



## FEV1 (FORCE EXPIRATORY VOLUME)/FEV6 AND FEV6 AS AN ALTERNATIVE FOR FEV1/FVC (FORCED VITAL CAPACITY) AND FVC IN THE DETECTION OF OBSTRUCTIVE AIRWAY DISEASE.

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**ABSTRACT... Objectives:** To evaluate the use of FEV<sub>6</sub> and FEV<sub>1</sub>/FEV<sub>6</sub> as an alternative of FVC and FEV<sub>1</sub>/FVC in determining airways restriction and obstruction. **Study Design:** Cross sectional Study. **Setting:** Department of pulmonology, DHQ Hospital Faisalabad. **Period:** 6 months (January-June, 2017). **Material & Methods:** Sample size of 250 patients, with 45-80 years of age who can exhale for 6 seconds were included in the study. Reference equations were used to detect lower normal limits (LNL) of FEV<sub>6</sub>, FVC, FEV<sub>1</sub>/FEV<sub>6</sub> and FEV<sub>1</sub>/FVC. A person was said to have obstruction if FEV<sub>1</sub>/FVC was below LNL. We considered a person to have restriction if FVC was below LNL without any obstructive pattern. FEV<sub>1</sub>/FEV<sub>6</sub> and FEV<sub>6</sub> sensitivity and specificity were determined from this data. **Results:** Sensitivity of FEV<sub>1</sub>/FEV<sub>6</sub> was 97.4% while specificity was 85.2%, in case of airway obstruction positive predictive value was 96.5% and negative predictive value was 88.5%. In case of restrictive pattern detected by spirometry a sensitivity of FEV<sub>6</sub> was 96.5 % and 85.71 % was specificity 97.6% was PPVs and 80% was NPVs .Values were close to LNL in case when difference was noted between two indexes. **Conclusion:** Instead of FEV<sub>1</sub>/FVC, FEV<sub>1</sub>/FEV<sub>6</sub> can be used for diagnosing airway obstruction, particularly for screening population having high risk for COPD. For determining restrictive pattern by spirometry FEV<sub>6</sub> can also be used instead of FVC by providing less confusing and easier results.

**Key words:** Asthma, COPD, Disease, FVC, FEV1, FEV6, Forced Expiratory Volume, Obstructive Restriction, PFT, Spirometry.

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## INTRODUCTION

Spirometry is frequently used to detect pulmonary functions. It measures the volume of air exhaled after full inhalation as a function of time. To detect airway obstruction and restriction spirometry is very helpful.<sup>1</sup>

Spirometric results are dependent on patient efforts and technician. In some patients it's very difficult to completely empty the lungs in order to achieve the FVC. Spirometry is used to screen COPD in high risk patient's i.e having age greater than 40 with smoking history and person having COPD symptoms. Now a days it is studied that FEV<sub>6</sub> can replace FVC.<sup>1</sup>

In countries like Pakistan, as technical staff is short in number and are not well trained, especially

in the primary healthcare setups, FVC could be difficult and costly, on the other hand FEV<sub>6</sub> is cheap, and equally effective measurement. Question still remains regarding its efficacy, as universal reference equations are not available.<sup>2</sup>

Reference values to be used have become now available from the third national health and nutrition examination survey (NHANES III) including LNL of FEV<sub>6</sub> and FEV<sub>1</sub>/FEV<sub>6</sub> ratio and also for forced expiratory flow between 25% and 75% of maximum observed volume in first six seconds of FVC maneuver((FEF 25-75%6).<sup>3,4</sup>

FEV<sub>1</sub>/FEV<sub>6</sub> ration is almost equal to FEV<sub>1</sub>/FVC ratio shown by data from this study. Swamney and coworkers study showed that FEV<sub>6</sub> is comparable with FVC in determining airway

restriction and obstruction.<sup>5</sup> The FEV<sub>1</sub>/FEV<sub>6</sub> ratio can be used as a valid alternative for FEV<sub>1</sub>/FVC in the diagnosis of airway obstruction in adults when the realization of the Broncho dilatation test is limited in screening study in primary care.<sup>6</sup>

We know that the spirometry is recommended for the diagnosis and management of chronic obstructive pulmonary disease (COPD). The specialists of respiratory medicine such as the American Thoracic and European Respiratory Societies (ATS/ERS) have published guidelines on standards of spirometry.

