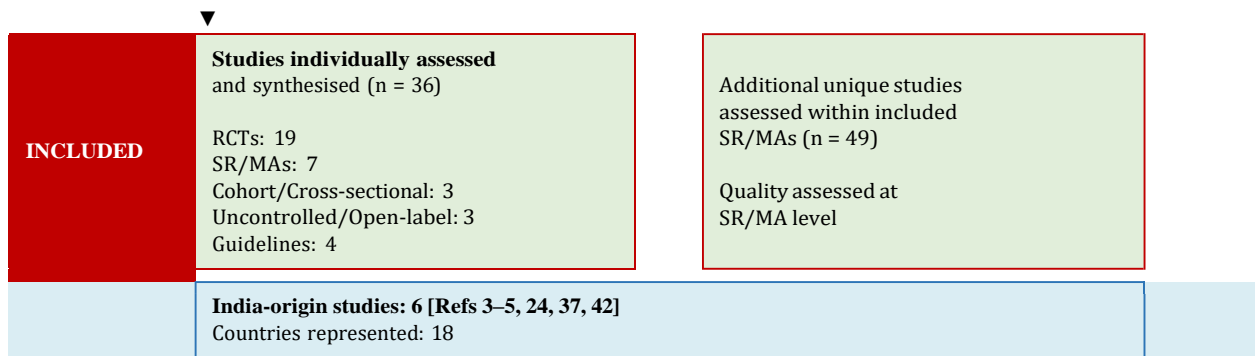
3. RESULTS

3.1. Study Characteristics

The search identified 4,520 database records and 48 additional records. After deduplication and screening, 540 full texts were assessed; 504 excluded. The study selection process is presented in Figure 1.

Figure 1. PRISMA 2020 Flow Diagram





CENTRAL = Cochrane Central Register of Controlled Trials; IJEM = Indian Journal of Endocrinology and Metabolism; JHRS = Journal of Human Reproductive Sciences; JOGI = Journal of Obstetrics and Gynaecology of India; SR/MA = systematic review/meta-analysis.

Figure 1. PRISMA 2020 flow diagram. CENTRAL = Cochrane Central Register of Controlled Trials; IJEM = Indian Journal of Endocrinology and Metabolism; JHRS = Journal of Human Reproductive Sciences; JOGI = Journal of Obstetrics and Gynaecology of India; SR/MA = systematic review/meta-analysis; WoS = Web of Science.

Final inclusion: 36 individually assessed studies and reviews (19 RCTs, 7 SR/MAs, 3 cohort/cross-sectional, 3 uncontrolled/open-label, 4 guidelines) from 18 countries. Six studies originated from India. [3-5,24,37,42] An additional 49 unique primary studies were assessed within the included SR/MAs (detailed in Additional file 1). Risk of bias among the

32 individually assessed primary studies and reviews (excluding 4 guidelines) was low in 14 (44%), moderate in 13 (41%), and high in 5 (16%) (Table 4). Key study characteristics: Table 1. Complete characteristics are provided in Additional file 1.

Table 1. Characteristics and risk of bias of key included studies.

Study [Ref] (Year)	Design	Country	n	Follow-up	RoB / Quality
Unfer et al. [22] (2012)	SR / 6 RCTs (5 analyzed)	Multi	617 (334 analyzed)	12–24 wk	AMSTAR-2: High
Kachhawa et al. [24] (2022)	Open-label RCT	India	70	6 mo + 3 mo f/u	RoB 2.0: Moderate
Pundir et al. [23] (2018)	MA / 10 RCTs	Multi	601	12–24 wk	AMSTAR-2: High
Wehr et al. [26] (2011)	Uncontrolled pilot	Austria	57 (46 comp.)	24 wk	High (no control)
Marsh et al. [16] (2010)	Quasi-RCT (alternation)	Australia	96 (49 comp.)	12 mo	RoB 2.0: Moderate
Moran et al. [17] (2003)	RCT	Australia	28	12 wk	RoB 2.0: Low
Jakubowicz et al. [19] (2013)	RCT	Israel	60	90 days	RoB 2.0: Low
Wei et al. [32] (2012)	RCT	China	89	3 mo	RoB 2.0: Moderate
An et al. [33] (2014)	RCT (3-arm)	China	150	3 mo pre-IVF	RoB 2.0: Moderate
Jamilian et al. [34] (2020)	RCT	Iran	60	12 wk	RoB 2.0: Moderate
Swaroop et al. [37] (2015)	Open-label	India	50	90 days	NOS: 4/9 (High RoB)
Khani et al. [28] (2017)	RCT (double-blind)	Iran	88	6 mo	RoB 2.0: Low

