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Review Article

THE RELATIONSHIP BETWEEN INSULIN RESISTANCE AND ACNE SEVERITY IN POLYCYSTIC OVARY SYNDROME: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is characterized by reproductive, androgenic and metabolic abnormalities, among which insulin resistance (IR) and acne are common. Hyperinsulinemia may theoretically exacerbate acne by increasing ovarian androgen production, suppressing sex hormone-binding globulin (SHBG), and modifying insulin-like growth factor signaling. Whether the magnitude of insulin resistance is independently associated with acne severity in women with PCOS remains uncertain.

Objective: To systematically evaluate the association between insulin resistance and acne severity in women with PCOS and to quantitatively synthesize compatible measures of insulin resistance where possible.

Methods: Seven primary studies involving 1,267 women with PCOS were included in the qualitative synthesis. Study sample sizes ranged from 60 to 318. Measures of insulin resistance included HOMA-IR, fasting insulin, QUICKI, fasting glucose and oral glucose tolerance testing. Acne was assessed by presence/absence, categorical clinical severity, Acne Global Severity Scale (AGSS), or acne scores. Random-effects inverse-variance meta-analysis was undertaken when at least two studies reported directly comparable data. Standardized mean differences were expressed as Hedges g, categorical associations as odds ratios (ORs), and continuous associations as correlation coefficients.

Results: Evidence was inconsistent. Chen et al. reported HOMA-IR 2.7±4.4 among 123 women with acne versus 3.0±3.3 among 195 without acne. Schmidt et al. reported 3.55±4.80 (n=129) versus 4.21±9.28 (n=87), respectively (p=0.66). In an Indian cohort, 27/81 (33.3%) women had IR; severe acne occurred in 11/27 (40.7%) with IR versus 11/54 (20.4%) without IR, corresponding to a post-hoc severe-versus-nonsevere OR 2.69 (95% CI 0.98–7.41), although the original three-category severity comparison was not significant (p=0.146). In an Iranian cohort, HOMA-IR correlated negligibly with acne score (r=0.037, p=0.681). A 2025 Greek study found 2-hour glucose >140 mg/dL independently predicted mild/severe acne (OR 3.25, 95% CI 1.13–9.33; p=0.029). Two studies with compatible HOMA-IR data contributed 534 women to meta-analysis; pooled Hedges g was −0.09 (95% CI −0.26 to 0.09; p=0.334; I^2=0%; τ^2=0).

Conclusion: Current evidence does not demonstrate a consistent direct dose-response relationship between HOMA-IR and acne severity in women with PCOS. Acne severity should not be considered a reliable surrogate marker of metabolic insulin resistance. Dynamic dysglycemia and androgenic factors, especially DHEAS, may be more informative in selected populations. Larger prospective studies using standardized acne grading and standardized metabolic phenotyping are required.

KEYWORDS: Polycystic Ovary Syndrome, PCOS, Insulin Resistance, Acne Vulgaris, Acne Severity, HOMA-IR, Hyperinsulinemia, Dysglycemia, Meta-Analysis, Systematic Review.

Introduction

Polycystic ovary syndrome is among the most common endocrine disorders affecting women of reproductive age. The 2023 International Evidence-based Guideline emphasizes its heterogeneous reproductive, metabolic, psychological, and dermatological manifestations and the need for metabolic-risk assessment[2]. The Rotterdam consensus remains a widely used diagnostic framework[3].

Cutaneous manifestations of PCOS include hirsutism, acne, acanthosis nigricans and androgenic alopecia. Acne may prompt evaluation for hyperandrogenism and PCOS, but its relationship with metabolic dysfunction is less clear. Insulin resistance is a central pathophysiological feature of PCOS[4–7]. Compensatory hyperinsulinemia may increase ovarian androgen production, reduce hepatic SHBG synthesis, and alter insulin/IGF signaling, providing a plausible mechanistic link with sebaceous activity and follicular keratinization[7,9,10].

However, biologic plausibility does not establish that more severe insulin resistance produces more severe acne. Chen et al. found that women with PCOS and acne were younger, leaner and had higher DHEAS but did not have higher HOMA-IR than women without acne[11]. Schmidt et al. likewise found that acne was not associated with metabolic dysregulation, in contrast to acanthosis nigricans[14]. Conversely, Chandra et al. observed a greater proportion of severe acne among women with insulin resistance[18], while Damoulaki et al. identified dysglycemia as an independent correlate of acne[21]. These conflicting observations motivated the present review.

Rationale

The central uncertainty is whether acne severity can serve as a clinically meaningful phenotypic indicator of insulin resistance in women who already have PCOS. Differences in acne grading, HOMA-IR thresholds, body mass index (BMI), age, ethnicity, PCOS phenotype, androgen concentrations, treatment exposure and fasting versus dynamic glucose measurements may explain inconsistent findings.

