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Assay Methodology Drives Interleukin-17 Heterogeneity in Psoriasis: A Meta-Analysis

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Abstract

Psoriasis is a chronic immune-mediated skin disorder in which interleukin-17 (IL-17) plays a central role in disease pathogenesis through the TNF-α/IL-23/IL-17 inflammatory axis. Despite broad consensus on IL-17 elevation in psoriasis, reported circulating levels vary markedly across studies, and the contribution of assay methodology to this variability remains underexplored. This systematic review and meta-analysis evaluated circulating IL-17 levels in psoriasis patients compared to healthy controls, with a primary objective of estimating the pooled effect size and a secondary objective of identifying assay methodology as a potential driver of inter-study heterogeneity. A systematic search of PubMed and Scopus identified 26 eligible studies involving 1,466 psoriasis patients and 1,083 healthy controls. The pooled standardised mean difference was 1.22 (95% CI: 0.78 to 1.66, $p < 0.001$), confirming significantly elevated circulating IL-17 in psoriasis patients. Substantial heterogeneity was observed ($I^2 = 95.31\%$), prompting comprehensive moderator analysis. Diagnostic tool type (ELISA versus non-ELISA) and study sample size emerged as significant moderators, while geographic region, psoriasis subtype, sex distribution, patient age, and methodological quality score did not significantly contribute to variability. Sensitivity analysis confirmed the robustness of the pooled estimate, and no publication bias was detected. Incomplete reporting of disease severity, treatment history, and disease duration across included studies limited full characterisation of heterogeneity sources. These findings support the role of IL-17 as a biomarker and therapeutic target in psoriasis, and indicate that assay methodology represents a key source of variability in circulating IL-17 measurement. Standardised immunoassay protocols and comprehensive clinical reporting are needed in future primary research to improve the reliability and comparability of IL-17 estimates across studies.

Keywords: biomarker, ELISA, heterogeneity, interleukin-17, psoriasis

Abstrak

Psoriasis adalah gangguan kulit kronis yang dimediasi oleh sistem imun, di mana interleukin-17 (IL-17) memainkan peran sentral dalam patogenesis penyakit melalui poros inflamasi TNF-α/IL-23/IL-17. Meskipun terdapat konsensus luas mengenai peningkatan kadar IL-17 pada psoriasis, kadar yang beredar dalam sirkulasi yang dilaporkan sangat bervariasi antar penelitian, dan kontribusi metodologi pemeriksaan terhadap variabilitas ini belum banyak diteliti. Tinjauan sistematis dan meta-analisis ini mengevaluasi kadar IL-17 dalam sirkulasi pada pasien psoriasis dibandingkan dengan kontrol sehat, dengan tujuan utama mengestimasi pooled effect size *(ukuran efek gabungan) dan tujuan sekunder mengidentifikasi metodologi pemeriksaan sebagai faktor potensial penyebab heterogenitas antarpenelitian. Pencarian sistematis pada PubMed dan Scopus mengidentifikasi 26 penelitian yang memenuhi syarat, yang melibatkan 1.466 pasien psoriasis dan 1.083 kontrol sehat.* Pooled standardised mean difference *(selisih rerata terstandarisasi gabungan) adalah 1,22 (IK 95%: 0,78 hingga 1,66; p < 0,001), yang mengonfirmasi adanya peningkatan signifikan kadar IL-17 dalam sirkulasi pada pasien psoriasis. Heterogenitas yang substansial teramati ($I^2 = 95,31\%$), sehingga mendorong*

dilakukannya analisis moderator yang komprehensif. Jenis alat diagnostik (ELISA versus non-ELISA) dan ukuran sampel penelitian teridentifikasi sebagai moderator yang signifikan, sedangkan wilayah geografis, subtipe psoriasis, distribusi jenis kelamin, usia pasien, dan skor kualitas metodologis tidak berkontribusi secara signifikan terhadap variabilitas tersebut. Analisis sensitivitas mengonfirmasi ketahanan estimasi gabungan tersebut, dan tidak ditemukan adanya bias publikasi. Pelaporan yang tidak lengkap mengenai tingkat keparahan penyakit, riwayat pengobatan, dan durasi penyakit pada penelitian-penelitian yang disertakan membatasi karakterisasi menyeluruh mengenai sumber heterogenitas. Temuan ini mendukung peran IL-17 sebagai biomarker dan target terapeutik pada psoriasis, serta menunjukkan bahwa metodologi pemeriksaan merupakan sumber utama variabilitas dalam pengukuran kadar IL-17 dalam sirkulasi. Protokol immunoassay *yang terstandarisasi dan pelaporan klinis yang komprehensif diperlukan dalam penelitian primer di masa mendatang untuk meningkatkan reliabilitas dan komparabilitas estimasi IL-17 antarpenelitian.*

