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Original Article

Escalation of Treatment in Children with Exacerbation of Asthma

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ABSTRACT

Background: An exacerbation of asthma in age group 5-12 years is defined by GINA guidelines (2022) as episodes characterized by a progressive increase in symptoms of shortness of breath, cough, wheezing or chest tightness and progressive decrease in lung function, i.e. they represent a change from the patient`s usual status that is sufficient to require a change in treatment. Severe exacerbations are medical emergencies, often require hospitalization and further treatment escalation. There are very few studies that have estimated escalation of treatment in exacerbation of asthma in pediatric age group.

Methods: A prospective observational cross-sectional study conducted over 18 months. Patients aged 5-12 years with exacerbation of asthma (as defined by GINA guidelines 2022) presented to emergency department for treatment were enrolled into the study. The objective of the study was to estimate the proportion of children requiring escalation of treatment in exacerbation of asthma and to evaluate risk factors in patients having escalation of treatment and compare it with patients who do not require escalation of treatment in exacerbation of asthma. Escalation of treatment will be defined as patient with exacerbation of asthma who required intravenous (IV) corticosteroids, IV MgSO4, IV bronchodilator, IV ketamine, non-invasive mechanical ventilation and invasive mechanical ventilation (intubation). Assessment of severity of asthma was done by pulmonary score.

Result: The mean (SD) of age (years) was 8.24 (2.45) while median (IQR) was 8.00 (6-10). The age (years) ranged from 5 – 12. 54.8% of the participants were male. The mean (SD) of pulmonary score was 4.61 ± 2.00 while median (IQR) was 4.00 (3-6). The pulmonary score ranged from 2 - 9. The proportion of escalation of treatment in acute exacerbation of asthma was 29%. There was a significant difference between the 2 groups in terms of distribution of duration of hospital stay ($\chi 2$ = 72.665, p = <0.001). A room air oxygen saturation level below 90% was identified as a significant risk factor, demonstrating a statistical significance between the groups that required treatment escalation and those that did not. Poor adherence to medication (29.8%) and seasonal variation (28.8%) were the most common risk factors for asthma exacerbations in this study; however, neither demonstrated statistical significance when compared between the two groups.

Conclusion: Children presenting with an asthma exacerbation may require treatment escalation, as observed in 29% of patients in this study. Early identification of these patients is crucial to prevent the deterioration of their condition. One way to identify such patients is by identifying risk factors that are more prevalent in escalated patients compared to non-escalated ones.

Keywords*: Escalation; Children; Exacerbation; Asthma.*

INTRODUCTION

Asthma is a chronic inflammatory condition of the airways, characterized by episodes of reversible airway obstruction and increased airway responsiveness, leading to symptoms like recurrent wheezing, coughing and shortness of breath [1].

India bears a disproportionately higher asthma burden, with three times higher mortality and over double the Disability-Adjusted Life Years (DALYs) compared to global figures [2]. In children, asthma is more prevalent among males less than 10 years, with 8.4% of boys affected compared to 5.5% of girls [3].

An exacerbation of asthma in age group 5-12 years is defined by GINA guidelines (2022) as episodes characterized by a progressive increase in symptoms of shortness of breath, cough, wheezing or chest tightness and progressive decrease in lung function, i.e. they represent a change from the patient`s usual status that is sufficient to require a change in treatment. Exacerbations may occur in patients with a pre-existing diagnosis of asthma or, occasionally, as the first presentation of asthma [1,4]. Exacerbations can occur in those with a known asthma diagnosis or sometimes represent the initial presentation of asthma. Severe exacerbations are medical emergencies, impacting a child's quality of life, emotional health, school attendance and daily activities [5].

The severity of exacerbations varies and is typically assessed based on clinical presentation and respiratory function. Accurate recognition of severe exacerbations is crucial, as these are associated with worse outcomes [6]. Pulmonary score is commonly used to estimate severity, with scores below 4 indicating mild exacerbations, scores 4-6 indicating moderate exacerbations, and scores 7-9 reflecting severe cases [7]. Moderate and severe asthma exacerbations require hospital care. Life threatening asthma is identified by red flag signs of asthma. These include oxygen saturation levels below 92%, inadequate respiratory effort, a silent chest, cyanosis, confusion, altered mental status, low blood pressure, and bradycardia. Patients exhibiting these symptoms need urgent care in a pediatric ICU and require rapid escalation of treatment to manage their severe condition effectively [8].

Children experiencing severe asthma exacerbations often require hospitalization and further treatment escalation, which may include intravenous corticosteroids, magnesium sulfate, bronchodilators or advanced respiratory support like noninvasive or invasive mechanical ventilation [4]. The rates of intravenous therapy use vary between countries, ranging from 3.4% in the UK to 10.5% in the USA, although similar data from India are lacking [9].

