

# Comparison of lower limit of normal values with a fixed ratio assessed by spirometry in obstructive and restrictive lung diseases in Indian population

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## Abstract

**Background and Aim:** Spirometric parameters are approximated by the normal distribution and using lower limit of normal (LLN) minimize the misclassification with fixed-ratio protocol in interpretation of spirometry results. This study investigates prevalence and characterization of obstructive and restrictive lung function impairments, and dissimilarities between two guidelines interpreting spirometry.

**Methods:** This study was conducted to assess the lung function in students and patients ( $n = 74$ ) of MGM Medical College, Kishanganj, Bihar, between September 2012 and May 2014, using computerized Spirometer.

**Results:** Forced vital capacity (FVC), forced expiratory volume in the 1<sup>st</sup> s ( $FEV_1$ )/FVC, forced expiratory flow<sub>25-75%</sub> ( $FEF_{25-75\%}$ ), peak expiratory flow rate (PEFR) were normally distributed with inflection at their mean  $\pm$  standard deviation.  $FEF_{25-75\%}$  and PEFR were higher in normal individuals compared to individuals with respiratory disease.  $FEV_1$ /FVC were lower, and FVC were higher in obstructive disease while the reverse results were obtained in restrictive disease category. Restrictive disease by fixed-ratio was found with 55% negative predictive value (NPV) and 5% positive predictive value (PPV), while the normal cases by fixed-ratio criteria was found with 91% NPV and 15% PPV versus LLN criteria. There were 58 individuals with normal spirometries under the LLN method but a discrepant of only 12 fixed-ratio normal results. Concordance analysis by kappa statistics yielded a  $\kappa = 0.017$ .

**Conclusion:** Older adults are more pulmonary susceptible. The performance of LLN criteria in differentiating respiratory diseases is better than the fixed-ratio criteria. Poor agreement exist between the fixed-ratio and LLN protocols in interpreting spirometric results. There is the difference between the LLN and fixed-ratio criteria which need to be redressed with population-specific reference values.

**Key words:** Concordance, fixed-ratio, lower limit of normal, obstructive, restrictive

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## INTRODUCTION

The fixed-ratio of forced expiratory volume in the 1<sup>st</sup> s to forced vital capacity ( $FEV_1$ /FVC%), combined with %predicted (PP) values for FVC (fixed-ratio), is commonly used as cut-off points for the detection of lung functional

abnormalities in routine clinical practice.<sup>[1]</sup> However, there are reports of misclassification with fixed-ratio based cut-offs in interpretation of spirometry results.<sup>[2-8]</sup> In an effort to standardize interpretation of pulmonary function tests (PFT), American Thoracic Society (ATS) proposed guidelines based on the values below the lower 5<sup>th</sup> percentile, that is, lower limit of normal (LLN), characterized as abnormal, derived from the equations based on the Third National Health and Nutrition Examination Survey (NHANES III).<sup>[9,10]</sup> The fixed-ratio value for  $FEV_1$ /FVC% approach has been reported to over-diagnose obstructive defect, compared with LLN, especially in older population because the process of aging affect lung volumes.<sup>[2-4]</sup>

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Continuous distributions such as PFT data parameters are characterized by an infinite number of possibilities, represented by a probability density function.<sup>[7]</sup> Many such random variables take only positive values and thus are approximated by a normal distribution.<sup>[7,8]</sup> Using LLN values based on the normal distribution of the lung function parameters and classifying the bottom 5% of the healthy population as abnormal, is one way to minimize the potential misclassification.<sup>[4,8]</sup> Limited data are available from this region of the globe, pertaining to the comparative investigation of the fixed cut-off ratio combined with PP value algorithm versus the LLN criterion for the classification of spirometric abnormalities. This study thus investigates the prevalence and characterization of obstructive and restrictive lung function impairments, and dissimilarities between the two guidelines interpreting PFT in a population from Kishanganj, Bihar.

