Systemic Corticosteroids in Children With Pneumonia

A Systematic Review and Meta-analysis

Maria Geropeppa, MD, Panagiota Tsagkli, MD,* Ioanna Papadatou, MD, PhD,*† Vasiliki Efthymiou, BSc, MA, MSc,†‡ Alfredo Tagarro, MD, PhD,§¶ Emmanouil Galanakis, MD, MSc, PhD,‖ and Vana Spoulou MD, MPhil, PhD,*†*

Background: Corticosteroids are effective adjunct treatment for certain infectious diseases. However, their role in children with community-acquired pneumonia (CAP) remains unclear. We aim to assess the efficacy and safety of adjunct corticosteroid therapy in pediatric CAP.

Materials and Methods: A systematic literature search was conducted on MEDLINE to retrieve studies assessing systemic corticosteroid therapy, given alongside antimicrobial regimens, in pediatric CAP (last search date December 31, 2024). Literature screening, quality assessment, and data extraction were conducted by 2 independent reviewers. Heterogeneity and publication bias were detected by I^2 and Egger's tests. The data were pooled using the random-effects model for the conduction of meta-analysis.

Results: Twenty-two articles (N = 75.353) of 3799 screened studies were included in the systematic review; 7 of 22 studies providing data on length of hospital stay (LOS) and duration of fever for corticosteroid-treated versus control patients were included in the meta-analysis. Significant heterogeneity was observed regarding the regimen, dosage and duration of corticosteroid therapy. Regarding meta-analysis, LOS and time to defervescence were significantly decreased in patients receiving corticosteroids compared to controls in randomized clinical trials (Cohen's d value = −0.59, 95% confidence interval: −0.96 to −0.23, $P = 0.001$, $I^2 = 52.6\%$; Cohen's d value =-0.54, 95% confidence interval: −0.83 to −0.26, $P < 0.001$, $I^2 = 26.1\%$, respectively), but not in observational studies. Corticosteroid administration was associated with a shorter radiologic and clinical recovery time especially for *Mycoplasma pneumoniae* and viral pneumonia with wheezing. Corticosteroid-related adverse events were infrequent and manageable.

Conclusions: Our analysis suggests a possible advantage for corticosteroid therapy in selected pediatric patients with CAP. Further studies are needed to clarify how, when, and where corticosteroids should be added to the treatment plan of pediatric CAP.

Key Words: corticosteroids, pediatric community-acquired pneumonia, systematic review, meta-analysis

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Despite advances in prevention and treatment, pneumonia remains a leading cause of morbidity and mortality in children worldwide.[1] The World Health Organization reports that community-acquired pneumonia (CAP) causes 14% of deaths in children under 5 years of age, with approximately 750,000 fatalities in 2019.[2] Pneumonia etiology varies by age: neonatal cases are mostly bacterial from the birth canal,[3] while viruses predominate in infants and older children.[4] Among bacteria, *Streptococcus pneumoniae* and *Haemophilus influenzae* type B are common in children aged 2–5 years, while *Mycoplasma pneumoniae* (MP) mainly affects older children and adolescents.[4]

CAP develops when pathogens enter the lower respiratory tract via inhalation, aspiration, or direct invasion of the respiratory epithelium.[5] Once in the lower airways, microorganisms replicate in alveoli, triggering innate immune responses, including alveolar macrophage phagocytosis and pro-inflammatory cytokine release, leading to inflammation, alveolar fluid accumulation, and lung injury.[6]

Corticosteroids, especially synthetic glucocorticoids, are known for their anti-inflammatory action, as they inhibit the leukocyte migration and the production of pro-inflammatory mediators.[7,8] Therefore, the theoretical benefit of this anti-inflammatory action has been investigated in the setting of several infectious diseases. For some, such as meningitis due to *S. pneumoniae, H. influenza*, and *Mycobacterium tuberculosiss*, as well as fulminant sepsis, the benefit of corticosteroids has been established, and in extent, their use has been incorporated in clinical practice.[9–11] However, for other infections, such as pediatric pneumonia, their role remains unclear. Proposed mechanisms include cytokine suppression, inhibition of immune cell lung infiltration, and modulation of the hypothalamus–pituitary–adrenal axis, similar to septic shock treatment.[12,13]

In adults hospitalized for CAP, several meta-analyses have shown that corticosteroids significantly reduced complications such as acute respiratory distress syndrome and multiorgan failure, as well as morbidity.[14–17] Moreover, the beneficial role of corticosteroids has been documented in adults with underlying conditions, such as chronic obstructive pulmonary disease, which may predispose them to exaggerated inflammatory responses.[18]

However, the evidence from adult studies cannot be directly extrapolated to children, due to significant differences in immune response, comorbidities, and disease severity associated with age.

