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Research Article

Pre- & post- bronchodilator pulmonary function test in Indian females: a survey in and around Jaipur

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ABSTRACT

Background: Nonsmoker COPD in people is a continued point of concern. Recent standards prescribe that spirometry should be population specific, recent origin and methodically derived (prescribed by GOLD) with influencing factors specified – which this study aims to do.

Methods: From a random sample of 4,500 adults, subjects were invited into study through a 16 point questionnaire. After inclusion/ exclusion criteria applied to 3,733 total responders, 244 rural and 240 urban healthy non-smoker females were enrolled. Spirometry with reproducibility testing before and after bronchodilator (salbutamol) was done as per GOLD prescription. As normality of distribution was disproved, non-parametric methods were used in statistics.

Results: Mean FEV1 and FVC were 2.25 and 2.69 liters respectively in rural females, while it was 2.06 and 2.44 liters in urban females. Post-bronchodilator (after 0.3 mg salbutamol) values in rural females were 2.32 and 2.70 liters respectively while the same were 2.13 and 2.45 liters in urban cases.

Conclusion: PFT of rural females resulted better on FEV1 and FVC, pre as well as post-bronchodilator. Possibly biomass fuel exposure in the rural females might not be causing a generalized decrease in PFT parameters or urban chemical pollution which might have more than counterbalanced in urban side.

Keywords: Biomass fuel, Indian female, Urban, Rural, FEV1, FVC

INTRODUCTION

During the last 30 years, numerous sets of spirometry reference values have been published. Some of them[1] used spirometry after reversibility testing but none was there for Indian population where ruro-urban disparities are still obvious. Even the scarce available data are not standardized by GOLD (Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease).[2,3]

The use of post-bronchodilator spirometry facilitates the distinction between 'fully reversible asthma' and 'poorly reversible' COPD, and may lead to a reduction in misclassification of individuals with reversible obstruction as COPD cases. Predicted FEV1 is calculated on reference values for normal lung function.[5]

That's why recent international guidelines have emphasized the importance of post-bronchodilator pulmonary function measurements in the diagnosis and severity classification of chronic obstructive pulmonary disease (COPD).[2-4]

But it seems unlikely that the difference between pre- and post-bronchodilator lung function is constant. Racial and genetic factors also have significant impact on these values[1,2,31,32] and these effects were further detailed for different regions of India.[33]

Moreover, studies have shown that reversibility decreases with age in adults[7,8], indicating a different relationship between lung function and age before and after bronchodilation.

Reversibility testing and post bronchodilator assessment being relatively recent regulations for standardization, they have not been applied widely – especially in Indian population as explained earlier.

Secondly, as populations change over time regarding both anthropometric characteristics and environmental exposures – it is prudent to update reference values regularly.[6]

For example, age pattern of a given population also keeps changing – mostly due to increase in the life expectancy and thus increase in elderly population due to better medical intervention.[27,28]

Therefore in addition to the need for regularly updated reference values, there was also a need for specific post-bronchodilator reference values with geographical and racial references according to age and height.

Chest dimensions, together with height and race explained 90% of the variation in forced vital capacity (FVC) and 86% of the variation in total lung capacity (TLC).[39] The rest difference remains to be explained by other plausible reasons like environmental factors of pollutants and food pattern.

As rural pollution of biomass fuel is different from vehicular and industrial pollution of urban setting and rural people mostly miss the processed food with synthetic additives commonly used by urban people, Indian ruro-urban differences provide a virgin field for tentative exploration.

With globalization and rapid urbanization, western countries have lost these ruro-urban disparities in their lifestyle and thus are least expected to exhibit any such difference and accordingly such studies are scarce, if any as explained earlier.

The background issue for this study was to identify and quantify the disparity of pulmonary function test (PFT) parameters like FEV1 and FVC, if any, due to this difference of lifestyle and environment in rural versus urban population.

METHODS

Ethical clearance for the study was obtained from the Human Ethical Committee of the SMS Medical College and Hospital. 3 points in the each of the 8 municipal zones of Jaipur city were selected as urban study centers.

10 days of campaigning for free universal participation camps were organized under the slogan "know your lung" to invite the potential subjects. Posters, banners and loudspeakers were used to motivate the commonality. Similar campaigning for motivation and mobilization of rural subjects was done in 25 villages.

Standard sampling procedures and data collection in this transverse epidemiological study has been used – applying a 16 point questionnaire as per modified ATS-DLD-78 and supplied to 4,500 random samples taken from these camps.[30]

The participants supplied information on disease history, respiratory symptoms, occupational exposure to airborne agents, and smoking history. Standing height and weight was measured at the clinical examination.

As rural people mostly represented the biomass users, 'persons using biomass fuels like dung, wood, leaves etc in urban setting' as well as 'non-biomass fuels like LPG in rural setting' were excluded to make the study more robust.