### MATERIAL AND METHODS

All the patients who were having respiratory complaints like dyspnea (shortness of breath), cough or expectorations presenting in the pulmonology department DHQ Hospital Faisalabad were included in the study and pulmonary function tests were performed. Adults with age ranges from 45 to 80 years were included. Data was collected during January 2017 to June 2017. Any patient who cannot exhale for 6 seconds, history of chest injuries; clinically relevant alterations of the physical examination of the heart and chest wall; major ECG abnormalities; pitting ankle edema; and the use of diuretics, cardiac glycosides or  $\beta$ -adrenergic blocking agents were excluded from study.

NHANESIII reference equation was used to determine the low-normal-limits LNL for, FEV<sub>1</sub>, FVC, FEV<sub>1</sub>/FVC, FEV<sub>6</sub> and FEV<sub>1</sub>/FEV<sub>6</sub>.

Forced vital capacity, or FVC, is defined as the volume of air in the lungs that can be exhaled following a deep inhalation. FVC is normal at or above 80% and a value below 80%, shows restrictive lung disease.

Forced expiratory volume-one second (FEV<sub>1</sub>) is the measurement of volume of air that can be exhaled in one second following a deep inhalation.

FEV<sub>1</sub>/ FVC ratio is the percentage of the lung size (FVC) that can be exhaled in one second. It is calculated by dividing FEV<sub>1</sub> with FVC. Its

normal value is more than 70%. Less than 70% is in obstructive lung disease.

FEV<sub>6</sub> is the measurement of volume of air in liters that can be exhaled in six seconds following a deep inhalation.

FEV<sub>1</sub>/FEV<sub>6</sub> ratio is ratio of FEV<sub>1</sub> and FEV<sub>6</sub>; it is calculated by dividing FEV<sub>1</sub> with FEV<sub>6</sub>. We took 72% as the cut off value for this ratio and patient with <72% will be labeled as obstructive lung disease. Depending on severity of obstruction of airways obstructive group was further divided according to European respiratory society definition.

Patients were labeled as having airway obstruction or obstructive lung disease if FEV<sub>1</sub>/FVC ratio was below its LNL, similarly those patients with respiratory complaints and having normal FEV<sub>1</sub>/FVC but FVC below low normal limits was labeled as having restriction or restrictive lung disease.

Spirometry was performed with Mir Spiro lab III (model 2200; Sener Mechis Yorba Lindo CA) by technicians well trained in performing pulmonary function test according to guidelines by European society of respiration. Three recordings were taken after each spirometric measurement and the spirometric measurement with the largest sum of FEV<sub>1</sub> and FVC was taken as final. FEV<sub>6</sub> was also taken from along with it. Spirometry flow/volume loops were conducted in accordance with American Thoracic Society (ATS) recommendations.

Sensitivity is the proportion of true positives out of all those who truly have the obstructive or restrictive lung disease. Specificity is the proportion of true negatives out of all those who truly don't have obstructive or restrictive lung disease. Positive predictive value is the proportion of true positives out of all those who are positive on FEV<sub>1</sub>/FEV<sub>6</sub> (for obstructive disease) or FEV<sub>6</sub> (for restrictive disease). Negative predictive value is the proportion of true negatives out of all those who are negative on FEV<sub>1</sub>/FEV<sub>6</sub> (for obstructive disease) or FEV<sub>6</sub> (for restrictive disease). True positives (TP) are those individuals who are

positive on FEV<sub>1</sub>/FEV<sub>6</sub> (for obstructive disease) or FEV<sub>6</sub> (for restrictive disease) as well as on FEV<sub>1</sub>/FVC (for obstructive disease) or FVC (for restrictive disease). True negatives (TN) are those individuals who are negative on FEV<sub>1</sub>/FEV<sub>6</sub> (for obstructive disease) or FEV<sub>6</sub> (for restrictive disease) as well as on FEV<sub>1</sub>/FVC (for obstructive disease) or FVC (for restrictive disease). False positives (FP) are those individuals who are positive with FEV<sub>1</sub>/FEV<sub>6</sub> (for obstructive disease) or FEV<sub>6</sub> (for restrictive disease) but negative FEV<sub>1</sub>/FVC (for obstructive disease) or FVC (for restrictive disease). False negatives (FN) are those individuals who are negative on FEV<sub>1</sub>/FEV<sub>6</sub> (for obstructive disease) or FEV<sub>6</sub> (for restrictive disease) but positive with FEV<sub>1</sub>/FVC (for obstructive disease) or FVC (for restrictive disease).

