

## Original Research Article

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# Peak expiratory flow rate monitoring can predict asthma exacerbation better as compared to monitoring by symptoms, prospective cohort study

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## ABSTRACT

**Background:** Global initiative for asthma (GINA) guidelines suggest to use peak expiratory flow rate (PEFR) monitoring to assess response to treatment, to identify triggers for exacerbation and to have a baseline value for action plan (especially for the poor perceivers). In comparison to adults, there are less evidence in support of the routine use of PEFR recording for the diagnosis and monitoring level of control of asthma in children. This study was conducted with objective to assess the effect of PEFR monitoring on numbers of exacerbations in comparison to monitoring by symptoms in asthma.

**Methods:** This was a prospective cohort study done for a in department of pediatrics and respiratory medicine, of a tertiary care hospital, North India. Prior to recruitment ethical approval and informed consent/assent was taken. Study subjects were children with partial and uncontrolled asthma aged 5-12 years of age. Patients were divided into two groups on their first visit by using random allocation number. In group "A" monitoring was done with symptoms only, while in group "B" monitoring was done by symptoms and PEFR. Number of exacerbations during study period was noted. At baseline and follow up, CACT score was calculated. Spirometry was done at the end of 3 months.

**Results:** Group B had statistically significant lesser exacerbation during study period as compared to group A (OR=0.23; 95% CI=0.06-0.81; p=0.020).

**Conclusions:** PEFR based monitoring can be used as a potential tool for aborting or decreasing the severity of episodes of exacerbations of asthma especially in resource limited areas.

**Keywords:** Asthma, Exacerbation, Peak expiratory flow

## INTRODUCTION

Global initiative for asthma (GINA) guidelines suggest to use PEFR monitoring to assess response to treatment, to identify triggers for worsening symptoms and to have a baseline value for action plan (especially for the poor perceivers).<sup>1</sup> The PEFR is expressed in litres/min and indicated the highest flow rare achieved when the child blows with maximum effort. PEFR is the maximum expiratory flow rate after a full inspiration and it correlate with forced expiratory volume in 1 second (FEV1).<sup>2</sup> In a child who is on regular inhaled corticosteroid controller

(ICS), personal best PEF is reached within 2 weeks. In 3 months, average PEF is increased and diurnal PEF variability is decreased.<sup>3,4</sup> Persistent excessive variability of PEFR point towards sub-optimal asthma control and increased risk of exacerbation.

PEFR measurement is easy to perform, less time consuming, and low cost. A recent study in adults has demonstrated that low PEFR variability could be a useful indicator of good asthma control.<sup>5</sup> Unfortunately, the bulk of the available evidence pertains to the adult population, with limited data in children. In Contrary to adults,

evidence is lacking in children to support the routine use of PEFR recording in diagnosis and monitoring of asthma in children. Therefore, most of protocols in children are either directly extrapolated from adults, or sometimes based on personal experience of individual pediatricians.

Factors accounting for exacerbation include inaccurate assessment of asthma severity and low perception of dyspnea.<sup>6</sup> Often asthma exacerbations happen without warning, and many children with asthma are not able to perceive it at the earliest. The identification of children at risk of exacerbation may help in early diagnosis and intervention. The PEFR is a valuable tool for assessing asthma status, even in patients with low perception of respiratory symptoms. If PEFR decreases by >20% of the personal best, then it is likely to be an onset of exacerbation.<sup>1</sup> Personal best PEFR is obtained by recording PEFR twice a day during a period of 2-3 weeks when asthma is "controlled". The highest PEFR value was the 'personal best'. PEFR is a tool which can predict exacerbation early at home and aids in its early management to prevent severity.<sup>7</sup> Utility of PEFR to monitor the disease and decrease the rate of severe exacerbations in both children and adults has been acknowledged during COVID-19 pandemic lockdown.<sup>8</sup>

This study was conducted with objective to assess the effect of PEFR monitoring on numbers of exacerbations in comparison to monitoring by symptoms in asthma.

## METHODS

This was a prospective cohort study done for a year (April 2019-March 2020) in department of pediatrics and respiratory medicine, of a tertiary care hospital, North India. Prior to recruitment ethical approval (Ref. code 97<sup>th</sup> ECM II B-P126) and informed consent/assent was taken. Study subjects were children with partial and uncontrolled asthma aged 5-12 years of age. Bronchial asthma for the present study was defined as presence of one or more of the following: (a) current presence of wheeze in any child with a history of more than three episode of documented wheeze or use of bronchodilator in the preceding 12 months, or (b) relief with bronchodilators with or without short course oral steroid or on any regular medication for asthma, or (c) currently hospitalized and diagnosed as case of bronchial asthma.<sup>9</sup> Children having other respiratory disease-causing recurrent breathing difficulty (bronchiectasis foreign body aspiration, bronchopulmonary dysplasia, cystic fibrosis, congenital heart disease) and who were not able to do/ willing to do PEFR monitoring at home excluded.