Risk factors for severe exacerbations include a history of previous exacerbations, viral infections, vitamin D deficiency, tobacco smoke exposure, psychological stress, poor medication adherence, allergens, and air pollution [10]. Preventive strategies include developing individualized asthma action plans highlighting danger signs to parents, ensuring regular follow-up, monitoring inhaler technique and addressing modifiable risk factors like exposure to tobacco smoke. Adjusting treatment with controller medications is critical for children with poor symptom control or frequent exacerbations [11].

There are very few studies that have estimated escalation of treatment in exacerbation of asthma in pediatric age group. So this study is planned to estimate the proportion of escalation of treatment in exacerbation of asthma in pediatric age group (5-12 years) and will also evaluate risk factors in patients having escalation of treatment and compare it with patients who do not require escalation of treatment in exacerbation of asthma.

METHODS

This was a prospective observational cross-sectional study conducted over 18 months. Patients aged 5-12 years with exacerbation of asthma (as defined by GINA guidelines 2022) presented to emergency department of a tertiary care hospital in Delhi for treatment were enrolled into the study after taking informed consent from the parents/guardian. Children with congenital or acquired heart disease, foreign body aspiration, tuberculosis, pneumonia or other chronic lung disease were excluded from the study [Figure 1]. The data collected was recorded in patient's proforma sheet and the quantitative data collected was analyzed later.

The ethical clearance was taken by institute ethical committee (S. No. IEC/VMMC/SJH/Thesis/2023-03/CC-213 dated 27.03.2023). The primary objective of the study was to estimate the proportion of children requiring escalation of treatment in exacerbation of asthma and secondary objective was to evaluate risk factors in patients having escalation of treatment and compare it with patients who do not require escalation of treatment in exacerbation of asthma. Escalation of treatment will be defined as patient with exacerbation of asthma who required intravenous (IV) corticosteroids, IV MgSO4, IV bronchodilator, IV ketamine, non-invasive mechanical ventilation and invasive mechanical ventilation (intubation). Assessment of severity of asthma is done by Pulmonary score [7] [Table – 1].

Management of life-threatening asthma in children emphasizes the importance of ensuring airway, breathing and circulation. Oxygen is delivered via nasal cannula or facemask to keep saturation levels above 95%. Intravenous fluids may be necessary to maintain euvolemia. Treatment typically begins with nebulization using a beta-2 agonist, such as salbutamol, at a dose of 0.15 mg/kg every 20 minutes for up to three doses. Alternatively, a metered-dose inhaler (MDI) with salbutamol can be used, delivering 2-4 puffs (100 µg each) every 20 minutes for the first hour, followed by nebulization with budesonide. If the child is unresponsive to initial therapy, nebulization with ipratropium bromide may be administered at three doses every 20 minutes. If the child can take oral medication, systemic corticosteroids should be

started at 1-2 mg/kg/day (maximum 40 mg). In cases where the child is unstable or unable to take medication orally, intravenous hydrocortisone can be given at 10 mg/kg as an initial dose, followed by 5 mg/kg every six hours. However, they should not be used as the sole treatment for acute asthma due to their delayed bronchodilator effects. For patients who remain unresponsive to initial therapies, intravenous magnesium sulphate may be administered at a dose of 50 mg/kg (max 2 grams) over 20 minutes with normal saline to facilitate smooth muscle relaxation [8]. If further escalation required then we used IV bronchodilator, IV ketamine, non-invasive mechanical ventilation and invasive mechanical ventilation (intubation). Additionally, monitoring serum electrolytes is important when a child receives multiple nebulisations of salbutamol to ensure potassium levels remain stable [1].

Sample size

The sample size for the study was based on a study by Craig S et al, who reported the proportion of subjects with treatment escalation as 7.3% [9]. The sample size was calculated according to the formula given by Lemeshow et al, 1990 [12].

Sample size $N = \frac{(z_{(1-\alpha/2)})^2 \times p \times (1-p)}{\delta^2}$

Proportion of subjects with treatment escalation: p = 0.073 (7.3%)
Precision: δ = 0.05 (5%)
Type I error: α = 0.05 (5%), = 1.96

Based on the formula and values given above:
Sample size required N = [1.96² x 0.073 x (1-0.073)] / 0.05² = 103.98 ≈ 104
Thus, 95% confidence interval, the proposed sample size for the study was **104**.

Statistical analysis

Data will be coded and recorded in MS Excel spreadsheet program. SPSS v21 (IBM Corp.) will be used for data analysis. Descriptive statistics will be elaborated in the form of means/standard deviations and medians/IQRs for continuous variables, and frequencies and percentages for categorical variables. Association between two categorical variables will be explored using Chi-squared test. In case the expected frequency in the contingency tables will be found to be <5 for >25% of the cells, Fisher's Exact test will be used instead. Association between variables where one is continuous and one is categorical will be explored using independent sample 't' test when the categorical variable has two categories, and One-Way ANOVA when it has more than 2 categories. Post-Hoc pairwise analysis will be performed using Tukey's HSD test in case of One-Way ANOVA to control for alpha inflation. If data will be found to be non-normally distributed, appropriate non-parametric tests in the form of Wilcoxon Mann-Whitney U Test/Kruskal Wallis test will be used for these comparisons. Linear correlation between two continuous variables will be explored using Pearson's correlation (if the data will be normally distributed) and Spearman's correlation (for non-normally distributed data). Statistical significance will be kept at $p<0.05$.

