Indian J Physiol Pharmacol 2019; 63(2) : 160–167

Original Article

Prediction Equations for Pulmonary Function Parameters in Central Indian Adult Population

Manish Sawane* and Tasneem Ansari

NKP Salve Institute of Medical Sciences & Research Centre,
Nagpur

Abstract

Introduction: The prediction equations for spirometry currently used may have lost significance as they are several decades old. Also the lung health of the population has changed over the years. Moreover prediction equations for Central Indians have never been proposed.

Aims: To develop prediction equations for pulmonary function parameters in Central Indian adult population and to compare them with equations currently used for Indian population.

Materials and Methods: Spirometry was performed using Helios 401 machine on 445 healthy male & female subjects aged between 18 to 60 years residing in Central India using the current guidelines as recommended by ATS. Prediction equations for males & females were developed separately for FVC, FEV1, PEFR, FEF 25-75 %, FEF 0.2-1.2 litres, FEF 25%, FEF50%, FEF75% and MVV. Final models were selected considering simplicity and ease of clinical application, highest predictive capability (R2), highest F value, lowest AIC value and satisfaction of assumptions of regression analysis. Age related decline and height related increase for all the pulmonary function parameters was observed. These equations were also compared for agreement with currently used Recorders equations for Indians using Bland Altman method.

Conclusion: All the observed values of pulmonary function parameters were less in central Indians as compared to the reference values suggesting either an ethnically lower values or a decline in the lung health of the population. We propose that the prediction equations for pulmonary function parameters developed in this study must be used as reference for Central Indians.

Introduction

Pulmonary function tests are the fundamental tool to evaluate the respiratory system of an individual and of all the tests, spirometry is by far the most common one used in the diagnosis, assessment and management of patients with different lung diseases. To make an assessment or interpretation of an observed value it is compared with a reference value, defined as 'normal' and is derived from a representative sample of healthy subjects. Unlike most other measurements in medicine where

***Corresponding author :**

Dr. Tasneem Ansari, NKP Salve Institute of Medical Sciences & Research Centre, Nagpur Email: dr.tasneem2@gmail.com

(Received on Feb. 27, 2018)

universally applicable normal ranges are available, lung function shows wide variations even in 'normals' not only due to technical factors related to equipment and procedures, but also due to biological and environmental factors. These include racial, ethnic, sex, anthropometric factors, socio-economic, geographical, climatic and nutritional conditions so that prediction equations developed in one set of population may not be applicable to a different set of population (1). Several prediction equations have been described for northern, eastern, western and southern regions of India with different prediction but none for central Indian adult population (2-7). In our previous works in normal healthy individuals and in control groups of occupational studies, it was conspicuous that recorded values of PFT parameters were lower than the predicted values (8-10), justifying the need for revision of prediction equations for the region. Further, considering the recent measurement protocols and the equipments available, the current utility and validity of some of the equations in vogue is questionable as these studies have varied in study population, sample size, instrumentation and statistical techniques that may no longer be useful. Also there are evidences of a cohort effect where some evidences show improvement in lung health of a population over a long period of time (11, 12), while some have proved deterioration in lung health (13). The other major factors that significantly affect PFTs are diet, obesity, air pollution and physical activity (14). There has been general improvement in nutritional status as a result of expansive industrialisation and rapid global economic growth but on the contrary the physical activity has reduced and exposure to air pollution has enormously increased. In light of changes in socioeconomic status, anthropometric changes, lifestyle modifications, environmental influences and the measurement instruments and protocols, the present study was taken up to formulate new prediction equations for various pulmonary function parameters for the Central Indian adult population.