Kata kunci: biomarker, ELISA, *heterogenitas, interleukin-17,* psoriasis

I. INTRODUCTION

Autoimmune diseases affect around 5% of the world's population and cause significant morbidity and mortality.[1] These disorders arise from aberrant immune responses, in which the immune system mistakenly targets self-antigens, leading to tissue damage and chronic inflammation. Among autoimmune diseases, psoriasis is one of the most prevalent immune-mediated skin conditions, with prevalence varying considerably across geographic regions and ethnic populations.[2] Psoriasis is a chronic inflammatory skin disorder characterized by dysregulated interactions between immune cells and keratinocytes, resulting in persistent inflammation and abnormal epidermal proliferation. Although it is more frequent in adults, psoriasis can occur at any age.[3] Clinically, psoriasis presents as erythematous, well-demarcated, scaly plaques that are difficult to cure, prone to relapse, and substantially impair patients' quality of life.[4]

The development of psoriasis involves a complex interplay between immune cells, keratinocytes, and a network of pro-inflammatory cytokines.[5] Among these, interleukin-17 (IL-17) occupies a central position in the TNF-α/IL-23/IL-17 inflammatory axis. IL-17 is primarily produced by T helper 17 (Th17) cells, though other immune cell populations also contribute.[6,7] Upon binding to its receptor IL-17R on keratinocytes, IL-17 drives keratinocyte hyperproliferation and induces the release of additional inflammatory mediators, sustaining the chronic inflammatory cycle of psoriasis.[5,8,9] The clinical relevance of this pathway is further supported by the efficacy of IL-17-targeted biologics, including monoclonal antibodies against IL-17A and IL-17R, in reducing plaque burden and systemic inflammation.[10,11]

Despite broad consensus on IL-17 elevation in psoriasis, reported circulating levels vary markedly across published studies, even among those using nominally similar methodologies.[12,13] Inconsistencies also persist in the correlation between IL-17 levels and disease severity[14–16], attributed to differences in study populations, psoriasis subtypes, sample sizes, and specimen source.[17] A critically underexplored contributor to this variability is the measurement methodology itself. The type of immunoassay employed is known to affect cytokine quantification. Differences in antibody specificity, kit sensitivity, calibration standards, and laboratory protocols can each produce divergent IL-17 estimates across studies.

Two prior meta-analyses have examined circulating IL-17 in psoriasis.[18,19] Zhou et al.[19] reported elevated IL-17 levels across nine studies, excluding one study that used a method other than ELISA, while Liu et al.[18] conducted a broader cytokine analysis with only eleven studies, which pooled the IL-17, and without a dedicated moderator analysis focused on assay methodology. Neither study systematically evaluated the contribution of diagnostic tool type to inter-study heterogeneity, nor did they incorporate evidence published after 2022. The moderating role of study-level factors such as sample size, geographic region, and psoriasis subtype on the magnitude of IL-17 elevation also remains incompletely characterized. To address these gaps, we performed a systematic review and meta-analysis of circulating IL-17 levels in psoriasis patients compared to healthy controls. The primary objective was to estimate the pooled effect size for IL-17 elevation in psoriasis. The secondary objective was to evaluate whether ELISA or non-ELISA assay methodology is a significant driver of heterogeneity across studies.

II. METHODS

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 (PRISMA 2020) guidelines and prospectively registered in the PROSPERO database (CRD420251000274).

