

## Protocol

# Comparative efficacy of nebulised salbutamol, salbutamol plus budesonide and salbutamol plus fluticasone in the management of acute exacerbation of bronchial asthma in children: a study protocol of a randomized controlled trial

Rachna Pasi<sup>1\*</sup>, Thirunavukkarasu Arun Babu<sup>2</sup>

<sup>1</sup>Department of Pediatrics, AIIMS Delhi, New Delhi, India

<sup>2</sup>Department of Pediatrics, AIIMS, Mangalagiri, Andhra Pradesh, India

**Received:** 20 May 2026

**Revised:** 27 July 2026

**Accepted:** 10 August 2026

### \*Correspondence:

Dr. Rachna Pasi,

E-mail: [rachna.pasi@gmail.com](mailto:rachna.pasi@gmail.com)

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

## ABSTRACT

**Background:** Acute exacerbation of asthma in children is one of the most common emergencies in children. Use of inhaled corticosteroids (ICS) in combination with bronchodilator as initial therapy has shown to be beneficial when compared to oral corticosteroids. ICS commonly used in acute exacerbation in children are budesonide and fluticasone. Pediatric respiratory assessment measure (PRAM) Score is widely used standardized score in clinical and as well in research studies for 2-17years children. It has five parameters with total scores from 0-10 where higher scores indicate sicker patient.

**Methods:** This study is planned to study efficacy of nebulised salbutamol vs salbutamol plus budesonide vs salbutamol plus fluticasone in management of acute exacerbation of asthma in children. After written informed consent, participants will be enrolled by computerized block randomization list to three groups. Each group will be administered the medication as per their allocation and weight band. Vitals and PRAM score will be recorded 0, 2 and 4 hours from the start of treatment. PEFR will be recorded with help of peak flowmeter at 2 hours and 4 hours from initiation of treatment. At the end of 4 hours, patient outcome will be noted. After 3 months, child will be followed to know level of control of symptoms as per GINA guidelines. Concealment will be disclosed after statistical analysis performed and results are locked.

**Conclusions:** If this intervention study shows evidence of a significant difference between three arms of treatment, then it may guide first line of treatment of acute exacerbation of paediatric asthma.

**Trial Registration:** CTRI/2023/07/054624 registered prospectively.

**Keywords:** Budesonide, Fluticasone, Asthma, Salbutamol, Corticosteroids

## INTRODUCTION

Bronchial asthma in children is one of the most common chronic diseases presenting to paediatric department. It frequently presents with episodic wheezing, cough, breathlessness routinely and with acute exacerbations to emergency department.<sup>1</sup> The recent Global Burden of Disease (GBD, 1990-2019) estimated the total burden of

asthma in India as 34.3 million, accounting for 13.09% of the global burden.<sup>2</sup> The data pertaining to exact prevalence of asthma in children is still lacking. One study estimated prevalence of current wheeze in (6-7 years) children and adolescents (13-14 years) were 3.16% and 3.63% respectively.<sup>3</sup> There are many modalities of treatment for management of acute exacerbation like short acting beta-2 agonist, anticholinergic, steroids or

magnesium sulphate which can be used as per response to these medications. Generally, anticholinergic like ipratropium bromide or inhalational steroids are used as an adjunct treatment to short acting beta-2 agonist, considering their additive effect in the control of symptoms.<sup>4,5</sup> Use of ICS in combination with bronchodilator as initial therapy has shown to be beneficial in terms of reducing length of stay, improvement of PEFV values when compared to oral corticosteroids.<sup>6,7</sup> ICS also has rapid onset of action, selective drug action to target organ with minimal systemic side effects as compared to systemic CS.<sup>7,8</sup> ICS commonly used in acute exacerbation in children are budesonide and fluticasone. Budesonide has been most common and widely studied ICS for acute and chronic control of symptoms. Fluticasone has been introduced as an inhaled CS in 1993 with superior therapeutic effect to other ICS as it has selective affinity for glucocorticoids receptors but low oral bioavailability. Few studies have also demonstrated the better immunological efficacy of ICS over systemic CS in terms of better induction of T regulatory cell response and reduction of cytokines levels.<sup>9</sup>

