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Review Article

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Revealing the Atopic Nexus: A Systematic Review and Meta-Analysis of Pityriasis Alba

Prathyusha Prabhakar [1], Archana Suresh [1], Darsan S [1], Noula Rahim [2], Jamila Hameed *[1]

[1]Department of Dermatology, Karuna Medical College, Vilayodi, Kerala, 678103, India.
[2]Department of Biochemistry, Karuna Medical College, Vilayodi, Kerala, 678103, India.

*Corresponding Author: Jamila Hameed; *hameedjamila78@gmail.com*

Abstract

Background: Pityriasis alba (PA) is a benign and common dermatosis predominantly occurring in children in association with atopy. Although it is very common, there is limited systematic investigation into its association with atopic dermatitis (AD) and other atopic disorders. ***Aim and Objective:*** The aim of this research is to determine the prevalence of pityriasis alba (PA) and its association with atopy, with the question in mind: "What is the strength of the association between pityriasis alba and atopy in studies from 2014 to 2023?". ***Methods:*** Systematic review was performed using PubMed, Embase, and Scopus for 2014-2023 studies according to PRISMA 2020 guidelines. Full-text PDF studies with focus on PA prevalence or atopy association were included. Four studies with atopy data were meta-analysed using a random-effects model. ***Results:*** We had eight studies, and three of them were included in meta-analysis. The overall prevalence of atopy in PA patients was 0.66 (66%), 95% CI: 0.62-0.70, $I^2 = 0\%$. PA was always linked with atopy, especially AD. ***Conclusion:*** PA is highly correlated with atopy, thus supporting its status as a minor manifestation of AD. Moreover, further large-scale studies are required to support this correlation.

Keywords: ***Atopy, Pityriasis alba, Atopic dermatitis, Meta-analysis, Prevalence, Systematic review, Children, Skin disorder.***

Introduction

Pityriasis alba (PA) is the development of scaly patches especially in children. The global prevalence is about 1% to 9.9% and increased rates are reported in tropical countries like Mali (20%) and Egypt (18%) (Givler D N *et al.*, 2024).

While it is typically a benign disorder, the pathogenesis of PA is poorly elucidated, with numerous putative causes described, including xerosis, ultraviolet exposure, and microbial effects (Shashikumar MB *et al.*, 2024). There is strong evidence that PA is linked to atopy, especially atopic dermatitis (AD), occurring in approximately 15-20% of children worldwide (Abdelwahab AA *et al.*, 2023). This coincidence has been the grounds for hypotheses that PA is a milder variant of AD, as postulated by diagnostic criteria proposed by Hanifin and Rajka (Hanifin JM *et al.*, 1980).

The rising global prevalence of atopic conditions highlights the need to identify PA's place in this category. Recent studies indicate that impaired skin barrier function, typical of AD, is also likely to be implicated in PA's etiology, with abnormal ceramide levels and filaggrin mutations shared between them. Environmental causes such as overexposure to the sun or inadequate hygiene also contribute to its presentation, especially in resource-poor areas. Developments in dermatological science have taken center stage with inflammatory mechanisms in hypopigmented disorders, with cytokines such as IL-6 and TNF-α potentially providing a link between PA and atopy. Systematic reviews of these associations over the last decade, however, are limited in the face of available large cohort studies and molecular studies since 2014.

Clinically, PA treatment is still empirical, with low-potency corticosteroids and emollients, a reflection of its overlap with AD treatment strategies. It is up to 90% prevalence in paediatric populations in some series requires improved understanding of its epidemiology and risk factors.

Our systematic review and meta-analyses aimed to conclude the association between pityriasis alba and atopy in studies published between 2014 and 2023 so that the study focused on evidence-based management of the chronic skin disease.

Methodology

A systematic review and meta-analysis were conducted following PRISMA 2020 guidelines (**Figure 1 a**). Databases (PubMed, Embase, Scopus) were searched for studies from 2014 to 2023, using keywords: "pityriasis alba", "atopy", "atopic dermatitis", and "prevalence". Full-text PDFs were retrieved, and data were extracted by two reviewers (P.P and A.S). Meta-analysis was performed using REML (random-effects model) on studies reporting atopy prevalence. The quality of the selection of the studies was assessed using the New-Castle Ottawa Scale (**Figure 1 b**). The first author's name with year of publication, study design with period of study, country of study, sample size and study characteristics were tabulated (**Table 1**).