RoB 2.0 = Cochrane Risk of Bias 2.0. NOS = Newcastle-Ottawa Scale. SR = systematic review; MA = meta-analysis. Key limitations are discussed in text and Additional file 1.

3.2. Dietary and Lifestyle Interventions

3.2.1. Weight Reduction and Physical Activity.

Lifestyle modification is endorsed as first-line therapy for all PCOS phenotypes.^[1,13] A 5–10% weight reduction has been associated with restoration of ovulation in a substantial proportion of anovulatory women in lifestyle intervention trials.^[14,15] The 2023 Guideline recommends tiered targets: 150–300 min/week moderate-intensity or 75–150 min/week vigorous-intensity aerobic activity, with resistance training on two non-consecutive days; for weight management, ≥ 250 min/week moderate-intensity.^[1] Among modalities, aerobic exercise has the strongest evidence for

HOMA-IR improvement; resistance training independently reduces total testosterone and improves body composition, though effects on other androgens are mixed^[48]; and HIIT demonstrates superior cardiorespiratory and metabolic improvements per unit time.^[43] A meta-analysis of 33 studies confirmed exercise benefits are more dependent on intensity than dose.^[44]

3.2.2. Mediterranean and Low-Glycaemic-Index Diets.

Marsh et al.'s 12-month trial (n = 96; 49 completers) demonstrated approximately threefold greater improvement in ISI^{OGTT} ($+2.2 \pm 0.7$ vs. $+0.7 \pm 0.6$; P =

0.03); 95% achieved improved menstrual regularity versus 63% ($P = 0.03$).^[16] Biochemical androgens did not differ significantly between groups. Moran *et al.* confirmed metabolic improvements with energy-restricted higher-protein diets.^[17] Evidence Level: A. For Indian women, dietary adaptation requires attention to preparation-dependent glycaemic impact.^[42] Based on Indian population GI data, whole pulses are reliably low-GI: chana (reported GI 28–36), moong dal (GI 29–42). Millet GI varies critically by preparation: ragi roti (GI ~65) and jowar idli (GI ~61) are meaningfully lower than polished white rice (GI 72–80), but finely ground ragi porridge (GI up to 98) and jowar roti (GI ~84) can exceed white rice, likely due to differences in starch gelatinization and particle size. Clinicians should prescribe specific preparations, not merely ‘switch to millets’.^[13]

3.2.3. Low-Carbohydrate, Time-Restricted, and Anti-Inflammatory Approaches.

A pilot study by Mavropoulos *et al.* ($n = 11$ enrolled; 5 completers) suggested improvements in body weight, free testosterone, and LH/FSH ratio with a ketogenic diet over 24 weeks; however, 55% attrition severely limits generalizability.^[18] Jakubowicz *et al.*'s RCT ($n = 60$ lean PCOS) demonstrated that distributing ~80% of calories to breakfast reduced postprandial insulin AUC by 54%, free testosterone by 50%, and increased SHBG by 105% over 90 days, with no weight change.^[19] Anti-inflammatory patterns incorporating omega-3-rich and fermented foods are supported by gut-ovary axis evidence.^[20,21] Evidence Levels: B (time-restricted); B–C (anti-inflammatory).

Table 2. Dietary interventions in PCOS: evidence summary and Indian-context adaptations.

