



Severe Persistent Bronchial Asthma: Literature Review

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Article Info	Abstract
<p>Article History: Received: 09 Desember 2024 Revised: 20 Desember 2024 Accepted: 22 Desember 2024</p> <p>Keywords: Severe persistent asthma, biological therapy, phenotype, montelukast, children</p> <p>Corresponding Author: Siti Maryam Iribaram Mandala Waluya University</p> <p>Email: sitimaryamiribaram03@gmail.com</p>	<p>Background: Severe persistent asthma is the most complex form of asthma, characterized by symptoms that cannot be optimally controlled despite the administration of high-dose standard therapy such as inhaled corticosteroids (ICS) combined with long-acting beta-2 agonists (LABA) and/or oral corticosteroids. This type of asthma significantly impacts the patient's quality of life, increases the frequency of exacerbations, and leads to higher healthcare costs.</p> <p>Purpose: To evaluate the impact of combination therapy and biological therapy approaches on key clinical outcomes such as reduction in exacerbations, improvement in quality of life, and decreased use of systemic corticosteroids.</p> <p>Methods: Articles were collected from the PubMed, ScienceDirect, and other peer-reviewed journal databases, with a publication range from 2021 to 2025.</p> <p>Results: The search yielded 10 articles that met the specified criteria and keywords. Biologic therapy has been proven effective in reducing exacerbations, improving lung function, and decreasing dependence on systemic corticosteroids.</p> <p>Conclusion: The importance of early intervention, accurate diagnostic approaches, and careful use of biologic therapy highlights the need for timely detection and treatment to prevent long-term damage.</p>

Background

Asthma is the most common chronic respiratory disease worldwide, affecting more than 300 million people of all ethnic groups and across all ages. It is the most prevalent chronic disease in children. Despite the various phenotypes of asthma in children, the condition is generally recognized as a chronic inflammatory disease of the airways characterized by variable symptoms such as wheezing, shortness of breath, chest tightness, and/or coughing, associated with expiratory airflow limitation that may resolve spontaneously or in response to treatment.

Severe asthma accounts for 5–10% of the asthma population, yet it contributes significantly to morbidity, healthcare costs, and reduced quality of life. Phenotypes such as eosinophilic and non-eosinophilic asthma show different responses to therapy. Therefore, a phenotype-based approach and targeted therapies are crucial. Severe asthma not only affects patients individually but also places a heavy burden on the overall healthcare system. Patients with severe asthma have higher hospitalization rates, more frequent emergency department visits, and more intensive use of systemic medications. The identification of asthma phenotypes, such as eosinophilic and non-eosinophilic, has enabled more targeted treatment strategies, especially through endotype-based approaches involving specific immunological mechanisms. The eosinophilic phenotype responds well to anti-IL5 therapy, while the non-eosinophilic phenotype remains clinically challenging.

Pediatric asthma is not a single disease but a heterogeneous disorder with diverse presentations throughout childhood. Asthma affects 8.3% of children in the United States and is the most common chronic disease of childhood. Pediatric asthma accounts for \$50 billion in annual healthcare expenditures and is a leading cause of emergency room visits, hospitalizations, school absences, and missed workdays for parents.

Asthma is characterized by inflammation that leads to bronchoconstriction, edema, and increased mucus production in the airways. Interestingly, the condition is more prevalent in boys during the first decade of life. However, after puberty and into the second decade of life, asthma appears to be more common among young women. Asthma disproportionately affects children from minority and low-income backgrounds, with African American and Hispanic children experiencing the highest rates of prevalence, morbidity, and mortality due to the disease.

The objective of this literature review is to evaluate the impact of combination therapy and biologic therapy approaches on key clinical outcomes such as reduction in exacerbations, improvement in quality of life, and decreased use of systemic corticosteroids.

Method

This type of study is a narrative literature review. Articles were collected from the PubMed, ScienceDirect, and other peer-reviewed journal databases, with a publication range from 2021 to 2025. Inclusion criteria included full-text journals discussing the therapy, diagnosis, and management of severe persistent asthma. Keywords used in the search included: 'severe persistent asthma', 'biologic therapy', 'eosinophilic asthma', 'pediatric asthma', 'stepwise treatment', and 'airway remodeling'.