The search was conducted in PubMed and Scopus to identify relevant studies published up to March 2025. No restrictions were applied to publication year or geographic region. Only studies published in English were considered. The search strategy combined terms related to psoriasis ("Psoriasis vulgaris" OR "Plaque Psoriasis" OR "Psoriasis" OR "Pustular Psoriasis" OR "Generalized Pustular Psoriasis" NOT "Psoriatic Arthritis") with the cytokine term "Interleukin-17". Unpublished data, case reports, animal studies, review articles, conference abstracts, and book chapters were excluded from consideration.

Studies were eligible for inclusion if they met all of the following criteria: (i) the case group consisted of patients with a confirmed diagnosis of psoriasis; (ii) the control group consisted of healthy individuals; (iii) IL-17 levels were measured in peripheral blood samples; and (iv) the study design was cohort, case-control, cross-sectional, or observational. Studies were excluded if they involved: (i) psoriasis patients who were pregnant, had a history of cancer or other autoimmune diseases, or had received psoriasis therapy within two weeks prior to the study; (ii) patients diagnosed with psoriatic arthritis; (iii) IL-17 measurement from non-peripheral blood samples, such as skin tissue; or (iv) non-primary study formats, including reviews, book chapters, case reports, conference abstracts, and animal studies.

Records retrieved from both databases were imported into the Rayyan AI web-based screening tool for title and abstract screening. Records deemed irrelevant were excluded at this stage. Full texts of potentially relevant studies were subsequently assessed against the predefined eligibility criteria. The first reviewer performed the initial screening, and the second reviewer independently verified all inclusion and exclusion decisions. Discrepancies were resolved through discussion between the two reviewers. Where consensus could not be reached, a third reviewer provided the final decision. The complete study selection process is illustrated in the PRISMA flow diagram (Fig. 1).

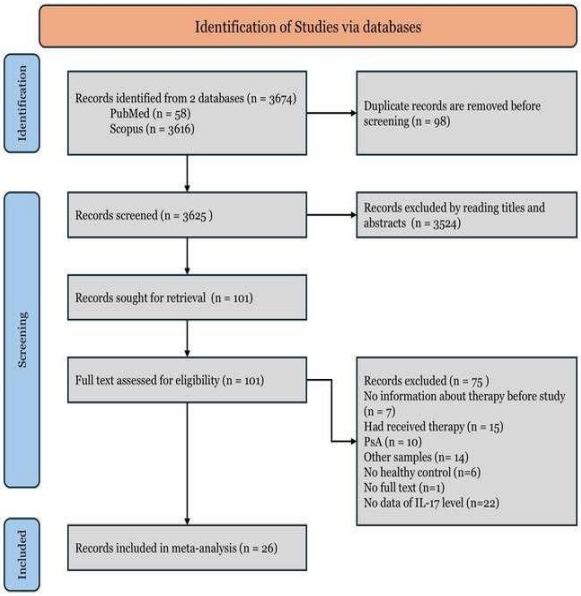

FIGURE 1. PRISMA FLOW DIAGRAM.

The methodological quality and risk of bias of the included studies were independently quantified by two reviewers using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist appropriate for each study design. Each checklist item was scored categorically as 'Yes' (1 point), 'No' (0 points), or 'Unclear' (0 points). Inter-rater agreement was statistically evaluated using Cohen's kappa coefficient, with any discrepancies resolved via consensus. To evaluate the impact of study quality on the pooled estimates, the cumulative quality scores were converted into a mathematical proportion of the maximum attainable score, and a predefined threshold of ≥70% was utilized to dichotomize studies into low and high risk of bias for subsequent subgroup analyses.

The following data were extracted from each included study: first author, year of publication, country, number of psoriasis patients and healthy controls, psoriasis type, sex distribution, mean age of participants, diagnostic method used to measure IL-17, and IL-17 levels. IL-17 levels were recorded as mean ± standard deviation (SD) where available. For studies reporting IL-17 as median with interquartile range (IQR) or median with minimum-maximum range, data were converted to mean and SD using the Meta-Analysis Accelerator web-based.[20] Data extraction was performed by the first reviewer and verified by the second reviewer, with discrepancies resolved as described above.