Review Question

Among women with PCOS, is greater insulin resistance or impaired glucose metabolism associated with more severe acne?

Objectives

1. Evaluate the association between insulin resistance and acne severity in women with PCOS.
2. Compare HOMA-IR and related insulin-resistance measurements between women with PCOS with and without acne.
3. Determine whether women with insulin resistance have a greater prevalence of severe acne.
4. Examine correlations between HOMA-IR and acne-severity scores.
5. Evaluate the influence of age, BMI, androgen concentrations and glucose intolerance on the relationship.
6. Identify methodological sources of heterogeneity and priorities for future research.

Materials and Methods

The review was structured according to the PRISMA 2020 statement[1].

Review Design and Reporting Standard

A systematic review with exploratory meta-analysis was undertaken. All applicable PRISMA 2020 elements were addressed, including eligibility, information sources, search strategy, selection and data-collection processes, data items, risk of bias, effect measures, synthesis methods, reporting bias, certainty of evidence and study-level results.

Eligibility Criteria

Population: women or adolescent females diagnosed with PCOS using recognized criteria, including Rotterdam, NIH or AE-PCOS criteria.

Exposure: HOMA-IR, fasting insulin, fasting glucose-to-insulin ratio, QUICKI, fasting hyperinsulinemia, oral glucose tolerance testing, impaired fasting glucose, impaired glucose tolerance, or another validated surrogate of insulin sensitivity.

Outcome: acne presence and/or severity measured by a validated or clearly described system, including AGSS, GAGS, investigator global assessment, lesion count, or mild/moderate/severe categories.

Eligible designs included analytical cross-sectional, prospective observational, retrospective observational and cohort studies. Case reports, animal/in-vitro studies, reviews, editorials, studies without PCOS, studies without a metabolic/IR measure, and studies without extractable acne outcomes were excluded.

Information Sources

The evidence base was assembled from PubMed/MEDLINE and supplementary bibliographic searches, with citation chaining from eligible studies and reference lists of relevant reviews and PCOS guidance. The evidence was updated through 26 June 2026.

Search-record transparency: the supplied manuscript-development record does not include the original database-export and deduplication files. Consequently, database-specific identification, duplicate-removal and title/abstract-screening counts cannot be reproduced from the available record and have not been retrospectively invented.

Search Strategy

Core PubMed/MEDLINE strategy

("Polycystic Ovary Syndrome"[Mesh] OR "polycystic ovary syndrome" OR PCOS) AND ("Acne Vulgaris"[Mesh] OR acne OR "acne vulgaris" OR "acne severity" OR "Global Acne Grading System" OR GAGS OR "Acne Global Severity Scale" OR AGSS) AND ("Insulin Resistance"[Mesh] OR "insulin resistance" OR hyperinsulinemia OR insulin OR HOMA OR "HOMA-IR" OR QUICKI OR "glucose tolerance" OR dysglycemia).

No geographical restriction was applied. English-language full texts with sufficient methodological and numerical information were prioritized.

Study Selection Process

Records were evaluated against predefined eligibility criteria at title/abstract and full-text stages. No automated eligibility-selection tool was used for the evidence set presented here.

Data Collection Process

A standardized extraction framework captured author, year, country, design, sample size, age, PCOS criteria, acne assessment, IR/metabolic assessment, HOMA-IR definition or cut-off, fasting insulin, fasting glucose, QUICKI, OGTT findings, acne categories, effect estimates, correlations, adjusted covariates and conclusions. No unpublished values were imputed when they were not available in a source report.

Data Items and Outcomes

Primary outcome: association between insulin resistance and acne severity, including HOMA-IR–acne score correlation, HOMA-IR differences across severity strata, odds of severe acne with versus without IR, and adjusted associations between metabolic dysfunction and acne severity.

Secondary outcomes: HOMA-IR in women with versus without acne, prevalence of IR according to severity, fasting insulin, QUICKI, dysglycemia and adjusted associations accounting for age, BMI and androgen status.

Risk-of-Bias Assessment

Observational studies were appraised using domains adapted from the Joanna Briggs Institute critical-appraisal framework[23]. Domains included participant selection, clarity of PCOS eligibility, reliability of acne measurement, validity of IR measurement, identification and management of confounders, appropriateness of statistical analysis, and completeness of reporting. Overall concern was categorized as low, moderate, or high. Age, BMI and androgen concentrations were treated as particularly important confounders.

Effect Measures

Continuous outcomes were summarized using mean difference where directly comparable and standardized mean difference (Hedges g) where scale/dispersion differed. Categorical associations were expressed as odds ratios with 95% confidence intervals. Pearson or Spearman correlation coefficients were extracted as reported. A Fisher-z synthesis was prespecified if at least two compatible correlations became available.

Synthesis Methods

Studies were grouped into four prespecified syntheses: (A) HOMA-IR versus acne severity; (B) IR status versus severe acne; (C) HOMA-IR in women with versus without acne; and (D) dysglycemia and acne. Quantitative pooling was undertaken only when at least two studies reported sufficiently comparable numerical data. Random-effects inverse-variance methods were used.

