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Hospital.**ADMINISTRATIVE INFORMATION****Support** - NA.**Review Stage at time of this submission** - Piloting of the study selection process.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202660003**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 2 June 2026 and was last updated on 2 June 2026.**INTRODUCTION**

Review question / Objective To systematically review and quantitatively synthesize the evidence on serum ECP levels across different clinical states of childhood asthma. Four clinical questions are addressed: (1) Is serum ECP elevated in asthmatic children compared with healthy controls? (2) Does ECP differ between acute exacerbation and stable disease? (3) Does ECP correlate with objective measures of airway obstruction and bronchial hyperresponsiveness? (4) Does anti-inflammatory treatment reduce serum ECP levels, and do corticosteroids and leukotriene receptor antagonists differ in their effects?

Rationale Childhood asthma is the most common chronic respiratory disease in children and is characterized by eosinophilic airway inflammation. Eosinophil cationic protein (ECP), a cytotoxic granule protein released by activated eosinophils,

has been proposed as a non-invasive serum biomarker of airway inflammation. However, individual studies report inconsistent findings regarding its association with disease severity, exacerbation, treatment response, and lung function, partly due to differences in assay methods, patient populations, and inhaled corticosteroid use at sampling. The only prior systematic review (Koh et al., 2007) did not perform quantitative meta-analysis, pooled adult and pediatric data without stratification, and did not assess the impact of assay methodology. Several additional pediatric studies have since been published. This study therefore aims to provide the first quantitative meta-analysis specifically evaluating serum ECP as a biomarker of asthma severity in children.

Condition being studied Childhood asthma – a chronic inflammatory airway disease of the pediatric population characterized by eosinophilic

airway inflammation, variable airflow obstruction, and bronchial hyperresponsiveness.

METHODS

Search strategy Electronic databases: PubMed, Embase, Web of Science, and the Cochrane Central Register of Controlled Trials, from database inception through 11 April 2026. Core terms: ("eosinophil cationic protein" OR "ECP" OR "RNase 3") AND ("asthma" OR "wheezing" OR "bronchial hyperreactivity") AND ("child*" OR "pediatric" OR "paediatric" OR "infant"). No language restrictions. Reference lists of included studies and relevant reviews were hand-searched.

Participant or population Children aged 0–18 years with a diagnosis of asthma.

Intervention Not an interventional review per se; the "exposure/index" of interest is serum ECP measurement. Where treatment is evaluated, the interventions are anti-inflammatory therapies – inhaled corticosteroids and leukotriene receptor antagonists (montelukast).

Comparator Healthy controls; stable or post-treatment disease periods; and pre-treatment versus post-treatment timepoints. For the treatment subgroup, corticosteroids versus montelukast.

Study designs to be included Cross-sectional studies, prospective cohort / before-after studies, and randomized controlled trials reporting serum ECP.

Eligibility criteria Inclusion: (a) children aged 0–18 years with diagnosed asthma; (b) measured serum ECP concentration; (c) compared ECP between asthmatic children and controls, between severity states, or between pre- and post-treatment timepoints; (d) reported sufficient data for extraction (mean \pm SD, geometric mean with range, or median with IQR/range). Exclusion: (a) adult-only subjects (>18 years); (b) ECP measured exclusively in non-serum specimens (BAL fluid, sputum, urine) without concurrent serum measurement; (c) reviews, editorials, or case reports; (d) ECP mRNA expression rather than protein concentration; (e) duplicate or overlapping cohorts.

Information sources Electronic databases (PubMed, Embase, Web of Science, Cochrane Central); manual searching of reference lists of included studies and relevant reviews. No

additional grey literature or trial registers were systematically searched.

Main outcome(s) Pooled weighted mean difference (MD) in serum ECP ($\mu\text{g/L}$) for: (a) asthmatic children versus healthy controls; (b) acute exacerbation versus stable disease; (c) pre-versus post-anti-inflammatory treatment. Effect measure: mean difference with 95% confidence interval, random-effects model.

Additional outcome(s) Pooled correlation (Fisher's z transformation) between serum ECP and pulmonary function / bronchial hyperresponsiveness indices; qualitative comparison of FeNO versus serum ECP.

Data management Records were managed and de-duplicated using reference management software, and screening was conducted in Rayyan. Two reviewers independently screened titles/abstracts and full texts, with disagreements resolved by consensus. Data were extracted into a standardized extraction form and stored for analysis in RevMan 5.4 and Python.

Quality assessment / Risk of bias analysis Assessed independently by two reviewers using: the Newcastle–Ottawa Scale (NOS) for cohort and case-control studies; the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for cross-sectional studies; and the Cochrane Risk of Bias 2.0 (RoB 2) tool for randomized controlled trials. Traffic-light and summary plots generated using robvis.

Strategy of data synthesis DerSimonian–Laird random-effects model. Weighted mean differences with 95% CIs for group comparisons; correlation coefficients transformed to Fisher's z, pooled by inverse-variance weighting, and back-transformed. Heterogeneity assessed by Cochran Q and quantified by I^2 . Where geometric means were reported, arithmetic means/SDs estimated using log-normal properties; where medians with IQR/range were reported, means/SDs estimated using the Wan et al. (2014) method. Analyses in RevMan 5.4, verified with Python 3.11 (NumPy, SciPy).

Subgroup analysis Pre-specified subgroups by ECP assay method (FEIA/CAP vs RIA vs Other/not reported) and by treatment type (ICS/corticosteroid vs montelukast).

Sensitivity analysis Leave-one-out analysis and restriction to studies reporting original mean \pm SD data.

Language restriction No language restriction applied.

Country(ies) involved Taiwan (primary institution).

Other relevant information None

Keywords eosinophil cationic protein; asthma; children; biomarker; meta-analysis; severity; eosinophilic inflammation.

Dissemination plans The results will be submitted for publication in a peer-reviewed journal.

Contributions of each author

Author 1 - MIN-HAO YANG - Conceived and designed the study, developed the search strategy, performed study screening and selection, and drafted the manuscript.

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Author 2 - CHIA-TA WU - Performed study screening and selection, carried out data extraction, and conducted the risk-of-bias assessment.

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