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Original Research Article

Study of spirometry parameters in suspected asthmatic children in a tertiary care hospital

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ABSTRACT

Background: Asthma in children is difficult to diagnose due to inability of young children to successfully perform spirometry. However some parameters in the spirometry which are relatively effort independent can be very helpful in confirming the diagnosis of asthma. This study was conducted to find out the most commonly affected spirometry parameter in the suspected cases of childhood asthma.
Methods: Total 56 children were studied between 7 to 18 years who came for outpatient visit or admitted in the paediatric ward and were clinically suspected to be asthmatic based on asthma predictive index. They were subjected to spirometry in our institute. Baseline and post bronchodilator values of spirometry parameters were studied and analysed using standard statistical tests.
Results: Baseline Forced expiratory flow between 25% and 75% of vital capacity ($FEF_{25-75\%}$) was found to be the most commonly affected spirometry parameter in confirming the diagnosis of suspected asthmatics and correlated with the clinical diagnosis of childhood asthma.
Conclusions: $FEF_{25-75\%}$ can aid in confirming the diagnosis of suspected asthmatic children who are otherwise not treated as asthmatics and remain undiagnosed in view of not meeting the established spirometry criteria for asthma due to poor performance and ignorance of looking at this important and effort independent parameter.

Keywords: Asthma, Bronchodilator, $FEF_{25-75\%}$, Spirometry

INTRODUCTION

Asthma is one of the most common chronic diseases of childhood and accounts for one of the top ten causes for disability adjusted life years in mid childhood age 5-14 years.[1] Though most prevalent still it is one of the most difficult disorders to diagnose, one of the major reasons being inability of young children to perform a successful spirometry and hence fail to meet the diagnostic criteria. Clinically asthma is diagnosed by using Asthma Predictive Index (API), based on history and clinical examination of the child.[2] These clinically diagnosed/suspected asthmatic children when subjected to spirometry to confirm the diagnosis, did not exactly meet the criteria and hence reported as restrictive lung disease. However based on the clinical diagnosis the children who continue to receive the treatment for asthma, inhalational corticosteroids and bronchodilators, respond well to the treatment given. Hence on reanalysing the same spirometry reports in a different way we found that looking at the relatively independent part of the forced vital capacity (FVC) curve matches the

clinical diagnosis in maximum children. As Forced expiratory flow between 25% and 75% of vital capacity ($FEF_{25-75\%}$) represents flow over sizeable middle part of the FVC curve it was preferred to study. Hence the present study was done with the objective of finding the most affected spirometry parameter in the suspected asthmatic children.

In children it is difficult to exhale with maximum effort for 3 seconds and hence difficult to get a reliable forced vital capacity. This makes ratio of forced expiratory volume in 1 second to forced vital capacity (FEV_1/FVC), which is an established criterion for diagnosis of asthma, unreliable in diagnosing airway obstruction in children. However, $FEF_{25-75\%}$ which represents the middle part of the FVC curve is relatively effort independent, hence should be more relevant parameter to assess airway obstruction in children. Although there are no recommendations regarding the utility of $FEF_{25-75\%}$ by the American Thoracic Society (ATS) or the National Asthma Education and prevention program (NAEPP) this measurement may have clinical significance in diagnosing childhood asthma. Rao D et al tested the utility of $FEF_{25-75\%}$ in predicting childhood morbidity and severity of asthma in the setting of normal FEV_1 and bronchodilator responsiveness as defined by $FEF_{25-75\%}$ and identified more childhood asthmatics than does bronchodilator response defined by Forced expiratory volume in 1 second (FEV_1).They found that $FEF_{25-75\%}$ is reflective of small airway patency and is reduced in asthmatics with a history of wheezing.[3]