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From the *Immunobiology and Vaccinology Research Laboratory, Infectious Diseases Department "MAKKA," First Department of Paediatrics, "Aghia Sophia" Children's Hospital, Athens Medical School, Athens, Greece; †University Research Institute of Maternal and Child Health and Precision Medicine, "Aghia Sophia" Children's Hospital, National and Kapodistrian University of Athens, Athens, Greece; ‡First Department of Pediatrics, Center for Adolescent Medicine and UNESCO Chair in Adolescent Health Care, Medical School, National and Kapodistrian University of Athens, Aghia Sophia Children's Hospital, Athens, Greece; §Fundación de Investigación Biomédica Hospital 12 de Octubre, Instituto de Investigación 12 de Octubre (IMAS12), Madrid, Spain; ¶Department of Pediatrics, Infanta Sofía University Hospital, Fundación Para la Investigación Biomédica e Innovación Hospital Universitario Infanta Sofía y Hospital del Henares (FIIB HUIS HHEN), Universidad Europea de Madrid. Madrid, Spain; and ‖Pediatric Infectious Diseases Unit, Heraklion University Hospital, University of Crete, Heraklion, Greece

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M.G. and P.T. contributed equally to this work.

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Address for correspondence: Maria Geropeppa, MD, Immunobiology and Vaccinology Research Laboratory, Infectious Diseases Department "MAKKA," First Department of Paediatrics, "Aghia Sophia" Children's Hospital, Athens Medical School, Athens 11527, Greece. E-mail: mgeropeppa@med.uoa.gr.

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Data on the role of corticosteroids in pediatric CAP are limited, with great variability in methodology and significant heterogeneity regarding the regimen, dosage, and duration of corticosteroid therapy.[14]

To our knowledge, no systematic review or meta-analysis has exclusively focused on children with pneumonia treated with corticosteroids. This systematic review evaluates the published data on the efficacy and safety of systemic corticosteroids as adjunctive therapy to antibiotic treatment in pediatric patients with CAP, aiming to provide evidence for optimization of clinical practice for the benefit of young patients.

MATERIALS AND METHODS

Study Design

This systematic review was conducted in accordance with the statement of the Preferred Reporting Items for Systematic Review and Meta-Analysis guidelines. Relevant published scientific articles were retrieved via the PubMed database (MEDLINE) up to December 31, 2024, using both MeSH terms and Boolean operators with relevant keywords including "corticosteroids," "pneumonia," "parapneumonic effusion," "children" (see text, Supplemental Digital Content 1, https://links.lww.com/INF/G461). Reference lists of the included studies were hand-searched for additional potentially eligible articles. The protocol of this systematic review was registered in PROSPERO (CRD42024599130).

Selection Criteria

This study aimed to evaluate the efficacy and safety of systemic corticosteroids as adjunctive therapy to antibiotics in children with CAP. Studies were considered eligible if they were randomized clinical trials (RCTs), case–control studies, and cohort studies reporting data on the administration of systemic corticosteroids for bacterial or viral pneumonia. The systematic search was conducted according to the following Population, Intervention, Comparison, Outcomes approach. Population: Children under 18 years old with radiographically confirmed pneumonia, including CAP treated in the hospitals or intensive care units; Intervention: Systemic corticosteroids, given as adjunctive therapy to antibiotic treatment. The following corticosteroids will be included: betamethasone, dexamethasone, hydrocortisone, methylprednisolone, prednisolone, and prednisone. Corticosteroids may have been administered at any dose, mode, and for any duration; Comparison: Systemic corticosteroid administration, given as adjunctive therapy to antibiotic treatment in children with pneumonia, was compared with antibiotics given alone or antibiotics with placebo. Primary outcomes: morbidity, defined as length of hospital stay (LOS), duration of fever, and mortality. Secondary outcomes: radiographical and clinical response to treatment, development of parapneumonic effusion, readmission to the hospital, and adverse events, including hyperglycemia, gastrointestinal bleeding, and cardiac events. Factors investigated included corticosteroid dose, timing of initiation, and duration of corticosteroid therapy. Exclusion criteria included studies written in any other language than English, case series, case reports, preprints, and studies published before 2003. Studies including neonates, children living with human immunodeficiency virus, and children with CAP treated in the community were also excluded from our analysis.

Data Extraction and Quality Assessment

Two reviewers (M.G., P.T.) independently and blinded to each other conducted the screening and selection of the studies, the extraction of required information, and quality assessment. Any disagreements were resolved by discussion or with the consultation of a third independent reviewer (I.P.).