## MATERIALS AND METHODS

A total of 74 participants belonging to the age group (18–60 years) among patients attending the MGM Medical College for treatment of respiratory troubles and under graduate medical students attending the classes at Physiology department for PFT, were recruited in the present study between the period September 2012 and May 2014. Clearance from the Institutional Ethical Committee was obtained prior to the study. Written consent were obtained from the participants, and a questionnaire was used to collect basic demographic information of each participant on their height, weight, gender, and smoking histories.

Spirometry was done using computerized spirometer (RMS Spirometer Helios 401, Chandigarh, India). The acceptability of the tests and the reproducibility criteria were maintained following ATS guidelines.<sup>[9]</sup> PFT results were interpreted using the fixed-ratio criteria and the LLN algorithm [Table 1] and the fixed-ratio based classification of the restrictive degree in the current study were as depicted in Table 2.<sup>[5,6,10,11]</sup>

Reference LLN values are based on data collected from population studies of healthy people without physiologic lung impairment and matched to patient's demographic data by the NHANES III.<sup>[12]</sup> A correction factor of 0.9 was multiplied with the LLN values of FEV<sub>1</sub> and FVC parameters, matched with corresponding age and height to adjust for Caucasian reference values to be suitable for application to the Indian population.<sup>[13]</sup> The LLN values for FVC and FEV<sub>1</sub>/FVC for the current study population involving disease free individuals were self-estimated from the 5<sup>th</sup> percentile = predicted mean – 1.645 × standard residual (SR), where SR is the difference between the observed and predicted value

**Table 1:** Fixed-ratio and LLN criteria for PFT interpretation

Category	Fixed ratio LLN			
	FEV <sub>1</sub> /FVC %		FVC % predicted	
Restrictive	>95	>LLN	<80	<LLN
Obstructive	<95	<LLN	>80	>LLN
Normal	>95	>LLN	>80	>LLN

FVC: Forced vital capacity, FEV<sub>1</sub>: Forced expiratory volume in the 1<sup>st</sup> s, LLN: Lower limit of normal, PFT: Pulmonary function test

**Table 2:** Fixed-ratio based classification of restrictive degree

Restrictive degree	FEV <sub>1</sub> /FVC %	FVC % predicted
Mild	>95	<80
Moderate	>95	<64
Severe	>95	<44

FVC: Forced vital capacity, FEV<sub>1</sub>: Forced expiratory volume in the 1<sup>st</sup> s

divided by the standard deviation (SD) of the predicted value. In a healthy population, 90% of the measured values fall between a SR of –1.64 and +1.64.<sup>[14]</sup> The PP values for PFT parameters such as FVC, FEV<sub>1</sub>/FVC, forced expiratory flow<sub>25–75%</sub> (FEF<sub>25–75%</sub>), and peak expiratory flow rate (PEFR), estimated from disease-free population in the present study were tested if these data were normally distributed, and the observed distribution were compared with the corresponding expected theoretical distribution; calculated on the basis of frequency density

as the ordinate (equal to  $\frac{1}{s\sqrt{2\pi}} \exp\left[-\frac{(x-\bar{x})^2}{2s^2}\right] = \frac{1}{s} \phi(\tau)$ ,

for some appropriate values of x; mean =  $\bar{x}$  and SD = s;  $\tau = \frac{(x-\bar{x})}{s}$ ) on the secondary vertical axis, superimposed on the histogram of the observed distribution at each class interval of the PP values. The ordinates were multiplied with n for comparing ordinates with frequency density of the observed distribution.<sup>[7]</sup> The probabilities for general normal distribution were computed using the principle of standardization as  $P(a < X < b) = \Phi\left(\frac{b-\mu}{\sigma}\right) - \Phi\left(\frac{a-\mu}{\sigma}\right)$ ;  $P(X < a) =$

$\Phi\left(\frac{a-\mu}{\sigma}\right)$ ;  $P(X > b) = 1 - P(X < b) = 1 - \Phi\left(\frac{b-\mu}{\sigma}\right)$ .<sup>[7]</sup> The values of  $\Phi(\tau)$  and  $\phi(\tau)$  were obtained from the tables of the normal deviate.