All statistical analyses were performed using JAMOVI Desktop for Windows (version 2.6), with the Mean Analysis function in the MAJOR module. The effect size was expressed as the standardized mean difference (SMD) with 95% confidence intervals (CI), comparing IL-17 levels between psoriasis patients and healthy controls. Statistical heterogeneity was comprehensively evaluated using the Cochrane Q test, the I^2 statistic, and the between-study variance (tau^2). A random-effects model was fitted to the data, utilizing the restricted maximum-likelihood (REML) estimator to calculate tau^2. Whenever heterogeneity was detected $tau^2 > 0$, a 95% prediction interval for the true outcomes was provided.

To explore potential sources of heterogeneity, moderator analyses were conducted using study-level characteristics as moderating variables. Categorical moderators included geographic region (Asia versus others), sex distribution (proportion of female versus male participants), psoriasis type (psoriasis vulgaris versus others), and diagnostic tool (ELISA versus non-ELISA). Continuous moderators included mean age of psoriasis patients, JBI score, and total number of psoriasis patients per study. The robustness of pooled estimates was examined through sensitivity analysis, in which individual studies were sequentially omitted to assess their influence on the overall result. Outliers were identified based on standardized residuals, and influential studies were assessed using Cook's distances. Publication bias and funnel plot asymmetry were statistically verified using the rank correlation test and Egger's regression test.

III. RESULT

A total of 3,674 records were initially identified from PubMed and Scopus using the predefined search strategy. After removing 98 duplicate records, 3,625 unique articles were available for screening. During title and abstract screening, 3,524 records were excluded as irrelevant, consisting mainly of review articles, animal studies, case reports, and studies that did not investigate IL-17 in the context of psoriasis. The remaining 101 full-text articles were assessed for eligibility. Of these, 75 articles were excluded. The most common reasons for exclusion were failure to fulfill the predefined selection criteria, absence of information regarding psoriasis therapy prior to sample collection, and failure to report IL-17 levels in a usable format (mean ± SD, median with IQR, or median with minimum-maximum range). One additional study was excluded because the full text could not be retrieved. Ultimately, 26 studies fulfilled all eligibility criteria and were included in the quantitative synthesis, collectively involving 1,466 psoriasis patients and 1,083 healthy controls. Detailed characteristics of the included studies are presented in Table 1.

The methodological quality of the κ=26 included studies demonstrated a low overall risk of bias, with a mean JBI quality score of μ= 94.71% (SD = ±7.15%; range: 75% – 100%). Statistically, 100% of the included studies (n=26) achieved a high-quality score above the predefined ≥70% threshold, indicating a highly robust internal validity across the evidence base. Minor methodological deficiencies were isolated and exclusively observed in a few studies,

such as Wojciechowska et al. (2023), which presented a lower but acceptable score of 75%. This uniform high-quality profile confirms that the observed inter-study heterogeneity was not driven by discrepancies in methodological rigor, as further validated by the detailed study-specific JBI scores presented in Table 1.

The pooled analysis yielded an SMD of 1.22 (95% CI: 0.78 to 1.66, $p < 0.001$), indicating that circulating IL-17 levels were significantly higher in psoriasis patients than in healthy controls. The distribution of individual study effect sizes and the overall pooled estimate are illustrated in the forest plot (Fig. 2).

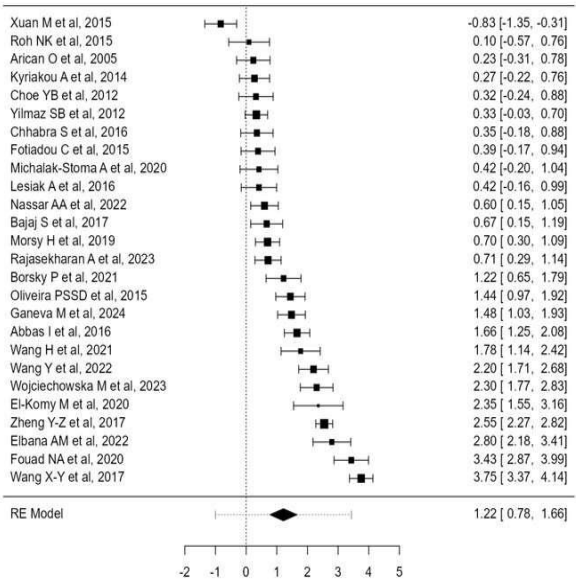

FIGURE 2. THE FOREST PLOT. THE SMD RESULTS OF IL-17 LEVELS IN PSORIASIS FROM 26 ARTICLES.