Dietary Pattern [Refs]	Core Features	Primary Outcome	n Range	Evidence	Indian Adaptation (GI values)
Mediterranean / Low-GI [1,13–17]	High MUFA, fibre, polyphenols; low refined CHO	Restores ovulation ~33–50%; ISI ^{OGTT} +2.2 vs +0.7; menstrual regularity 95% vs 63%	28–96	A	Chana (GI 28–36), moong dal (GI 29–42); ragi roti (GI ~65), jowar idli (GI ~61); mustard/olive oil [42]
Low-CHO / Ketogenic [18]	CHO <50 g/day; high fat; moderate protein	Reduces free testosterone; improves menstrual cyclicity (pilot; 5 completers)	11 (5 comp.)	B (pilot)	Paneer, eggs, full-fat curd, non-starchy vegetables
Time-restricted (breakfast-heavy) [19]	~80% calories at breakfast	Insulin AUC –54%; free testosterone –50%; SHBG +105%; improved ovulation	60	B	Consistent with traditional Indian heavy-morning-meal pattern
Anti-inflammatory / High-fibre [20,21]	Omega-3-rich, polyphenols, fermented foods, legumes	Reduces CRP; improves HOMA-IR; gut microbiome diversity	Varied	B–C	Flaxseeds, walnuts, dahi, idli/dosa batter, turmeric + black pepper

CHO = carbohydrate; MUFA = monounsaturated fatty acid; GI = glycaemic index; SHBG = sex hormone-binding globulin. GI values from Indian population data [42]. Evidence per OCEBM hierarchy.

3.3. Nutraceutical Interventions

The 2023 guideline ^[1] characterizes nutraceutical certainty as low to very low and recommends shared decision-making.

3.3.1. Myo-Inositol and MYO: DCI 40:1.

MYO mediates FSH signaling via PI3K/Akt and GLUT4. ^[22] Hyperinsulinaemia depletes follicular MYO — the ‘inositol paradox’. Unfer *et al.*'s systematic review identified 6 RCTs ($N = 617$; 5 analyzed after exclusion of one using a multivitamin formulation) and demonstrated that MYO 2–4 g/day improves ovulation, reduces testosterone, and improves HOMA-IR.^[22] Pundir *et al.*'s meta-analysis (10 RCTs; $n = 601$) confirmed that inositol more than doubled ovulation rates versus placebo (RR 2.3, 95% CI 1.1–4.7).^[23] The Indian open-label RCT by Kachhawa *et al.* from AIIMS ($N = 70$ young PCOS women aged 15–24) demonstrated that 6 months of

MYO:DCI combination improved menstrual regularity and insulin resistance comparably to combined hormonal contraceptive, providing Indian-context data on inositol acceptability.^[24] OCEBM Level A; however, the Fitz *et al.* systematic review (30 RCTs; $n = 2,230$) informing the guideline rated all outcomes as low-to-very-low certainty,^[41] and the SOGC 2025 Position Statement concurs.^[46]

3.3.2. Vitamin D3.

Deficiency affects 60–90% of Indian adults. ^[6,25] In an uncontrolled pilot study ($N = 57$; 46 completers), Wehr *et al.* observed improved menstrual frequency in 50% of participants after 24 weeks of cholecalciferol 20,000 IU/week ^[26]; however, without a control arm, causation cannot be established. Trummer *et al.*'s subsequent RCT confirmed HOMA-IR improvements.^[27] Dosing: 2,000–4,000 IU/day targeting 40–60 ng/mL. Evidence Level: B

(supported primarily by Trummer et al. and other controlled data).

3.3.3. Omega-3 Fatty Acids.

In a double-blind RCT (N = 88, 6 months), Khani et al. demonstrated that EPA + DHA (2 g/day) significantly improved lipid profiles and menstrual interval versus placebo.^[28] Indian diets are structurally omega-3-deficient. Evidence Level: B.

3.3.4. N-Acetylcysteine.

NAC (1.8 g/day) improves insulin sensitivity ^[29] and is effective as CC adjunct ^[30] but inferior to metformin alone for ovulation induction (ovulation 6.7% vs. 51.6% in CC-resistant PCOS). ^[31] Level B (CC adjunct only).