Quality assessment of the included studies was performed using the Newcastle–Ottawa Scale for case–control and cohort studies; for the evaluation of randomized controlled studies, Consolidated Standards of Reporting Trials statement was used (Figure, Supplemental Digital Content 2, https://links.lww.com/INF/G462). A meta-analysis of studies that compared patients who received corticosteroids with patients who did not receive steroid therapy (control patients) was performed regarding LOS and time for defervescence.

Statistical Analysis

Statistical analysis was performed using SPSS version 28.0 (IBM Corp. Released 2021, IBM SPSS Statistics for Windows, Version 28.0, IBM Corp, Armonk, NY). The association of LOS and duration of fever between the group receiving steroids and control group was calculated using Cohen's *d* value with a 95% confidence interval (CI). The significance was determined by the *Z* test. A random-effect model was applied, respectively, for heterogeneous data after calculating Cochran's Q-statistic ($P < 0.05$ for significant) and I^2 test (0%, no heterogeneity; 100%, maximal heterogeneity). Egger's test was used to estimate the publication bias. The statistical significance level was set at 5% ($P < 0.05$). Transformation of the median and interquartile range was based on Wan et al.'s[19] formula. For the transformation of logarithmic standard deviation, Cochrane Handbook was used.[20]

RESULTS

The search yielded 3786 articles from the database, from which 3657 references were excluded based on the title and abstract screening. After assessing the full texts of the remaining 129 articles and 13 references from the snowball procedure for eligibility, 22 articles (N = 75.353; MP cases: 54.042, various bacterial causes cases: 20.762, viral causes cases: 392, cases with parapneumonic effusion: 157; treated with corticosteroids: 21.686/75.353) were included in our analysis (Fig. 1). The characteristics of the eligible studies are presented in Table, Supplemental Digital Content 3, https://links.lww.com/INF/G463.

Bacterial Pneumonia

Seventeen of 22 studies included in this analysis referred to bacterial pneumonia cases (15/17: MP cases, 2/17: various bacterial causes). Thirteen out of the 17 studies were observational studies,[21–33] and 4 were RCTs.[34–37] Sample sizes ranged from 12 to 20,703 hospitalized children, aged mostly 4–8 years old, and with a slight predominance of males. Methylprednisolone or prednisolone (1–2 mg/kg/day) was administered in 9 of 17 studies for 3–21 days; higher doses (>2 mg/kg/d) were administered in 5 studies, methylprednisolone pulse therapy (30 mg/kg) in 1, while dosing was unspecified in 2studies. Initiation timing varied across studies: 8 studies started treatment 7–10 days after onset, 4 at 5–7 days, 2 within 5 days, and 2 did not report timing.

Primary Outcomes

Length of Hospital Stay

In general, LOS was recorded in 14 out of 17 studies; mean LOS was estimated to be less than 10 days in 10 out of 14 studies and over 10 days in 4 out of 14 studies.

Among the eligible studies, 3 RCTs[34,36,37] were included in the meta-analysis for the length of hospitalization in days (Fig. 2). A random-effects model revealed a moderate estimate of effect size (Cohen's *d* value = −0.59, 95% CI: −0.96 to −0.23, $P = 0.001$), indicating that the length of hospitalization was significantly shorter in the group with corticosteroids compared with control group. Significant heterogeneity was identified across included studies ($P <$