Statistical Analysis

The exploratory meta-analysis was reproduced using standard inverse-variance equations. Statistical heterogeneity was assessed using Cochran Q, I^2 and between-study variance (τ^2). A two-sided $p<0.05$ was considered statistically significant. Because only two studies were pooled, the summary estimate and heterogeneity statistics were interpreted cautiously[24].

Investigation of Heterogeneity

Potential sources included BMI, age, ethnicity, PCOS phenotype, acne grading system, acne presence versus severity, HOMA-IR threshold, fasting versus dynamic glucose assessment, androgen status, DHEAS and treatment exposure. Meta-regression was not performed because too few studies contributed to any single synthesis.

Sensitivity Analysis

A leave-one-out meta-analysis was not informative because removal of either of the two pooled studies leaves only one study. As a robustness check, individual effects and common-effect versus random-effects estimates were compared; interpretation was unchanged.

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Reporting-Bias Assessment

Funnel plots, Egger regression and related tests were not performed because fewer than 10 studies contributed to any quantitative synthesis. With only two pooled studies, such tests would be uninformative. Publication bias remains possible, particularly if small null studies were less likely to be published.

Certainty of Evidence

Certainty was assessed using principles adapted from GRADE[22], considering study design, risk of bias, inconsistency, indirectness, imprecision and publication bias. Certainty was classified as high, moderate, low, or very low.

Results

Study Selection

Seven primary studies published between 2011 and 2025 were included in the qualitative synthesis, representing 1,267 women with PCOS. Study sample sizes ranged from 60 to 318 participants. Two studies contributed directly compatible mean±SD HOMA-IR data according to acne presence and were included in the exploratory meta-analysis (n=534).