3.3.5. Berberine.

Berberine (1,500 mg/day) activates AMPK with equivalent metabolic effects to metformin. ^[32,33] Importantly, berberine holds no FDA or EMA pharmaceutical approval; it is a dietary supplement in the US/EU. It inhibits CYP3A4, CYP2D6, and P-glycoprotein. Evidence Level: B.

3.3.6. Curcumin.

Jamilian et al. (n = 60) demonstrated significant reductions in fasting glucose, HOMA-IR, insulin, total cholesterol, and LDL with 500 mg/day curcumin over 12 weeks.^[34] Sohrevardi et al. confirmed benefits of nanocurcumin added to metformin.^[35] Ghanbarzadeh-Ghashti et al. demonstrated improved menstrual characteristics in a double-blind RCT.^[47] Oral

bioavailability is extremely poor; piperine co-administration enhances absorption markedly but with limited reproducibility.^[36] Case reports document suprathreshold INR with warfarin. Evidence Level: C.

3.3.7. Fenugreek.

Fenugreek contains diosgenin (steroidal sapogenin with putative anti-androgenic activity) and 4-hydroxyisoleucine (glucose-dependent insulin secretagogue). An Indian open-label study (n = 50) achieved 71% regular cycles.^[37] Fenugreek stimulates oxytocin secretion and uterine contractility; caution is warranted in pregnancy.^[45] Evidence Level: C.

3.3.8. Additional Agents.

CoQ10 (100 mg/day for 12 weeks) improved fasting glucose, serum insulin, and HOMA-IR in a double-blind RCT of 60 PCOS women.^[38] Resveratrol (1,500 mg/day for 3 months) reduced total testosterone by 23.1% and fasting insulin by 31.8% in a placebo-controlled trial of 34 PCOS women (30 completers).^[39] Zinc and magnesium^[40] carry Level C evidence as targeted adjuncts.

3.4. Contraindications and Safety

Myo-inositol at 4 g/day is well tolerated and safe in pregnancy. Vitamin D >10,000 IU/day without monitoring risks hypercalcaemia. Berberine inhibits CYP3A4/CYP2D6/P-gp (cyclosporine trough ↑89%); avoid with narrow-therapeutic-index drugs. Curcumin inhibits platelet aggregation and potentiates warfarin (case reports of INR >10 and major bleeding); contraindicated with anticoagulants.

Table 3. Nutraceutical evidence summary for PCOS management.

Agent [Refs]	Dose	Primary Outcome	Hormonal / Metabolic	OCEBM / GRADE	Safety / CI
Myo-inositol [22-24]	2-4 g/day	Improves ovulation; menstrual regularity	Reduces T, LH; raises SHBG; reduces HOMA-IR	A / Low-very low	Well tolerated; mild GI >12 g/d; safe in pregnancy
MYO:DCI 40:1 [22,24]	MYO 550 + DCI 150 mg BID	Improved menstrual regularity comparable to OCP (N=70, 6 mo)	Reduces LH:FSH; reduces IR	B / —	As myo-inositol
Vitamin D3 [25-27]	2,000-4,000 IU/d	Improves menstrual regularity	Reduces T, AMH, HOMA-IR	B / —	IOM UL 4,000 IU/d; toxicity >10,000 IU/d; 25(OH)D >150 ng/mL
Omega-3 [28]	2 g/day EPA+DHA	Improved lipids, menstrual interval (N=88, 6 mo RCT)	Modest T and DHEA-S reduction	B / —	Fishy eructation; caution with anticoagulants >3 g/d
NAC [29-31]	1.8 g/day	CC adjunct; inferior to metformin alone	Reduces T; improves insulin sensitivity	B (CC adjunct) / —	Well tolerated; not a metformin substitute
Berberine [32,33]	500 mg TID	Equivalent to metformin for HOMA-IR	Reduces T, DHEA-S; PCSK9 suppression	B / —	CYP3A4/2D6/P-gp inhibitor; cyclosporine ↑89%; not FDA/EMA approved
Curcumin† [34-36,47]	500 mg/d (+piperine)	Menstrual regularity; FPG and LDL reduction	Reduces T; reduces HOMA-IR	C / —	Inhibits platelet aggregation; INR elevation with warfarin; avoid anticoagulants