Assessment of between-study variability revealed substantial heterogeneity, with an I^2 value of 95.31% and a statistically significant Cochrane Q test ($p < 0.001$). As the I^2 value exceeded 50%, a random-effects model was applied to account for both within-study and between-study variance. Accordingly, a 95% prediction interval for the true outcomes was evaluated, yielding a range from -1.0007 to 3.4362.

Moderator analysis was performed to explore potential sources of the observed heterogeneity. Four categorical moderators were examined: geographic region (Asia versus others), sex (female versus male), psoriasis type (psoriasis vulgaris versus others), and diagnostic tool (ELISA versus non-ELISA). Three continuous moderators were also examined: mean age of psoriasis patients, JBI score, and total number of psoriasis patients per study. Due to incomplete reporting of sex and age data across studies, these two moderators were examined using a reduced set of studies.

Among the categorical moderators, geographic region did not significantly moderate the association ($p = 0.995$; $I^2 = 95.45\%$). Sex distribution showed no significant moderation ($p = 0.431$; $I^2 = 95.63\%$), nor did psoriasis type ($p = 0.904$; $I^2 = 95.46\%$). Among continuous moderators, the mean age of psoriasis patients was not a significant moderator ($p = 0.312$; $I^2 = 95.4\%$), and JBI score similarly showed no meaningful contribution ($p = 0.282$; $I^2 = 95.28\%$).

In contrast, diagnostic tool type was a significant moderator ($p = 0.011$; $I^2 = 94.32\%$), with ELISA-based studies reporting larger effect sizes than non-ELISA studies. The pooled effect size of the ELISA-based studies, after excluding the non-ELISA studies, is an SMD of 1.44 (95% CI: 0.98 to 1.89; $p < 0.001$; $I^2 = 95.03\%$). The pooled effect size of the non-ELISA-based studies, after excluding the ELISA-based studies, is an SMD of -0.01 (95% CI: -0.58 to 0.55; $p = 0.959$; $I^2 = 75.12\%$). The total number of psoriasis patients per study also emerged as a significant moderator ($p = 0.005$; $I^2 = 93.68\%$), suggesting that study sample size contributed to variability in observed effect sizes.

Sensitivity analysis was conducted by sequentially omitting individual studies. Based on standardized residuals, no study exceeded a value of ±3.1019, indicating the

absence of statistical outliers. Based on Cook's distances, one study (Wang X-Y et al., 2017 [21]) was identified as potentially influential. Exclusion of this study did not materially alter the pooled effect size, supporting the robustness of the overall findings.

Publication bias was assessed using Egger's regression test and visual inspection of the funnel plot. The Egger's regression intercept was -0.356 ($p = 0.722$), exceeding the threshold of $p > 0.1$. Funnel plot inspection revealed no apparent asymmetry (Fig. 3). These results indicate no evidence of publication bias in the present meta-analysis.

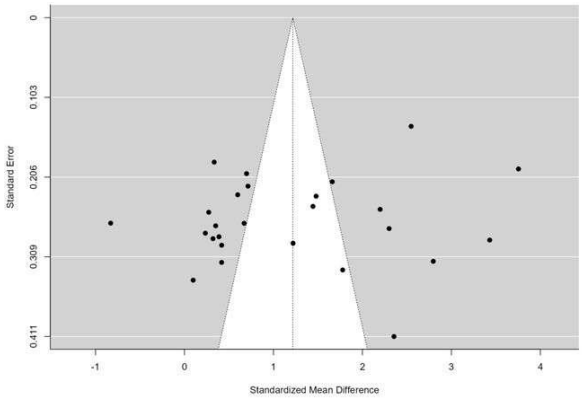

FIGURE 3. THE FUNNEL PLOT

IV. DISCUSSION

Psoriasis is a chronic immune-mediated skin disorder with a multifactorial etiology, in which the interplay between genetic, epigenetic, and environmental factors triggers immune dysregulation and activates pro-inflammatory pathways.[22] Among these, the TNF-α/IL-23/IL-17 axis is one of the most extensively studied in psoriasis pathogenesis. IL-17 acts as a downstream effector in this axis, directly interacting with keratinocytes to induce hyperproliferation and excessive production of inflammatory mediators, which manifest clinically as thickened, scaly plaques. This mechanistic understanding has informed the development of IL-17-targeted biologic therapies, including inhibitors that block IL-17 binding to its receptor on keratinocytes.[23]