According to the ATS guidelines, subjects who were examined to generate reference values should be lifetime nonsmokers without respiratory symptoms and disease.[6]

In the present study, we excluded ever-smokers, as well as never-smokers reporting physician-diagnosed respiratory disease, dyspnea grades 1 to 4, morning cough, or wheeze.

Normal health without chronic or acute disease/ disability was the criteria for inclusion while smoking was the criteria for exclusion. Out of 4,500 invited patients, 767 denied participation in the experiment or didn't accomplish up to conclusion of the experiment due to various reasons (non-compliance to technique etc).

Out of rest 3,733 subjects, 2,073 were urban and 1,660 were rural. Out of 2,073 urban subjects, 865 were females. From these 865 subjects, respiratory disease was the reason of exclusion in 541 and non-reproducibility of the test was the reason in 84 subjects. Thus finally 240 urban females completed study.

Out of 1,660 rural subjects, 633 were females out of whom 168 failed on reproducibility and 221 were excluded due to respiratory diseases. Thus finally 244 rural females completed the full protocol after application of exclusion criteria.

The spirometer was computerized and printed the FEV1 and FVC values after the forced expiration had been performed. There was no time lag between the onset of forced expiration and the onset of timing for FEV1.

FVC and FEV1 were measured according to the American Thoracic Society (ATS) criteria[23] with

EasyOne Spirometer from ndd Medizintechnik, Switzerland at a maintained temperature around 30°C.

The subject breathed in from room air and then exhaled into the spirometer. No extrapolation was performed. Spirometry was performed before and 15 min after inhalation of 0.3 mg salbutamol aerosol from metered dose inhaler.

Asthalin inhaler from Cipla Ltd was used which delivered salbutamol sulphate equivalent to salbutamol IP 100 µgm/ puff on actuation with nonflammable ozone friendly propellant 134a aka 1,1,1,2-tetrafluoroethane. [Cipla]. Such 3 puffs are applied one after another at a gap of 2 minutes each.

Both pre as well as post bronchodilator values of FEV1 and FVC were plotted against the cited non-PFT parameters. The data collection continued from April 2009 to April 2010.

Statistics

Assumption of distributional normality in PFT and non-PFT variables was tested with the probability plot correlation co-efficient (PPCC) on PAST 2.10 version from Hammer & Harper, Palaentologia electonica, which suggested non-normal distribution and preference of mean over mode or median as a measure of the central tendency.

Testing on Excel based NormQuant from Microsoft Office 2003, witnessed homogenous scattering with insignificant central tendency and Blom's plot revalidated this basic assumption of nonparametric distribution. As Blom's plot is better than Shapiro-Francia and Filliben plots for the same indication[29], further reconfirmations were avoided.

Hence, Pearson's correlation coefficient, which is used for normal aka Gaussian distribution, was not used. Seeing the non-parametric and continuous nature of the data with unequal sample size, which didn't sufficiently transform even by logarithm or residual methods, option of statistical tests were chosen.

To correlate pre as well as post bronchodilator PFT parameters to non-PFT parameters, Spearman's rank correlation (ρ) and Kendall's correlation (τ) for bivariate analysis were performed using SPSS for Windows version 13.0.

Ruro-urban differences in PFT trends were initially assessed by Spearman's rank correlation (ρ) and Kendall's correlation (τ) for bivariate analysis and were processed using SPSS for Windows version 13.0.

Ruro-urban as well as pre-post values are re-elucidated in box-whisker plot drawn using SigmaXL 6.11. To assist this estimate of ruro-urban differences, Fligner Killeen test for coefficient of variation and Mann Whitney U test for rank mean was used.

RESULTS

As tables 1A and 1B show, all the PFT as well as non-PFT parameters in rural as well as urban population were non-parametric i.e not following normal distribution.

Table 1A: Result of normality test (rural female).

Non-PFT parameters		PFT parameters	
Parameter	PPCC	Parameter	PPCC – pre(post)
Age	0.9705	FEV1	0.9876 (0.9912)
Height	0.9879	FVC	0.9791 (0.9818)
Weight	0.9776		
PPCC = probability plot correlation co-efficient (on Past 2.10);			
(on NormQuant, using α = 0.10, critical value was 0.996827123)			

Table 1B: Result of normality test (urban female).

Non-PFT parameters		PFT parameters	
Parameter	PPCC	Parameter	PPCC – pre(post)
Age	0.9777	FEV1	0.9983 (0.9988)
Height	0.9965	FVC	0.9978 (0.9976)
Weight	0.9930		
PPCC = probability plot correlation co-efficient (on Past 2.10);			
(on NormQuant, using α = 0.10, critical value was 0.996729573)			

Pre-bronchodilator as well as post bronchodilator Spearman's (ρ) and Kendall's (τ) correlation coefficient for bivariate analysis for the PFT versus non-PFT parameters in Table 2A and Table 2B show the correlation of FEV1 and FVC with age and height far better than weight.