Fenugreek† [37]	500–1000 mg/d	71% regular cycles (uncontrolled)	Reduces T and LH	C / —	May potentiate hypoglycaemics; uterotonic—avoid in pregnancy [45]
CoQ10 [38]	100 mg/d	Improved FPG, insulin, HOMA-IR (N=60, 12-wk RCT)	Improves glucose metabolism and lipid profiles	C / —	Well tolerated; may reduce warfarin efficacy
Resveratrol [39]	1,500 mg/d	Fasting insulin -31.8%; ISI (Matsuda) +66.3%	T -23.1%; DHEA-S -22.2%	C / —	GI discomfort; theoretical oestrogenic activity
Zn / Mg [40]	Zn 25–50; Mg 250–400 mg/d	Zn: hirsutism; Mg: FPG	Reduces DHT and T	C / —	Zn: Cu depletion >50 mg/d; Mg: diarrhoea

† Indian-context agents. CC = clomiphene citrate; T = testosterone; SHBG = sex hormone-binding globulin; FPG = fasting plasma glucose; CI = contraindications; ISI = Insulin Sensitivity Index. OCEBM/GRADE shows OCEBM level / GRADE certainty (from [1]) where available; ‘—’ = no GRADE rating.

Table 4. Risk of bias summary across individually assessed primary studies.

Study Design (n)	Tool Used	Low RoB	Moderate	High RoB
RCTs (n = 19)	Cochrane RoB 2.0	8 (42%)	9 (47%)	2 (11%)
SR/MAs (n = 7)	AMSTAR-2	5 (71%)	2 (29%)	0 (0%)
Cohort/Cross-sectional (n = 3)	Newcastle-Ottawa	1 (33%)	1 (33%)	1 (33%)
Uncontrolled/Open-label (n = 3)	NOS or descriptive	0 (0%)	1 (33%)	2 (67%)
Guidelines (n = 4)	N/A	—	—	—
TOTAL (n = 32, excluding guidelines)		14 (44%)	13 (41%)	5 (16%)

RoB 2.0 = Cochrane Risk of Bias 2.0. NOS = Newcastle-Ottawa Scale. AMSTAR-2 = A Measurement Tool to Assess Systematic Reviews 2. N/A = not applicable. Domain-level RoB judgements for individual RCTs are available on request.

4. DISCUSSION

The synthesis supports a hierarchical approach: lifestyle modification as universal foundation, evidence-matched nutraceuticals as adjuncts, and culturally adapted strategies for Indian women.^[1,13] Tissue-selective insulin resistance defines the mechanistic logic: dietary patterns attenuating postprandial insulin surges reduce hyperinsulinaemic ovarian androgen synthesis,^[7,16,19] while nutraceuticals acting on AMPK, glutathione, and PPAR γ address the same upstream derangement.

The divergence between OCEBM Level A and GRADE low-to-very-low certainty for myo-inositol — the ‘inositol paradox’ — is the central methodological issue. OCEBM Level A requires consistent evidence from multiple RCTs, which myo-inositol satisfies (>30 RCTs). However, GRADE downgrades certainty based on risk of bias, inconsistency, imprecision, and suspected publication bias.^[41] The SOGC 2025 Position Statement notes myo-inositol ‘may be considered’ given limited harm, while evidence remains insufficient for a strong recommendation.^[46] Clinicians should understand that OCEBM Level A indicates the evidence *exists* in quantity, while GRADE low certainty indicates it may not be *reliable* in quality.

The Indian context requires emphasis proportionate to its disease burden: insulin resistance at lean BMI,^[5] near-universal vitamin D deficiency,^[6,25] and urban prevalence of 22.5%.^[3] Empirical vitamin D repletion, pulse-based dietary prescriptions,

metabolic screening irrespective of BMI,^[13] and culturally familiar supplements must become routine practice.