RESULTS

The mean (SD) of age (years) was 8.24 (2.45). The median (IQR) of age (years) was 8.00 (6-10). The age (years) ranged from 5 – 12. 54.8% of the participants were male while 45.2% of the participants were female. 30 (28.8%) of the participants had escalation of treatment during exacerbation of asthma while 74 (71.2%) of the participants did not have escalation of treatment. The mean (SD) of pulmonary score was 4.61 ± 2.00. The median (IQR) of pulmonary score was 4.00 (3-6). The pulmonary score ranged from 2 - 9. 12.5% of the participants had a pulmonary score ≤3 indicating mild severity, 66.3% had a pulmonary score in the moderate category, and 21.2% had a pulmonary score 7-9 indicating severe exacerbation. The mean (SD) pulmonary score was 7.00 (1.36) in the patients receiving escalation of treatment group and 3.66 (1.40) in the non-escalated group. The median (IQR) pulmonary score in patients receiving escalation of treatment was 7 (6-8), while it was 3 (3-4) in non-escalated group. The range of pulmonary scores was 2 to 9 in the escalated group. There was a significant difference in pulmonary scores between the two groups ($W = 2109.000$, $p < 0.001$), with the median pulmonary score being highest in the group receiving escalation of treatment. The strength of association, as measured by Point-Biserial Correlation, was 0.74, indicating a large effect size. The Box-and-Whisker plot illustrates the distribution of pulmonary scores in the two groups [Figure 2]. The middle horizontal line represents the median pulmonary score, the upper and lower bounds of the box represent the 75th and 25th percentiles, respectively, and the whiskers indicate the Tukey limits for the pulmonary score in each group.

Chi-squared test was used to explore the association between 'Escalation of Treatment' and 'Pulmonary Score Category'. There was a significant difference among the escalated and non-escalated group in terms of distribution of Pulmonary Score Category ($\chi2 = 46.328$, $p = <0.001$). Larger proportion of participants (78.4%) in the non-escalated group had moderate category of pulmonary score while larger proportion of participants (63.3%) in the escalated group had severe category of pulmonary score [Table 2]

Summary of Basic Details

33 (31.7%) of the participants had accompanied fever. 70 (67.3%) of the participants had cough. 91 (87.5%) of the participants had difficulty breathing at presentation to emergency. 6(5.8%) of the participants had chest pain. 8 (7.7%) of the participants had vomiting. 82 (78.8%) of the participants had history of similar illness in past. 82 (78.8%) of the participants had history of recurrent nebulization. 13 (12.5%) of the participants had positive history of atopy. 20 (19.2%) of the participants had family history of asthma. 49 (47.1%) of the participants were already on treatment who presented with an asthma exacerbation. 64 (61.5%) of the participants had length of hospital stay less than a day. 19 (18.3%) of the participants had length of hospital stay for 1-2 Days. 20 (19.2%) of the participants had length of hospital stay for 3-5 days. 1 (1.0%) of the participants had duration of stay: >5 days.

Summary of Illness Related Factors

27 (26.0%) of the participants had URI. 30 (28.8%) of the participants had seasonal variation. 2 (1.9%) of the participants had food allergy.1 (1.0%) of the participants had psychological stress. 11 (10.6%) of the participants had overuse of SABA. None (0.0%) of the participants had obesity/OSA. 45(43.3%) of the participants had rural residence. 59 (56.7%) of the participants had urban residence. 1 (1.0%) of the participants had previous history of mechanical ventilation. The mean saturation at room air (%) was 94.76 ± 5.01. 18 (17.3%) of the participants had saturation at room air ≤90 %. 25 (24.0%) of the participants had saturation at room air 91-94 %. 61 (58.7%) of the participants had saturation at room air ≥95 %. Air pollution was identified as a risk factor for asthma exacerbation in 13 participants, representing 12.5% of the total. 31 (29.8%) of the participants had poor adherence to medication. 7 (6.7%) of the participants had smoking exposure. 2 (1.9%) of the participants had pet exposure. 27 (26.0%) of the participants had dust allergy. Asthma exacerbations were most frequently observed in July with 25 cases (24%), followed by 19 cases (18.3%) in April, 17 cases (16.3%) in May, and 12 cases (11.5%) in June.