Paediatric respiratory assessment measure (PRAM) Score is the widely used score in clinical and as well in research studies to know the outcome of patient presented to emergency as acute exacerbation of asthma. It has been standardized, validated score for use in children aged 2-17years. It has five parameters like oxygen saturation, suprasternal retraction, scalene muscle contraction, air entry and wheezing. Each parameter has scoring 0-2, with total scores from 0-10 where higher scores indicates sicker patient (Table 1). It has good inter-rater reliability and good prognosticating values for severity of illness.<sup>10</sup> As per recent updates of GINA and IAP guidelines for management of acute severe asthma, inhalational bronchodilator therapies like beta-2 agonist and corticosteroids are to be used. Details of which corticosteroids are preferable over other, or any flow chart for management is not provided due to paucity of data. We hereby have planned this study to know efficacy of various modalities of inhalational medicines over each other to achieve better and rapid relief of symptoms in the children with acute exacerbation. This will help us to pick the best drug combination among all the approved first line drugs.

**Table 1: PRAM score.<sup>10</sup>**

| Severity                           |          | PRAM score         |                            |                                                |
|------------------------------------|----------|--------------------|----------------------------|------------------------------------------------|
| <b>Mild</b>                        |          | 1-3                |                            |                                                |
| <b>Moderate</b>                    |          | 4-7                |                            |                                                |
| <b>Severe/life-threatening</b>     |          | 8-12               |                            |                                                |
| <b>Signs</b>                       | <b>0</b> | <b>1</b>           | <b>2</b>                   | <b>3</b>                                       |
| Suprasternal indrawing             | Absent   |                    | Present                    |                                                |
| Scalene retractions                | Absent   |                    | Present                    |                                                |
| Wheezing                           | Absent   | Expiratory only    | Expiratory +/- inspiratory | Audible wheeze/ silent chest/minimal air entry |
| Air entry                          | Normal   | Decreased at bases | Widespread decrease        | Absent/minimal                                 |
| Room air O <sub>2</sub> saturation | >94%     | 92-94%             | <92%                       |                                                |

### Research question

Is nebulised salbutamol plus fluticasone/salbutamol plus budesonide is more effective than salbutamol alone than in management of acute exacerbation of asthma in children?

### Aim

Aim was to study the efficacy of nebulised salbutamol vs salbutamol plus budesonide vs salbutamol plus fluticasone in management of acute exacerbation of asthma in children.

### Objectives

Primary objective is to assess the efficacy of nebulised salbutamol vs salbutamol plus budesonide vs salbutamol

plus fluticasone in management of acute exacerbation of asthma in children using PRAM score.

Secondary objective is to assess the effect of nebulised salbutamol vs salbutamol plus budesonide vs salbutamol plus fluticasone in management of acute exacerbation of asthma in children by calculating the improvement in peak expiratory flow rate and also to assess the short-term outcome at 2 hours and 4 hours followed by assessing the long-term level of control of symptoms in these patients on follow up at 3 months.

### METHODS

#### Place of study

Study conducted at AIIMS Mangalagiri, paediatrics department.

### **Study population**

Children aged 4 years to 14 years who will be coming to paediatric OPD/emergency department in acute exacerbation of asthma.

### **Inclusion criteria**

Children with known asthma as defined by British Thoracic Society who will be presenting as acute exacerbation of asthma in pediatric OPD/Emergency department (Table 2).<sup>11</sup> Children with past history of two or more episodic wheeze responsive to inhaled  $\beta_2$  agonist and now presenting as acute exacerbation of asthma. All children presenting with acute exacerbation of asthma whose parents will give written informed consent to participate in this study.