India critically lacks proportionate research output. The AIIMS myo-inositol study^[24] demonstrates that Indian PCOS trials are feasible. Institutions with infrastructure — AIIMS Delhi, PGIMER Chandigarh, CMC Vellore, KEM Mumbai — have the capability to address this gap. We propose a National PCOS Registry, modelled on the UK Biobank.

Specific limitations: (a) no PROSPERO registration; (b) no meta-analytic pooling, precluding formal publication bias quantification; (c) most nutraceutical RCTs involve small samples and short durations; (d) the majority were conducted in non-Indian populations; (e) studies within included SR/MAs were assessed at the SR/MA level rather than individually re-extracted.

As a *recommendation of the present authors* based on this evidence synthesis, a three-step clinical hierarchy for Indian clinicians is proposed. This hierarchy represents a pragmatic clinical synthesis of heterogeneous evidence rather than a formal guideline recommendation. **Step 1 (universal):** pulse-based low-GI diet, 150–300 min/week moderate aerobic activity with twice-weekly resistance training. **Step 2 (assess and correct):** measure 25(OH)D universally; supplement 2,000–4,000 IU/day; ensure omega-3 intake. **Step 3 (nutraceutical adjuncts via shared decision-making):** myo-inositol 2–4 g/day; berberine 1,500 mg/day where metformin is poorly tolerated; NAC 1.8 g/day as CC adjunct. Curcumin and fenugreek

may be discussed as culturally familiar options with preliminary evidence.

5. CONCLUSIONS

1. Lifestyle modification (low-GI diet, 150–300 min/week exercise, resistance training) is the Level A first-line intervention. [1,14,15] For Indian women, a pulse-based pattern (chana GI 28–36, moong dal GI 29–42) is recommended. [13,42]
2. Myo-inositol (2–4 g/day) currently has the strongest nutraceutical evidence (OCEBM Level A; GRADE low–very low), though certainty remains limited. [1,22,23,46] Recommended as first-line nutraceutical adjunct via shared decision-making.
3. Vitamin D3, omega-3, NAC, and berberine carry Level B evidence. [26–33] Universal 25(OH)D assessment is recommended in all Indian PCOS patients, with supplementation at 2,000–4,000 IU/day.
4. Curcumin and fenugreek (Level C) are the highest-priority targets for Indian multicentre RCTs: double-blind, placebo-controlled, $n \geq 200$, 6-month duration, ≥ 3 centers. [34,37]
5. India's PCOS burden, thin-fat phenotype, and pharmacognostic resources constitute a scientific opportunity. A National PCOS Registry is recommended. [3,5,13]

Declarations

Funding: This research received no specific funding.

Conflicts of Interest: The authors declare no conflicts of interest.

Data Availability: Complete study characteristics are provided in Additional file 1, and the completed PRISMA 2020 checklist in Additional file 2. The full search strategy, screening log with inter-rater

agreement data, and domain-level risk-of-bias judgements are available from the corresponding author on reasonable request.

Additional Files

Additional file 1: Complete characteristics of all individually assessed studies. Study design, country of origin, sample size, diagnostic criteria, intervention details, primary outcomes, follow-up duration, risk-of-bias assessment, and key limitations for all 36 individually assessed studies organized by intervention type (dietary, exercise, myo-inositol, vitamin D, omega-3, NAC, berberine, curcumin/fenugreek, other nutraceuticals, SR/MAs, guidelines). (DOCX)

Additional file 2: Completed PRISMA 2020 checklist for this narrative review with systematic literature search. (DOCX)

Plain Language Summary

Polycystic Ovary Syndrome (PCOS) is a common hormonal condition affecting up to one in five Indian women of reproductive age. This review examined published studies to identify the best non-drug treatments. We found strong evidence that eating foods with a low glycaemic index (such as lentils, chickpeas, and appropriately prepared millets rather than polished white rice), combined with regular exercise, is the most important first step. Among supplements, myo-inositol has the most evidence for improving ovulation, though experts consider overall evidence quality low. Vitamin D supplementation is particularly important for Indian women, most of whom are deficient. Turmeric (curcumin) and fenugreek (methi) show early promise but need larger studies from Indian institutions.

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