METHODS

This cross sectional study was conducted in a tertiary care hospital with a dedicated pulmonary function test laboratory between June 2017 and October 2018.The study included children both boys and girls between ages of 7 to 18 years who were clinically suspected of asthma based on asthma predictive index, coming to outdoor clinic for follow up or admitted in the pediatric ward of the hospital. All children with grossly enlarged tonsils, adenoids and structural deformity of thoracic cage like kyphosis, scoliosis or that of oral cavity, known case of cardiac disease or those who refused to be a part of study were excluded. Children taking bronchodilators were asked to stop the treatment for specified time before attempting the test (previous 4 hours for short acting and 12 hours for long acting Beta2- agonist). For indoor patients, spirometry was done once the patients became asymptomatic, after initial workup and treatment was given. The child performed baseline and post bronchodilator spirometry on the same day. The protocol was approved by the Institutional Ethics committee. After due counselling, the written informed consent was obtained from the caretaker of the studied subjects.

Spirometry was performed with a rolling seal volume sensing USB PC based spirometer. The manoeuvres were identical for indoor as well as outdoor patients. Standard spirometry instructions were given prior to efforts. Spirometry was performed in the seated upright position with a nose clip. The subject was prompted to "blast", not just "blow" air from their lungs, and then was encouraged to fully exhale making sure no coughing during the first second of exhalation. Throughout the manoeuvre enthusiastic coaching of the subject was done. Multiple manoeuvres i.e. blowing in the spirometer to obtain graphs were obtained from each patient (maximum 8 trials) and the spirometry values based on the acceptability criteria, only were put into the Pulmonary Function Test database to minimize bias.[4] Minimum of three acceptable curves with difference between the largest and next largest FVC <0.150 L were obtained. The largest FVC and the largest FEV_1 was selected. $FEF_{25-75\%}$ was selected from the curve with the largest sum of FEV_1 and FVC. After giving inhaled rapid onset Beta2- agonist (2 puffs of salbutamol, 200 micrograms) by metered dose inhaler and spacer post bronchodilator reading were taken 15 minutes later in the same sitting on the same day. Post bronchodilator reversibility (BDR) was calculated as the percent change from baseline for FEV_1 and $FEF_{25-75\%}$ given by the following equation using FEV_1 as an example:

$$BDR = \frac{(\text{Post-bronchodilator } FEV_1 - \text{Pre-bronchodilator } FEV_1) * 100}{(\text{Pre-bronchodilator } FEV_1)}$$

A 12% improvement in FEV_1 or 25% improvement in $FEF_{25-75\%}$ was considered significant.

The sample size was calculated using following formulae:

$$n = (Z2 \times P (1 - P))/e^2$$

n- Sample size, Z - Z value at 5% error (1.96), P - Taken as 90% (expected true proportion).[3]

e - Allowable error (taken as 10%; power of study - 90%)

It was planned to enroll minimum of 50 cases for the present study. Quantitative data included baseline and post bronchodilator values of FEV_1, FEV_1/FVC% and $FEF_{25-75\%}$. Comparison of Quantitative data was done using Paired t-test, if the data passed 'Shapiro–Wilk Normality test' or by Wilcoxon Signed Rank Test if the data failed 'Shapiro–Wilk test Normality' test. Appropriate statistical software, including but not restricted to MS Excel, PSPP version 1.0.1 was used for statistical analysis. Graphical representation was done in MS Excel package included in Microsoft Office 365. An alpha value (p-value) of <=0.05 was used as the cut-off for statistical significance.

RESULTS

The study population included 56 clinically suspected asthmatic children. Age group (7-9 years) represented majority of cases (35.7%) while no child was found

between 15- 18 years of age. The male female ratio was 1.67:1. Most of the children had wheezing (55.4%) or history of atopy (71.4%), important parameters in asthma predictive index. The demographic parameters of study population are given in Table 1.

Table 1: Demographic parameters of clinically suspected asthmatic children enrolled in the study.