Standardized questionnaire form was developed to collect data. At the time of recruitment all the children were assessed for level of control of asthma. Level of control of asthma was assessed as per GINA guideline.<sup>1</sup> At the time of recruitment all the children were assessed for level of control of asthma. Asthma was considered to be controlled when daytime symptoms are twice a week or

less, no limitations of activities, no nocturnal symptoms or awakenings and need for reliever/rescue treatment twice a week or less. Asthma was considered to be partly controlled if any of these measures were present in any week: daytime symptoms more than twice a week, any limitations of activities, any nocturnal symptoms or awakenings and need for reliever/rescue treatment more than twice a week. Asthma was considered to be uncontrolled if three or more features of partly controlled asthma was present in any week.

Patients were divided into two groups on their first visit by using random allocation number. On the first visit, patients and parents were trained for correct technique of using inhaler. On the same day baseline spirometry was performed. Spirometry measurement was done using spirometer (Cosmed pulmonary function equipment) in respiratory medicine department following the standard guidelines including COVID-19 precautions.<sup>10</sup> Reduced FEV1/FVC ratio (<0.90), FEV1 <80% predicted, and increase in FEV1 by 12% was taken as criteria of obstructive airway disease.

In group "A" monitoring was done with symptoms only, while in group "B" monitoring was done by symptoms and PEFR. The age and gender matched subjects in both groups were recruited. Group B subjects and their parents were trained in the skill of measuring PEFR. Patients were educated on how to use the PEFR meter by a trained researcher and a technician expert in doing lung function assessment. They were trained about monitoring and maintenance of PEFR diary. After explaining the procedure to child and parents, they were demonstrated technique of using peak flow meter (Breathometer). Afterwards they were asked to repeat the same. The procedure explained to them was: fix the mouth piece to peak flow meter, move the "indicator" to '0' (zero) or at the base level, take a deep breath, followed by placing the peak flow meter in the mouth with tight lips seal around it, blow as "Hard and fast" as possible, check the position of indicator against the number written on peak flow meter; for e.g. 150, repeat above steps 2 more times, finally, note down the highest of the three values obtained in the PEFR diary, morning and evening at a fixed time before receiving their daily dose of controller in the morning and evening.<sup>10</sup> At follow up visit, the peak flow diary was reviewed to determine patient's "personal best" PEFR value. Personal best PEFR was the highest PEFR value achieved when over a period of 2-3 weeks when asthma was controlled. The skill of measuring PEFR and maintenance of PEFR diary was rechecked and reemphasized at every follow up. Group A patients were assessed at follow up visit for symptoms-based monitoring. Number of exacerbations during study period of 1 year in all were noted. For group A, asthma exacerbation was defined as the rapid worsening of symptoms including cough, breathing difficulty, chest pain and/or audible wheeze particularly in the setting of an upper respiratory infection or exposure to a known asthma trigger for the child. For group B asthma

exacerbation was defined as rapid worsening of symptoms and/or reduction in PEFR of less than 80% of personal best. Parents of both groups were instructed to administer inhaled short-acting beta agonist via metered dose inhaler with spacer in case of exacerbation.

First follow up visit was done in 7-10 days, especially to check patients and parents' compliance with inhaler therapy in both groups. In group B this follow up visit was utilized to check PEFR monitoring technique too. All the children were followed in outdoor and by telephonic (audio/video) conversation (due to covid pandemic) monthly. At baseline and follow up, childhood asthma control test (CACT) score was calculated. Spirometry was done at the end of 3 months.

Prior to uses of CACT, permission was taken from author. CACT score was calculated on the basis of seven questions, which denotes the previous 4 weeks status of asthma of child. First part was filled in by the child himself/herself and consisted of four questions, based on perception of asthma control, limitation of activities, coughing and awakenings at night. The 2<sup>nd</sup> part was filled by the parent or caregiver and it consisted of three questions (daytime complaints, day time wheezing and awakenings at night) and have six response options. The child give response to survey question by using a response scale of 0-3 points ranging from sad face to smiling face. Caregiver responsible for the child's care assigned a score between 0 and 5 for each question for last 3 question. The sum of all scores yielded the total CACT score, which ranges from 0 (poorest asthma control) to 27 (optimal asthma control). A cut-off point  $\leq 19$  indicates uncontrolled asthma.<sup>11</sup>

Outcome were number of exacerbations during study period and improvement in the level of control of asthma as evident on change in mean score of CACT questionnaire, improvement in PEFR value from personal base line value in category B patients and improvement of spirometry parameters.