We used two by two (2 x 2) tables to calculate sensitivity and specificity for FEV<sub>1</sub>/FEV<sub>6</sub> below its LNL as a predictor for obstruction. Similarly sensitivity and specificity were determined for FEV<sub>6</sub> as predictor for a restrictive spirometric pattern. Positive predictive value and negative predictive value was also calculated. Female, male and total populations result was calculated. Statistical software (SPSS II.0; SPSS; Chicago IL) was used for statistical analysis.

**Following formulas were used**

a (TP)	b(FP)
c(FN)	d(TN)

- Sensitivity= a/a+c\*100
- Specificity= d/b+d\*100
- Positive predictive value= a/a+b\*100
- Negative predictive value=d/c+d\*100

**RESULTS**

In this cross sectional validation study conducted at the DHQ hospital department of chest medicine, data collected from 250 patients regarding spirometry was entered on a Performa and was later using SPSS. Due to exhalation time of less than 6 seconds in 10 patients, data of these 10 cases were excluded from the study. Rests of

the 240 test cases were included in the study. We consider only 1 test per patient. NHANES III reference equation defined LLN on FEV<sub>1</sub>, FVC, and FEV<sub>1</sub>/FVC were used to determine restrictive and obstructive pattern. Depending on severity of obstruction of airways obstructive group was further divided according to European respiratory society definition. Possible normal variant (FEV<sub>1</sub> > 100% predicted). Mild obstruction shown by FEV<sub>1</sub> > 70% to <100 predicted); Moderate obstruction FEV<sub>1</sub> > 50% to < 70% predicted) and severe obstruction by FEV<sub>1</sub> <50% predicted.

Among all the cases included in the study, 144 (60%) were men and 106 (40%) were women.

Gender	Frequency	Percentage
Male	144/240	60%
Female	106/240	40%

**Table-I. Showing the gender distribution in the study population.**

Among all the patients included in our study, more than half were diagnosed to have an obstructive disease 140 out of 240, i.e. the prevalence of obstruction in our study population was 58.33%. Taking FEV<sub>1</sub>/FVC as gold standard in diagnosing obstructing lung disease, 2 x 2 table was used to calculate the sensitivity and specificity. Sensitivity of FEV<sub>1</sub>/FEV<sub>6</sub> came to be 97.4% and specificity of 85.2% along with PPV of 96.5% and a NPV of 88.5%.

When FEV<sub>1</sub>/FVC was normal in subjects FEV<sub>6</sub> was used as alternative for FVC to determine restrictive pattern. Taking FVC as a gold standard for diagnosis of restrictive lung disease, 2 x 2 table was used to calculate sensitivity and specificity of FEV<sub>6</sub>, sensitivity of 96.5% and 85.71% specificity. 97.65% was PPV and 80% was NPV.

**DISCUSSION**

Aim of this study was to check whether FEV<sub>1</sub>/FEV<sub>6</sub> can be used instead of FEV<sub>1</sub>/FVC. Results were quite satisfactory. In addition almost all of the discordant cases were close to the LNL. American thoracic society guidelines shows that LNL are variable so cannot be considered

arbitrary limits that correctly divide patients as abnormal and normal. Subjects with value close of LNL should be calculated with caution. Diurnal, day to day differences in spirometric data can change outcome across LNL.<sup>7</sup>

Comparing with Swanney and coworkers specificity and sensitivity of ours was 85.2% and 97.4% while theirs were 97.4% and 95.8%. PPV was 96.5% as compared to 98.6% in their study and NPV in our study was 88.5% and 91.1% in theirs. Our study showed obstruction in 58.33% and 65.1% in swanney cl al. So it was expected to have low PPV in our study. Our study is applicable to population with airway obstruction prevalence of 58.33% (33.8% females and 43.3% males).

Decreased total lung volume/capacity is used to diagnose restriction. American thoracic society guidelines say that when  $FEV_1/FVC$  is normal and FVC is reduced suggest restrictive but not diagnosed restrictive problem. According to study by aaron and coworkers<sup>8</sup>, it can be seen that <60% of people were actually having restriction when using total lung capacity measurement while there spirometry shows restriction. (58% was PPV of FVC).

But NPV was 95.4% which favors that spirometry is helpful to exclude restriction. Our study show high NPV in when comparing FVC and  $FEV_6$  as a marker of restriction. So  $FEV_6$  can be used to exclude restriction.