Material & Methods

A cross-sectional study was carried out in Department of Physiology of a tertiary care hospital attached to a medical college on normal, healthy male & female subjects aged between 18 to 60 years over a period of 3 years. An ethical approval to conduct the study was taken from Institutional Ethics Committee. A written informed consent was taken from all the subjects. For feasibility reasons convenient sampling technique was used to sample the subjects. All the available Indian studies have also used convenient sampling technique (2-7). The hospital where the study was conducted caters to the patients coming from different districts of Vidarbha, parts of Madhya Pradesh and Chhattisgarh. Therefore, the subjects included were healthy relatives of patients attending the hospital OPD and IPD so as to make the sample representative of Central Indian population. Some of the teaching and non teaching staff members of the institute were also included in the study so as to have a mix of urban and rural population. All the subjects included were permanent residents of Central India and originally hailed from the region. Detailed history of all the subjects was taken along with thorough clinical examination and only those found to be normal and healthy were included in the study. The exclusion criteria included smokers, subjects with clinical abnormalities of vertebral column and thoracic cage; subjects with pulmonary tuberculosis, bronchial asthma, subjects who had undergone vigorous exercise, abdominal or chest surgery and subjects suffering from any active respiratory tract infection and or having respiratory symptoms like cough, sputum production, dyspnoea, and wheezing as assessed by American Thoracic Society, Division of Lung Diseases questionnaire for respiratory symptoms (ATS-DLD-78A). Exclusion criteria were in conformity with the guidelines recommended by ATS (1). Spirometry was performed using Helios 401 (Recorders and Medicare systems Private Limited, Chandigarh, India), a computerized electronic type of spirometer, which was attached to a laptop. It is a dry type of spirometer with an internal correction of volumes. Before beginning the tests, demonstrations were given to each subject separately and it was confirmed whether he had understood the procedure. They were familiarized with the instruments and pulmonary function tests were performed. The data of the subject like name, age, sex, height, weight, the atmospheric temperature were entered into the software program of computerized spirometer. The standing height of the subject was measured by making the subject stand against a wall on which measuring scale was marked. The subjects stood barefoot and his feet were approximated together with heels, buttocks and occiput touching the wall firmly. Head was held erect and subject was asked to look straight in front without tilt. The highest point on the head was marked on the wall with a plastic ruler and then height was measured up to nearest centimetre. Weight was measured without shoes and was rounded to the nearest kilogram. Age was rounded to the nearest date of birth.

On the day of spirometry, subjects were instructed to have breakfast in the morning and the tests were done in between 10 am to 12 noon after rest of one hour in the laboratory. All the tests were performed in sitting position. The subjects were asked to place the mouthpiece attached to the spirometer in their mouth. Nose was closed by nose clip. The subject was asked to take deep full inspiration which was followed by as much rapid and forceful expiration as possible through the mouth piece. Since spirometry is an effort dependent manoeuvre, proper instructions were given and it was ensured that the subject understood the procedure and performed according to the current ATS acceptability (individual spirograms free from artifacts, having good starts & satisfactory exhalation) and reproducibility criteria (two largest FVC & FEV_1 within 0.2 l of each other). The criteria were very rigidly applied to all the spirograms. Three consecutive readings were taken and best among them was selected. Subjects who failed to perform with desired acceptability & reproducibility were rescheduled for another day & who still failed to perform were dropped out. Proper hygiene and infection control was maintained. The spirometer was calibrated daily with a 3 litre syringe. The parameters of the pulmonary function tests included in the study were Forced vital capacity (FVC), Forced Expiratory volume at the end of first second (FEV1), Peak expiratory flow rate (PEFR), Forced expiratory flow rate (FEF) 25-75 %, FEF 0.2-1.2 litres, Forced expiratory flow rate 25%, FEF50%, FEF75% and Maximum voluntary ventilation (MVV). A total of 470 subjects were screened, out of which 17 subjects didn't meet the inclusion criteria, 8 subjects failed to return to perform the test next day. Thus data of 445 subjects (274 males & 171 females) were used in the study for statistical analysis.

