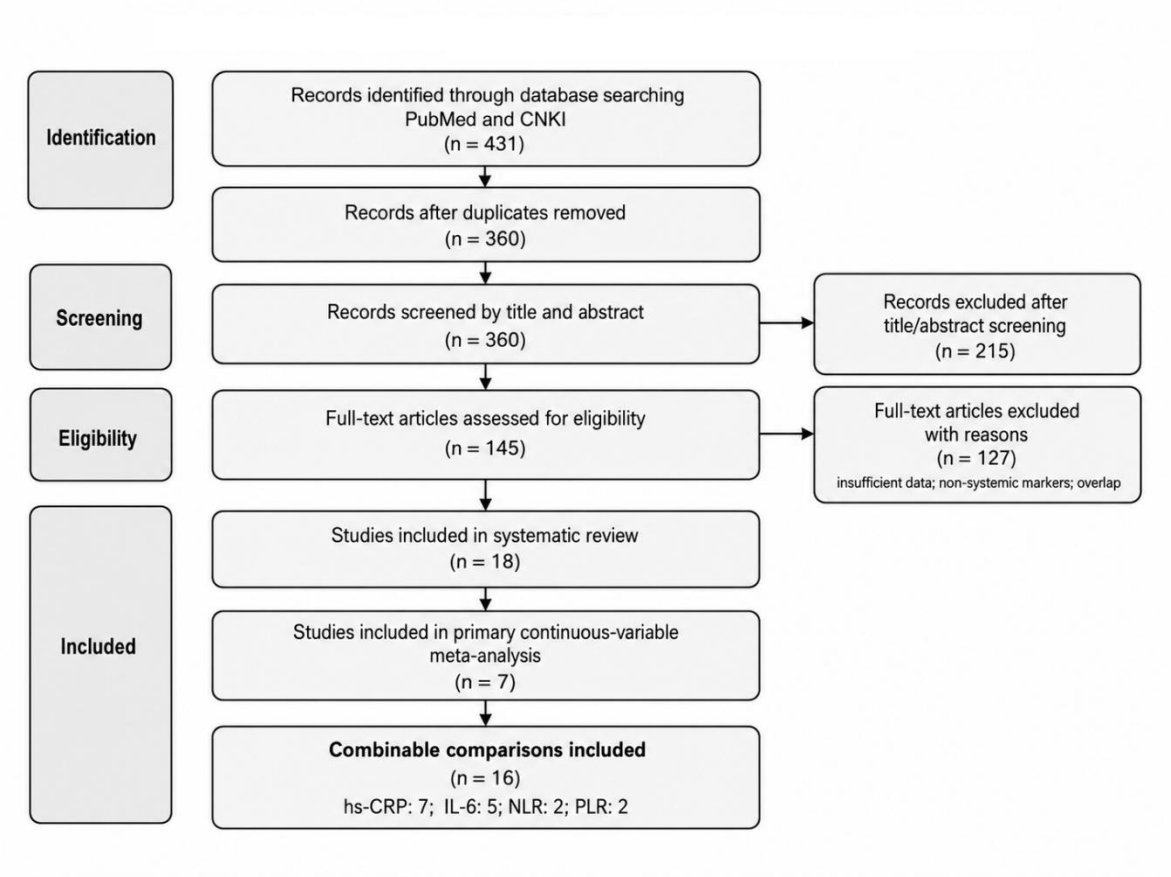
Supplementary Table 1. Methodological quality assessment of included observational studies using the Newcastle–Ottawa Scale or an adapted Newcastle–Ottawa Scale framework