### Statistical analysis of data

Spirometric variables were expressed as mean ± SD and ranges. Student's unpaired *t*-test was used to compare the measured respiratory function characteristics of the participants classified according to the type of respiratory diseases, and a *P* < 0.05 was considered statistically significant. Predictive values of the fixed-ratio spirometric algorithms with respect to LLN were determined through estimation of sensitivity, specificity, positive predictive value (PPV), and

negative predictive value (NPV). Concordance between fixed-ratio and LLN spirometry algorithms was assessed for restrictive, obstructive and normal cases using kappa statistics;  $\kappa = 0$  and 1 indicated nil and perfect reproducibility respectively while a  $\kappa > 0.75$  indicated excellent, between 0.4 and 0.75 good, and  $<0.4$  poor reproducibility, respectively.

## RESULTS

Between September 2012 and May 2014, a total of 74 participants in the age group (18–60 years) with 41 (53.95%) and 7 (9.21%) number of males belonging to the age group  $>18$  years (19–60 years) and  $\leq 18$  years, respectively, and with mean age  $\pm$  standard error of mean (SEM) of  $32.02 \pm 2.30$  years were included in the study. Twenty four (31.58%) females  $>18$  years (19–55 years) and 4 (5.26%) females  $\leq 18$  years with mean age  $\pm$  SEM of  $25.96 \pm 2.24$  years respectively, were involved in the investigation of pulmonary function testing.

Table 3 depicts the measured respiratory function characteristics of participants classified according to the presence of respiratory disease. The values are represented as their mean and SEM of FVC (L), and FEV<sub>1</sub>/FVC %. The FVC values have been found to be  $3.15 \pm 0.13$  L in normal individuals, and  $2.04 \pm 0.18$  L and  $3.27 \pm 0.42$  L in restrictive and obstructive disease, respectively. The

measured mean  $\pm$  SEM values of FEV<sub>1</sub>/FVC ratios have been found to be  $93.46\% \pm 0.95\%$  in normal individuals and  $97.06\% \pm 1.07\%$  and  $75.2\% \pm 1.73\%$  in restrictive and obstructive disease, respectively. The FEF<sub>25–75%</sub> and PEFR values were  $3.24 \pm 0.34$  L/s and  $4.73 \pm 0.53$  L/s in restrictive diseases compared with  $4.01 \pm 0.11$  L/s and  $6.87 \pm 0.11$  L/s in normal population.

A normal curve was obtained for the expected distribution of the percent predicted values for FVC, FEV<sub>1</sub>/FVC, FEF<sub>25–75%</sub>, PEFR as depicted in Figure 1 that was superimposed on the histogram of the observed distribution of the measured values at each class interval. The points of inflection of the normal density at their respective mean  $\pm$  SD are represented in Table 4. The maximum expected and observed frequencies were obtained for FEV<sub>1</sub>/FVC at 114.5%, for FVC at 84.5%, for FEF<sub>25–75%</sub> at 109.5%, and for PEFR at 72% of predicted values. The corresponding range of values with approximate probability of 68%, 95%, and 99.7% are depicted in Table 4. The normally distributed random variable FVC lies, within 70.64 – 112.36% predicted values with 68% probability, within 49.78 – 133.22% predicted values with 95% probability, within 28.92 – 154.08% predicted values with 99.7% probability.