Predictors considered were age, sex, height and weight. Multiple regression models for different parameters were selected separately for males and females with backward selection i.e. all three independent parameters viz. Age, height and weight were included to get the better fit and then one parameter with non-significant p value was removed to get linear regression with two parameters.

Best fit model was selected using Akaike Information Criteria (AIC) (16). Lower AIC values indicate a better model. Thus, for all the parameters different models were developed and a best fit for each parameter was selected on the basis of AIC.

Analysis of variance was carried out for each model to evaluate the significance of the regression equation and standard errors of the estimate (SEE) were also calculated. Estimates of regression coefficients for individual predictor variables were obtained and their significance was determined by student's 't' test. Highest F value was also considered as best fit of the model. Final models were selected considering simplicity and ease of clinical application, highest predictive capability (adjusted R^2), highest F value, lowest AIC value and satisfaction of assumptions of regression analysis.

The goodness of fit for the selected models was tested by studying independence of predictor variables and plotting residuals against each predictor variable as a corollary. The model was finally selected if the plot did not show any specific pattern suggesting that a linear model is suitable for the parameter under consideration. Agreements between current and previous equations were tested by Bland-Altman method (17).

All the statistical calculations were done with the help of statistical tools of Microsoft Excel using Add-In Analysis Toolpak.

Results

Total 445 subjects (274 males and 171 females) were included for analysis in the study after strictly applying inclusion and exclusion criteria as well as the acceptability criteria for spirometry. As sex is the most important independent criteria for PFT prediction, males and females groups were analysed separately for obtaining prediction equations. Age-wise composition of both the groups is given in Table I.

TABLE I : Age-wise composition of the study population.

Age (yrs)	*Males (N=274): No. (%)*	*Females (N=171): No.(%)*
18-20	10 (3.6)	10 (5.8)
21-30	77 (28.1)	48 (28.1)
31-40	86 (31.4)	68 (39.8)
41-50	91 (33.2)	38 (22.2)
51-60	10 (3.6)	7 (4.1)

Height and weight being other important anthropometric independent variables, mean values of height and weight in males and females are depicted in Table II.

Mean values of different PFT parameters in males and females are given in Table III.

TABLE II : Anthropometric data of study population.

Parameter	*Males : Mean±SD*	*Females : Mean±SD*
Age	36.75±8.88	33.90±8.64
Height	168.62±7.49	153.79±6.28
Weight	64.24±9.66	53.66±10.23

TABLE III : Mean±standard deviation of Spirometry parameters in males & females.

Parameter	*Males : Mean±SD*	*Females : Mean±SD*
FVC (Litres)	3.10±0.48	2.07±0.29
FEV1 (Litre/Sec)	2.60±0.42	1.73±0.28
PEFR (Litre/Sec)	6.97±1.13	4.94±0.95
FEF25-75% (Litre/Sec)	3.23±0.85	2.31±0.53
FEF0.2-1.2 (Litre/Sec)	5.64±1.11	3.83±0.87
FEF25% (Litre/Sec)	5.92±1.07	4.27±0.88
FEF50% (Litre/Sec)	4.07±0.98	3.20±0.72
FEF75% (Litre/Sec)	1.88±0.78	1.53±0.52
MVV (Litres)	109.73±21.65	82.04±13.59

All the multiple linear regression models for different PFT parameters were found to have best fit with age and height as the predictors. All the prediction equations for 9 different parameters in males and females are given in Table IV and V respectively.

TABLE IV : Regression equations formulated for PFT parameters in males.