Summary of Management [Table 3]

All 30 participants (100.0%) received intravenous (IV) corticosteroids, with a mean duration of 48.00 ± 0.00 hours. Nineteen participants (63.3%) were administered IV magnesium sulphate, with 10 of them (52.6%) receiving a single dose and 9 (47.4%) receiving two or more doses. 7 participants (23.3%) were treated with IV aminophylline, with 5 (71.4%) having a duration of 0-6 hours, and 2 (28.6%) receiving it for more than 6 hours. Subcutaneous adrenaline was administered to 10 participants (33.3%), and IV ketamine was given to 1 participant (3.3%). Non-invasive mechanical ventilation was used for 3 participants (10.0%), while 1 participant (3.3%) required invasive mechanical ventilation. Regarding admission status, 64 participants (61.5%) were not admitted, while 40 (38.5%) were hospitalized. Of those admitted, 28 (26.9%) were in the PICU and 12 (11.5%) were in the Paediatric High Dependency Unit (HDU). The mean pulmonary score was 4.62 ± 2.05. In terms of asthma severity, 13 participants (12.5%) experienced mild exacerbations, 69 (66.3%) had moderate exacerbations, and 22 (21.2%) had severe exacerbations. Respiratory support was required by 83 participants (79.8%), with 56 (53.8%) using a face mask for oxygen delivery, 15 (14.4%) requiring nasal prongs, and 12 (11.5%) using a non-rebreather mask. As for nebulization treatments, 53 participants (51.0%) received only salbutamol, 15 (14.4%) were given both salbutamol and budesonide, 8 (7.7%) received salbutamol and ipratropium, and 28 (26.9%) received all three nebulisations (salbutamol, budesonide, and ipratropium).

Comparison of risk factors between Escalated and Non-escalated group [Table 4]

Various risk factors were evaluated between the escalated and non-escalated groups. Room air oxygen saturation (%) showed statistically significant differences between the two groups. Poor adherence to medication (29.8%) and seasonal variation (28.8%) were the most common risk factors for asthma exacerbations in our study; however, neither demonstrated statistical significance when compared between the two groups.

Legend Tables

Asthma Severity Score (Pulmonary Score) (Table 1)

Score	Respiratory rate/min		Wheezing	Accessory muscle use
	<6yrs	>6yrs		
0	<30	<20	None	No apparent activity
1	31-45	21-35	Terminal expiration with stethoscope	Questionable increase
2	46-60	36-50	Entire expiration with stethoscope	Increase apparent
3	>60	>50	During inspiration and expiration without stethoscope	Maximum activity

Score 1-3: Mild, 4-6: Moderate, >6: Severe. If wheezing absent (due to minimal flow or silent chest), score = 3

Association between 'Escalation of Treatment' and 'Pulmonary Score Category' (Table – 2)

Pulmonary Score Category	Escalation of Treatment			Chi-Squared Test	
	Positive	Negative	Total	$\chi 2$	P Value
Mild	0 (0.0%)	13 (17.6%)	13 (12.5%)	46.328	<0.001
Moderate	11 (36.7%)	58 (78.4%)	69 (66.3%)		
Severe	19 (63.3%)	3 (4.1%)	22 (21.2%)		
Total	30 (100.0%)	74 (100.0%)	104 (100.0%)		

Summary of Management (Table 3)

Management	Mean ± SD || Median (IQR) || Min-Max OR N (%)
IV Corticosteroid (Yes)	30 (100.0%)
IV Corticosteroid Duration (Hours)	48.00 ± 0.00 || 48.00 (48.00-48.00) || 48.00 - 48.00
IV Magnesium Sulphate (Yes)	19 (63.3%)
IV Magnesium Sulphate Doses	
1 Dose	10 (52.6%)
≥2 Doses	9 (47.4%)
IV Aminophylline (Yes)	7 (23.3%)
IV Aminophylline Duration	
0-6 Hours	5 (71.4%)
>6 Hours	2 (28.6%)
Subcutaneous Adrenaline	
Received	10 (33.3%)
Not Received	20 (66.7%)
IV. Ketamine (Positive)	1 (3.3%)
Non Invasive Mechanical Ventilation (Positive)	3 (10.0%)
Invasive Mechanical Ventilation (Positive)	1 (3.3%)
Place of Admission	
Not Admitted	64 (61.5%)
Admitted	40 (38.5%)
Place of Admission Category	
Not Admitted	64 (61.5%)
PICU	28 (26.9%)
Pediatric HDU	12 (11.5%)
Pulmonary Score	4.62 ± 2.05 || 4.00 (3.00-6.00) || 2.00 - 11.00
Pulmonary Score Category	
Mild	13 (12.5%)
Moderate	69 (66.3%)
Severe	22 (21.2%)
Respiratory Support (Yes)	83 (79.8%)
Respiratory Support Category	
None	21 (20.2%)
Face Mask	56 (53.8%)
Nasal Prongs	15 (14.4%)
Non-Rebreather Mask	12 (11.5%)
Type of Nebulisation Received	
Salbutamol	53 (51.0%)
Salbutamol + Budesonide	15 (14.4%)
Salbutamol + Ipratropium	8 (7.7%)
Salbutamol + Budesonide + Ipratropium	28 (26.9%)

Comparison of risk factors between Escalated and Non-escalated group (Table 4)