The measured FVC and FEV<sub>1</sub>/FVC values of disease free individuals in the current study population were compared with predicted values using self-estimated LLN from the

**Table 3:** Measured respiratory function characteristics, age and gender of the participants

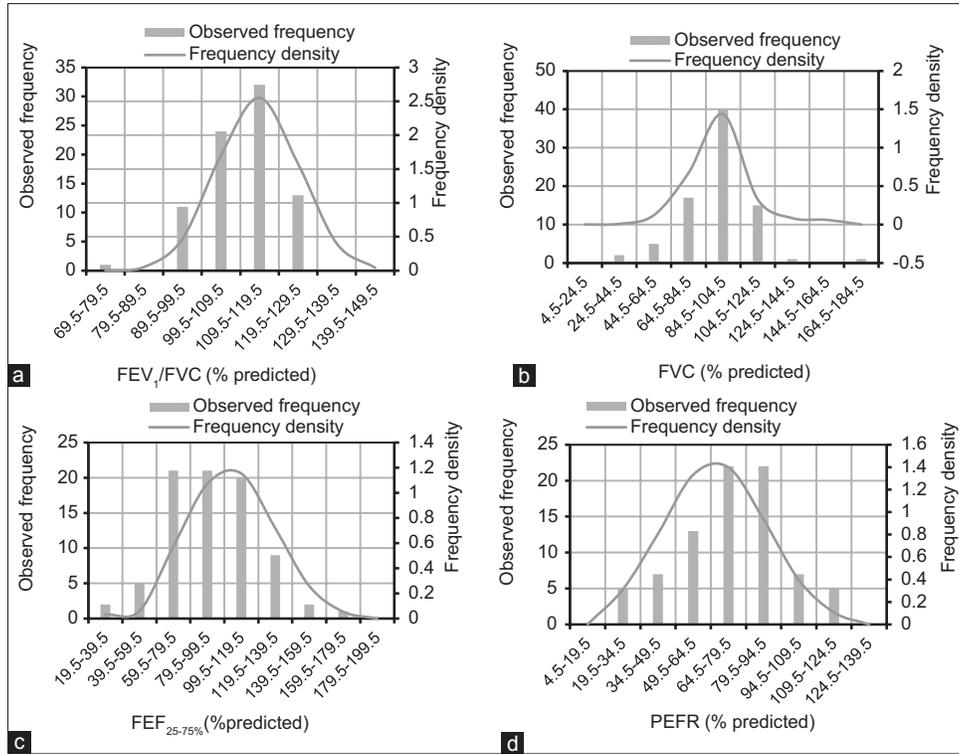
Characteristic	Overall (n=74)	Normal (n=18)	With respiratory disease		
			ESAO (n=37)	Restrictive (n=16)	Obstructive (n=3)
Age (years)	29.5 $\pm$ 1.98	24.69 $\pm$ 1.91	37.24 $\pm$ 3.03 <i>P</i> <0.05	29.44 $\pm$ 4.12 <i>P</i> <0.05	38.33 $\pm$ 8.74 <i>P</i> <0.05
Male, %	65	64.1	60.7	27.3	100
FVC (L)	2.76 $\pm$ 0.22	3.15 $\pm$ 0.13	2.59 $\pm$ 0.14 <i>P</i> <0.05	2.04 $\pm$ 0.18 <i>P</i> <0.05	3.27 $\pm$ 0.42 <i>P</i> <0.05
FEV <sub>1</sub> /FVC (%)	88.69 $\pm$ 1.27	93.46 $\pm$ 0.95	89.04 $\pm$ 1.31 <i>P</i> <0.05	97.06 $\pm$ 1.07 <i>P</i> <0.05	75.2 $\pm$ 1.73 <i>P</i> <0.05
FEF <sub>25–75%</sub> (L/s)	3.05 $\pm$ 0.32	4.01 $\pm$ 0.11	2.82 $\pm$ 0.17 <i>P</i> <0.05	3.24 $\pm$ 0.34 <i>P</i> <0.05	2.12 $\pm$ 0.66 <i>P</i> <0.05
PEFR (L/s)	5.14 $\pm$ 0.75	6.87 $\pm$ 0.11	4.62 $\pm$ 0.29 <i>P</i> <0.05	4.73 $\pm$ 0.53 <i>P</i> <0.05	4.33 $\pm$ 2.05 <i>P</i> <0.05