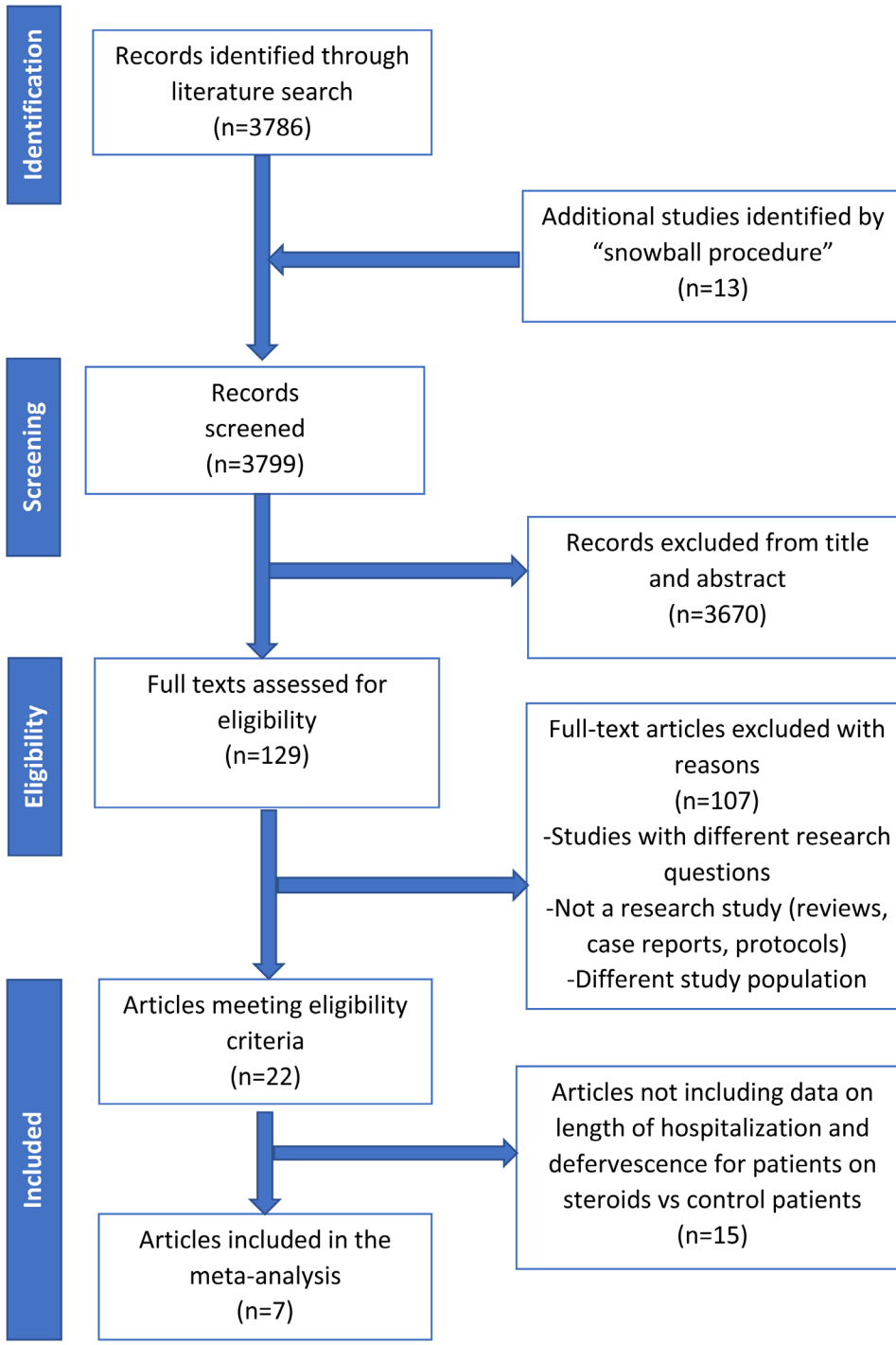

FIGURE 1. Flowchart of literature search and enrolled studies. full color online

0.001, $I^2 = 52.6\%$). Egger's test ($P = 0.702$) indicated no significant publication bias over all included studies.

For retrospective studies[22,27,29,30] (Fig. 3), a random-effects model revealed a moderate estimate of effect size (Cohen's d value = 0.53, 95% CI: 0.18–0.87, $P = 0.003$), indicating that the length of hospitalization was significantly higher in the group with corticosteroids compared with control group. Significant heterogeneity was identified across included studies ($P < 0.001$, $I^2 = 94.1\%$). Egger's test ($P = 0.179$) indicated no significant publication bias over all included studies.

Duration of Fever

Fever duration data were available in 14 of 17 studies. Eight reported total fever duration, 8 reported time to defervescence after steroid initiation, and 2 reported both parameters. Of those reporting total duration, 4 found a mean under 10 days, and 4 over 10