Inclusion Criteria

- PDF-published full-text articles from 2014 to 2023
- Primary research articles (e.g., case-control, cross-sectional, cohort)

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- Studies of PA prevalence, clinical presentation (e.g., lesion distribution, duration), or atopy associations (e.g., AD, asthma, allergic rhinitis) in humans
- At least 20 PA patients are required to ensure the results are valid, with definite rules for diagnosis (such as clinical and histopathological).
- English articles

Exclusion Criteria

- Case reports, case series with fewer than 20 PA patients, letters to the editor, editorials, or commentaries without original data or statistical analysis.
- Pre-2014 publications, to emphasize recent findings that correlate with advances in dermatological diagnostics and research into atopy.
- Non-specific studies not addressing PA as a primary outcome (e.g., general dermatoses studies with no PA-specific findings) or not distinguished from other similar conditions (e.g., vitiligo, post-inflammatory hypopigmentation).
- Non-human literature (e.g., animal model), non-English publications without translation, or duplicate reports using the same datasets.

No ethical approval was needed since we conducted a systematic review and meta-analyses.

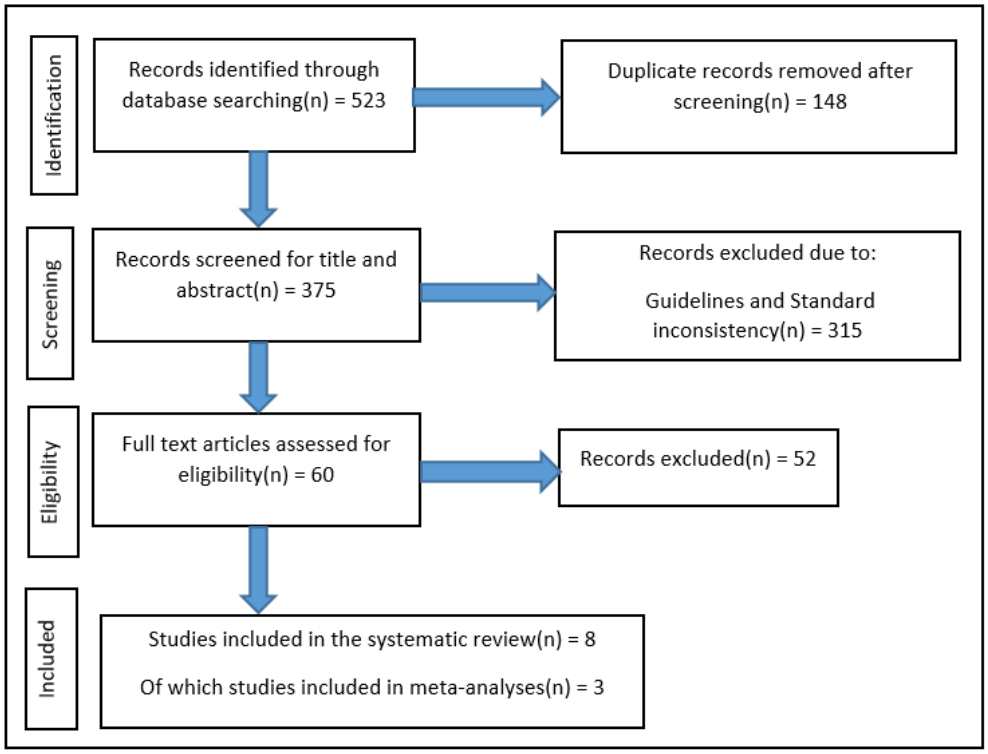

Figure 1 a): Flowchart for selection of studies

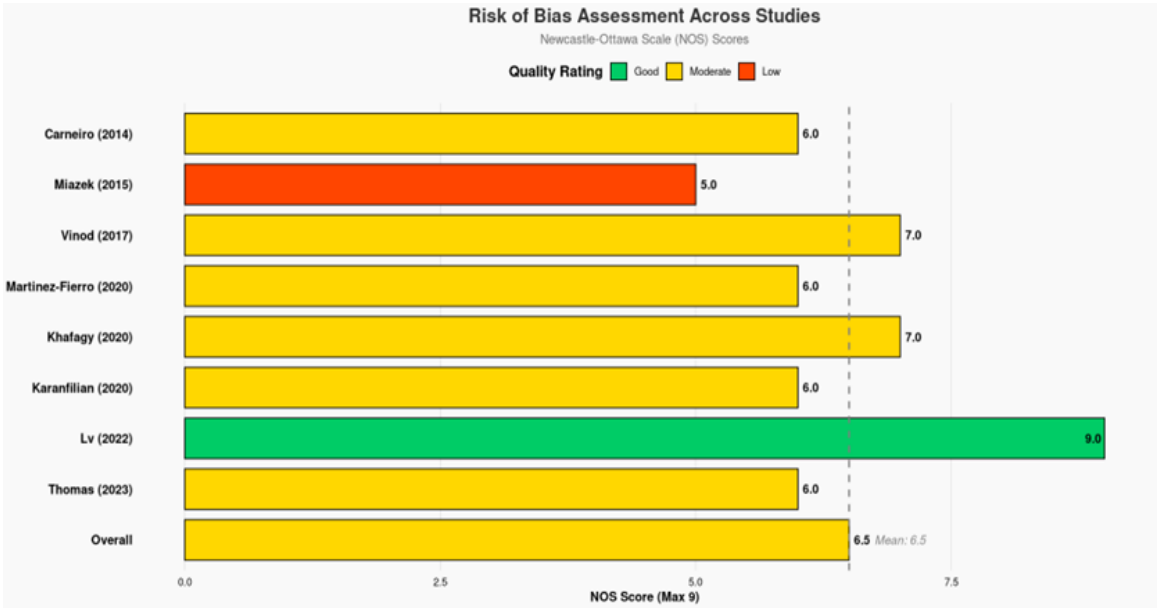

Figure 1 b): Risk of bias

Results

Eight studies met inclusion criteria, with three suitable for meta-analysis on atopy.

The PA-atopy prevalence for the three studies taken in meta-analyses were 69%, 66% and 73% respectively (Khafagy GM *et al.*, 2020, Lv Y *et al.*, 2022 and Martinez-Fierro ML *et al.*, 2020).

Screening Flow