Parameters	Sub parameters	Number	Percentage
Age	7 to 9 years	20	35.7%
	9 to 11 years	14	25.0%
	11 to 13 years	05	8.9%
	13 to 15 years	17	30.4%
Sex	Males	35	62.5%
	Females	21	37.5%
Family history of asthma	Present	26	46.4%
	Absent	30	53.6%
Wheezing at presentation	Yes	31	55.4%
	No	25	44.6%
Skin rash or atopy	Present	40	71.4%
	Absent	16	28.6%

On studying the spirometry parameters we found that 44 of these 56 children showed abnormality in baseline or bronchodilator reversibility of at least one quantitative parameter being studied. We considered them as asthmatics in our study while those children who showed no abnormality in any one of FEV_1, FEV_1/FVC or $FEF_{25-75\%}$ were referred as non-asthmatics. It is evident from Table 2 that the mean baseline FEV_1 was below 80% (77.1%) as seen in asthma. On the contrary mean baseline FEV_1/FVC was 88.12, much higher than the cut off set for the diagnosis of asthma (<80%).

The mean baseline $FEF_{25-75\%}$ was found to be as low as 65.8%. The mean of Peak expiratory flow rate (PEFR), the parameter mainly useful to assess the control of asthma rather than diagnosis was found to be 82.8%. The difference between pre and post bronchodilator value for all the parameters was found to be significant by Wilcoxon- signed rank Test (Table 2).

Among asthmatics 43 children (97.7%) had low baseline $FEF_{25-75\%}$ (<75%) while 28 children (63.6%) had low baseline FEV_1 (<80%) (Figure 1).

Table 2: Baseline and post bronchodilator reversibility of spirometry parameters among study population (n=56).

Parameter	Time	No.	Mean	SD	Median	IQR	t-value	p-value
FEV_1	Baseline	56	77.16	13.94	79.74	25.03	-6.635	1.49E-08
	Post Bronchodilator	56	82.87	11.20	84.37	14.10	Difference is significant	
FVC ^	Baseline	56	78.41	11.49	80.50	17.06	-5.044	4.55E-07
	Post Bronchodilator	56	81.58	10.74	81.94	12.68	Difference is significant	
FEV_1/ FVC% ^	Baseline	56	88.12	9.55	91.90	11.47	-4.466	7.97E-06
	Post Bronchodilator	56	91.16	6.51	92.49	9.55	Difference is significant	
$FEF_{25-75\%}$ ^	Baseline	56	65.81	23.88	65.25	24.89	-6.354	2.09E-10
	Post Bronchodilator	56	85.67	22.58	84.50	24.30	Difference is significant	
PEF ^	Baseline	56	82.83	15.73	82.95	22.21	-4.349	1.37E-05
	Post Bronchodilator	56	88.10	15.66	86.50	16.72	Difference is significant	

*(p-value of 1.49E-08 implies 1.49 x 10-08)

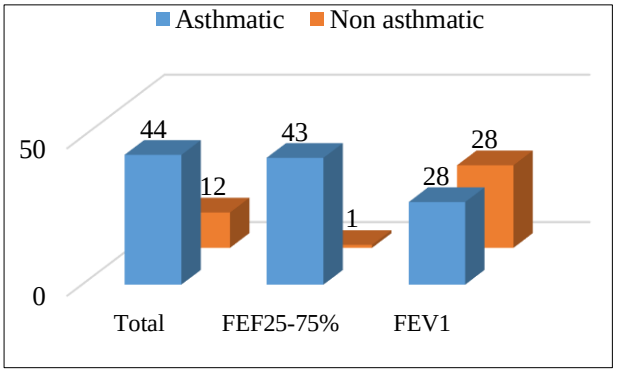

Figure 1: Role of baseline FEV_1 and $FEF_{25-75\%}$ in identifying Asthmatics and Non asthmatics in the study group.

Among the study population of 44 asthmatics and 12 non asthmatics, $FEF_{25-75\%}$ identified 97.7% (n=43) asthmatics while FEV_1 identified 50% (n=28) of asthmatic children.