Variable	Parameter	Total	Escalation of Treatment		Difference (95% CI)	Significance
			Positive	Negative		
URI	Yes	27 (25.96%)	7 (23.33%)	20 (27.03%)	-3.69% (-100.00% to 14.51%)	χ^2 = 0.020, p = 0.808[f]
	No	77 (74.04%)	23 (76.67%)	54 (72.97%)	3.69% (-100.00% to 21.90%)	χ^2 = 0.020, p = 0.808[f]
Seasonal Variation	Yes	30 (28.85%)	11 (36.67%)	19 (25.68%)	10.99% (-100.00% to 30.90%)	χ^2 = 0.778, p = 0.340[f]
	No	74 (71.15%)	19 (63.33%)	55 (74.32%)	-10.99% (-100.00% to 8.92%)	χ^2 = 0.778, p = 0.340[f]
Food Allergy	Positive	2 (1.92%)	0 (0.00%)	2 (2.70%)	-2.70% (-100.00% to 0.99%)	χ^2 = 0.015, p = 1.000[f]
	Negative	102 (98.08%)	30 (100.00%)	72 (97.30%)	2.70% (-100.00% to 6.40%)	χ^2 = 0.015, p = 1.000[f]
Pyschological Stress	Positive	1 (0.96%)	1 (3.33%)	0 (0.00%)	3.33% (-100.00% to 9.76%)	χ^2 = 0.220, p = 0.288[f]
	Negative	103 (99.04%)	29 (96.67%)	74 (100.00%)	-3.33% (-100.00% to 3.09%)	χ^2 = 0.220, p = 0.288[f]
Overuse of SABA (>200 Puff/Year)	Positive	11 (10.58%)	4 (13.33%)	7 (9.46%)	3.87% (-100.00% to 17.75%)	χ^2 = 0.053, p = 0.726[f]
	Negative	93 (89.42%)	26 (86.67%)	67 (90.54%)	-3.87% (-100.00% to 10.00%)	χ^2 = 0.053, p = 0.726[f]
Obesity/ OSA	Positive	0 (0.00%)	0 (0.00%)	0 (0.00%)	0.00% (-100.00% to 0.00%)	χ^2 = NaN, p = 1.000[f]
	Negative	104 (100.00%)	30 (100.00%)	74 (100.00%)	0.00% (-100.00% to 0.00%)	χ^2 = NaN, p = 1.000[f]
Residence	Urban	59 (56.73%)	16 (53.33%)	43 (58.11%)	-4.77% (-100.00% to 16.32%)	χ^2 = 0.051, p = 0.669[f]
	Rural	45 (43.27%)	14 (46.67%)	31 (41.89%)	4.77% (-100.00% to 25.87%)	χ^2 = 0.051, p = 0.669[f]
Previous History of Mechanical Ventilation	Positive	1 (0.96%)	0 (0.00%)	1 (1.35%)	-1.35% (-100.00% to 1.28%)	χ^2 = 0.000, p = 1.000[f]
	Negative	103 (99.04%)	30 (100.00%)	73 (98.65%)	1.35% (-100.00% to 3.98%)	χ^2 = 0.000, p = 1.000[f]
Saturation at Room Air (%)	Mean ± SD	94.76 ± 5.01	91.07 ± 6.73	96.26 ± 3.09	-5.19 (-7.79 to -2.59)	W = 395.000, p = <0.001[m]
	Median (IQR)	96.00 (92.00 - 94.00)	92.00 (90.00 - 94.00)	97.00 (94.25 - 98.00)		
Saturation at Room Air	≤90 %	18 (17.31%)	14 (46.67%)	4 (5.41%)	41.26% (-100.00% to 59.84%)	χ^2 = 22.591, p = <0.001[f]