A total of 523 records were identified from the electronic databases of Pubmed, Embase and Scopus (192, 165 and 166 respectively) using the keywords "pityriasis alba", "atopy," "atopic dermatitis", and "prevalence" following the 2020 PRISMA guidelines (**Figure 1 a**). A total of 148 duplicates were removed. During the title and abstract screening, a total of 315 articles were excluded from 375 records. About 60 articles were evaluated for full-text eligibility of which 51 were removed due to lack of data and full text. Finally, a total of eight studies were selected for the systematic review of which three were taken for the meta-analyses.

The overall prevalence in the forest plot for atopy in PA patients was 0.66 (66%), 95% CI: 0.62-0.70, $I^2 = 0\%$ with only three studies included in the meta-analyses making the tests less reliable and limiting the scope of data analyses (**Figure 2**).

Funnel's and Egger's test

The funnel plot shows asymmetry attributed to geographical and chronological variations (**Figure 3**). However, the Egger's test intercept was 0.738 with a p value higher than 0.05 indicating no significant publication bias. The results should be interpreted with caution due to the inclusion of small number of studies in the meta-analyses. The bubble meta regression graph was also plotted (**Figure 4**).

Table 1: Study Characteristics

Sl No	First Author (Year)	Study Design (Period)	Country	Sample Size (PA)	Study Characteristics (M:F, Mean Age in Years)
1	Carneiro FR *et al.* (2014)	Histopathological (2012-13)	Brazil	20	12:8, 8.5
2	Miazek N *et al.* (2015)	Review (NA)	Poland	NA	NA
3	Vinod K *et al.* (2017)	Case-control (2015-16)	India	50	28:22, 9.8
4	Martinez-Fierro ML *et al.* (2020)	Molecular (2018-19)	Mexico	30	16:14, 11.3
5	Khafagy GM *et al.* (2020)	Case-control (2018-19)	Egypt	60	5530:25, 10.1
6	Karanfilian KM *et al.* (2020)	Histologic (2018-19)	USA	25	13:12, 12.1
7	Lv Y *et al.* (2022)	Epidemiological (2019-21)	China	2726	1400:1326, 8.7
8	Thomas IN *et al.* (2023)	Observational (2021-22)	India	100	52:48, 9.2