The present meta-analysis confirms that circulating IL-17 levels are significantly elevated in psoriasis patients compared to healthy controls, with a pooled SMD of 1.22 (95% CI: 0.78 to 1.66, $p < 0.001$). These findings are consistent with two prior meta-analyses that similarly reported elevated circulating IL-17 in psoriasis.[18,19] The present analysis, however, extends this evidence base in two important respects. First, it incorporates a larger number of studies (26 studies) and a broader patient population (1,466 psoriasis patients) than either prior analysis. Second, and more critically, it is the first to systematically evaluate assay methodology as a categorical moderator of heterogeneity, identifying diagnostic tool type as a significant contributor to inter-study variability. The geographic diversity of included studies, spanning Asia, Africa, the Americas, and Europe, further strengthens the generalisability of the pooled estimate.

The substantial heterogeneity observed in this meta-analysis ($I^2 = 95.31\%$) warrants careful interpretation of the pooled SMD. Although a random-effects model was applied to account for between-study variance, an I^2 of this magnitude indicates that the true effect size likely varies considerably across studies. The sources of this variability were therefore examined through a comprehensive moderator analysis.

Among the moderators evaluated, diagnostic tool type emerged as a significant contributor to heterogeneity ($p = 0.011$), with ELISA-based studies reporting larger effect sizes and being the primary driver of heterogeneity, whereas non-ELISA-based studies showed smaller effect sizes and less heterogeneity. This finding is consistent with evidence that cytokine quantification is highly sensitive to assay-related factors,

including antibody specificity, kit sensitivity, calibration curve parameters, sample preparation procedures, and inter-laboratory protocols.[24] Whether these assay-related differences account for the full magnitude of tool-dependent variability observed across the included studies warrants further investigation.

The total number of psoriasis patients per study also emerged as a significant moderator ($p = 0.005$). Studies with smaller sample sizes tended to report larger effect sizes, consistent with well-documented small-study effects in meta-analytic literature [25]. Whether this pattern reflects genuine biological variability in smaller study populations or methodological instability in underpowered designs remains an open question in the interpretation of IL-17 data across studies.

By contrast, geographic region, psoriasis type, sex distribution, mean patient age, and JBI methodological quality score did not significantly moderate the association between IL-17 levels and psoriasis. The absence of a significant regional or disease-subtype effect suggests that IL-17 elevation may represent a consistent biological feature of psoriasis regardless of geographic background or clinical variant.[26,27] The non-significant contribution of JBI score indicates that the observed heterogeneity was not primarily attributable to differences in study quality, though this finding does not diminish the importance of rigorous study design in primary research.

Several moderators of potential clinical relevance could not be fully assessed due to incomplete reporting across included studies. Variables such as disease duration, severity indices, prior systemic or biologic therapy, and comorbid inflammatory conditions were not consistently reported.[12,14,15,17,21,28–48] As these factors are known to influence cytokine expression[49,50], their absence limits the ability to fully characterize sources of heterogeneity and may affect the precision of the pooled estimate. The extent to which these unreported variables contributed to the residual heterogeneity observed in this analysis cannot be determined from the available data.

The robustness of the pooled findings was supported by sensitivity analysis. Sequential omission of individual studies did not materially alter the overall effect size, and no statistical outliers were identified based on standardized residuals. Wang X-Y et al. 2017[21] was identified as a potentially influential study based on Cook's distances; however, its exclusion did not change the direction or significance of the pooled estimate.