	91-94 %	25 (24.04%)	10 (33.33%)	15 (20.27%)	13.06% (-100.00% to 32.26%)	χ^2 = 1.344, p = 0.206[f]
	≥95 %	61 (58.65%)	6 (20.00%)	55 (74.32%)	-54.32% (-100.00% to -36.89%)	χ^2 = 23.784, p = <0.001[f]
Air Pollution	Positive	13 (12.50%)	4 (13.33%)	9 (12.16%)	1.17% (-100.00% to 15.43%)	χ^2 = 0.000, p = 1.000[f]
	Negative	91 (87.50%)	26 (86.67%)	65 (87.84%)	-1.17% (-100.00% to 13.09%)	χ^2 = 0.000, p = 1.000[f]
Poor Adherence to Medication	Positive	31 (29.81%)	9 (30.00%)	22 (29.73%)	0.27% (-100.00% to 19.70%)	χ^2 = 0.000, p = 1.000[f]
	Negative	73 (70.19%)	21 (70.00%)	52 (70.27%)	-0.27% (-100.00% to 19.16%)	χ^2 = 0.000, p = 1.000[f]
Smoking Exposure	Positive	7 (6.73%)	1 (3.33%)	6 (8.11%)	-4.77% (-100.00% to 4.17%)	χ^2 = 0.201, p = 0.670[f]
	Negative	97 (93.27%)	29 (96.67%)	68 (91.89%)	4.77% (-100.00% to 13.72%)	χ^2 = 0.201, p = 0.670[f]
Pet Exposure	Positive	2 (1.92%)	2 (6.67%)	0 (0.00%)	6.67% (-100.00% to 15.59%)	χ^2 = 2.116, p = 0.081[f]
	Negative	102 (98.08%)	28 (93.33%)	74 (100.00%)	-6.67% (-100.00% to 2.26%)	χ^2 = 2.116, p = 0.081[f]
Dust Allergy	Positive	27 (25.96%)	5 (16.67%)	22 (29.73%)	-13.06% (-100.00% to 3.86%)	χ^2 = 1.276, p = 0.220[f]
	Negative	77 (74.04%)	25 (83.33%)	52 (70.27%)	13.06% (-100.00% to 29.98%)	χ^2 = 1.276, p = 0.220[f]
History of Atopy	Positive	13 (12.50%)	6 (20.00%)	7 (9.46%)	10.54% (-100.00% to 26.33%)	χ^2 = 1.312, p = 0.190[f]
	Negative	91 (87.50%)	24 (80.00%)	67 (90.54%)	-10.54% (-100.00% to 5.25%)	χ^2 = 1.312, p = 0.190[f]
Family History of Asthma	Positive	20 (19.23%)	8 (26.67%)	12 (16.22%)	10.45% (-100.00% to 28.37%)	χ^2 = 0.903, p = 0.273[f]
	Negative	84 (80.77%)	22 (73.33%)	62 (83.78%)	-10.45% (-100.00% to 7.46%)	χ^2 = 0.903, p = 0.273[f]