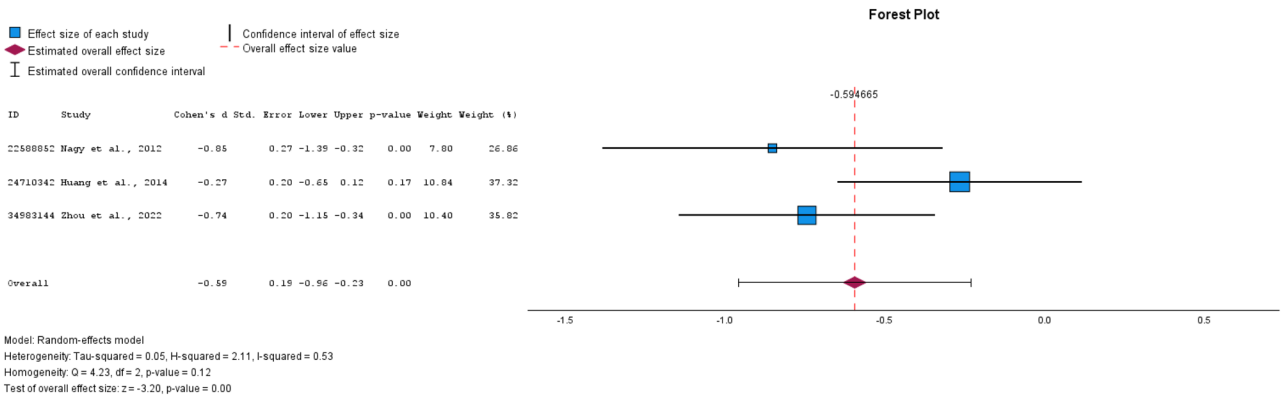

FIGURE 2. Forest plot presenting the meta-analysis based on Cohen's *d* value for the effect of length of hospitalization (days) for the subgroup of bacterial pneumonia in RCTs. full color online

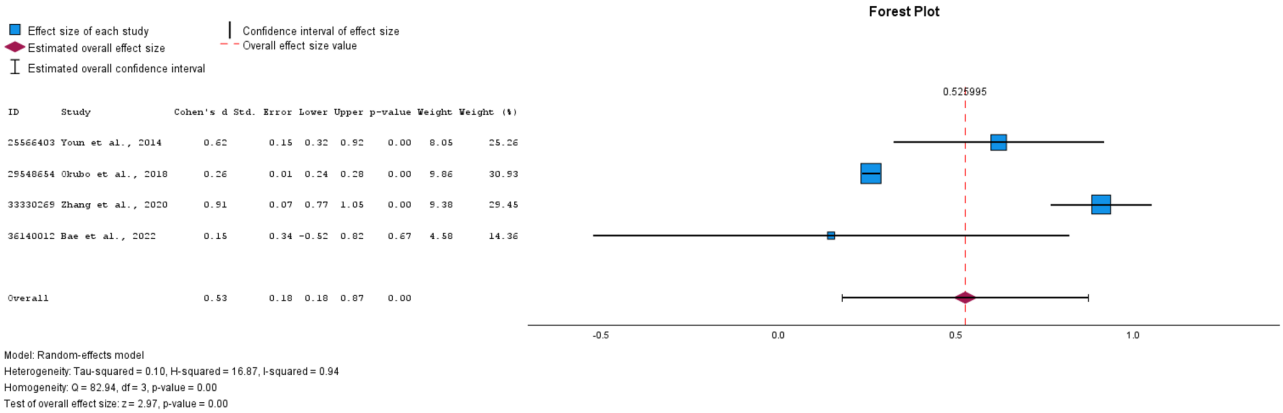

FIGURE 3. Forest plot presenting the meta-analysis based on Cohen's *d* value for the effect of length of hospitalization (days) for the subgroup of bacterial pneumonia in retrospective studies. full color online

days. For defervescence after steroid initiation, 5 studies reported a mean under 2 days, and 3 over 2 days.

The ensuing conducted meta-analysis of the duration of fever was performed among the 3 RCTs.[34,36,37] A random-effects model revealed a moderate estimate of effect size (Cohen's *d* value = −0.54, 95% CI: −0.83 to −0.26, $P < 0.001$), indicating that the duration of fever was significantly higher in the control group compared to the group receiving corticosteroids. Nonsignificant heterogeneity was identified across included studies ($P = 0.244$, $I^2 = 26.1\%$). Egger's test ($P = 0.544$) indicated no significant publication bias over all eligible studies (Fig. 4).

For retrospective studies,[22,27,30] a random-effects model revealed a moderate estimate of effect size (Cohen's *d* value = 0.17, 95% CI: −0.34 to 0.68, $P = 0.516$), indicating that the length of hospitalization was nonsignificantly different in the group with corticosteroids compared with the controls. Significant heterogeneity was identified across included studies ($P < 0.001$, $I^2 = 88.0\%$). Egger's test ($P = 0.093$) indicated no significant publication bias over all included studies (Fig. 5).

Mortality

No deaths were reported in any of the studies, neither in the corticosteroid nor in the control group.

Secondary Outcomes

Radiologic and Symptomatic Response to Treatment

Pooled data from 3 RCTs[34–36] and 2 observational studies[24,27] show that corticosteroid administration resulted in more rapid radiographical improvement, although this was evaluated at different time-points in each of the 5 studies, ranging from 2 to 60 days after first presentation. Corticosteroid administration was also associated with a shorter period of coughing and faster improvement of hypoxemia and dyspnea in 2 studies.[24,34]

Readmission

Readmission was examined by 2 studies. Of note, the RCT by Huang et al.[36] showed that there was no difference in 7-day readmission risk postdischarge, although Okubo et al.[29] retrospectively reported an increased 30-day readmission risk for patients who received corticosteroids (risk difference 0.4%; 95% CI: 0.1%–0.7%).