From a clinical standpoint, the confirmed elevation of circulating IL-17 in psoriasis strengthens the rationale for IL-17-targeted therapy.[26,51] IL-17 inhibitors have demonstrated efficacy in reducing plaque severity[52,53], improving quality of life[54], and attenuating systemic inflammation.[55,56]. It remains unclear, however, whether circulating IL-17 levels consistently correlate with disease severity, therapeutic response, or long-term prognosis, which represents an important gap in the current evidence base.

The variability in IL-17 estimates observed across studies also raises broader considerations for clinical practice. Standardized measurement protocols, including consistent ELISA kit calibration and uniform sample processing procedures, are necessary to ensure that circulating IL-17 assessments are reliable and comparable across settings. How stratification by age, sex, psoriasis subtype, and treatment history might further clarify IL-17 dynamics in future studies remains to be examined.

Several limitations of the present meta-analysis should be acknowledged. The reliance on published data meant that studies with incomplete IL-17 reporting could not be

included, which may have introduced selection bias. The high residual heterogeneity not explained by the examined moderators suggests that additional sources of variability remain unidentified. Longitudinal data on IL-17 trajectories in relation to disease course and treatment response were also unavailable from the included cross-sectional and case-control studies. Future meta-analyses incorporating individual patient data and standardized cytokine measurement protocols would be better positioned to address these gaps.

TABLE 1. CHARACTERISTICS OF 26 RESEARCH STUDIES

Author	Year	Region	Psoriasis Type	Diagnostic Tools	JBI Score	Healthy Controls		Psoriasis Patients				
						n	IL-17 level (pg/ml)	Age	Male	Female	n	IL-17 level (pg/ml)
Arican O et al[28]	2005	Turkey	PV	ELISA	87,5	23	7,4 ± 3,76	35 ± 15,5	18	12	30	8,3 ± 3,8
Choe YB et al[29]	2012	South Korea	PV	Other	87,5	15	3,7 ± 2	36,3 ± 14	41	30	71	6,4 ± 9,1
Yilmaz SB et al[17]	2012	Turkey	PsO	ELISA	87,5	50	4,4 ± 4,1	39,9 ± 14,9	36	34	70	6,64 ± 8
Kyriakou A et al[30]	2014	Greece	PV	ELISA	100,0	32	1,8 ± 2,81	44,53 ± 15,6	9	23	32	2,67 ± 3,46
Xuan M et al[31]	2015	China	PV	Other	100,0	20	37,04 ± 71,24	37,11 ± 12,82	42	20	62	7,44 ± 7,58
Fotiadou C et al[32]	2015	Greece	PV	Other	100,0	20	0	47 ± 16	28	7	35	91,8 ± 291,2
Roh NK et al[33]	2015	South Korea	PsO	Other	87,5	10	1,42 ± 2,36	36,6 ± 14,2	-	-	68	1,73 ± 3,23
Oliveira PSSD et al[14]	2015	Brazil	PV	ELISA	100,0	35	3,9 ± 0[b]	50,2 ± 13,3	30	23	53	885,42 ± 778,17[b]
Chhabra S et al[34]	2016	North India	PV	ELISA	87,5	24	1,31 ± 1,00	37,5 ± 13,5	27	7	34	1,81 ± 1,63
Lesiak A et al[35]	2016	Poland	PPP	ELISA	87,5	29	0,75 ± 1,72	51,8	0	20	20	2 ± 4,13
Abbas I et al[36]	2016	Iraq	PsO	ELISA	100,0	60	22,7 ± 4,96	-	29	31	60	346,02 ± 273,46
Bajaj S et al[37]	2017	India	PV	ELISA	100,0	30	1,69 ± 0,45	37	-	-	30	2,53 ± 1,69
Zheng Y-Z et al[38]	2017	China	PV	ELISA	100,0	175	8,14 ± 1,79	39,5 ± 12,7	120	74	194	16,82 ± 4,37
Author	Year	Region	Psoriasis Type	Diagnostic Tools	JBI Score	Healthy Controls		Psoriasis Patients				
						n	IL-17 level (pg/ml)	Age	Male	Female	n	IL-17 level (pg/ml)
Wang X-Y et al[21]	2017	China	PV	ELISA	100,0	109	16,52 ± 6,54	36,7 ± 10,07	106	83	189	80,79 ± 20,84
Morsy H et al[12]	2019	Egypt	PV	ELISA	100,0	50	32,5 ± 12,82[a]	40,75 ± 15,4	28	17	55	128,03 ± 187,2[a]
Fouad NA et al[39]	2020	Egypt	PV	ELISA	100,0	60	15,1 ± 2,1	48,9 ± 1,6	32	28	60	25,7 ± 3,8
Michalak-Stoma	2020	Poland	PV	ELISA	100,0	20	3,06 ± 1,19	50,14 ± 14,51	21	0	21	4,24 ± 3,69