Parameter	*Equation*	*Standard Error of Estimate*
FVC	–1.9494–(0.0161×Age)+(0.0334×Height)	0.357
FEV1	–0.3654–(0.0222×Age)+(0.0224×Height)	0.305
PEFR	0.8725–(0.02809×Age)+(0.04227×Height)	1.045
FEF25-75%	3.506753–(0.0578×Age)+(0.010966×Height)	0.659
FEF0.2-1.2	1.107523–(0.0452×Age)+(0.036727×Height)	0.981
FEF25%	2.098073–(0.02551×Age)+(0.028244×Height)	1.021
FEF50%	3.541099–(0.0511×Age)+(0.014289×Height)	0.857
FEF75%	2.08743–(0.05233×Age)+(0.010156×Height)	0.606
MVV	–5.57895–(0.97999×Age)+(0.89739×Height)	17.965

TABLE V : Regression equations formulated for PFT parameters in Females.

Parameter	*Equation*	*Standard Error of Estimate*
FVC	–1.9292–(0.00888×Age)+(0.02797×Height)	0.218
FEV1	–0.87031–(0.0222×Age)+(0.019087×Height)	0.241
PEFR	1.720658–(0.03497×Age)+(0.028668×Height)	0.891
FEF25-75%	0.916903–(0.03242×Age)+(0.016186×Height)	0.444
FEF0.2-1.2	2.100173–(0.046×Age)+(0.021417×Height)	0.767
FEF25%	1.814412–(0.0279×Age)+(0.022087×Height)	0.842
FEF50%	1.018297–(0.02108×Age)+(0.01884×Height)	0.687
FEF75%	0.225902–(0.02791×Age)+(0.01464×Height)	0.452
MVV	39.91172–(0.39279×Age)+(0.36054×Height)	13.039

Standard error of estimate (SEE) is also given for calculation of Lower Limit of Normal (LLN). The lower limits of normal for each spirometric variable can be determined by a 90% confidence interval (CI). The confidence interval is calculated using the SEE according to the formula:

90% CI = predicted or reference value±(1.645 * SEE)

Thus the lower limit of normal (LLN) = Predicted Value – (1.645 * SEE)