Vandevoorde J, et al reported after a study done to know the fixed cut-off values for  $FEV(1) / FEV_6$  and  $FEV_6$  to see whether it can be used as an alternate of  $FEV(1) / FVC$  and FVC while dealing with suspected cases of airway obstruction and restriction, respectively, that in about eleven thousand spirometric studies in adult patients, ROC curves showed the  $FEV(1) / FEV(6) < 73%$  and  $FEV(6) < 82%$  of the predicted value can be taken as alternate to  $FEV(1) / FVC < 70%$  and FVC  $< 80%$  predicted cut off limits in the diagnosis of obstruction and restriction, respectively. With a prevalence of obstruction of 45.9%,  $FEV(1) / FEV(6)$  sensitivity and specificity were 94.4 and 93.3%, respectively; PPV 92.2; NPV 95.2%.

Similarly, with a prevalence of restrictive disease of 14.9%,  $FEV(6)$  sensitivity and specificity were 95.9 and 98.6%, respectively; PPV 92.2 and NPV 99.3%, respectively.<sup>9</sup>

Stupnytska G, et al reported that after analysis of data collected from 250 spirometric tests performed in the patient with COPD, divided into smokers and non-smokers, that all of the parameters of  $FEV_6$  and  $FEV_1/FEV_6$  ratio in these patients were almost similar to FVC and  $FEV_1/FVC$ ; and the sensitivity and specificity of  $FEV_1/FEV_6$  was 92.0% and 90.1%. The positive predictive value and negative predictive value was 88.6% and 92.0%, respectively.

In another study, Vandevoorde J, et al. reported, after analyzing about eleven thousand spirometric cases of white race, of age between 20-80 years with 7,010 males and 4,666 females who were able to exhale unto at least 6 sec, obstructive lung disease can be labeled if  $FEV_1/FVC$  is below LLN and any patient can be labeled as having restrictive lung disease if FVC is below its LLN, in the absence of obstruction. In this study, sensitivity and specificity of  $FEV_1/FEV_6$  and  $FEV_6$  for the spirometric diagnosis of airway obstruction,  $FEV_1/FEV_6$  sensitivity was 94.0% and specificity was 93.1%; the positive predictive value (PPV) and negative predictive value (NPV) were 89.8% and 96.0%, respectively. The prevalence of obstruction in the entire study population was 39.5%, unlike our study. Almost similar to our results were observed in this study regarding diagnosis of restrictive lung disease.  $FEV_6$  sensitivity was 83.2% and specificity was 99.6%; the PPVs and NPVs were 97.4% and 96.9%, respectively. But prevalence of this restriction was 15.7%, unlike our study. Both male and female population had equal results. They concluded that  $FEV_1/FEV_6$  ratio can be used as an alternate for  $FEV_1/FVC$  in the airway obstruction and  $FEV_6$  as an alternate for FVC in the diagnosis of restricted lung disease.  $FEV_6$  is more defined and is easier to achieve.<sup>10</sup>

Spirometry indices are influenced by age, height, sex, and ethnicity.<sup>11</sup> Therefore, discovering the cut-off value of  $FEV_1/FEV_6$  for detecting airway



obstruction in a nationwide, representative population sample in Pakistan is worthwhile.

After review of many studies, the prevalence in smoker population of COPD is 30 to 58% if spirometry is used as diagnostic tool. So  $FEV_1/FEV_6$  can be used instead of  $FEV_1/FVC$  in population having high risk of COPD for example smoker with age greater than 45 and having respiratory symptoms.<sup>12,13,14</sup>

## CONCLUSION

The results of our study clearly recommends that the ratio of forced expiratory volume in one second/forced expiratory volume in six seconds and forced expiratory volume in six seconds, both can be used as a clear alternate of forced expiratory volume in one second/forced vital capacity and forced vital capacity predicted, as fixed cut-off terms for the detection of an obstructive or restrictive spirometric pattern in adults. It's easy for subjects and for the operator specifically in older patients and subject with respiratory disease in severe form.<sup>2</sup>

## Annexure Abbreviations

$FEV_6$ =forced expiratory volume at 6 sec of exhalation;

FET = forced expiratory time;

LNL= lower normal limit;

NHANES III =third National and Nutrition Examination Survey;

NPV= negative predictive value;






PPV=positive predictive value.

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