Safety

No corticosteroid-related adverse events were noted in any of the studies that reported this parameter,[23,24,27,28,34] except for hyperglycemia, which was more common with corticosteroids in 1 study (50% vs 20%, $P = 0.02$).[38]

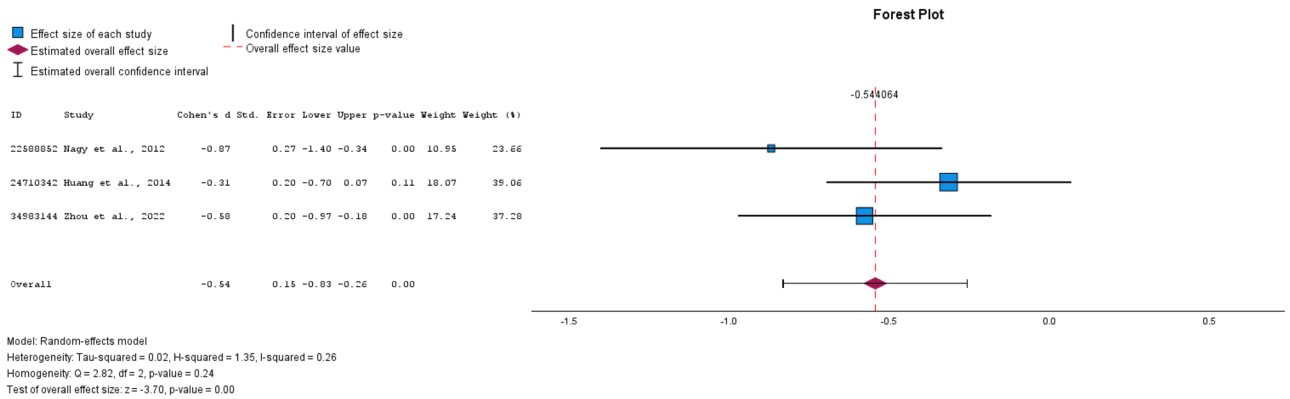

FIGURE 4. Forest plot presenting the meta-analysis based on Cohen's *d* value for the effect of duration of fever (days) for the subgroup of bacterial pneumonia in RCTs. full color online

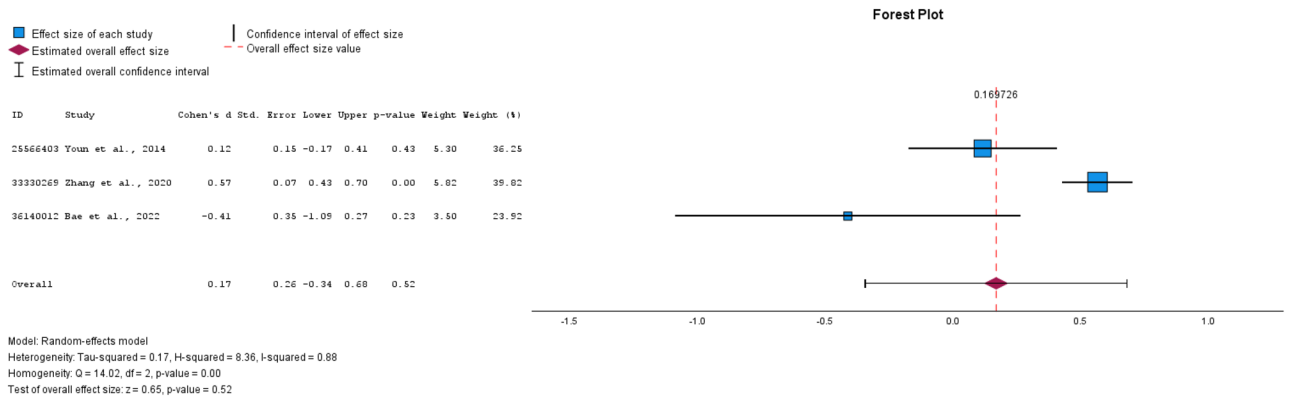

FIGURE 5. Forest plot presenting the meta-analysis based on Cohen's *d* value for the effect of duration of fever (days) for the subgroup of bacterial pneumonia in retrospective studies. full color online

Effect of Corticosteroid Dose and Timing

Two observational studies assessed methylprednisolone dosing in refractory MP pneumonia with conflicting results. Zhu et al.[26] associated high-dose methylprednisolone (10 mg/kg/d) with prolonged LOS (13.5 vs 8 days, $P < 0.05$) and defervescence (13 vs 11 days, $P < 0.001$). In contrast, Okumura et al.[28] reported that moderate dosing (2.8 mg/kg/d) reduced LOS (8.2 vs 10.7 days, $P < 0.001$) and fever duration (0.8 vs 1.5 days, $P = 0.01$).