Table 2: Important Findings

Sl No	First Author (Year)	Key Findings
1	Carneiro FR *et al.* (2014)	Factor XIIIa+ dendrocytes were increased in PA lesions, suggesting inflammation (80% of 20 cases).
2	Miazek N *et al.* (2015)	PA prevalence ranged 1-5%, strongly linked to atopy in 70-90% of cases (review-based).
3	Vinod K *et al.* (2017)	Zinc levels were lower in 50 PA patients (mean 72 µg/dL) vs. controls (88 µg/dL, $p<0.05$).
4	Martinez-Fierro ML *et al.* (2020)	Inflammatory genes (e.g., IL-6) upregulated in 73% of 30 PA cases, linked to atopy.
5	Khafagy GM *et al.* (2020)	Lower hemoglobin, ferritin, zinc, copper, magnesium in 55 PA patients vs. controls; zinc deficiency increased PA risk >15-fold ($p<0.001$).
6	Karanfilian KM *et al.* (2020)	Histologic changes in 25 PA cases showed spongiosis in 68%, suggesting early inflammation.
7	Lv Y *et al.* (2022)	66% of 2726 PA patients had atopy; prevalence 3.8%; AD in 40%.
8	Thomas IN *et al.* (2023)	Dermoscopy aided PA diagnosis in 100 cases; 60% had atopy, mean duration 6 months.

Table 3: Merits and Gaps

Sl No	First Author (Year)	Merits	Gaps
1	Carneiro FR *et al.* (2014)	Novel histologic insight	Small sample, no atopy focus
2	Miazek N *et al.* (2015)	Comprehensive review	No primary data
3	Vinod K *et al.* (2017)	Trace element analysis	No atopy association
4	Martinez-Fierro ML *et al.* (2020)	Molecular evidence	Small sample, costly methodology
5	Khafagy GM *et al.* (2020)	Broad trace element analysis, Limited atopy exploration, small sample	Broad trace element analysis. Limited atopy exploration, small sample
6	Karanfilian KM *et al.* (2020)	Detailed histology	Small sample, no prevalence data
7	Lv Y *et al.* (2022)	Large sample, epidemiology	No molecular data
8	Thomas IN *et al.* (2023)	Diagnostic innovation	Observational, no control group