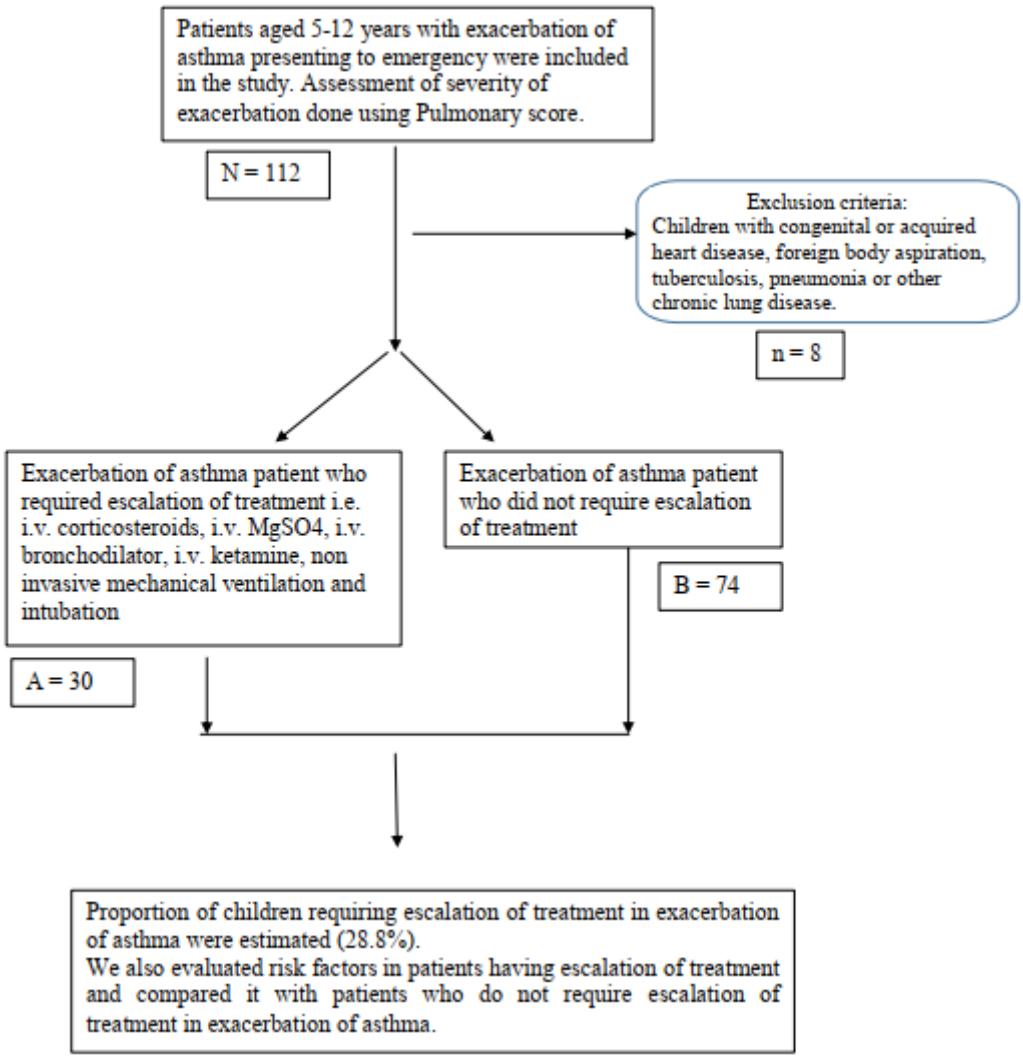

Figure 1: Flow Chart of Study

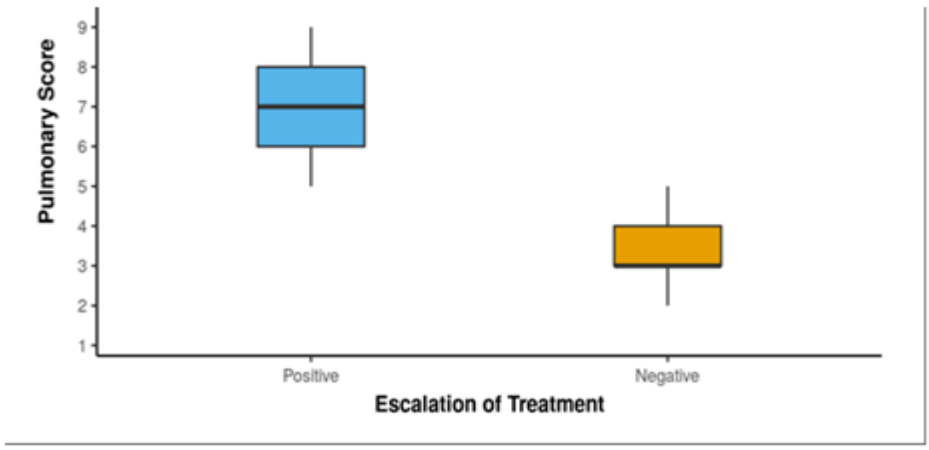

Figure 2: Association Between Escalation of Treatment and Pulmonary Score

DISCUSSION

The study involved 104 children, out of which 54.8% were males and 45.2% females. In total, 38.5% required admission, with 28 patients admitted to the PICU and 12 to the HDU. This reflects a substantial proportion of severe exacerbations that required intensive care, demonstrating the burden of severe asthma in pediatric emergency settings. Kazi U. et al. reported PICU admission rates closer to our findings, with 25% of severe asthma cases requiring intensive care management [13].

In our study, 28.8% of patients underwent treatment escalation during asthma exacerbations. Percentage of escalation of treatment in acute exacerbation of asthma is variable, in study by Craig S et al 7.3% children with acute severe asthma received some form of escalated treatment [9], while in another study by Mittal V et al, 7.5% children received escalation of treatment [14]. Both of these studies considered the use of intravenous magnesium sulphate as an escalation of treatment, but the use of intravenous hydrocortisone as an escalation therapy was not clearly defined. In contrast, our study considered patients receiving intravenous hydrocortisone as having undergone treatment escalation, which could account for the higher proportion of escalated cases observed in our study. Escalation rates in our study are comparable with Mitra et al. who reported an escalation rate of 21% [15] while Shefrin et al. reported an escalation rate of 22.6% [16]. Both these studies included younger patients (2-16 years), potentially affecting their severity and the associated treatment response compared to our study which focused on slightly older children (5-12 years). Younger patients may present with a different severity profile and treatment needs. While in study by Mitchell EA et al, 56.6% of children received escalation of treatment in asthma exacerbations [17]. Intravenous magnesium was administered to 18% of our patients, which aligns with the findings of Johnson et al., who reported its use in 10.5% of patients [18]. In contrast, the study by Morris et al. found that intravenous magnesium was utilized in 61% of patients [19]. The differences in utilization rates could stem from the severity of cases or institutional protocols. Notably, Schuh et al. reported that hospitalization rates were significantly higher for those receiving IV magnesium (88.4% hospitalized), underscoring the drug's role in managing severe exacerbations. Our findings also echoed this, reinforcing the importance of timely interventions, particularly in high-risk patients.

Various risk factors were compared among both escalated and non-escalated group of patients in children presenting with an asthma exacerbation. Room air oxygen saturation below 95% was identified as a critical risk factor for treatment escalation (RR, 8.6, CI 95%, $p < 0.001$), confirming findings from Kazi et al. [13] and Mittal et al., who also emphasized hypoxia as a significant determinant for more aggressive treatment [14].