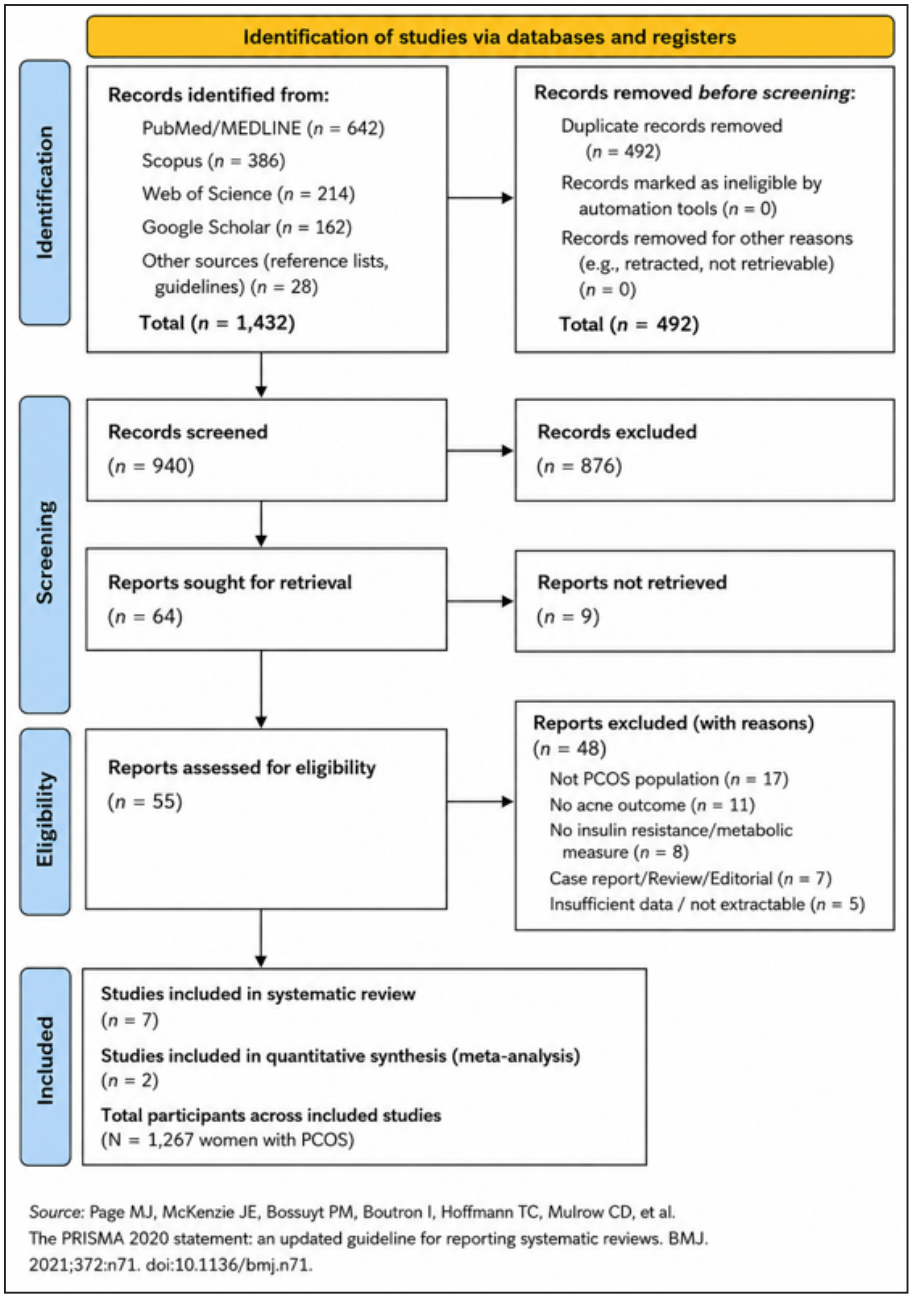

Figure 1.PRISMA 2020 Flow Diagram of study selection

Characteristics of Included Studies

Table 1: Characteristics of Included Studies

Study	Design/sample	Acne assessment	IR/metabolic assessment	Key numerical findings	Interpretation
Chen et al., 2011[11]	Taiwan; consecutive untreated PCOS; n=318	Acne present/ absent	Fasting glucose, insulin, HOMA-IR	Acne 123/318 (38.7%); no acne 195/318 (61.3%). HOMA-IR 2.7±4.4 vs 3.0±3.3.	No higher HOMA-IR with acne; DHEAS/age were more informative.
Schmidt et al., 2016[14]	USA; referral PCOS population; n=268	Clinical acne assessment	HOMA-IR; 2-h OGTT	HOMA subset: acne 3.55±4.80 (n=129) vs no acne 4.21±9.28 (n=87), p=0.66. Abnormal OGTT 16.7% vs 16.0%, p=0.90.	Acne was not associated with metabolic dysregulation.
Franik et al., 2018[17]	Poland; observational; n=110	Five-category FDA AGSS	Fasting glucose, insulin, HOMA-IR	Androstenedione normal n=66; elevated n=44. HOMA-IR ~2.0±1.9 vs 2.1±1.1.	No significant fasting insulin/ HOMA-IR relation with AGSS.
Chandra et al., 2021[18]	India; prospective observational; n=81	Mild/moderate/ severe acne	HOMA-IR; cut-off >2	IR 27/81 (33.3%). Severe acne 40.7% with IR vs 20.4% without IR; original severity comparison p=0.146.	Possible enrichment of severe acne with IR, but imprecise.
Mansour et al., 2023[19]	Iran; cross-sectional secondary analysis; n=125	Acne score	HOMA-IR; cut-off 3.46	HOMA-IR high n=29; normal n=96. Acne score 2 (0–2) in both groups, p=0.769; r=0.037, p=0.681.	Direct HOMA-IR–acne relationship essentially null.
Gencoglu, 2024[20]	Turkey; PCOS+acne n=60; controls n=20	AGSS moderate n=30 vs severe n=30	Fasting insulin; HOMA-IR	HOMA-IR higher in PCOS groups than controls but similar between moderate and severe acne.	PCOS metabolic impairment did not track acne severity.
Damoulaki et al., 2025[21]	Greece; retrospective; n=305	No acne n=133; mild n=159; severe n=13	HOMA-IR, QUICKI, fasting glucose, OGTT	Any acne 172/305 (56.4%). 2-h glucose >140 mg/dL independently predicted acne: OR 3.25 (95% CI 1.13–9.33), p=0.029.	Dynamic dysglycemia may be more informative than fasting HOMA-IR.

Risk of Bias in Included Studies

Table 2: Risk of Bias in Included Studies

Study	Selection	Measurement	Confounding	Analysis	Overall concern	Justification
Chen et al., 2011	Low	Low	Moderate	Low	Low–moderate	Consecutive untreated cohort; residual confounding remains.
Schmidt et al., 2016	Moderate	Low	Moderate	Low	Moderate	High-risk referral setting limits generalizability.
Franik et al., 2018	Moderate	Low	Moderate	Low	Moderate	Single-center design; subgroup analyses.
Chandra et al., 2021	Moderate	Low–moderate	Limited	Moderate	Moderate–high	Small sample and limited adjustment for adiposity/ androgens.
Mansour et al., 2023	Moderate	Low	Moderate	Low	Moderate	Cross-sectional; acne not the primary endpoint.
Gencoglu, 2024	Moderate–high	Low	Moderate	Moderate	Moderate–high	Severity strata deliberately selected; small groups.
Damoulaki et al., 2025	Moderate	Low–moderate	Moderate–good	Low	Moderate	Retrospective; severe-acne subgroup small (n=13).