Values are expressed as mean $\pm$ SEM. *P*<0.05 was considered statistically significant. SEM: Standard error of mean, ESAO: Early small airway obstruction, FVC: Forced vital capacity, FEV<sub>1</sub>: Forced expiratory volume in the 1<sup>st</sup> s, FEF<sub>25–75%</sub>: Forced expiratory flow<sub>25–75%</sub>, PEFR: Peak expiratory flow rate, *n*: Sample size

**Table 4:** Distribution of % predicted FVC, FEV<sub>1</sub>/FVC, FEF<sub>25–75%</sub>, PEFR is approximately normal

Parameter	Mean $\pm$ SD	Range of values with approximate probability of		
		68%	95%	99%
FVC (L)	91.5 $\pm$ 20.86	70.64, 112.36	49.78, 133.22	28.92, 154.08
FEV <sub>1</sub> /FVC (%)	109.6 $\pm$ 10.63	98.97, 120.23	88.34, 130.86	77.71, 141.49
FEF <sub>25–75%</sub> (L/s)	92.22 $\pm$ 27	65.22, 119.22	38.22, 146.22	11.22, 173.22
PEFR (L/s)	73.61 $\pm$ 22.3	51.31, 95.91	29.01, 118.21	6.71, 140.51

Values are expressed as mean $\pm$ SD. SD: Standard deviation, FVC: Forced vital capacity, FEV<sub>1</sub>: Forced expiratory volume in the 1<sup>st</sup> s, FEF<sub>25–75%</sub>: Forced expiratory flow<sub>25–75%</sub>, PEFR: Peak expiratory flow rate



**Figure 1:** Fitted normal curve together with the histogram of the percent predicted values of the observed distribution for the %predicted values of (a) forced expiratory volume1/forced vital capacity ( $FEV_1/FVC$ ), (b) FVC, (c) forced expiratory flow<sub>25-75%</sub> ( $FEF_{25-75\%}$ ), (d) peak expiratory flow rate (PEFR), FVC: FVC,  $FEV_1$ : 1<sup>st</sup> s of FVC,  $FEF_{25-75\%}$ : mean FEF during the middle of the FVC; PEFR

5<sup>th</sup> percentile = predicted mean – 1.645 × SR; LLN for FVC values were 2.5309 L and LLN for  $FEV_1/FVC$  values were 76.126% [Table 5]. Among 18 participants showing obstructive disease by LLN criteria, a 94.4% (17/18) of individuals did not exhibit obstructive disease by fixed-ratio criteria. A three out of overall participants had pulmonary obstruction following FVC >80% +  $FEV_1/FVC$  <95% guidelines. Only one patient showed concordance between the two protocols in having obstructive disease. None of the participants exhibited pulmonary restriction by the LLN criteria. A 20% of the total participants suffered from pulmonary restriction in any form according to fixed %age guidelines. A 90% of the total number of patients could not be categorized under any of the criteria mentioned above.

A 19% sensitivity indicated the probability that the fixed %age criteria would be positive given that the LLN criteria was positive and a 20% specificity indicated the probability that the fixed %age criteria would be negative given that the LLN criteria was negative for the detection of airway respiratory disease. The probability that the fixed %age criteria would be positive or negative given that the LLN criteria was positive or negative, respectively, for the detection of obstructive disease was nil. An 83% sensitivity indicated the probability that the fixed %age criteria would be positive given that the LLN criteria was positive and a 25% specificity indicated the probability

**Table 5:** Number of patients categorized under LLN and fixed percentage guidelines for the detection of respiratory diseases

Type of respiratory disease	Criteria	No
<b>Pulmonary restriction</b>		
Restrictive	FVC < LLN+ $FEV_1/FVC$ ≥ LLN	0
Not restrictive	FVC < LLN+ $FEV_1/FVC$ ≥ LLN	4
Mild	FVC <80+ $FEV_1/FVC$ >95	7
Moderate	FVC <64+ $FEV_1/FVC$ >95	5
Severe	FVC <44+ $FEV_1/FVC$ >95	2
	LLN+fixed percentage	0
<b>Pulmonary obstruction</b>		
Obstructive	FVC ≥ LLN+ $FEV_1/FVC$ < LLN	1
Not obstructive	FVC ≥ LLN+ $FEV_1/FVC$ < LLN	17
Obstructive	FVC >80+ $FEV_1/FVC$ <95	3
	LLN+fixed percentage	1
Neither restrictive nor obstructive	Any of the above criteria	72