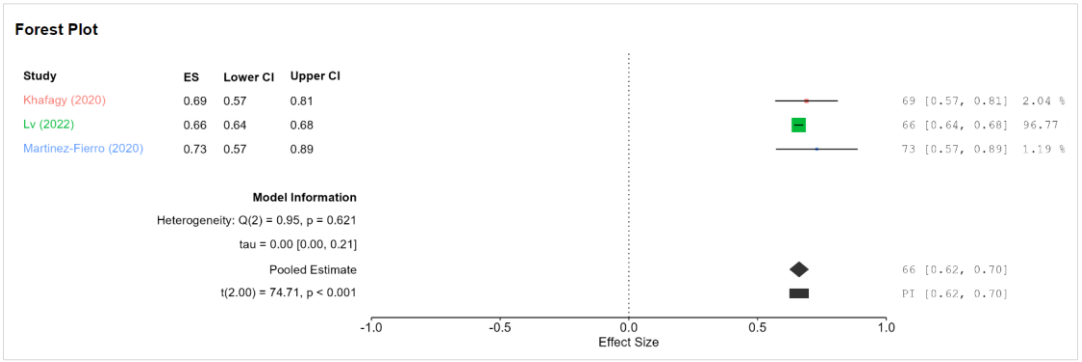

Figure 2: Forest plot for meta-analyses

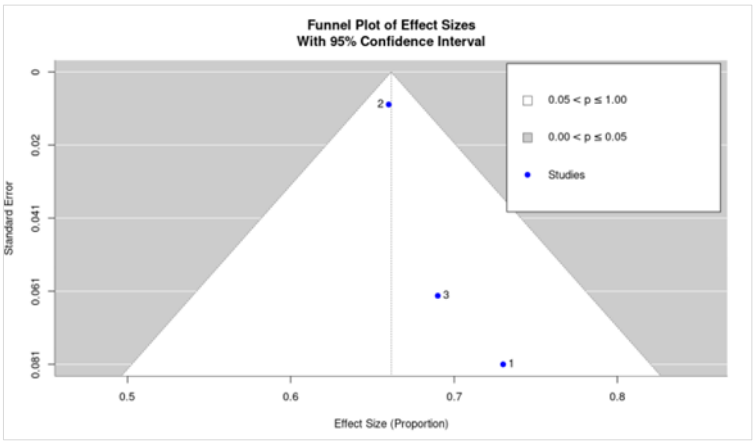

Figure 3: Funnel plot

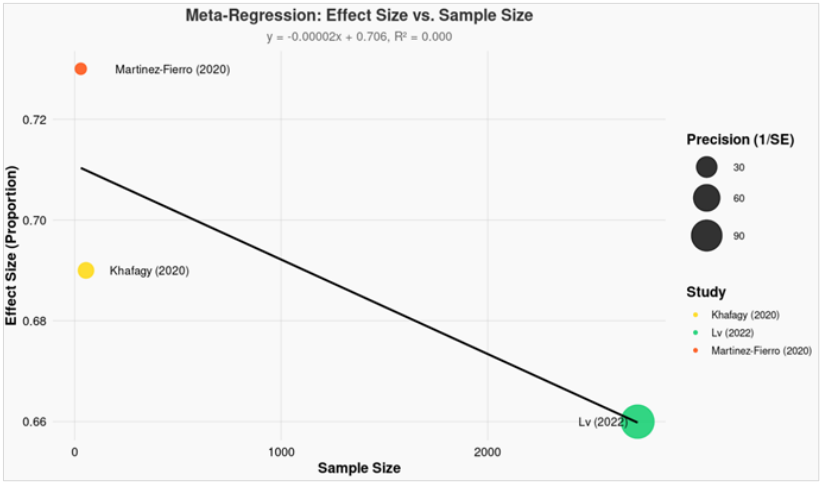

Figure 4: Bubble-meta regression plot

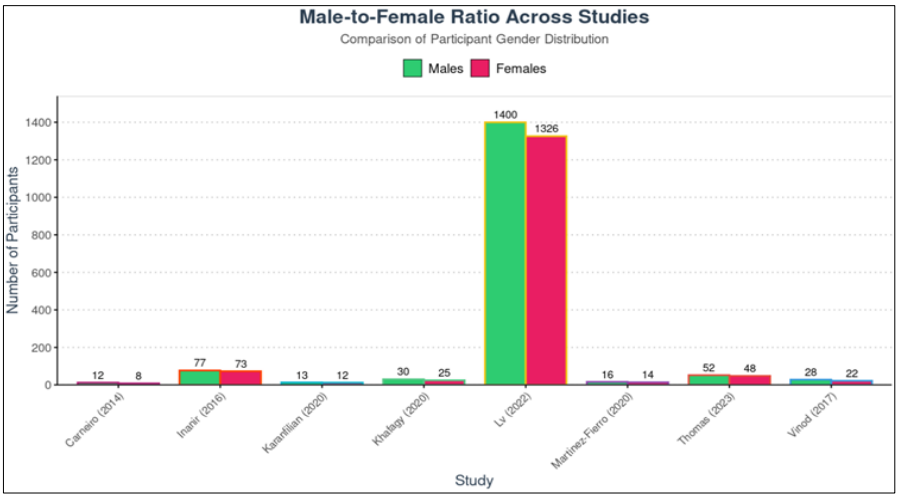

Figure 5: PA male to female ratio across various studies

Statistical analysis

Statistical analysis was performed with the SPSS version 28.0 and the data were presented using descriptive statistics such as number and percentage. R Studio was used for the preparation of graphs.

Discussion

The articles included in this systematic review and meta-analysis collectively point to pityriasis alba (PA) as a disorder which is predominantly associated with inflammatory, atopic, nutritional, and diagnostic disorders, thus providing a balanced view towards its pathogenesis and epidemiology between 2014-2023. An author demonstrated an increased number of Factor XIIIa+ dendrocytes in 80% of the 20 cases of PA examined, indicating an inflammatory process in the dermal layer (Carneiro FR *et al.*, 2014). This was further elucidated in another article (Quatresooz P *et al.*, 2008). This inflammatory component is the foundation for further studies on PA beyond its clinical presentation, speculating that the subclinical changes may be the reason for its hypopigmented nature, a feature which may be evocative of atopic conditions. Based on this assumption, another author approximated PA prevalence at 1-5%, citing a strong 70-90% correlation with atopy, thus positioning PA as a common dermatosis of atopic persons and highlighting its epidemiological relevance (Miazek N *et al.*, 2015). This assumption had already been made in a study carried out much earlier (Vargas Ocampo FR *et al.*, 1993). The dietary factor is another point of overlap with another author's study, finding low zinc levels (mean 72 µg/dL vs. control 88 µg/dL) in 50 PA patients, indicating trace element deficiencies may compound skin barrier impairments, one recognized feature of atopic dermatitis (AD) (Vinod K *et al.*, 2017). This nutritional factor overlaps with the inflammatory and atopic aspects, indicating multifactorial etiopathogenesis. This was also found in another study (Jadotte *et al.*, 2011).