Table 3 shows that there was significant difference in PFT parameters of rural and urban females - thus they can't be considered as samples from "essentially similar" population. Table.4 gives average on all PFT and non-PFT parameters for rural and urban population of females.

Table 2A: Spearman's (ρ) and Kendall's (τ) Correlation Coefficient (Pre-bronchodilator).

	Age - τ (ρ)	Height - τ (ρ)	Weight - τ (ρ)
FEV1 (rural female)	−0.417** (−0.586**)	0.343** (0.482**)	0.037 (0.058)
FEV1 (urban female)	−0.481** (−0.661**)	0.375** (0.517**)	−0.155** (−0.234**)
FVC (rural female)	−0.256** (−0.363**)	0.332** (0.472**)	0.106* (0.153*)
FVC (urban female)	−0.358** (−0.507**)	0.392** (0.545**)	−0.053 (−0.093)
FEV1/ FVC (rural female)	−0.467** (−0.638**)	0.102* (0.157*)	−0.123** (−0.174**)
FEV1/FVC (urban female)	−0.354** (−0.497**)	0.089* (0.128*)	−0.210** (−0.315**)
Correlation significant at ** 0.01 level or *0.05 level (both 2 tailed)			

Table 2B: Spearman's (ρ) and Kendall's (τ) Correlation Coefficient (Post-bronchodilator).

|	Age - τ (ρ)	Height - τ (ρ)	Weight - τ (ρ)
FEV1 (rural female)	−0.407** (−0.571**)	0.337** (0.473**)	−0.034 (−0.055)
FEV1 (urban female)	−0.495** (−0.671**)	0.396** (0.543**)	−0.148** (−0.223**)
FVC (rural female)	−0.258** (−0.368**)	0.335** (0.466**)	−0.105* (−0.155*)
FVC (urban female)	−0.347** (−0.493**)	0.410** (0.561**)	−0.022 (−0.046)
FEV1/FVC (rural female)	−0.469** (−0.637**)	0.103** (0.156**)	−0.118** (−0.173**)
FEV1/FVC (urban female)	−0.413** (−0.580**)	0.086 (0.121)	−0.299** (−0.440**)
Correlation significant at ** 0.01 level or *0.05 level (both 2 tailed)			

Table 3: Ruro-urban disparity.

	FEV1	FVC	Post FEV1	Post FVC
Coefficient of variation*	19.066# (R) 20.850# (U)	16.427^ (R) 18.558^ (U)	18.614 (R) 20.102 (U)	16.289# (R) 18.007# (U)
Mean Rank**	136.3 (R) 106.2 (U)	140.7 (R) 101.8 (U)	136.2 (R) 106.3 (U)	140.9 (R) 101.6 (U)

*For coefficient of variation, Fligner Killeen test has been used

(P for one tailed test was < 0.05# or < 0.01^ for significant cases)

**For mean rank, Mann Whitney U test has been used

**Table 4: Summary of PFT and non-PFT parameters in urban versus rural population.**

Parameters	Rural average (Mean)	Urban average (Mean)
Age	35.59836 ±13.41313	37.25 ±13.84689
Height	155.6516 ±6.067992	154.8667 ±5.97825
Weight	52.77459 ±9.296356	59.26667 ±11.94985
FEV1	2.250176 ±0.429011	2.067096 ±0.430996
FVC	2.693803 ±0.442524	2.446075 ±0.453942
Post FEV1	2.32375 ±0.432546 (Δ = + 3.2697 %)	2.138633 ±0.429905 (Δ = + 3.4607 %)
Post FVC	2.704344 ±0.440521 (Δ= + 0.3913 %)	2.454754 ± 0.442032 (Δ = + 0.3548 %)

In rural females, % of significantly improved cases, i.e. showing >12% improvement in post-FEV1 value compared to pre FEV1 value was 14/244 = 5.7377% while in urban females the same was 20/240 = 8.3333%. Thus more reversible impairment was seen in urban population.