### **Exclusion criteria**

Children with known asthma who will be presenting as acute exacerbation of asthma but whose parents will not give consent to participate. Children who will be having symptoms of acute life-threatening asthma (Table 3), chronic respiratory illness and those who took short/long acting beta 2 agonist or steroids within 6 hours prior to admission. Children who will be having symptoms or radiological evidence of acute alternate diagnosis i.e., bronchopneumonia or pleural effusion. Any deviation from the study treatment protocol necessitated due to clinical situation.

### **Operational definitions**

#### *Acute exacerbation of asthma*

The operational definition for the recruitment of participants in this study will be, any patient with suggestive history or confirmed case of asthma now complaining of cough or respiratory difficulty and on examination found to have wheezing will be considered as acute exacerbation of asthma.

### **Sample size**

Sample size was calculated using G\*Power software version 3.1.9.7 based on previously published RCT by Amir Najim Abood HA et al on Effects of nebulized budesonide plus salbutamol and nebulized salbutamol monotherapy on acute exacerbation of asthma in children. Based on the mean improvement and standard deviation in both groups, acceptable alpha error of 5% and power of 80%, with allocation ratio of 1:1, to prove non-inferiority, a minimum sample size needed was found to be 34 in each group.<sup>12</sup>

### **Ethical consideration**

This study has received clearance from institute ethical committee. (AIIMS/MG//IEC/2022-23/230). Written

informed consent and assent (wherever applicable) will be taken from parents of all participants and children.

### **Name of registry and reg. no.**

This RCT is registered under clinical registry trials, India. (CTRI/2023/07/054624).

### **Status and timeline of study**

Study is still recruiting participants. (a)Expected to finish participant recruitment in next 2 months followed by (b) data analysis for next 2 months (c) Result will be expected by end of 4months. Study will be completed in next 4 months (August 2026).

### **Randomization and group assignment**

#### *Randomization*

The block randomization will be done through computer automatic randomization table generation. Sequence generation will be done through randomization software.

#### *Allocation concealment mechanism*

The list generated through software will be kept concealed at a place. The sealed envelopes will be made for randomly allocating participants to one of the groups. The opaque envelopes will be carrying a paper written either A or B or C which will allocate the participants to respective group.

#### *Implementation*

Out of three randomly assigned groups, one group will be administered nebulised salbutamol, other group will be administered nebulised salbutamol plus fluticasone and third group will receive nebulised salbutamol plus budesonide. The physical characteristics of all will be made same. The groups will be coded as A, B and C which will be concealed from the investigator assigning the group, performing intervention, documenting data and statistician. The allocation ration would be 1:1:1.

### **Methodology**

At first, written informed consent will be taken from the participants. The participants who will agree to be the part of the study will be asked to take out one sealed envelope which will be opened to allocate one of the either group. Vitals (Heart rate, pulse rate, respiratory rate) and PRAM scoring will be done. Each group will be administered the medication labelled either A or B or C as per their allocation through nebulisation. Patient will be receiving medications as per weight band. Each medication will be given through nebulisation thrice in the interval of 20 mins. During this, vitals of patients will be monitored regularly. Vital and PRAM score will be recorded 0, 2 and 4 hours from the start of treatment. All

scoring will be done by same trained person and will be recorded on study proforma. PEFR will be recorded with the help of peak flowmeter at 2 hours and 4 hours from initiation of treatment. All the patients will receive treatment as per standard protocol and treatment will be upgraded too, if clinical condition demands so. The CONSORT flow diagram can be found in Figure 1.

#### ***Dose of salbutamol per dose***

Concentration of nebulised salbutamol will be used in the study is 2.5 mg (for less than 30 kg) or 5 mg (for more than 30 kg) plus distilled water (2 ml).