Agreement between current equations and Recorders

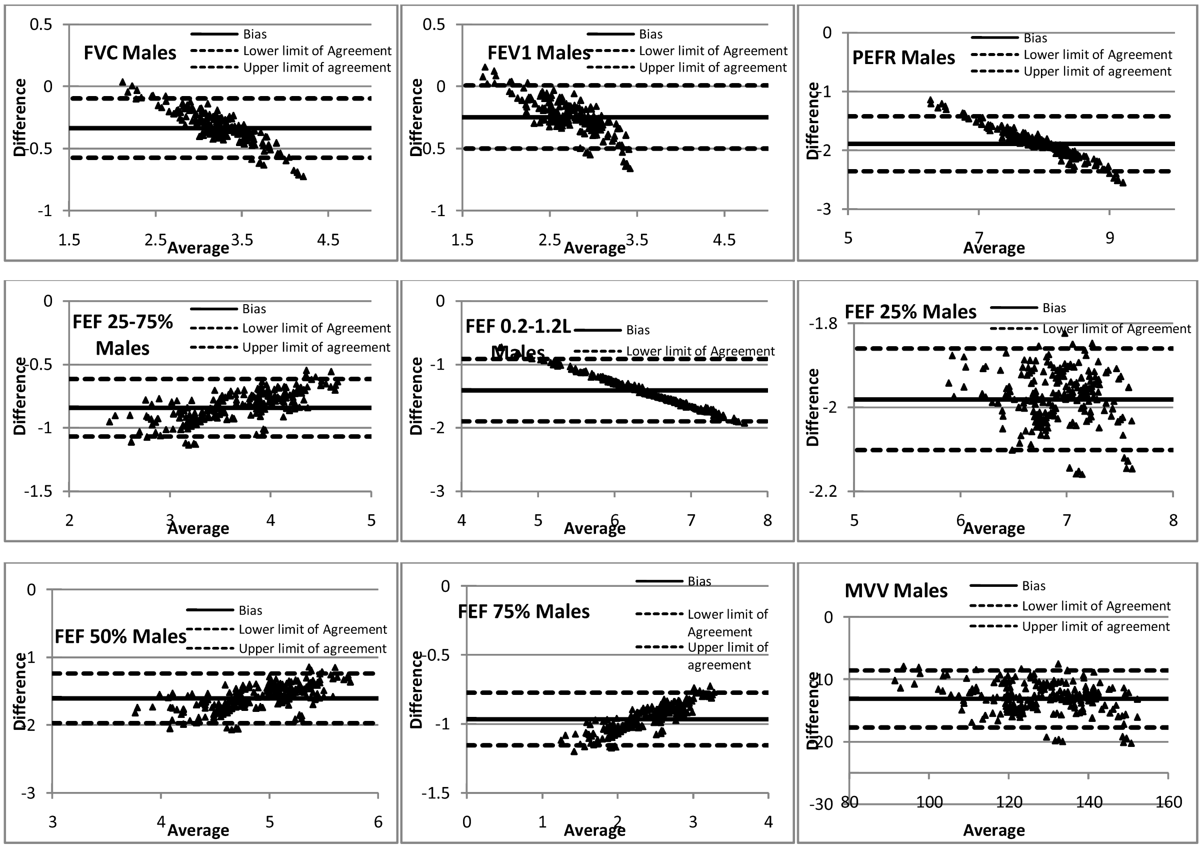

Fig. 1: Bland Altman Plot for current prediction equations as compared to Recorders equations for males.

equations incorporated in software of a popular spirometer Helios (Recorders and Medicare System, India) for FVC, FEV1, PEFR, FEF25-75%, FEF0.2-1.2L, FEF 25%, FEF50%, FEF75% and MVV were assessed using Bland-Altman method. Bland Altman plots for males and females with mean bias and lower and upper limits of agreement are given in Fig. 1 and Fig. 2 respectively.

Discussion

The current study has proposed prediction equations for pulmonary function parameters for both males and females adults of Central Indian origin within the age group of 18 to 60 years for males and females. To the best of our knowledge the RMS Helios 401 machine is the only machine in India which has prediction equations of Indian standard configured in it in the name of Recorders (18) and so in our study we performed spirometry with Helios 401 in accordance with the current standardisation recommendations by ATS-ERS. The Recorders prediction equations are widely used for Indian population irrespective of understanding the intricacies of the factors affecting pulmonary functions. However, from the results it is clear that the values of pulmonary function parameters were quite less in our subjects of Central India when compared with the reference values incorporated in the instrument. When we compared the reference equations of Helios 401 machine with that given by Kamat et al. in 1977 we found that the equations for few parameters were exactly similar (4). Their study population mainly represented south Indian population and prediction equations were formulated almost 40 years ago with old instrumentation that is outdated now. In other words, the two groups are incomparable and so formulation of an appropriate prediction equation for comparison as a reference was imperative.

Our study also shows that apart from gender and ethnicity, age and height of the individual are the