#### Statistical analysis

Data was entered in Microsoft excel and was analyzed using statistical software SPSS version 23 (Chicago, IL,

USA). Data was assessed for normalcy of distribution. For continuous variables independent t test, "paired t" test or Mann Whitney u test were applied as required. Chi square test was used to compare the categorical variable. Univariate, binary and multivariate logistic regression analysis was performed. Difference in  $p < 0.05$  was considered as statistically significant.

#### RESULTS

This study was done for a period of one year from April 2019 to March 2020. Total 98 subjects were screened. Out of screened subjects, 70 were enrolled in the study. About 18 subjects were lost to follow up and follow up spirometry could not be done in 10 subjects. Group A (symptom-based monitoring) included 36 subjects while group B (symptom + PEFR based monitoring) included 34 subjects.

Table 1 represent basic, demographic and asthma exacerbation details of recruited subjects. All the variables were equally distributed among the two groups except the occurrence of exacerbation during study period. Group B had lesser exacerbation during study period as compared to group A and it was statistically significant (OR=0.23; 95% CI=0.06-0.81;  $p=0.020$ ).

Table 2 represents the comparison of mean difference and mean percentage change of CACT scores at baseline and follow up visits among recruited subjects in two groups. From baseline to follow up at 3 month and 6 months, percentage of controlled asthma increase progressively in group B as compared to group A and it was statistically significant.

Table 3 represent change in PFT parameters of the recruited subjects at 3<sup>rd</sup> month follow from baseline. As compared to group A, group B had statistically significant improvement in FEV1 (% predicted change), and FEF 25-75% (% predicted change).

Table 4 represent the mean change in PEFR value (actual and percent predicted) for group B from baseline to follow up at end of 3<sup>rd</sup> month and 6<sup>th</sup> month. It depicts that on follow up visit, PEFR parameter improved and it was statistically significant.

**Table 1: Basic, demographic and asthma exacerbation details of recruited subjects.**

Characteristics	Category A, n=36 (%)	Category B, n=34 (%)	P value
<b>Age (in years), mean<math>\pm</math>SD</b>	8.5 $\pm$ 2.31	8.3 $\pm$ 2.02	0.779
<b>Gender-Male</b>	24 (66.7)	18 (52.9)	0.241
<b>Weight (kg), mean<math>\pm</math>SD</b>	24.32 $\pm$ 6.04	25.24 $\pm$ 6.58	0.511
<b>Height (cm), mean<math>\pm</math>SD</b>	123.18 $\pm$ 9.87	123.13 $\pm$ 12.72	0.739
<b>BMI (kg/m<sup>2</sup>), mean<math>\pm</math>SD</b>	15.83 $\pm$ 3.2	16.55 $\pm$ 2.6	0.629
<b>*Socioeconomic status</b>			
Upper	7 (19.4)	7 (20.6)	
Upper middle	28 (77.8)	27 (79.4)	0.618
Lower middle	1 (2.8)	0 (0)	

Continued.

Characteristics	Category A, n=36 (%)	Category B, n=34 (%)	P value
<b>Distance of residence from traffic distance <math>\leq</math> 1 km</b>	5 (13.9)	4 (11.8)	1.000
<b>Separate cooking space</b>	34 (94.4)	33 (97.1)	1.000
<b>Exclusive use of LPG for cooking</b>	28 (79.3)	32 (94.1)	0.156
<b>Second hand cigarette smoke exposure</b>	13 (36.1)	14 (41.1)	0.663
<b>Ever given asthma action plan</b>	0 (0)	0 (0)	NA
<b>Prior use of regular controller medication</b>	6 (16.7)	11 (32.3)	0.126
<b>Allergic rhinitis</b>	20 (55.6)	15 (44.1)	0.338
<b>GERD</b>	2 (5.6)	2 (5.9)	1.000
<b>Family history of atopy</b>	10 (27)	7 (20.5)	0.483
<b>Previous systemic steroid use</b>	14 (38.9)	11 (32.3)	0.568
<b>Previous 1 year exacerbations</b>	12 (33.3)	9 (26.4)	0.535
<b>Exacerbations during study duration</b>	13 (36.1)	4 (11.8)	0.020

\*There were no subjects belonging to upper lower and lower socioeconomic status-Category A (symptom based monitoring)-36 and category B (symptom + PEFR based monitoring)-34.