The literature search strategy in this review was based on the PICO approach to focus the research and clarify its scope. The PICO components used are:

- P (Patient) : *Pediatric with severe persistent asthma.*
- I (Intervention) : *Biological therapy.*
- C (Comparison) : *Standard high-dose ICS/LABA therapy or placebo.*
- O (Outcome) : *Symptom control, reduction in exacerbations, improvement in lung function, quality of life.*

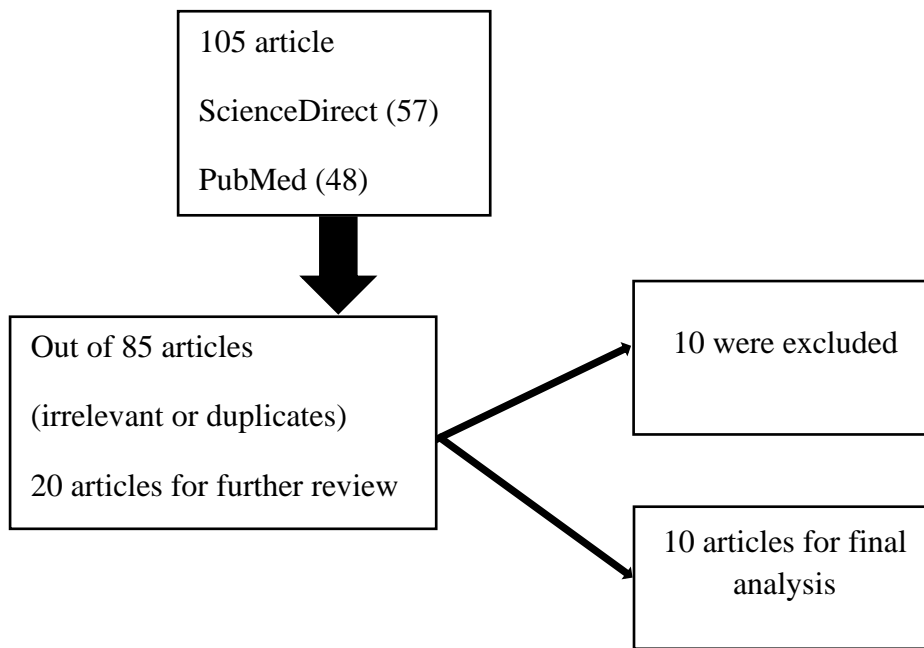


Figure 1. Literature Search Diagram

Results

Based on the results of the literature selection, ten articles were identified that discuss severe persistent bronchial asthma. Yamaguchi et al. (2024), the study discusses the effectiveness and safety of benralizumab in patients with severe eosinophilic asthma. The study results showed improvements in asthma control scores (ACQ-5) and lung function following therapy administration. These findings strengthen the evidence that benralizumab can be a safe and effective treatment option in real-world clinical practice in Japan.

Savin et al. (2023) presented a classification of phenotypes and endotypes of severe asthma and a therapy approach based on molecular profiling. They emphasized the importance of precision therapy using biomarkers such as eosinophils, IgE, and FeNO to determine optimal treatment, including the use of biologic therapies like anti-IL5 and anti-IgE.

Sardon-Prado et al. (2023) discussed the effectiveness of various biologic therapies in controlling severe asthma. The main focus was on the T2-high phenotype, which showed significant response to anti-IL5, anti-IL4R, and anti-IgE. The article emphasizes the importance of phenotype identification in determining the optimal biologic therapy.

Pelaia et al. (2021), through an international registry study, described patterns of biologic therapy use and switching. Many patients changed biologic treatments due to suboptimal response or side effects. This underscores the importance of regular evaluation and personalized approaches in severe asthma therapy.

From all the articles, it can be concluded that multidisciplinary collaboration among nurses, doctors, nutritionists, pharmacists, and psychologists is essential to ensure the success of long-term care. In addition, with an appropriate approach and optimal family support, the quality of life of children with severe persistent asthma can be improved, and the risk of recurrent exacerbations can be minimized.