First author	Year	Study design	Selection	Comparability	Exposure/outcome assessment	Total score	Overall quality
Takemura[5]	2006	Cross-sectional/case-control	3	1	2	6	Moderate
Ramirez[13]	2010	Cross-sectional	3	1	2	6	Moderate
Sigari and Ghasri[8]	2013	Cross-sectional	3	1	2	6	Moderate
Bai and Chen[14]	2015	Grouped clinical study	3	1	2	6	Moderate
Naik et al[15]	2015	Case-control	3	1	2	6	Moderate
Liu et al[16]	2016	Retrospective study	3	1	2	6	Moderate
Monadi et al[7]	2016	Case-control	3	1	2	6	Moderate
Peters et al[3]	2016	Pooled cross-sectional analysis	3	2	2	7	Moderate to high
Shi et al[17]	2017	Case-control/cross-sectional	3	1	2	6	Moderate
Ren et al[18]	2018	Case-control with follow-up	3	1	2	6	Moderate
Jackson et al[9]	2020	Post-hoc cohort analysis	3	2	2	7	Moderate to high
Esmaeilzadeh et al[19]	2021	Cross-sectional	3	1	2	6	Moderate
Yu et al[20]	2021	Retrospective study	3	1	2	6	Moderate
Arwas et al[21]	2023	Emergency database cross-sectional study	3	1	2	6	Moderate
Asseri[22]	2024	Case-control	3	1	2	6	Moderate
Xiao et al[23]	2024	Case-control	3	1	2	6	Moderate
Zhang and Ren[24]	2025	Cross-sectional	3	1	2	6	Moderate
Feng et al[25]	2026	Case-control	3	1	2	6	Moderate

[a]The Newcastle–Ottawa Scale or an adapted Newcastle–Ottawa Scale framework was used according to study design. Selection was scored from 0 to 4, comparability from 0 to 2, and exposure/outcome assessment from 0 to 3, with a maximum score of 9. Studies scoring 7–9 were considered moderate to high quality, 4–6 moderate quality, and 0–3 low quality. The main sources of potential bias were incomplete adjustment for confounders, heterogeneous definitions of asthma severity or control status, and inconsistent reporting of corticosteroid exposure.



Supplementary Figure 1. PRISMA flow diagram of study selection.

Supplementary Table 2. Studies included in the systematic review but not included in the primary continuous-variable meta-analysis

First author	Year	Country/region	Main markers	Main comparison or endpoint	Reason for exclusion from primary continuous-variable meta-analysis
Ramirez[13]	2010	United States	hs-CRP	Well-controlled asthma vs partly/uncontrolled asthma; association with airway inflammation and control indices	Data were mainly reported as association or control-related analyses and were not directly suitable for the primary mean/SD-based continuous-variable pooling.
Sigari and Ghasri[8]	2013	Iran	hs-CRP	Asthma control status based on GINA and ACT categories	Data format and grouping were not fully consistent with the primary pooling framework, and the results were therefore summarized descriptively.
Bai and Chen[14]	2015	China	IL-16, MCP-1	Acute exacerbation, remission, and healthy controls; mild vs moderate-to-severe acute asthma	Markers were not among the four primary pooled indicators, and available data were used as supplementary evidence.
Peters et al[3]	2016	United States	IL-6	High IL-6 expression group vs low-expression group; asthma severity and metabolic dysfunction	The study mainly reported IL-6 expression groups and adjusted associations rather than directly extractable mean/SD comparisons for the primary continuous-variable meta-analysis.
Ren et al[18]	2018	China	TNF-α, IL-8, ECP	Acute phase, chronic persistent phase, remission phase, and healthy controls; glucocorticoid efficacy	Markers and outcomes were not consistent with the primary pooled indicators and were summarized descriptively.
Jackson et al[9]	2020	United States	IL-6	IL-6 quartiles and future exacerbation risk in childhood asthma	The main outcome was future exacerbation risk by IL-6 quartiles rather than a directly comparable mean/SD-based disease-status comparison.
Esmaeilzadeh et al[19]	2021	Iran	NLR, eosinophils	Hospitalized vs non-hospitalized asthma exacerbation	The main results focused on hospitalization prediction and were not directly included in the primary continuous-variable pooling because of reporting and endpoint differences.
Yu et al[20]	2021	China	SII, CRP, neutrophils,	Mild, moderate, and severe asthma	SII and related blood-cell indices were summarized as supplementary evidence because

Supplementary Table 2. Studies included in the systematic review but not included in the primary continuous-variable meta-analysis