#### ***Dose***

Three doses will be given at interval of 20 minutes as per standard protocol recommended by GINA.<sup>13</sup>

#### ***Dose of salbutamol/fluticasone per dose***

Concentration of nebulised salbutamol will be used in the study is 2.5 mg (for less than 30 kg) or 5 mg (for more than 30 kg) plus 0.5 mg fluticasone respule.<sup>14</sup>

#### ***Dose***

Three doses will be given at interval of 20 minutes as per standard protocol recommended by GINA.<sup>13</sup>

#### ***Dose of salbutamol/budesonide per dose***

Concentration of nebulised salbutamol will be used in the study is 2.5 mg (for less than 30 kg) or 5 mg (for more than 30 kg) plus 0.5mg budesonide respule.<sup>14</sup>

#### ***Dose***

Three doses will be given at interval of 20 minutes as per standard protocol recommended by GINA.<sup>13</sup>

#### ***Blinding***

Groups will be blinded by giving them alphabetical naming. The person who will be doing intervention, administering medication, monitoring PRAM score, recording PEFR by peak flowmeter, collecting data and statistician will not be knowing which medication has been administered to the participant.

Concealment will be disclosed only after statistical analysis is performed and results are locked.

#### ***Outcomes***

Outcomes will be measured in terms of change in vitals and PRAM scores from initial recruitment to 2 hours and 4 hours from initiation of treatment, improvement in PEFR values from 2 hours and 4 hours from initiation of treatment.

At the end of 4 hours, patient outcome will be noted as can be discharged, need further admission to the hospital. After 3 months, child will be followed to know the level of control of symptoms as per GINA guidelines.<sup>13</sup>

#### ***Statistical analysis***

All data will be entered in excel sheet. Continues variables like age; PRAM will be summarized as mean and standard deviation and categorical variables like gender of study group will be summarized as frequency and percentage.

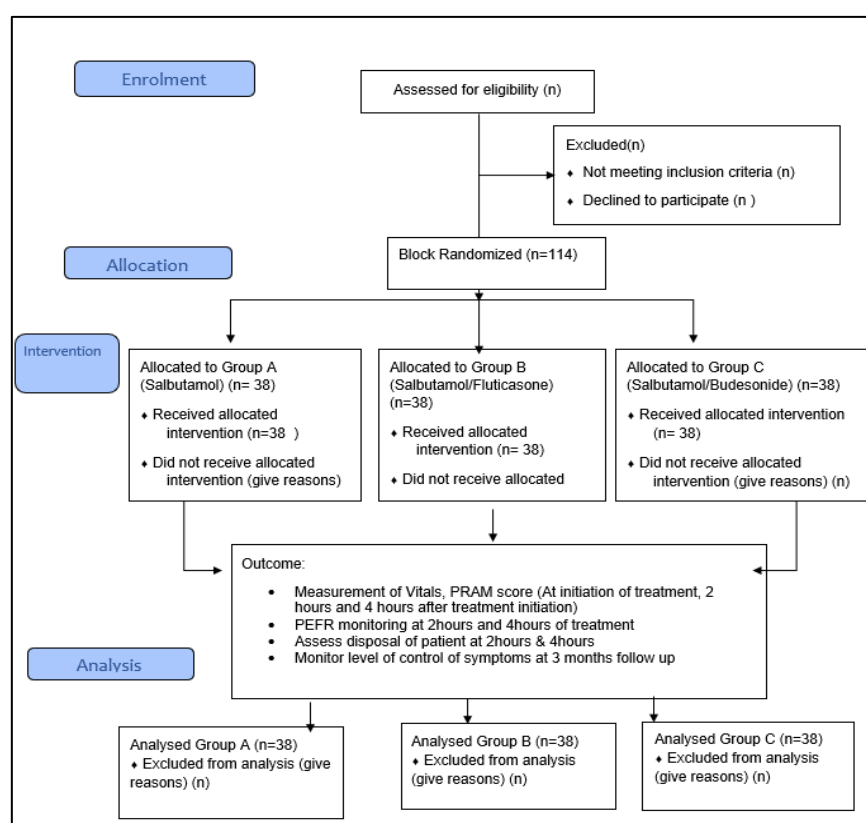
The association between continues variables and categorical variables will be analysed using ANOVA. The association between categorical variables will be analysed using Chi-square test. Intention to treat analysis method will be used.  $P < 0.05$  will be considered as a statistical significance. Analysis will be done using Epi-info and R-software.