Table 1. Journal Review

No	Authors	Title	Objective	Method	Results	Conclusion
1	Masao Yamaguchi et al. (2024)	<i>Real-World Safety and Effectiveness of Benralizumab</i>	To assess the effectiveness and safety of benralizumab in patients with severe eosinophilic asthma in Japan	Multicenter prospective observational study	Significant improvement in ACQ-5 and FEV1 scores; low annual exacerbation rate (0.42); no new safety concerns	Benralizumab is safe and effective as an add-on therapy for uncontrolled severe eosinophilic asthma
2	Mohsen Jafari et al. (2023)	<i>The Effect of Oral Montelukast in Controlling Asthma Attacks</i>	To evaluate the effectiveness of oral montelukast in controlling asthma attacks in children	Double-blind randomized clinical trial with montelukast and placebo groups	No significant difference in asthma attack scores or oxygen saturation between groups	Montelukast does not offer significant additional benefit compared to standard therapy in treating asthma attacks in children
3	Chung et al. (2022)	<i>Characteristics and Management of Severe Asthma</i>	To describe phenotype and endotype classification and therapies for severe asthma	Comprehensive literature review using data from multicenter studies and clinical trials	Severe eosinophilic asthma (T2-high phenotype) responds well to biologic therapy; non-T2 phenotype lacks effective targeted therapies	Understanding inflammatory phenotypes and endotypes is crucial for precision therapy in severe asthma; more research needed for non-T2 phenotypes
4	Thomas et al. (2022)	<i>Asthma Attack Prevention...</i>	To reflect on past experiences and highlight the	Narrative review synthesizing findings from previous	Many patients still experience attacks despite	A paradigm shift is needed in asthma attack

No	Authors	Title	Objective	Method	Results	Conclusion
			need for new therapies for exacerbation prevention	studies	standard therapy (ICS/LABA) ; early identification of high-risk patients emphasized	prevention; therapies targeting pathophysiology (e.g., biologics), patient education, and symptom monitoring are essential
5	Zokirov et al. (2025)	<i>Stepwise Treatment Methods for Children with Asthma</i>	To compare the effectiveness of stepwise treatment approaches in children	Multicenter prospective observational study on 500 children aged 6–15 years with persistent asthma	All regimens improved asthma control; initial combination of ICS + LABA led to faster improvement in lung function and fewer severe exacerbations	Initial ICS + LABA combination therapy is more effective and faster than traditional step-up therapy, suggesting the need to revise initial treatment strategies
6	Sardon-Prado et al. (2023)	<i>Severe Asthma and Biological Therapies</i>	To review available biologic therapies and their indications for severe asthma	Clinical review based on guidelines and clinical trials	Biologics like omalizumab, mepolizumab, benralizumab, dupilumab, and tezepelumab effectively reduce exacerbations and steroid dependence when targeted appropriately	Phenotype-based biologic therapy is a major advancement in managing severe pediatric asthma, highlighting the importance of accurate endotyping for treatment decisions
7	Pelaia et al.	<i>Tezepelumab : A Potential</i>	To analyze the	Literature review on	Tezepelumab blocks	Tezepelumab expands

No	Authors	Title	Objective	Method	Results	Conclusion
	(2021)	<i>Therapy for Severe Asthma</i>	mechanism of action and effectiveness of tezepelumab	clinical trials and molecular studies	TSLP signaling, reduces airway inflammation across various asthma phenotypes, effective even in non-eosinophilic cases	biologic therapy options by targeting upstream inflammatory triggers and is promising for patients unresponsive to conventional T2 therapies
8	Menzies-Gow et al. (2022)	<i>Real World Biologic Use in Severe Asthma</i>	To analyze real-world usage patterns and switching of biologic therapy	Observational study using data from the International Severe Asthma Registry and CHRONICLE study	Many patients switched biologics due to suboptimal response or side effects; dupilumab and benralizumab showed high retention rates	Individualized therapy selection and close monitoring are essential in biologic use for severe asthma, as real-world data show varied patient responses
9	Pijnenburg et al. (2022)	<i>Childhood Asthma: Pathogenesis and Phenotypes</i>	To review pathogenesis and phenotypes of childhood asthma	Comprehensive review of environmental, genetic, and immunologic factors	Multiple phenotypes and endotypes influenced by early-life exposure, infections, microbiome, and genetic susceptibility; data-driven approaches can enhance therapy	Personalized treatment based on phenotype and endotype classification offers new hope in diagnosis and therapy, moving beyond one-size-fits-all approaches
10	Savin et al. (2023)	<i>Bronchial Asthma, Airway Remodeling and Lung</i>	To explain the progressive relationship between	Literature review based on experimental and clinical	Remodeling and fibrosis play a major role in chronicity	Targeted molecular therapies addressing remodeling