This highlighted the fact that in the group of 44 asthmatics those 15 children who had normal baseline FEV_1 were diagnosed as asthmatic because of low baseline $FEF_{25-75\%}$. There was significant association between $FEF_{25-75\%}$ and asthma status with p value <0.05 according to Pearson's Chi square test (1.18X10-12) and Fischer exact test (2.33X10-11) (Table 3).

Out of study population, only 9 children had baseline FEV_1/FVC <80%, a parameter considered essential for asthma diagnosis. Sensitivity of FEV_1/FVC in identifying asthmatic among study population was found to be

20.45%. The association between baseline FEV_1/FVC and asthma status was found to be non-significant with p value of 0.087 according to Pearson's Chi-square test). Study of post bronchodilator reversibility of FEV_1 among total study population revealed that 26.8% children showed bronchodilator reversibility of more than 12% (BDR+). None of the child with normal baseline FEV_1 showed >12% bronchodilator reversibility suggesting that significant bronchodilator reversibility of FEV_1 was more common amongst those children who had low baseline FEV_1 (p value being 6.00X10-6 according to Pearson's Chi-square test) (Table 4).

Table 3: Comparison of baseline FEV1 with baseline FEF25-75% among asthmatics.

Baseline FEV_1	Baseline $FEF_{25-75\%}$		Total
	Asthmatics	Non asthmatics	
Asthmatics	27	1	28/44 (63.6%)
Non asthmatics	16	12	28
Total	43/44 (97.7%)	13	56 (100%)

Table 4: Study of bronchodilator reversibility of FEV_1 among normal and low baseline FEV_1 in the study population.

Baseline FEV_1		Bronchodilator Reversibility of FEV_1		Total
		BDR+	BDR-	
Low	No.	15	13	28
	%	53.6%	46.4%	100%
Normal	No.	0	28	28
	%	0.0%	100.0%	100%
Total	No.	15	41	56
	%	26.8%	73.2%	100.0%

*BDR+ implies positive significant bronchodilator reversibility
BDR - implies non significant bronchodilator reversibility.

Table 5: Study of bronchodilator reversibility of $FEF_{25-75\%}$ among normal and low baseline $FEF_{25-75\%}$ in the study population.

Baseline $FEF_{25-75\%}$		Bronchodilator Reversibility(BDR) $FEF_{25-75\%}$		Total
		BDR+	BDR-	
Low	No.	30	13	43
	%	69.8%	30.2%	100.0%
Normal	No.	5	8	13
	%	38.5%	61.5%	100.0%
Total	No.	35	21	56
	%	62.5%	37.5%	100.0%

*BDR+ implies positive significant bronchodilator reversibility
BDR - implies non significant bronchodilator reversibility.

Significant bronchodilator reversibility of >25% (BDR+) in $FEF_{25-75\%}$ was seen in 35 children of which 30 children had low baseline $FEF_{25-75\%}$, showing that bronchodilator reversibility of>25% was seen significantly more common amongst those children who had low baseline $FEF_{25-75\%}$ (p value being 0.041 according to Pearson's Chi-square test)(Table 5).

On comparing the bronchodilator reversibility of FEV_1 and $FEF_{25-75\%}$ it was found that among total 44 asthmatic children 15 had BDR+ for FEV_1 while 20 additional children had BDR+ for $FEF_{25-75\%}$ (Figure 2).

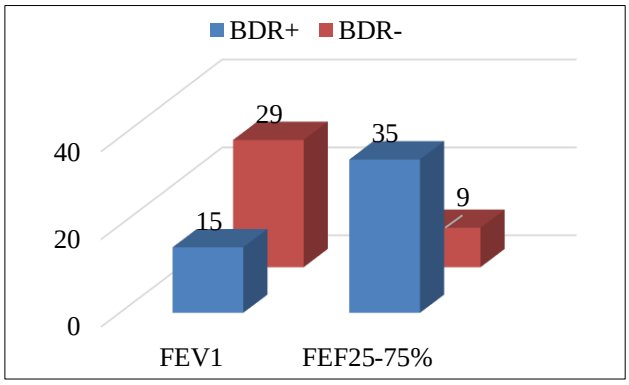

Figure 2: comparison of bronchodilator reversibility of $FEF_{25-75\%}$ and FEV_1 among asthmatics.