LLN=Predicted mean–1.645(standard residual), LLN for FVC values=2.5309 L, LLN for  $FEV_1/FVC$  values=76.126%. FVC: Forced vital capacity,  $FEV_1$ : Forced expiratory volume in the 1<sup>st</sup> s, LLN: Lower limit of normal

that the fixed %age criteria would be negative given that the LLN criteria was negative for the detection of individuals without any respiratory disorders [Table 6].

The fixed %age criteria matched 4.64% with LLN guidelines, while the fixed %age criteria not met implied 54.66% chances that the LLN criteria will not match for

the prediction restrictive disease. The fixed %age criteria did not either match or mismatch with LLN guidelines for the detection of obstructive disease. A 14.19% probability indicated that if the participant did not have any respiratory impairment by LLN criteria would not also be detected following fixed %age standard; similarly there were 90.78% chances that if the participant did not have any respiratory impairment by not following LLN criteria then he would not also follow the fixed %age criteria [Table 6].

Application of the LLN protocol using NHANES III reference values resulted in 58 (78.4%) normal variant results. Ten (13.5%) of those were concordant with the fixed-ratio interpretation whereas the remaining 2 (2.7%) were restrictive under the fixed-ratio criteria [Table 7]. Sixty two subjects (83.8%) were labeled as restrictive variant of which 12 (16.2%) were normal variants by the fixed-ratio criteria. Of the 74 test results, 10 (13.5%) and 12 (16.2%) number of individuals respectively were characterized as normal and restrictive variant by both the LLN and fixed-ratio criteria. Fourteen subjects (18.9%) were characterized as restrictive under the LLN method of which 2 (2.7%) were labeled as normal variant by the fixed-ratio criteria. Concordance between fixed-ratio and LLN spirometry algorithms assessed for the restrictive, obstructive and normal cases using kappa statistics showed a  $\kappa$  value of 0.017, indicating poor reproducibility.

## DISCUSSION

The measured respiratory function characteristics of the participants classified according to the presence

**Table 6:** PPV and NPVs of respiratory disease and normal by fixed ratio criteria in comparison with LLN

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Restrictive	18.75	20	4.64	54.66
Obstructive	0	0	0	0
Normal	83.33	25.4	14.19	90.78

PPV: Positive predictive value, NPV: Negative predictive value, LLN: Lower limit of normal

**Table 7:** Observed concordance between fixed ratio and LLN algorithm according to NHANES III reference values, using kappa statistics

		LLN			
		Normal	Obstructive	Restrictive	Total
Fixed ratio	Normal	10	0	48	58
	Obstructive	0	0	2	2
	Restrictive	2	0	12	14
	Total	12	0	62	74

LLN: Lower limit of normal, NHANES III: Third National Health and Nutrition Examination Survey

of respiratory disease, in the present study shows that there is an occurrence of respiratory disease in older adults ( $P < 0.05$ ) with mean  $\pm$  SEM of  $37.24 \pm 3.03$  years,  $29.44 \pm 4.12$  years,  $38.33 \pm 8.74$  years in individuals with early small airway obstruction (ESAO), restrictive and obstructive respiratory diseases, respectively, compared with younger adults ( $24.69 \pm 1.91$  years) without any respiratory symptoms. There are many age-associated changes in the respiratory and immune system including decreased volume of the thoracic cavity, reduced lung volumes, alterations in respiratory muscles, and increased susceptibility to pulmonary infections that causes impairment of lung function in the elderly population.<sup>[15]</sup>