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A et al[15]												
El-Komy M et al[40]	2020	Egypt	PV	ELISA	100,0	20	17,53 ± 3,47[b]	41,8 ± 12,25	15	5	20	26,35 ± 3,85[b]
Borsky P et al[41]	2021	Czech Republic	PV	ELISA	100,0	28	17,52 ± 3,09[a]	44,07 ± 35,15	17	11	28	23,08 ± 5,55[a]
Wang H et al[42]	2021	China	PsO	ELISA	100,0	20	68,9 ± 11,92	47,5 ± 3,36	21	15	36	237,28 ± 115,65
Wang Y et al[43]	2022	China	PV	ELISA	100,0	50	0,32 ± 0,12	45,47 ± 12,34	28	27	55	0,82 ± 0,29
Elbana AM et al[44]	2022	Egypt	PsO	ELISA	100,0	40	63,4 ± 20,1	45,48 ± 14,35	22	18	40	243,7 ± 88,04
Nassar AA et al[45]	2022	Egypt	PV	ELISA	100,0	40	170.100 ± 22.600	42,3 ± 13,7	28	12	40	212.700 ± 97.100
Rajasekharan A et al[46]	2023	South India	PsO	ELISA	100,0	45	4,12 ± 2,19[a]	41,3 ± 12,6	35	10	45	7,22 ± 5,68[a]
Wojciechowska M et al[47]	2023	Poland	PsO	ELISA	75,0	30	29.925 ± 8.063[b]	44,5	37	33	70	63.350 ± 16.372[b]
Ganeva M et al[48]	2024	Bulgaria	PV	ELISA	100,0	48	2,16 ± 0,95[a]	52,85 ± 10,81	30	18	48	5,02 ± 2,54[a]

PV for Psoriasis Vulgaris or Plaque Psoriasis; PsO for Psoriasis; PPP for Pustular Palmoplantar Psoriasis; n indicates number; age is presented as mean ± SD in years; IL-17 levels are presented as mean ± SD in pg/ml. Decimals are expressed using a comma. Data transformation used Meta-Analysis Accelerator [20]. [a]Median and IQR range used Interquartile Range (IQR) to Mean & Standard Deviation (SD) type of Meta-Analysis Accelerator. [b]Median and minimum-maximum range used Median & Range to Mean & Standard Deviation (SD) type of Meta-Analysis Accelerator.

V. CONCLUSIONS

The present systematic review and meta-analysis demonstrates that circulating IL-17 levels are significantly elevated in psoriasis patients compared to healthy controls, with a pooled SMD of 1.22 (95% CI: 0.78 to 1.66, $p < 0.001$) across 26 studies involving 1,466 psoriasis patients and 1,083 healthy controls. This finding is consistent with the established role of IL-17 in the TNF-α/IL-23/IL-17 inflammatory axis and supports its consideration as a biomarker for disease presence and a target for therapeutic intervention.

Beyond confirming IL-17 elevation, this analysis identified assay methodology and study sample size as significant moderators of inter-study heterogeneity, with ELISA-based studies yielding larger effect sizes and heterogeneity than non-ELISA studies. Geographic region, psoriasis subtype, sex distribution, patient age, and methodological quality score did not significantly contribute to variability. Substantial residual heterogeneity ($I^2 = 95.31\%$) nonetheless persisted, partly attributable to incomplete reporting of clinically relevant variables such as disease severity, treatment history, and disease duration across included studies. Future primary research incorporating standardized immunoassay protocols and comprehensive clinical reporting will be essential to address these gaps.

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