**Table 2: Definition of asthma (as per British Thoracic Society guidelines).<sup>11</sup>**

| Variables                | Definitions                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|--------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Episodic symptoms</b> | More than one of the symptoms of wheeze, breathlessness, chest tightness and cough occurring in episodes with periods of no (or minimal) symptoms between episodes. Note that this excludes cough as an isolated symptom in children. For example: a documented history of acute attacks of wheeze, with symptomatic and objective improvement with treatment recurrent intermittent episodes of symptoms triggered by allergen exposure as well as viral infections and exacerbated by exercise and cold air, and emotion or laughter in children. An historical record of significantly lower FEV1 or PEF during symptomatic episodes compared to asymptomatic periods provides objective confirmation of obstructive nature of the episodic symptoms. |
|                          | <b>Wheeze confirmed by a healthcare professional on auscultation</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|                          | It is important to distinguish wheezing from other respiratory noises, such as stridor or rattly breathing. Repeatedly normal examination of chest when symptomatic reduces the probability of asthma.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|                          | <b>Evidence of diurnal variability</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| <b>Atopic history</b>    | Symptoms which are worse at night or in the early morning.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|                          | Personal history of an atopic disorder (ie, eczema or allergic rhinitis) or a family/ history of asthma and/or atopic disorders, potentially corroborated by a previous record of raised allergen-specific IgE levels, Positive skin-prick tests to aeroallergens or blood eosinophilia.<br>Absence of symptoms, signs or clinical history to suggest alternative diagnoses (including but not limited to dysfunctional breathing, GERD, obesity).                                                                                                                                                                                                                                                                                                       |

**Table 3: Definition of acute severe asthma and life-threatening asthma (as per British thoracic society guidelines).<sup>11</sup>**

| Acute severe                                                             | Life-threatening           |
|--------------------------------------------------------------------------|----------------------------|
| SpO <sub>2</sub> <92%                                                    | SpO <sub>2</sub> <92%      |
| PEF 33-50% best or predicted                                             | PEF <33% best or predicted |
| Can't complete sentences in one breath or too breathless to talk or feed | Silent chest               |
|                                                                          | Cyanosis                   |
| Heart rate                                                               |                            |
| >125 (>5 years) or                                                       | Poor respiratory effort    |
| >140 (1-5 years)                                                         | Hypotension                |
| Respiratory rate                                                         |                            |
| >30 breaths/min (>5 years) or                                            | Exhaustion                 |
| >40 (1-5 years)                                                          | Confusion                  |

**Figure 1: CONSORT flow diagram.**

## DISCUSSION

There are many modalities of treatment for management of acute exacerbation like short acting beta-2 agonist, anticholinergic, steroids or magnesium sulphate which can be used as per response to these medications.<sup>3,6,7</sup> Inhaled CS have fewer side effects as compared to systemic steroids, so it will be better to use inhaled CS to prevent children with the side effects due to target delivery of drug.<sup>6,7</sup> It has also been shown that if inhaled bronchodilators are supplemented with ICS, it has several prognostic significances.<sup>6</sup> Fluticasone, budesonide and salbutamol are widely used drugs for control of acute exacerbation of asthma.<sup>8,9,12,14</sup> This study will indicate the most efficacious first line combination of bronchodilators with CS or if bronchodilator alone is effective in control

of acute symptoms. The symptom improvement will be quantified with the help of widely used PRAM score.

## Limitations

This is a single centre-based study. Similar large scale, multicentric studies are needed before this study findings can be generalized to other populations.