The first step when interpreting PFT results is to determine if the FEV<sub>1</sub>/FVC ratio is low, indicating an obstructive defect. The Global Initiative for Chronic Obstructive Lung Disease criteria uses a cut-off of  $<70\%$  for the FEV<sub>1</sub>/FVC ratio and for patients 5–18 years of age, the National Asthma Education and Prevention Program advocates the use of a ratio of  $<85\%$ .<sup>[16–18]</sup> In the present study the FEV<sub>1</sub>/FVC ratio showed lower results ( $75.2\% \pm 1.73\%$ ,  $P < 0.05$ ) and FVC showed higher results ( $3.27 \pm 0.42$  L,  $P < 0.05$ ) in the obstructive disease category while the reverse results were obtained in the restrictive disease category that is a higher FEV<sub>1</sub>/FVC ratio ( $97.06\% \pm 1.07\%$ ,  $P < 0.05$ ) and a lower FVC ( $2.04 \pm 0.18$  L,  $P < 0.05$ ) values when compared with the values in the controls. The spirometry results in a study on patients with airway obstruction were, mean FVC of  $3.017 \pm 1.020$  L, and FEV<sub>1</sub>/FVC of  $62.9\% \pm 5.5\%$ .<sup>[19]</sup> FVC is the maximum volume of air exhaled as forcefully and rapidly as possible after maximum inhalation. FVC is always lessened in restrictive lung disorder because of loss of lung volume, so as the disease progresses the FEV<sub>1</sub>/FVC ratio may become higher than normal. The spirometric characteristics in a study on nonchronic obstructive pulmonary disease, nonasthmatic participants were  $3.25 \pm 0.77$  L and  $83.8\% \pm 5.0\%$  of FVC and FEV<sub>1</sub>/FVC, respectively.<sup>[20]</sup> Another study reported an FVC value of  $3.36 \pm 0.83$  L and FEV<sub>1</sub>/FVC value of  $89.73\% \pm 6.89\%$  in healthy subjects within the age group of 20–65 years.<sup>[21]</sup> In the present study the measured values of pulmonary flow rate FEF<sub>25–75%</sub> is significantly diminished ( $P < 0.05$ ) in all types of respiratory diseases ( $2.82 \pm 0.17$  L/s,  $3.24 \pm 0.34$  L/s,  $2.12 \pm 0.66$  L/s in ESAO, restrictive and obstructive pattern physiology respectively) compared to disease free individuals ( $4.01 \pm 0.11$  L/s). An evaluation of the flow rates at various time intervals throughout the FVC measurement demarcates, the size of bronchi responsible for the obstructive state.<sup>[22]</sup> FEF<sub>50%</sub> flow rates represent the middle portion of exhalation, FEF<sub>75%</sub> values occur at late portion of exhalation, FEF<sub>25–75%</sub> are flow rates that take place near the 25–75% portion of expiration and their reductions imply obstruction of small airways, obstruction of the smallest bronchioles is indicated by

diminished  $FEF_{75-85\%}$ .<sup>[23]</sup> Similarly PEF<sub>R</sub>, the peak flow rate during expiration, in the present study is significantly reduced ( $P < 0.05$ ) in respiratory disease states. PEF<sub>R</sub> indicate first portion of expiration and their reductions imply either a poor expiratory effort or an obstruction of large airways. However, this value is highly variable among normal volunteers and is an unreliable measure to diagnose obstructive lung disease.<sup>[24]</sup>

Interpretation of pulmonary function are based on normal distribution of test results in a population.<sup>[8]</sup> In the current study, distribution of PP values of FVC,  $FEV_1/FVC$ ,  $FEF_{25-75}$ , PEF<sub>R</sub> are normal among the studied population of Kishanganj with scatter around the predicted value characterized by SD, creating a reference range of population specific normal values. The reference range of FVC,  $FEV_1/FVC$ ,  $FEF_{25-75}$ , PEF<sub>R</sub> values with 68%, 95%, 99% confidence interval for the current population are depicted in Table 4 and the PP values of the studied spirometric parameters below that reference range is considered abnormal for that specific population, leaving 16%, 2.5%, and 0.5%, respectively, of observations in the healthy population below the LLN and above the upper limit of normal. Analysis of PFT based on distribution of normal results in population and through LLN determination, are unbiased by age, height, sex and ethnic group, unlike the fixed cut-off criteria; and this approach is likely to circumvent over-diagnosis and overtreatment of elderly patients, and under-diagnosis of younger patients.<sup>[6]</sup>