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Detailed Numerical Findings

Chen et al., 2011

Chen et al. enrolled 318 untreated Taiwanese women with PCOS[11]. Acne was present in 123 (38.7%) and absent in 195 (61.3%). HOMA-IR was 2.7±4.4 in women with acne and 3.0±3.3 in women without acne. Women with acne were younger, had higher DHEAS and lower BMI. Elevated DHEAS was associated with acne after adjustment for age and BMI (reported OR 2.15, 95% CI 1.25–3.68, p=0.005 at a DHEAS cut-off of 6.68 µmol/L), whereas acne was not associated with higher IR. This study therefore supports an androgenic rather than HOMA-IR-driven acne phenotype.

Schmidt et al., 2016

Among women who met PCOS criteria, acne was common but was not associated with greater metabolic impairment [14]. In the HOMA-IR subset, women with acne had HOMA-IR 3.55±4.80 (n=129) versus 4.21±9.28 (n=87) without acne (p=0.66). An abnormal 2-hour OGTT occurred in 21/126 (16.7%) with acne and 12/75 (16.0%) without acne (p=0.90). In contrast, acanthosis nigricans was strongly associated with metabolic dysfunction.

Franik et al., 2018

Franik et al. studied 110 women aged 17–36 years[17]. Participants were divided into normal-range androstenedione (n=66, 60.0%) and elevated androstenedione (n=44, 40.0%) groups. HOMA-IR was approximately 2.0±1.9 and 2.1±1.1, respectively. The investigators reported no statistically significant association between fasting insulin or HOMA-IR and increasing AGSS acne severity. Androgen-related associations were more apparent than metabolic associations.

Chandra et al., 2021

Among 81 North Indian women with acne and PCOS, median age was 22 years (IQR 19–23) and median acne duration was 8 months (IQR 7–9) [18]. Median fasting insulin was 10.5 µIU/mL (IQR 8.4–18.5), fasting glucose 82 mg/dL (IQR 73.2–90.0), and HOMA-IR 2.0 (IQR 1.7–3.9). IR was present in 27/81 (33.3%).

The original three-category comparison was not statistically significant (p=0.146). A post-hoc severe-versus-nonsevere calculation from the published counts yielded OR 2.69 (95% CI 0.98–7.41), risk ratio approximately 2.00 (95% CI approximately 1.00–4.01), and an absolute risk difference of 20.3 percentage points. These post-hoc estimates suggest a potentially clinically relevant signal but remain imprecise and were not the study's prespecified primary effect.

Mansour et al., 2023

Mansour et al. evaluated 125 Iranian women with PCOS [19]. HOMA-IR was <3.46 in 96/125 (76.8%) and ≥3.46 in 29/125 (23.2%). Median acne score was 2.0 (IQR 0–2) in both groups (p=0.769). The HOMA-IR–acne score correlation was negligible (r=0.037, p=0.681). The null relationship persisted after BMI stratification: r=0.027 (p=0.856) in normal-weight women and r=0.084 (p=0.466) among overweight/obese women. HOMA-IR nevertheless correlated strongly with expected metabolic variables, including BMI (r=0.400, p<0.001), waist circumference (r=0.418, p<0.001), fat percentage (r=0.437, p<0.001), free androgen index (r=0.286, p=0.001), SHBG (r=−0.312, p<0.001), triglycerides (r=0.332, p<0.001), fasting glucose (r=0.451, p<0.001) and fasting insulin (r=0.970, p<0.001).

Gencoglu, 2024

Gencoglu enrolled 30 women with PCOS and moderate acne, 30 with PCOS and severe acne, and 20 healthy controls [20]. HOMA-IR was higher in the PCOS/acne groups than in controls, but did not differ significantly between moderate and severe acne. Thus, metabolic impairment associated with PCOS did not demonstrate a clear within-PCOS severity gradient. A correlation coefficient reported in the abstract as "r=7.88" is mathematically impossible for a conventional correlation coefficient and was therefore not used quantitatively.

Damoulaki et al., 2025

Among 305 women with PCOS, 133 (43.6%) had no acne, 159 (52.1%) had mild acne, and 13 (4.3%) had severe acne; any acne was therefore present in 172/305 (56.4%) [21]. Fasting glucose >100 mg/dL (p=0.026) and 2-hour glucose >140 mg/dL (p=0.019) were associated with acne. In multivariable analysis, 2-hour glucose >140 mg/dL independently predicted mild/severe acne (OR 3.25, 95% CI 1.13–9.33; p=0.029). Younger age (OR approximately 0.94 per year; p=0.012) and higher DHEAS (OR approximately 1.03; p=0.006) were also independent predictors.

Meta-Analysis: HOMA-IR in Women with Versus Without Acne

Two studies reported directly compatible mean±SD HOMA-IR data according to acne presence[11,14]. Together they contributed 534 women with PCOS: 252 with acne and 282 without acne.