**Table 2: Comparison of mean difference and mean percentage change of CACT scores at baseline and follow up visits among recruited subjects, (n=70).**

CACT score	Category A, n=36 (%)			Category B, n=34 (%)			P value
	Controlled asthma score $\geq$ 25	Partially controlled score 20-24	Uncontrolled score $\leq$ 19	Controlled asthma score $\geq$ 25	Partially controlled score 20-24	Uncontrolled score $\leq$ 19	
<b>Baseline (B)</b>	0 (0)	23 (63.9)	13 (36.1)	0 (0)	29 (85.3)	5 (14.7)	0.056
<b>3 MFU</b>	7 (19.4)	20 (55.6)	9 (25)	17 (34.3)	14 (41.2)	3 (8.8)	0.017
<b>6 MFU</b>	11 (30.6)	20 (55.6)	5 (13.9)	26 (76.5)	8 (23.5)	0 (0)	<0.001
<b>Mean<math>\pm</math>SD</b>							
B-3 MF	4.94 $\pm$ 2.3			5.8 $\pm$ 3.0			0.185
3-6 MF	3.4 $\pm$ 1.88			4.11 $\pm$ 2.1			0.076
B-6 MF	9.05 $\pm$ 2.6			9.25 $\pm$ 3.11			0.040

**Table 3: Change in PFT parameters of all the recruited patients at 3<sup>rd</sup> month follow from baseline.**

Variables	Category A, n=36 (%)		Category B, n=34 (%)		P value
	Mean difference $\pm$ SD	% mean change	Mean difference $\pm$ SD	% mean change	
<b>Change in FEV1(% predicted change) (Baseline to 1<sup>st</sup> FU)</b>	3.06 $\pm$ 5.33	18.88	7.65 $\pm$ 5.48	35.17	0.033
<b>Change in FEV1/FVC</b>	7.83 $\pm$ 6.45	8.89	8.38 $\pm$ 5.40	9.05	0.702
<b>Change in FEF 25%-75% (% predicted change) (Baseline to 1<sup>st</sup> FU)</b>	8.81 $\pm$ 20.35	19.27	18.94 $\pm$ 18.02	23.41	0.045

PFT was done 2 times (baseline and 1<sup>st</sup> FU-at the end of 3<sup>rd</sup> month). BD=bronchodilator

**Table 4: Mean change in PEFR parameters from baseline to follow up among group B subjects.**

Variables	Category B, n=34		P value
	Mean difference $\pm$ SD	% mean change	
<b>Change in actual PEFR (Baseline to 1<sup>st</sup> FU)</b>	15.59 $\pm$ 9.91	10.67	0.001
<b>Change in actual PEFR (1<sup>st</sup> to 2<sup>nd</sup> FU)</b>	16.18 $\pm$ 10.74	11.08	0.001
<b>Change in actual PEFR (Baseline to 2<sup>nd</sup> FU)</b>	31.76 $\pm$ 17.66	27.14	<0.000
<b>Change in percent predicted PEFR (Baseline to 1<sup>st</sup> FU)</b>	7.03 $\pm$ 3.94	9.97	0.001
<b>Change in percent predicted PEFR (2<sup>nd</sup> to 3<sup>rd</sup> FU)</b>	7.38 $\pm$ 4.10	10.5	0.001
<b>Change in percent predicted PEFR (1<sup>st</sup> to 3<sup>rd</sup> FU)</b>	14.41 $\pm$ 5.57	20.4	<0.000

## DISCUSSION

This study was done to assess the effect of PEFR monitoring on numbers of exacerbations in comparison to monitoring by symptoms in asthma. The idea of study was seeded in pre COVID period, however its utility was consumed during COVID period. In our study we observed that group B subjects who did monitoring for asthma exacerbation by symptoms as well as PEFR had lesser exacerbation as compared to group A and it was statistically significant (OR=0.11; 95%CI=0.01-0.57; p=0.003). Better asthma control of group B was reflected in improved CACT score, PFT and PEFR parameters (Table 2-4).