Box and whisker diagram in figure 1A (FEV1) and figure 1B (FVC) represent the pre- as well as post-bronchodilator ruro-urban differences with centrality (mean, median) and scattering. First and third quartile are represented by upper and lower limit of box respectively – with outliers as separate points.
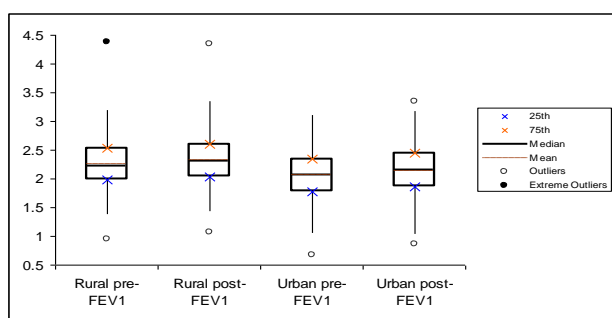
Figure 1A: Pre- and post-bronchodilator ruro-urban differences (FEV1).
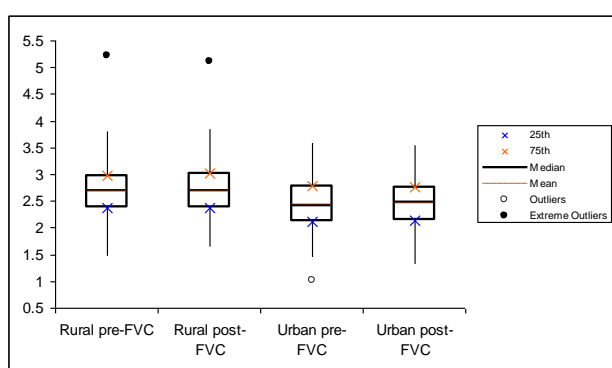
Figure 1B: Pre- and post-bronchodilator ruro-urban differences (FVC).

Table 5 gives the proportion of rural and urban females having FEV1/ FVC less than 70%.

Table 5: Females with FEV1/FVC value <70% (pre versus post).

Rural		Urban	
Pre FEV1/ FVC (yrs/cms)	Post FEV1/ FVC	Pre FEV1/ FVC (Age & Height)	Post FEV1/ FVC
64.24% (75/142)	64.98%	66.90 % (72/149)	64.92 %
66.14% (38/155)	74.40%		
69.71% (70/143)	78.51%		
69.81% (35/135)	75.63%		

DISCUSSION

FEV1 or FVC was best correlated to age and then height. Rural females were significantly better than urban counterpart on PFT. In rural females, FEV1 decline with age was slower as age was relatively less negatively correlated to FEV1 compared to their urban counterparts

both pre as well as post-bronchodilator as per table 2A and table 2B.

Notably, age related decline in FVC was less than FEV1 in both rural as well as urban females and here again decline in urban females was still faster. Thus finally, FEV1/FVC value declined faster both pre as well as post-bronchodilator in rural females who were otherwise healthier.

Thus paradoxically there were more such impaired people in rural population as shown in Table.5. This fact would be important in stage I COPD where FEV1/ FVC <70% but FEV1 is >80%.

Interestingly, weight was positively correlated to FEV1 in rural population –most probably because it was contributed by hard manual labor and muscle mass thereby. But FEV1 was negatively correlated in urban population – most probably contributed by sedentary life and consequential adiposity.

For ruro-urban difference on PFT parameters shown in Table.3, it can be argued that as bronchodilation reverses the physiological performance in reversibly impaired cases but hardly benefits already normal/ irreversibly impaired people.

Thus coefficient of variance was lesser in post bronchodilator PFT parameters in both rural as well as urban cases. Obviously mean rank won't change much in such cases but ruro-urban disparity was still significantly obvious. Urban females were more compromised and hence more reversible cases were seen in urban area.

Concerning Table 4, another plausible reason for the ruro-urban difference could be that despite insignificant difference in height of ruro-urban population, weight was significantly more in urban females which could have contributed to decrease of FEV1 as well as FVC.[24-26]

On average, urban population was a bit older, but even if the little age difference was compensated at the rate of 20ml/ year, PFT parameters were still lower in the urban females than their rural counterpart.

A plausible explanation to this discrepancy might be that urban females were exposed to more chemical pollution which could be more detrimental. Thus against repeatedly reported increased relative risk of COPD in female exposed to biomass fuel[34-38], it was not witnessed in our ruro-urban comparison of FEV1 and FVC.

Possibly biomass fuel exposure in the rural females might not be causing a generalized decrease in PFT parameters, though it might have caused some fall in susceptible individuals, in whom COPD could be a later manifestation.

CONCLUSION

All data sets were non-parametric i.e. don't follow ideal Gaussian scattering pattern and central tendency of a normal distribution. Age and height were re-validated as the best predictors of FEV1 and FVC both – pre as well as post bronchodilator.

Rural females, though more diverse in their exposure to the biomass fuel due to vast range of discrepancy in social status and economy, were on average better performers on spirometric PFT.

Reversible components in PFT parameters were more in urban females compared to their rural counterparts – thus post bronchodilators betterment was more obvious.

Probably effect of chemical pollution through industry and vehicles and food additives added to sedentary life in urban females has more than counterbalanced the decrease in lung function in rural population exposed to bio-mass fuel.

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