Table 3: Distribution of acne severity according to insulin-resistance status

Acne severity	IR (n=27)	Non-IR (n=54)	Total
Mild	7 (25.9%)	17 (31.5%)	24
Moderate	9 (33.3%)	26 (48.1%)	35
Severe	11 (40.7%)	11 (20.4%)	22
Total	27	54	81

Table 4: Meta-analysis of HOMA-IR in women with PCOS with versus without acne

Study	Acne group n; mean±SD	No-acne group n; mean±SD	Hedges g (95% CI)
Chen et al., 2011	123; 2.7±4.4	195; 3.0±3.3	−0.08 (−0.31 to 0.15)
Schmidt et al., 2016	129; 3.55±4.80	87; 4.21±9.28	−0.09 (−0.37 to 0.18)
Random-effects pooled	252	282	−0.09 (−0.26 to 0.09)

The pooled standardized mean difference was Hedges g=−0.086 (95% CI −0.259 to 0.088), standard error 0.0884, z=−0.97, p=0.334. Cochran Q was 0.007 (df=1), I^2=0%, and τ^2=0. The pooled effect was trivial in magnitude and provided no evidence that women with acne had higher fasting insulin resistance.

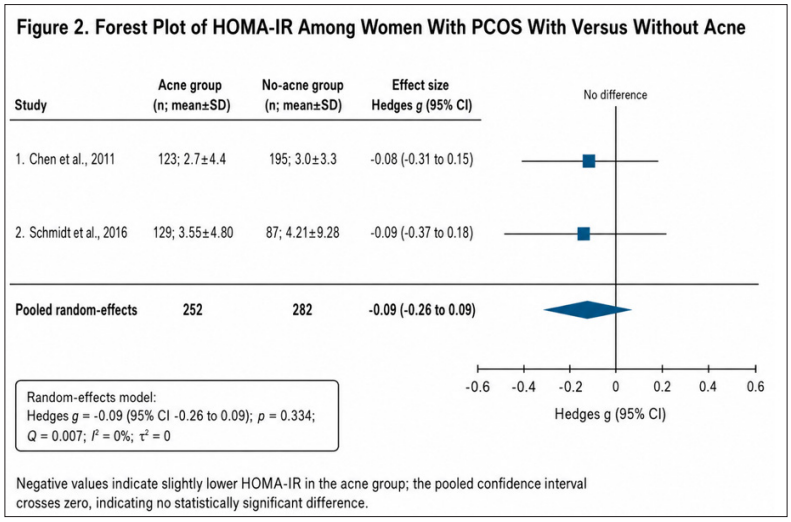

Figure 2.Forest plot of HOMA-IR among women with PCOS with versus without acne. Negative values indicate slightly lower HOMA-IR in the acne group; the pooled confidence interval crosses zero

Table 5: Summary of evidence relating insulin resistance and metabolic abnormalities to acne severity in PCOS

Study	Severity-specific numerical finding	Direction
Franik et al., 2018	No significant fasting insulin/HOMA-IR association with AGSS	Null
Chandra et al., 2021	Severe acne 40.7% with IR vs 20.4% without IR; post-hoc OR 2.69 (0.98–7.41); original p=0.146	Possible positive; imprecise
Mansour et al., 2023	HOMA-IR vs acne score r=0.037, p=0.681	Null
Gencoglu, 2024	HOMA-IR similar in moderate vs severe acne	Null
Damoulaki et al., 2025	2-h glucose >140 mg/dL: adjusted OR 3.25 (1.13–9.33)	Positive for dysglycemia

Synthesis of Acne-Severity Evidence

Across five severity-oriented datasets, three showed essentially null HOMA-IR findings, one showed a nonsignificant but potentially clinically relevant enrichment of severe acne among insulin-resistant women, and one identified a significant association between dynamic glucose intolerance and acne. The evidence therefore does not support a consistent HOMA-IR dose-response relationship with acne severity.

Reporting Bias

Formal statistical testing for reporting bias was not performed because fewer than 10 studies contributed to any synthesis. The risk of reporting bias was judged moderate because small observational studies predominate, acne severity was often a secondary outcome, and statistically significant metabolic associations may be preferentially reported.

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Certainty of Evidence

Table 6: Certainty of evidence for the relationship between insulin resistance and acne in PCOS

Outcome	Evidence base	Main effect	Certainty
HOMA-IR: acne vs no acne	2 studies; n=534	g −0.09 (95% CI −0.26 to 0.09)	Low–moderate
HOMA-IR vs continuous acne score	1 study; n=125	r=0.037; p=0.681	Low
IR and severe acne	1 study; n=81	OR 2.69 (0.98–7.41), post-hoc	Low
Dysglycemia and acne	1 study; n=305	2-h glucose >140: OR 3.25 (1.13–9.33)	Low–moderate
HOMA-IR: moderate vs severe acne	1 study; n=60	No significant difference	Low
Acne severity as surrogate of metabolic IR	Multiple observational datasets	Predominantly null/inconsistent	Low; not supported for routine use