Poor adherence to treatment was most common risk factor of asthma exacerbation present in 31(30%) patients but did not show statistical significance on comparison between escalated and non-escalated group (RR, 1.01, CI 95% $\chi 2 = 0.001$, $p = 0.978$). This differs from Kumar AP et al., where non-adherence was a significant risk factor ($p < 0.001$), highlighting potential differences in study populations or adherence measurement [20]. Seasonal variation was second most common 30 (28.8%) risk factors among asthma exacerbation but did not show statistical significance on comparison between escalated and non-escalated groups. Seasonal variation may not have shown significance due to a small sample size, broad categorizatio2n of seasonal factors, or geographic differences that might lessen the seasonal impact. Additionally, other dominant risk factors, like poor adherence, could have overshadowed the role of seasonal changes in treatment escalation. Upper respiratory infections (URIs) were identified in 26% of the study population, though they were not a significant predictor of treatment escalation (RR, 0.75, CI 95%, $\chi 2 = 0.152$, $p = 0.697$). This contrasts with Shankar et al., who reported a much higher prevalence of URIs (76%) in asthma exacerbations [21], though they did not analyze the association with treatment escalation. The lower incidence of URIs in this study might reflect seasonal or geographic variations in viral infections.

Asthma exacerbations peaked in the month of July with 25 cases (24%), followed by 19 cases (18.3%) in April, 17 cases (16.3%) in May, and 12 cases (11.5%) in June. The seasonal variation observed aligns with previous literature, where asthma exacerbations often rise in certain months due to environmental triggers, allergens, and respiratory infections. Our study demonstrated a significant difference in the duration of hospital stay between patients requiring treatment escalation and those who did not ($\chi^2 = 72.665$, $p < 0.001$). Among the patients who required treatment escalation, 60% stayed in the hospital for 3-5 days, whereas 86.5% of the non-escalated group had a significantly shorter median stay of less than 1 day. These results are consistent with the findings of Craig S et al., who also observed longer hospital stays in children receiving escalated care [9]. In their study, children who underwent treatment escalation had a median length of stay of 44.2 hours (IQR 27.3–63.2 hours), compared to 6.7 hours (IQR 3.5–16.3 hours) for those without escalation ($p < 0.001$). The longer hospital stay in our cohort, particularly for escalated cases, may be attributed to the greater severity of asthma exacerbations observed in our study population, necessitating more intensive treatment and extended monitoring.
The distribution of pulmonary scores in the present study revealed that most patients had moderate severity (66.3%), with 21.2% experiencing severe exacerbations. This is comparable to Craig S. et al., who also noted a significant burden of moderate-to-severe asthma cases in their cohort [9]. However, despite a similar distribution of severity, Craig et al. reported lower rates of treatment escalation. In the present study, a statistically significant difference was observed between the escalated and non-escalated groups regarding the distribution of pulmonary score categories ($\chi 2 = 46.328$, $p < 0.001$). Among those who required treatment escalation, 63.3% had severe pulmonary scores, while 36.7% had moderate scores. In contrast, among patients who did not undergo escalation, only 4.1% had severe scores, and the majority (78.4%) had moderate scores. Additionally, 17.6% of the non-escalated group had mild scores, reflecting the correlation between higher pulmonary scores and the need for more aggressive treatment.

Craig S. et al. found that salbutamol and ipratropium were commonly used in combination, especially in severe cases. In our study higher use of all three (salbutamol-budesonide-ipratropium) combinations (26.9%) reflects a more aggressive

approach to multi-drug nebulization. Kostakou E. et al. also noted frequent use of combination nebulisations in severe asthma, similar to our findings [11].

The utilization of intravenous corticosteroids was universal in our cohort, with all participants receiving them for a mean duration of 48 hours. This mirrors practices seen in the study by Kostakou et al., which demonstrated that corticosteroid administration is crucial in controlling inflammation during exacerbations [11]. Notably, our findings regarding the duration of corticosteroid treatment highlight a standardized approach in acute care settings. Our study demonstrated that 23.3% of escalated patients received intravenous aminophylline, reflecting reliance on this medication in refractory cases, as reported by Shankar et al. (10-15%) and Schuh et al. found that aminophylline was utilized in less than 20% of children experiencing severe exacerbations, often in conjunction with magnesium sulphate [22]. However, it should be noted that in our study, aminophylline was administered in only 6.7% of all asthma exacerbations, indicating a more selective use of this therapy. The use of IV corticosteroids, $MgSO_4$, and non-invasive mechanical ventilation in our study correlates with findings from studies like Mittal et al., which highlight the need of these therapies in severe cases of Asthma [14].

The strength of this study was being prospective in nature and sample size was adequate for primary outcome i.e. to estimate proportion of escalation of treatment in children aged 5-12 years with an exacerbation of asthma while limitations was single site study.

CONCLUSION

Children presenting with an asthma exacerbation may require treatment escalation, as observed in 29% of patients in our study. Early identification of these patients is crucial to prevent the deterioration of their condition. One way to identify such patients is by identifying risk factors that are more prevalent in escalated patients compared to non-escalated ones. A room air oxygen saturation of less than 90% was found to be statistically significant when comparing escalated and non-escalated patients. Overall, our study contributes to the understanding of how treatment escalation decisions are made in pediatric asthma care and reinforces the importance of timely, aggressive interventions for children at risk of severe exacerbations. By integrating international best practices and adding valuable data from our region, our research supports the development of more standardized, evidence-based guidelines for managing asthma in children.

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