Three studies examined the role of early versus delayed corticosteroid use in children with MP pneumonia. In the RCT by Huang et al.,[36] early initiation (within 24 hours of admission and 5 days of onset) was associated with shorter LOS (8 vs 10 days, $P = 0.001$) and time to defervescence (0 vs 2 days, $P < 0.01$) compared with initiation after 72 hours of admission. The observational study of Youn et al.[30] reported longer LOS (7 vs 5.8 days, $P < 0.001$) with early steroids (mean duration of symptoms 5 days) and no difference in fever duration (6.4 vs 6.1 days, $P = 0.5$). Zhang et al.[27] using retrospective logistic regression, found no differences in LOS or fever duration across steroid initiation at 1–5, 6–10, and >10 days after fever onset.

Effect on Parapneumonic Effusion

Two out of 22 studies examined the effect of corticosteroids in CAP-related pleural effusion. In the retrospective study by Thimmesch et al.,[39] 56.7% of children received methylprednisolone (2 mg/kg/d) for persistent fever despite drainage and fibrinolysis; most defervesced within 1 day; however, with no difference in time to defervescence and median LOS among corticosteroid and control patients. In the RCT of Tagarro et al.,[38] 60 children received antibiotics plus either dexamethasone (0.25 mg/kg every 6 hours for 48 hours) or placebo. Corticosteroids reduced median recovery time (109 vs 177 hours, $P = 0.037$).

Viral Pneumonia

Three of 22 studies referred to viral causes retrospectively. Ozsurekci et al.[40] studied patients diagnosed with severe coronavirus disease 2019 pneumonia and/or acute respiratory distress syndrome treated with either standard doses (2–4 mg/kg/d) or high doses (greater than 250 mg/d) of methylprednisolone. An H1N1 pneumonia pediatric patients included patients who received high-dose methylprednisolone (10 mg/kg/d) tapered within a week,[41] while Wang et al.[42] described clinical features and prognosis of adenoviral pneumonia in pediatric patients.

Primary Outcomes

Length of Hospital Stay

Mean LOS was reported from 6.4 to 16.5 days. No statistically significant differences were noted for the 2 studies that compared corticosteroid versus control patients.[40,41]

Duration of Fever

Data on defervescence were provided by 2 studies. Patients with adenoviral CAP required 10.7 days from disease onset to achieve defervescence.[42] In patients with influenza, high-dose methylprednisolone (10 mg/kg/d) tapered within a week resulted in significantly reduced duration of fever in patients with influenza (mean = 2.1 ± 0.8 vs 5.8 ± 4.8 days, $P = 0.009$).[41]

Mortality

None of the 3 studies reported any deaths.

Secondary Outcomes

Radiographic and Symptomatic Response to Treatment

In pediatric SARS-CoV-2 pneumonia, high-dose corticosteroids led to higher rates of clinical and radiologic improvement by day 7 (64.3% vs 28.9%, $P = 0.06$) and reduced requirement for invasive mechanical ventilation (46.7% vs 71.4%, $P = 0.03$) compared with standard doses.[40] In H1N1 pneumonia, corticosteroid administration shortened oxygen therapy duration (2.5 ± 0.6 vs 5.1 ± 4.6 days, $P = 0.04$) and accelerated resolution of infiltrates (88% vs 43%, $P = 0.01$).[41]

Safety

In the study by Ozsurekci et al., corticosteroid use in pediatric SARS-CoV-2 pneumonia was linked to increased bradycardia (37.5% vs 4.9%, $P = 0.03$). Moreover, Wang et al.[42] reported that intravenous corticosteroids were a risk factor for postinfectious bronchiolitis obliterans in severe adenovirus pneumonia (odds ratio = 4.45; 95% CI:1.70–11.68).

DISCUSSION

This systematic review is the first to comprehensively evaluate the use of systemic corticosteroids as adjunctive therapy in pediatric CAP, with particular attention to the underlying pathogen. Despite considerable heterogeneity across studies, the emerging evidence—particularly from RCTs—suggests that corticosteroids may confer clinical benefits in selected pediatric populations.