## CONCLUSION

This study will reveal which inhalational medications are more efficacious as first line treatment for management of acute exacerbation of paediatric asthma. This will also talk about long term level of control of symptoms in each category of treatment.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee (CTRI/2023/07/054624).*

## REFERENCES

1. Andrew HL, Ronina AC, Joseph DS, Scott HS. Childhood asthma. In: Kliegman R, Stanton B, Behrman RE, St. Geme JW, Schor NF editors. *Nelson's textbook of pediatrics*. 20<sup>th</sup> ed. Philadelphia: Saunders. 2016;1095-115.
2. GBD compare, Viz hub. Available at: <https://vizhub.healthdata.org/gbdcompare/>. Accessed on 03 July 2026.
3. Singh MS, Sundeep, Singh V. Prevalence, time trends and treatment practices of asthma in India: Global Asthma Network study. *ERJ Open Res*. 2022;8(2):00528-2021.
4. Inayat N, Shah RH, Rahu QA, Sahito R. Nebulized salbutamol with and without ipratropium bromide in the treatment of acute severe asthma. *Pak J Chest Med*. 2016;22:102-6.
5. Aaron SD. The use of ipratropium bromide for the management of acute asthma exacerbation in adults and children: a systematic review. *J Asthma*. 2001;38:521-30.
6. Sawanyawisuth K, Chattakul P, Khamsai S. Role of Inhaled Corticosteroids for Asthma Exacerbation in Children: An Updated Meta-Analysis. *J Emerg Trauma Shock*. 2020;13(2):161-6.
7. Arulparithi CS, Babu TA, Ravichandran C. Efficacy of Nebulised Budesonide versus Oral Prednisolone in Acute Severe Asthma. *Indian J Pediatr*. 2015;82:328-32.
8. Edmonds ML, Milan SJ, Camargo CA Jr, Pollack CV, Rowe BH. Early use of inhaled corticosteroids in the emergency department treatment of acute asthma. *Cochrane Database Syst Rev*. 2012;12(12):CD002308.
9. Demirca BP, Cagan H, Kiykim A. Nebulized fluticasone propionate, a viable alternative to systemic route in the management of childhood moderate asthma attack: A double-blind, double-dummy study. *Respir Med*. 2015;109(9):1120-5.
10. Alnaji F, Zemek R, Barrowman N, Plint A. PRAM score as predictor of pediatric asthma hospitalization. *Acad Emerg Med*. 2014;21(8):872-8.
11. British Thoracic Society Scottish Intercollegiate Guidelines Network. British guideline on the management of asthma Quick Reference Guide. 2016.
12. Amir Najim Abood HA, Al-Musawi ZM, Hussein AM, Hameed RM. Effects of nebulized budesonide plus salbutamol and nebulized salbutamol monotherapy on mild to moderate acute exacerbation of asthma in children: A comparative study. *J Pak Med Assoc*. 2021;71(9)12:S29-S34.
13. Global initiative for asthma. Global Strategy for Asthma Management and Prevention 2022. GINA Report. 2022.
14. Direkwattanachai C, Aksilp C, Chatchatee P, Jirapongsananuruk O, Kamalaporn H, Kamchaisatian W, et al. Practical considerations of nebulized corticosteroid in children with acute asthmatic exacerbation: A consensus. *Asian Pac J Allergy Immunol*. 2021;39(3):168-76.
15. Juszczak E, Altman DG, Hopewell S, Schulz K. Reporting of Multi-Arm Parallel-Group Randomized Trials: Extension of the CONSORT 2010 Statement. *JAMA*. 2019;321(16):1610-20.

**Cite this article as:** Pasi R, Babu TA. Comparative efficacy of nebulised salbutamol, salbutamol plus budesonide and salbutamol plus fluticasone in the management of acute exacerbation of bronchial asthma in children: a study protocol of a randomized controlled trial. *Int J Clin Trials* 2026;13(4):455-60.