There are few studies on assessment of utility of PEFR monitoring in asthmatic children. Most of these studies were done in last 10-15 years. They concluded that the measurements obtained by PEFR meters were effort dependent, could be manipulated by children and intrapersonal variability was substantial.<sup>12,13</sup> Though PEFR monitoring is an inexpensive way of monitoring asthma treatment, it cannot be sole primary tool for assessment of asthma control.<sup>13</sup>

One study demonstrated that serial peak flow recordings are more difficult to interpret in children and peak flow diaries are often not completed, not returned or unreliable after the monitoring period. Studies have demonstrated up to 25% of peak flow entries being incorrectly recorded, with mean differences between written and electronic recorded peak flows ranging from 72 to 34 liters per minute per patient.<sup>14</sup>

However, it is evident that patient education, consistent evaluations and feedback to patients may improve adherence to PEF monitoring.<sup>15</sup> An RCT on children with persistent asthma, who were followed for 3 months did not show good correlation between clinical assessment scores and FEV1/PEFR, but spirometry PEFR correlated with FEV1. They concluded that though FEV1 is superior to PEFR, it can be used at home when spirometry is not available.<sup>16</sup> During COVID pandemic, it was documented that PEFR monitoring may continue to be used by patients with asthma who were previously familiar with its measurement and tracking. It highlights that if PEFR monitoring is continuously monitored and reinforced by physician, it can be used to monitor asthma.<sup>17,18</sup> In another study, effect of mepolizumab in patients with severe eosinophilic, on lung function was assessed by documenting improvement in morning peak expiratory flow.<sup>19</sup> A study ascertain the seasonal patterns of asthma exacerbation by recording the percentage change in PEFR from baseline. They concluded that PEFR in children with asthma was lower in autumn than in winter.<sup>20</sup> The PEFR was significantly reduced in April and October than in January. A study in adult has demonstrated that low PEFR variability could be a useful indicator of good asthma control.<sup>21</sup> PEFR monitoring was utilized to assess therapeutic response to ICS in a study in

combination with improvement in asthma control test score.<sup>23</sup> A study demonstrated that PEFR percent predicted strongly correlates with FEV1 percent predicted. They concluded that it may be a suitable measure of lung function impairment and response to treatment during asthma exacerbations. However, both raw and adjusted models suggested that the absolute PEF percent predicted is not equivalent to absolute FEV1 percent predicted and that percent predicted values are not directly interchangeable.<sup>24</sup>

One of the systematic reviews evaluated the effect of written asthma action plan. It concluded that written action plan uses significantly reduced acute care visits per child as compared with control subjects and symptom-based plans worked better than peak flow-based plans, to reduce the risk of a patient requiring an acute care visit. They reported that asthma action plans based on peak flow monitoring, was most useful when a personal best baseline has recently been established using the same device. They concluded that PEFR measurements can be used to predict asthma exacerbation by comparing with personal best values.<sup>22</sup> One of the recent study concluded that pre-dose PEFR, can work as an alternative primary lung function endpoint for trials in adolescent and adult patients with asthma. They demonstrated a strong association between pre-dose FEV1 and pre-dose PEFR.<sup>25</sup>

In a resource limited setting, where pulmonary function test facility is not available everywhere; or if available not able to assess service because of financial issue, shortage of experts to advise and interpret spirometry, and where the asthmatic children have not been given asthma action plan to monitor their symptoms to predict worsening of level of control of asthma and to predict exacerbation, the result of the study reflected that PEFR monitoring may be a potential solution for early detection and management of exacerbation.

GINA guidelines and WHO-PEN guidelines had recommended use of PEFR in asthma diagnosis in low- and middle-income countries. GINA recommends that short term PEF monitoring may be used to assess response to treatment, to identify triggers and to establish a baseline for action plan.<sup>1,22,26,27</sup>

Utility of PEFR to predict respiratory compromise and to increase adherence to controller medications is reported by a study. It showed that feedback on PERF predictions may decrease under-perception of respiratory compromise and increase adherence to controller medications. Children and their families may shift their attention to asthma perception and management as a result of this intervention.<sup>28</sup> Similarly, an adult study concluded that being a rapid, inexpensive method, PEFR monitoring can be utilized to predict and detect hospitalized exacerbation of COPD, leading to early intervention.<sup>29</sup>

The strength of the study is a stringent definition of asthma used to avoid misclassification of other respiratory diseases. Another strength is that we monitored patient's use of PEFR to identify errors and ensured correct and precise use of PEFR measurement. The limitation was that being a single center study, generalizability to the community is limited.

## CONCLUSION

A patient who is poor perceiver of asthma symptoms may benefit from assessment of PEFR rather than relying solely on symptoms to guide therapy, especially in resource limited areas. PEFR based monitoring can be used as a potential tool for aborting the episodes of exacerbations of asthma.

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