Additionally, a study documented upregulated inflammatory genes (e.g., IL-6) in 73% of 30 PA cases, further incriminating inflammation in atopy, and hinting that PA's pathogenesis might be cytokine-mediated processes similar to those in AD (Martinez-Fierro ML *et al.*, 2020). The same conclusion was echoed in another study (IN Sl *et al.*, 2009).

Likewise, another author documented markedly lower hemoglobin, serum ferritin, zinc, copper, and magnesium in 55 PA patients compared to controls, and zinc deficiency augmenting PA risk by more than 15-fold and decreased hemoglobin by more than ninefold (Khafagy GM *et al.*, 2020). This affirms the nutritional hypothesis, with trace elements being key to skin health in atopic environments. This was also reported in another study (Guareschi E *et al.*, 2009).

Histologically, another study described 68% spongiosis in 25 cases of PA, in line with initial inflammatory changes of atopic disease, thus correlating microscopic to clinical atopy (Karanfilian KM *et al.*, 2020). On a larger scale, another author described 66% atopy in 2726 patients, with 3.8% prevalence and 40% AD, solidifying PA's epidemiological status and its continued atopic correlation in different populations (Lv Y *et al.*, 2022). Finally, another yet author contributed a diagnostic component, describing 60% atopy in 100 cases and emphasizing dermoscopy's utility in PA diagnosis, an easy tool to enhance clinical detection of its atopic associations (Thomas IN *et al.*, 2023).

Collectively, these findings paint a picture that defines PA as a condition with inflammation (Carneiro FR *et al.*, 2014; Martinez-Fierro ML *et al.*, 2020; Karanfilian KM *et al.*, 2020), increased atopy prevalence (Miazek N *et al.*, 2015; Lv Y *et al.*, 2022; Thomas IN *et al.*, 2023), dietary impact (Vinod K *et al.*, 2017), and improvement in diagnostic techniques (Thomas IN *et al.*, 2023). In total, this image presents PA not only as an innocuous dermatosis, but as a complex condition in the atopic model, which requires holistic approaches to its investigation and treatment.

The important findings, merits and gaps of various studies for systematic review were tabulated and the gender ratio for PA was depicted (**Table 2 and 3, Figure 5**)

Conclusion

This review confirmed a robust pooled atopy prevalence in PA, reaching the aim to quantify its relationship with atopy and positioning PA as a sentinel sign of AD. Integrating inflammatory, epidemiological, and nutritional insights, it bridged molecular and clinical disciplines, necessitating new management such as barrier-enhancing therapies (e.g., ceramide-based emollients) and screening for atopy in PA patients. Genetic polymorphisms (e.g., filaggrin) and microbiome effects should be explored in future studies using multi-omics, and randomized trials may assess targeted interventions such as zinc supplementation or anti-inflammatory agents, raising PA from an under-recognized entity to a model for atopic skin disease prevention.

Strengths and limitations

The major strength of our study was that the studies selected were published between 2014-2023 making it a study of ten years. The heterogeneity was 0% in the meta-analyses. However, this was linked to the limited number of three studies taken for the meta-analyses for pityriasis alba association with atopy making it a limitation. The results should be interpreted with caution as the study suggested no significant publication bias but the sample size was small.

Declarations

Ethical approval

Not Required since the study conducted was a systematic review and meta-analyses and included the studies selected from 2014-2023.

Source of funding

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Conflicts of interests

The authors report no conflict of interest.

Author contributions

Conceptualization and methodology P.P, A.S. and D.S.; Formal analysis P.P, A.S. and D.S.; Visualization and writing - original draft P.P, A.S. and D.S.; Writing - review and editing P.P, A.S., D.S., and J.H. All authors have read and agreed to the final version of the manuscript.

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