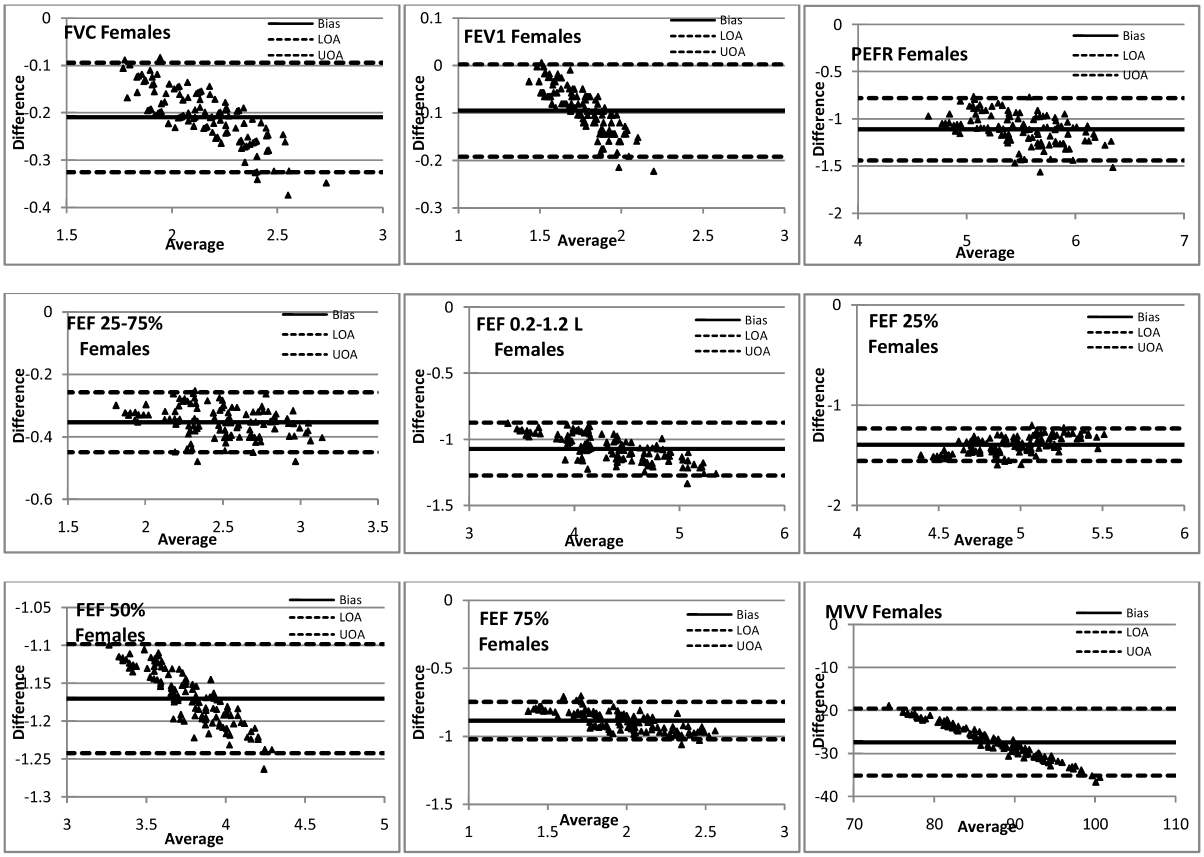

Fig. 2 : Bland Altman Plot for current prediction equations as compared to Recorders equations for females.

most important determinant variable for pulmonary function parameters while contribution of weight to the same is not of much importance. Age related decline and height related increase for all the pulmonary function parameters was observed. These findings are consistent with the other studies done in India on a different set of population (3, 4, 5, 6, 7). Our study has recorded lower pulmonary function parameter values suggesting that either the ethnic factors are responsible for these differences or the lung health of our study population may have declined due to environmental and lifestyle factors. Similar finding was recorded by Bandopadhyay et al (13). On comparison with the prediction equations proposed by Chhabra et al. (2014) (19), it was found that the observed values were lower than the predicted values particularly for FVC, FEV1, and PEFR (Data not given) in both males and females signifying the differences between different populations. In contrast to prediction equations of Chhabra et al., linear equations were having best fit in the current study as compared to quadratic and exponential equations proposed by them. Somewhat lower age range in the current study (18 to 60 years) as compared to study population in their study (18 to 71 years for males and 18 to 65 in females) may have been responsible for linear relationship.

Bland-Altman analysis for proposed prediction equations and existing equations being used in Central Indian population (Recorders equations) shows that there is disagreement for all the parameters in both males and females (Fig. 1 and 2). Disagreement was of a large degree for flow rates as compared to FVC and FEV1 as can be judged from the bias.

The anthropometric parameters like height, chest size, weight, physical activity of the individual, nutritional status that might affect the respiratory muscle strength of the individual, environmental exposures which include the tobacco smoke and other air pollutants, variety of respiratory tract infections as bacteria and viruses get mutated differing from region to region, immunization status of the individual and possibly other unknown factors also influence the pulmonary function of an individual.