First author	Year	Country/region	Main markers	Main comparison or endpoint	Reason for exclusion from primary continuous-variable meta-analysis
			platelets, lymphocytes		they were not part of the four primary pooled indicators.
Arwas et al[21]	2023	Israel	NLR	NLR quartiles and severe asthma exacerbation in children	The study used NLR quartiles and emergency-visit data, which were not directly compatible with the primary mean/SD-based pooling framework.
Zhang and Ren[24]	2025	China	FeNO, TNF-α, IL-8, blood eosinophils	Mild, moderate, and severe asthma	The main markers were not among the four primary pooled systemic inflammatory indicators and were summarized descriptively.
Feng et al[25]	2026	China	GRP78, IL-4, IL-13, IL-17, IFN-γ	Mild, moderate, and severe asthma; asthma vs healthy controls	The main markers were not included in the primary continuous-variable meta-analysis and were summarized as supplementary evidence.

[a]CRP: C-reactive protein; ECP: eosinophil cationic protein; FeNO: fraction of exhaled nitric oxide; hs-CRP: high-sensitivity C-reactive protein; IL-6: interleukin-6; IL-8: interleukin-8; IL-16: interleukin-16; MCP-1: monocyte chemoattractant protein-1; NLR: neutrophil-to-lymphocyte ratio; SD: standard deviation; SII: systemic immune-inflammation index; TNF-α: tumor necrosis factor-α.

Supplementary Table 3. Baseline and methodological heterogeneity across included studies

First author	Year	Country/ region	Study design	Age group	Main disease-status domain	Main markers	Included in primary meta-analysis	Potential source of heterogeneity
Takemura[5]	2006	Japan	Cross-sectional/ case-control	Adult or mixed adult population	Asthma vs healthy control; steroid-naive and ICS-treated asthma	hs-CRP	Yes	Medication exposure and asthma treatment status may influence inflammatory marker levels.
Ramirez[13]	2010	United States	Cross-sectional	Adult or mixed population	Asthma control status	hs-CRP	No	Control status definitions and outpatient disease activity may differ from severity-stratification studies.
Sigari and Ghasri[8]	2013	Iran	Prospective case-control	Adult or mixed population	Asthma control status based on GINA and ACT	hs-CRP	No	Different control classification systems and reporting formats may affect comparabilit.
Bai and Chen[14]	2015	China	Grouped clinical study	Adult or mixed population	Acute exacerbation, remission, and healthy control; mild vs moderate-to-severe acute asthma	IL-16, MCP-1	No	Different biomarkers and acute-phase grouping limited comparability with the primary pooled indicators.

Supplementary Table 3. Baseline and methodological heterogeneity across included studies

First author	Year	Country/ region	Study design	Age group	Main disease-status domain	Main markers	Included in primary meta-analysis	Potential source of heterogeneity
Naik et al[15]	2015	India	Case-control	Adult population	Moderate persistent vs severe persistent asthma; asthma vs healthy control	IL-6, MMP-9	Yes	Persistent asthma severity and assay differences may contribute to IL-6 heterogeneity.
Liu et al[16]	2016	China	Retrospective study	Adult or mixed population	Severity stratification and control status	hs-CRP	Yes	Multiple comparisons from one study may introduce non-independence.
Monadi et al[7]	2016	Iran	Case-control	Adult population	Asthma vs healthy control; poorly controlled vs well-controlled asthma	hs-CRP	Yes	Control status and comorbid inflammatory factors may influence hs-CRP.
Peters et al[3]	2016	United States	Pooled cross-sectional analysis	Adult population	IL-6 expression groups and severe asthma/metabolic dysfunction	IL-6	No	IL-6 may be strongly influenced by obesity, metabolic dysfunction, and phenotype composition.
Shi et al[17]	2017	China	Case-control/cross-sectional	Adult or mixed population	Critical vs non-critical acute exacerbation; healthy control	NLR, PLR	Yes	Acute exacerbation status and severity of acute illness may affect