In this figure out of total asthmatic children (n=44) only 15 children showed positive bronchodilator reversibility (BDR+) for FEV_1 while $FEF_{25-75\%}$ identified 35 children out of 44 who showed positive bronchodilator reversibility.

DISCUSSION

In this study low Baseline FEV_1 was defined as <80%.[5] FEV_1/FVC ratio of less than 80% was used to define airflow obstruction.[6] However, there are no published guidelines regarding normal values for $FEF_{25-75\%}$. While low $FEF_{25-75\%}$ and poor clinical outcomes have been previously described in asthmatic children, the absolute normal cut-off level for $FEF_{25-75\%}$ has not been firmly established. Previous studies have cut off values ranging from 60-80%.[3,7,8] As there is a lack of consensus of normal range for $FEF_{25-75\%}$we used $FEF_{25-75\%}$ cut-off of <75%, for our subjects based on the findings from other published studies.[9]

FEV_1/FVC was normal in most of the clinically suspected asthmatic children (83.9%) in our study. Use of FEV_1/FVC as the initial screen for adults is necessary because the differential diagnosis includes interstitial lung disease and chronic obstructive pulmonary disease, but these diseases are unlikely to be relevant in children hence it did not match with their asthma status.

Baseline FEV_1 was sensitive enough to identify half of the asthmatic children however failed to detect 15

asthmatic children who were additionally identified by low baseline $FEF_{25-75\%}$. These findings provide evidence that $FEF_{25-75\%}$ in the setting of a normal FEV_1 is useful in identifying asthmatic children. Hence using low baseline $FEF_{25-75\%}$ increases the number of asthmatics identified compared to only using FEV_1 and FEV_1/FVC. Bronchodilator reversibility of FEV_1>12% was used based on published data .[6]However, similar to baseline $FEF_{25-75\%}$ there is a lack of availability of data for BDR to $FEF_{25-75\%}$. We used a change of more than 25% of $FEF_{25-75\%}$ from baseline for our study based on the findings from other published studies.[10] Analysis of post bronchodilator reversibility showed that positive bronchodilator reversibility of $FEF_{25-75\%}$ (30 children) is twice as effective as positive bronchodilator reversibility of FEV_1 (15 children) in identifying asthmatics.

These are important findings from our study which could influence the way in which spirometry is used to diagnose and manage childhood asthma. The presence of normal baseline FEV_1 and FEV_1/FVC values in asthmatic children with low baseline $FEF_{25-75\%}$ is a finding where most clinicians do not suspect the presence of airflow obstruction. Study suggests that low baseline $FEF_{25-75\%}$ is a sensitive marker for airway obstruction. Our study also showed that significant bronchodilator reversibility of $FEF_{25-75\%}$ is twice as effective as significant bronchodilator reversibility of FEV_1. This helped in identifying more asthmatics that would have been described bronchodilator unresponsive otherwise. Baseline FEV_1 though a sensitive parameter yet FEV_1/FVC ratio solely cannot be relied upon for the diagnosis of asthma in children.

CONCLUSION

This study highlights that baseline $FEF_{25-75\%}$ is the most common parameter affected in the spirometry of clinically suspected asthmatic children as it does not involve the effort which children most often are unable to deliver and hence remain undiagnosed. Hence inclusion of $FEF_{25-75\%}$ and its bronchodilator reversibility can potentially identify many clinically suspected asthmatic children who are often missed by the usual effort dependent parameters of FEV_1 and FEV_1/FVC.

With the accessibility of better equipment and incentives, with adequate training, most children above 7 years of age can perform acceptable spirometry. Based on this study it is recommended to look for baseline $FEF_{25-75\%}$ and its reversibility to bronchodilator, as it is the parameter which is often overlooked and can aid in diagnosis and better management of clinically suspected asthmatic children.

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