No	Authors	Title	Objective	Method	Results	Conclusion
		<i>Fibrosis</i>	asthma, airway remodeling, and lung fibrosis	studies	and treatment resistance in severe asthma	and fibrosis are needed to prevent disease progression in severe asthma

Discussion

Based on the analysis of ten journals discussing severe pneumonia in children, it was found that recovery time and treatment success are significantly influenced by several key factors. These include early intervention, diagnostic approaches, and precise biologic therapies such as anti-IgE, anti-IL5, anti-IL4R, and anti-TSLP.

According to Yamaguchi et al. (2024), the study discusses the effectiveness and safety of benralizumab in patients with severe eosinophilic asthma. The study results showed improvements in asthma control scores (ACQ-5) and lung function following therapy administration. These findings strengthen the evidence that benralizumab can be a safe and effective treatment option in real-world clinical practice in Japan.

According to Jafari et al. (2023), the study investigated the effectiveness of oral montelukast in controlling acute asthma attacks in children. The study found no significant differences between the montelukast and placebo groups in terms of hospital stay duration or oxygen saturation. This indicates that montelukast is not effective as an adjunct therapy for acute asthma attacks.

Savin et al. (2023) presented a classification of phenotypes and endotypes of severe asthma and a therapy approach based on molecular profiling. They emphasized the importance of precision therapy using biomarkers such as eosinophils, IgE, and FeNO to determine optimal treatment, including the use of biologic therapies like anti-IL5 and anti-IgE.

According to Thomas et al. (2022), a new paradigm in asthma management has emerged, shifting from merely controlling symptoms to achieving asthma remission. For years, asthma therapy has focused on symptom reduction and exacerbation prevention without achieving a “cure.” Asthma remission is not identical to a complete cure, but rather a state of being symptom- and exacerbation-free for a certain period, with or without continued treatment.

Zokirov & Q (2025) compared the effectiveness of a stepwise therapy approach and immediate combination therapy in children with asthma. Results showed that initial combination of ICS and LABA provided faster symptom control and reduced exacerbations compared to the stepwise approach. The main recommendation is to initiate combination therapy early in moderate to severe asthma cases.

Sardon-Prado et al. (2023) discussed the effectiveness of various biologic therapies in controlling severe asthma. The main focus was on the T2-high phenotype, which showed

significant response to anti-IL5, anti-IL4R, and anti-IgE. The article emphasizes the importance of phenotype identification in determining the optimal biologic therapy.

Chung et al. (2022) discussed the effectiveness of Tezepelumab, a monoclonal antibody targeting TSLP. This therapy demonstrated efficacy in reducing exacerbations in both T2 and non-T2 phenotypes. Tezepelumab presents a new hope for refractory asthma treatment, especially in patients who do not respond to conventional biologics.

Pelaia et al. (2021), through an international registry study, described patterns of biologic therapy use and switching. Many patients changed biologic treatments due to suboptimal response or side effects. This underscores the importance of regular evaluation and personalized approaches in severe asthma therapy.

Menzies-Gow et al. (2022) outlined the importance of early understanding of asthma phenotypes and pathogenesis in children. Early identification allows for therapy approaches tailored to each patient's immunological profile, improving long-term outcomes.

Pijnenburg et al. (2022) highlighted the relationship between airway remodeling and pulmonary fibrosis in long-term asthma patients. Fibrosis is considered the end result of chronic inflammation and repeated epithelial damage, which, if left unaddressed, may lead to permanent lung function impairment.

Conclusion

Based on the analysis of 10 articles, we found that biologic therapy has been proven effective in reducing exacerbations, improving lung function, and decreasing dependence on systemic corticosteroids. However, responses to therapy vary, making regular evaluation and an individualized approach essential.

Acknowledgement

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