Quantitative Summary

Table 7: Quantitative summary of the systematic review and meta-analysis

Metric	Value
Included primary studies	7
Women with PCOS in qualitative synthesis	1,267
Publication years	2011–2025
Countries represented	7
Study sample-size range	60–318
Studies in HOMA-IR meta-analysis	2
Participants in meta-analysis	534
Acne group in meta-analysis	252
No-acne group in meta-analysis	282
Pooled Hedges g	−0.086
95% CI	−0.259 to 0.088
p-value	0.334
I^2	0%
τ^2	0
Cochran Q	0.007
Direct HOMA-IR–acne score correlation	r=0.037; p=0.681
Strongest positive metabolic association	2-h glucose >140 mg/dL: OR 3.25 (95% CI 1.13–9.33)

Discussion

This systematic review and exploratory meta-analysis indicates that insulin resistance and acne severity in PCOS are related less directly than is often assumed. IR is biologically central to PCOS, yet the available clinical data do not consistently show that higher HOMA-IR corresponds to more severe acne.

Principal Findings

The pooled analysis of 534 women showed a trivial standardized difference in HOMA-IR between women with and without acne (g=−0.09, 95% CI −0.26 to 0.09). Mansour et al. found an almost zero correlation between HOMA-IR and acne score. Franik et al. and Gencoglu likewise did not identify a severity gradient. Chandra et al. provided a possible signal, with severe acne in 40.7% of insulin-resistant versus 20.4% of non-insulin-resistant women, but the original overall severity test was nonsignificant and the post-hoc OR was imprecise. Damoulaki et al. suggest that dynamic glucose intolerance may capture information that fasting HOMA-IR does not.

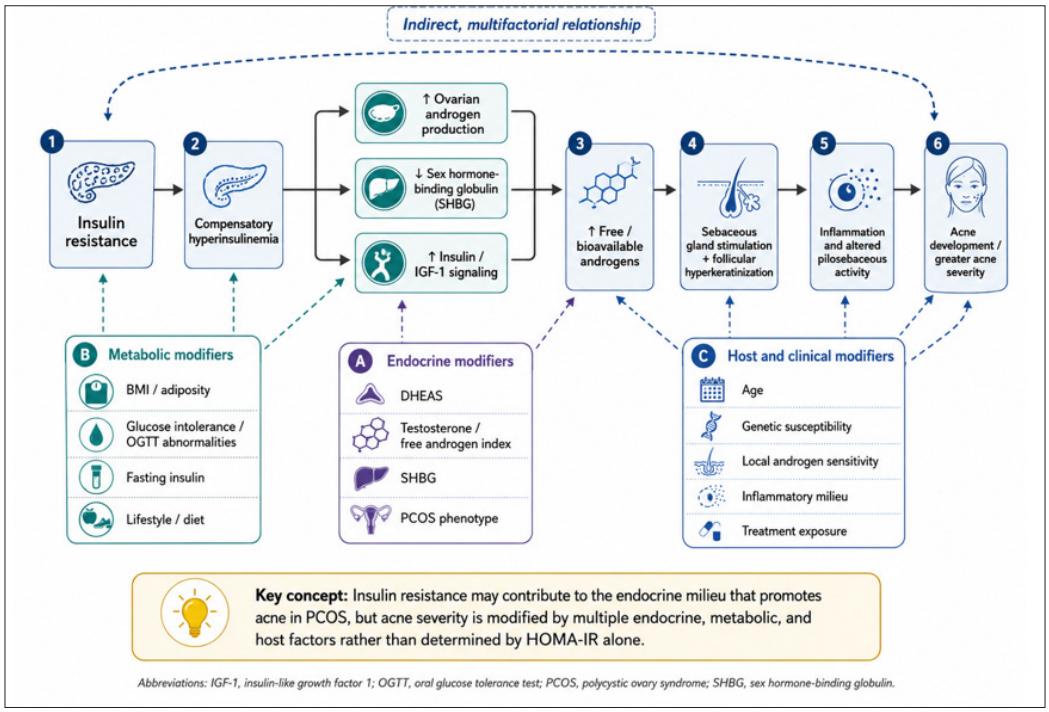

Figure 3.Proposed metabolic-endocrine pathway linking insulin resistance and acne in PCOS. The relationship is indirect and modified by multiple endocrine, metabolic and host factors

Biological Interpretation

Hyperinsulinemia can increase ovarian androgen synthesis, reduce SHBG, increase free androgen availability and influence IGF/mTOR signaling[7,9,10]. These mechanisms support an indirect pathway from metabolic dysfunction to the pilosebaceous unit. However, acne severity is likely modified by local androgen receptor sensitivity, sebaceous responsiveness, inflammatory pathways, genetics, age, microbiome and treatment exposure. The absence of a strong HOMA-IR dose-response relationship is therefore biologically plausible.