Restrictive disease characterized by fixed-ratio criteria was found in 12 out of 64 individuals (19%) with a NPV of approximately 55% but a PPV of only 5% versus LLN criteria; normal cases characterized by fixed-ratio criteria was in 10 out of 12 individuals (83%) with a NPV of approximately 91% but a PPV of only 15% versus LLN criteria. Therefore, the performance of fixed-ratio criteria in differentiating respiratory diseases seems to be poorer than the LLN criteria. Reduced FVC only, as a condition of restrictive defect, was found in 14.4% patients (sensitivity 59%, specificity 97%), reduced FVC together with increased  $FEV_1/FVC > 85\%$  was found in only 5.4% patients (sensitivity 23%, specificity 99%), indicating dual condition, that is, reduced FVC and increased  $FEV_1/FVC$ , significantly diminished the sensitivity of the test and hampered the diagnosis of restrictive defect.<sup>[25]</sup> Low sensitivity (0.32) and high specificity (0.95) were found in participants having bronchial obstruction with a PPV of 81% and NPV of 89%. Specificity was higher, sensitivity decreased to 28% in participants without bronchial obstruction.<sup>[26]</sup>

Application of the LLN protocol resulted in 78.4%, 2.7%, and 18.9%, respectively, normal, obstructive, and restrictive variant whereas the fixed-ratio criteria

showed 16.2% and 83.8% normal and restrictive results, respectively, and nil obstructive defects. The present study found 58 individuals with normal spirometries under the LLN method but a discrepant (only 12) fixed-ratio normal results indicating poor agreement ( $\kappa = 0.017$ ) between the two protocols. An increased risk of mortality was reported in individuals identified with obstructive airways or restrictive physiology pattern using the fixed-ratio criteria but normal airways under the LLN protocol substantiated with 128 normal spirometries under the LLN method but a discrepant fixed-ratio result.<sup>[27]</sup> All of those normal by the LLN method had results classified as obstructive under the fixed-ratio criteria ( $n = 63$ ).<sup>[28,29]</sup>

However, further studies with larger sample size are warranted to establish the population specific reference values for predicted and LLN  $FEV_1/FVC$  ratios matched with the age as well as height and age related predicted and LLN FVC values for individuals including older than 80 years. The newly developed population specific prediction equations and standards could be used in both epidemiological studies and clinical practice for characterizing spirometry results.

### Limitations of the study

The age of the subjects in the present study ranged between 18 and 60 years necessitating the age to be matched across the groups to account for the age related lung function decline as well as age-related comparison between two algorithms. Future studies incorporating response to bronchodilators in PFT can be taken up to distinguish between restrictive and obstructive diseases based on both the radiographic and lung volume findings. Moreover, measurement of total lung capacity as the standard criterion could be applied to detect pulmonary restriction using body plethysmography or helium wash-in or nitrogen wash-out techniques.

## CONCLUSION

To our knowledge this is the first cross-sectional survey to examine the use of spirometry to study the distribution of respiratory function characteristics and in the assessment of concordance between the fixed-ratio cut-off point with the fixed PP values (fixed-ratio) and the LLN algorithms in interpreting spirometry results among a population of Kishanganj, Bihar where there is scarcely any report on the studied area. In the present study, the performance of LLN criteria in differentiating respiratory diseases seems to be better than the fixed-ratio criteria. Poor agreement exists between the fixed-ratio and LLN protocols in interpreting spirometric results. There is difference between the LLN and fixed-ratio criteria needs to be redressed with population-specific reference values.

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