Supplementary Table 3. Baseline and methodological heterogeneity across included studies

First author	Year	Country/ region	Study design	Age group	Main disease-status domain	Main markers	Included in primary meta-analysis	Potential source of heterogeneity
								blood-cell-derived indices.
Ren et al[18]	2018	China	Case-control with follow-up	Adult population	Acute phase, chronic persistent phase, remission phase, and treatment efficacy	TNF-α, IL-8, ECP	No	Follow-up treatment response and glucocorticoid exposure may affect inflammatory markers.
Jackson et al[9]	2020	United States	Post-hoc cohort analysis	Pediatric population	IL-6 quartiles and future exacerbation risk	IL-6	No	Pediatric population and prospective exacerbation endpoint differ from cross-sectional severity comparisons.
Esmaeilzadeh et al[19]	2021	Iran	Cross-sectional	Adult or mixed population	Hospitalized vs non-hospitalized asthma exacerbation	NLR, eosinophils	No	Hospitalization reflects healthcare utilization and exacerbation severity rather than standard severity stratification.
Yu et al[20]	2021	China	Retrospective study	Adult population	Mild, moderate, and severe asthma	SII, CRP, neutrophils, platelets, lymphocytes	No	Different composite inflammatory index and retrospective design may affect

Supplementary Table 3. Baseline and methodological heterogeneity across included studies

First author	Year	Country/ region	Study design	Age group	Main disease-status domain	Main markers	Included in primary meta-analysis	Potential source of heterogeneity
								comparability .
Arwas et al[21]	2023	Israel	Emergency database cross-sectional study	Pediatric population	Severe asthma exacerbation based on NLR quartiles	NLR	No	Emergency-care setting and quartile-based analysis differ from mean/SD pooling.
Asseri[22]	2024	Saudi Arabia	Case-control	Pediatric population	Acute exacerbation vs stable asthma	NLR, PLR, WBC, ANC, ALC, platelets	Yes	Pediatric population and acute-vs-stable comparison may differ from adult severity-stratification studies.
Xiao et al[23]	2024	China	Case-control	Adult population	Asthma vs healthy control; mild, moderate, and severe asthma	miR-30, TGF-β1, IL-6, IL-33, TNF-α, eosinophils	Yes	Multiple severity comparisons and broad inflammatory marker panel may contribute to heterogeneity .
Zhang and Ren[24]	2025	China	Cross-sectional	Adult population	Mild, moderate, and severe asthma	FeNO, TNF-α, IL-8, blood eosinophils	No	Markers mainly reflect airway/type 2 inflammation rather than the primary systemic markers.
Feng et al[25]	2026	China	Case-control	Adult population	Asthma vs healthy	GRP78, IL-4, IL-13,	No	Different inflammatory

Supplementary Table 3. Baseline and methodological heterogeneity across included studies

First author	Year	Country/ region	Study design	Age group	Main disease-status domain	Main markers	Included in primary meta-analysis	Potential source of heterogeneity
					control; mild, moderate, and severe asthma	IL-17, IFN-γ		pathways and limited consistency with the primary pooled markers.

[a]ACT: Asthma Control Test; ALC: absolute lymphocyte count; ANC: absolute neutrophil count; CRP: C-reactive protein; ECP: eosinophil cationic protein; FeNO: fraction of exhaled nitric oxide; GINA: Global Initiative for Asthma; GRP78: glucose-regulated protein 78; hs-CRP: high-sensitivity C-reactive protein; ICS: inhaled corticosteroids; IFN-γ: interferon-γ; IL-4: interleukin-4; IL-6: interleukin-6; IL-8: interleukin-8; IL-13: interleukin-13; IL-16: interleukin-16; IL-17: interleukin-17; IL-33: interleukin-33; MCP-1: monocyte chemoattractant protein-1; miR-30: microRNA-30; MMP-9: matrix metalloproteinase-9; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; SD: standard deviation; SII: systemic immune-inflammation index; TGF-β1: transforming growth factor-β1; TNF-α: tumor necrosis factor-α; WBC: white blood cell.