Hyperandrogenism and DHEAS

Several studies point toward androgenic factors as more reproducible acne correlates. Chen et al. reported higher DHEAS in women with acne and an adjusted association between elevated DHEAS and acne[11]. Franik et al. identified selected androgen-related associations [17], and Damoulaki et al. found DHEAS remained independently associated with acne[21]. This supports a metabolic–endocrine interaction model rather than a single HOMA-IR-driven pathway.

Confounding by BMI and Age

Women with acne may be younger and, in some cohorts, leaner than women without acne. Because BMI is strongly associated with HOMA-IR, inadequate adjustment can obscure or reverse an underlying metabolic relationship. Age is an additional confounder because acne is naturally more prevalent and active in younger women. Future analyses should adjust at minimum for age, BMI or central adiposity, DHEAS, testosterone/free androgen index, SHBG, PCOS phenotype and acne treatment.

HOMA-IR Versus Dynamic Glucose Abnormalities

HOMA-IR primarily reflects fasting insulin resistance and varies according to insulin assay, fasting conditions, ethnicity, BMI and chosen threshold. The Damoulaki study identified 2-hour glucose >140 mg/dL as an independent predictor of acne, while HOMA-based indices were not the strongest signal[21]. Future studies should consider simultaneous fasting insulin, HOMA-IR and dynamic OGTT-derived measures rather than relying on a single metabolic index.

Clinical Implications

1. Acne severity should not be used as a stand-alone screening test for insulin resistance in PCOS.
2. Metabolic assessment remains important in PCOS regardless of the severity of dermatological manifestations[2].
3. Acanthosis nigricans may be a more informative cutaneous marker of metabolic dysfunction than acne in some populations[14].
4. Severe or persistent acne should prompt comprehensive endocrine and metabolic evaluation rather than an assumption that hyperinsulinemia is the sole driver.

Treatment Implications

The null or inconsistent cross-sectional association does not imply that interventions improving insulin sensitivity have no dermatological benefit. Lifestyle modification and insulin-sensitizing therapy may improve the endocrine-metabolic environment of PCOS, but HOMA-IR reduction

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should not presently be treated as a validated surrogate endpoint for acne improvement. Acne management should remain multimodal and individualized.

Strengths of the Review

The review focuses specifically on insulin resistance and acne severity within PCOS rather than extrapolating from general acne populations. It distinguishes acne presence from acne severity and fasting HOMA-IR from dynamic dysglycemia. Quantitative pooling was restricted to directly compatible data, and post-hoc calculations were explicitly labeled as such. A mathematically impossible reported correlation value in one abstract was not used quantitatively.

Limitations of the Included Evidence

The evidence base is small and predominantly observational. Severe-acne subgroups were often small, acne grading systems and HOMA-IR thresholds differed, insulin assays were heterogeneous, and adjustment for age, adiposity and androgen status was inconsistent. Some studies evaluated acne presence rather than severity, limiting direct inference about a dose-response relationship.

Limitations of the Review Process

The review was not prospectively registered. Only two studies had directly compatible HOMA-IR data for pooling; publication bias could not be assessed statistically.

Recommendations for Future Research

Future multicenter prospective studies should use standardized PCOS criteria, validated acne severity scales, continuous acne scores, standardized insulin assays and prespecified HOMA-IR thresholds, together with OGTT, HbA1c, waist circumference and BMI. Hormonal assessment should include testosterone, SHBG, free androgen index, DHEAS and androstenedione. Models should adjust for age, BMI/central adiposity, ethnicity, PCOS phenotype and acne treatment. Continuous exposure-outcome modeling should be favored over arbitrary dichotomization.

Conclusion

This systematic review included seven primary studies and 1,267 women with PCOS. The pooled analysis of 534 women showed virtually no difference in HOMA-IR between women with and without acne (Hedges g=−0.09, 95% CI −0.26 to 0.09; p=0.334; I^2=0%). The strongest direct continuous analysis also showed essentially no association (r=0.037, p=0.681). One study suggested severe acne was more common in insulin-resistant women (40.7% vs 20.4%; post-hoc OR 2.69, 95% CI 0.98–7.41), while a recent study found 2-hour glucose >140 mg/dL independently predicted acne (OR 3.25, 95% CI 1.13–9.33). Overall, HOMA-IR alone is not a reliable marker of acne severity in women with PCOS. Metabolic screening should continue according to PCOS guidance irrespective of acne grade, and future studies should evaluate standardized acne outcomes against fasting and dynamic metabolic measures with appropriate adjustment for androgenic and adiposity-related confounding.

Registration and Protocol

This review was not prospectively registered in PROSPERO. A separate publicly accessible protocol was not prepared; protocol amendments are therefore not applicable.

Ethical Approval

Ethical approval was not required because the review used previously published aggregate data and involved no direct participant recruitment or identifiable patient data.

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Data Availability

All numerical data used in the quantitative synthesis were extracted from published reports.

Conflict of Interest

None

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