Meta-analysis of RCTs involving children with bacterial pneumonia demonstrated that corticosteroid therapy was associated with reduced LOS and shorter duration of fever. In contrast, observational studies yielded less favorable outcomes, reporting prolonged LOS and no significant improvement in time to defervescence among steroid-treated patients. These discrepancies likely reflect methodologic differences, including selection bias and variability in treatment protocols; notably, corticosteroids may have been preferentially administered to more severely ill patients.

The potential role of corticosteroids in pneumonia complicated by parapneumonic effusion was explored in 2 studies,[38,39] both of which suggested improved recovery times. In such cases, corticosteroids may represent a valuable adjunctive, noninvasive therapeutic option—especially when standard antibiotic therapy or invasive interventions are insufficient. However, these findings should be interpreted cautiously due to the limited number of studies and small sample sizes.

The most consistent therapeutic benefit of corticosteroids was observed in children with refractory MP pneumonia—a condition thought to be driven by an exaggerated host immune response. In MP infections, excessive immune activation—including elevated levels of interleukin (IL)-1, IL-6, and tumor necrosis factor-α—may cause pulmonary damage, and early corticosteroid administration might mitigate this inflammatory response and improve clinical outcomes.[43] However, results regarding optimal dosing and timing of corticosteroid administration were inconsistent, possibly due to confounding and selection bias in non-randomized observational studies.

In children with viral pneumonia, adjunctive corticosteroid therapy was associated with more rapid defervescence and clinical improvement, including radiographic resolution.[40,41] Viruses and atypical pathogens often induce airway inflammation and wheezing, where corticosteroids may be particularly effective by modulating airway hyperreactivity rather than systemic cytokine production. Subgroup analyses also suggest that children with asthma or wheezing may derive additional benefit from corticosteroids, particularly when administered concurrently with β-agonists.[25,44] This aligns with established evidence supporting corticosteroid use in asthma exacerbations and highlights potential synergistic anti-inflammatory and bronchodilatory effects.[45,46]

Most studies assessing radiographic outcomes reported improved imaging findings with corticosteroid use. However, the timing of radiologic assessments varied widely, complicating interpretation. Experimental evidence from animal models supports these observations, demonstrating that adjunctive corticosteroids significantly reduce histologic markers of lung inflammation in MP infection.[47] Nonetheless, in clinical practice, the relevance of radiographic improvement is limited and should not be used as a clinical endpoint, since imaging abnormalities often outlast clinical recovery and radiographic resolution is not typically required for hospital discharge.

Unlike in adult populations, where corticosteroids may increase the risk of gastrointestinal bleeding, neuropsychiatric complications, or secondary infections,[14] the pediatric studies included in this review generally revealed a favorable short-term safety profile. This is likely due to shorter treatment durations and lower baseline comorbidity in children. Across studies, adverse events were infrequent and typically mild, including transient hyperglycemia and bradycardia that resolved without intervention. While rare, the potential for postinfectious bronchiolitis obliterans must also be considered—though its development is more plausibly related to the severity of the initial viral infection than to corticosteroid use itself.

This review has several limitations. There was substantial heterogeneity in patient age, corticosteroid regimens (dose, timing, and duration), outcome definitions (eg, defervescence, clinical and radiologic improvement), and follow-up durations. Also, $I^2 > 75\%$ indicates considerable heterogeneity, as noted in the Cochrane Handbook for Systematic Reviews of Interventions.[20] The lack of standardized protocols and inconsistent pathogen identification further limited comparability across studies. Moreover, as the review was limited to search in PubMed/MEDLINE, some relevant studies in other databases may not have been identified; to mitigate this limitation, manual screening of or reference lists was conducted to ensure comprehensive retrieval of relevant literature.

These discrepancies underscore the urgent need for well-designed RCTs that stratify patients based on disease etiology, timing of intervention, and relevant host factors. Future research should aim to confirm the causative pathogen, employ standardized corticosteroid protocols, and use clinically meaningful outcomes such as time to clinical stability, need for oxygen supplementation or intensive care, and treatment failure rates. Such trials will be critical to optimize the use of corticosteroids in pediatric CAP and inform pathogen-specific treatment strategies.

CONCLUSIONS

Although routine use of corticosteroids in all children with CAP is not currently supported, our findings emerging from meta-analysis of RCT studies—which provide stronger evidence—suggest a potential role for adjunctive corticosteroids in specific subgroups. Benefits appear to be largely confined to patients with MP pneumonia or parapneumonic effusion, and those with MP pneumonia and those with asthma or wheezing receiving β-agonists.

In these groups, corticosteroids may reduce hospital stay, fever duration, and radiographic recovery time. Short-term corticosteroid therapy appears to be safe, but further high-quality studies are needed to clarify long-term safety as well as optimal timing, dosing, and pathogen-specific efficacy.

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