Limitation of the study is the operational constraint in taking random sample in a multi-centric study which could have truly represented Central Indian population. However, an attempt was made to include representational sample of Central Indian origin. P H Quanjer et al. in their study on influence of sample size on reference equations have mentioned that for any ethnic group prediction equations derived from less than 150 individuals for each sex are unlikely to be reliable (20). In the present study sample size was more than 150 for both males and females making the results valid.

One important limitation of the study was inability to get healthy subjects with acceptable spirometry in ages above 60 making the equations valid up to 60 years of age only. This limitation must be kept in mind while using these prediction equations. An attempt will be made to recruit only elderly healthy people to formulate separate prediction equations for elderly adults in our future work.

Even with all these limitations, the present study is important as there is paucity of data on prediction equations for PFT in Indian subcontinent as quoted by Quanjer et al. (2012). These workers have formulated global prediction equations for Caucasians but failed to design the same for non Caucasians. They have suggested use of other equations for non-Caucasians (21).

The strength of the study is the valid current measurement protocol and statistical methods used to formulate prediction equations for PFT. Even more important is the fact that these are the first ever equations proposed for Central Indian population.

Conclusion

Prediction equations proposed in this study are in total disagreement with commonly used recorders equations which were derived from a different population. Interpretation of spirometry based on wrongly chosen prediction equations is a major clinical disadvantage. Therefore, the use of these prediction equations is advocated for Central Indian adult population till the generation of newer prediction equations in multi-centric study with random sampling involving a very large sample size.

References

1. American Thoracic Society. Medical Section of the American Lung Association. Lung function testing: Selection of reference values and interpretative strategies. *Am Rev Respir Dis* 1991; 144: 1202–1218.
2. Jain SK, Ramiah TJ. Normal standards of pulmonary function tests for healthy Indian men 15-40 years old: Comparison of different regression equations (prediction formulae). *Indian J Med Res* 1969; 57: 1453–1466.
3. Jain SK, Gupta CK. Age, height and body weight as determinants of ventilatory norms in healthy men above forty years of age. *Indian J Med Res* 1967; 55: 612–619.
4. Kamat SR, Sarma BS, Raju VR, Venkataraman C, Balkrishna M, Bhavsar RC, et al. Indian norms for pulmonary function: observed values, prediction equations and intercorrelation. *J Assoc Physicians India* 1977; 25: 531–540.
5. Chatterjee S, Saha D, Chatterjee BP. Pulmonary function studies in healthy non-smoking men of Calcutta. *Ann Hum Biol* 1988; 5: 365–374.
6. Udwadia FE, Sunavala JD, Shetye VM, Jain PK. The maximal expiratory flow-volume curve in normal subjects in India. *Chest* 1986; 89: 852–856.
7. Vijayan VK, Kuppurao KV, Venkatesan P, Sankaran K, Prabhakar R. Pulmonary function in healthy young adult Indians in Madras. *Thorax* 1990; 45: 611–615.
8. Gupta SS, Sawane MV. A comparative study of the effects of yoga and swimming on pulmonary functions in sedentary subjects. *Int J Yoga* 2012; 5(2): 128–133.
9. Jagzape A, SawaneM, Sawane A, Jagzape T. Impact of Bioaerosol exposure on respiratory status of vegetable market workers in Nagpur, India. *J Datta Meghe Inst Med Sci Univ* 2013; 8(3): 158–163.
10. Jagzape A, Sawane M. Respiratory status of workers in occupations with organic dust. Scholar's Press (November 28, 2014) ISBN-10: 3639668812, ISBN-13: 978-3639668810, Paperback Edition, 120 pages.
11. Glindmeyer HW, Diem JE, Jones RN, Weill H. Non-comparability of longitudinally and cross-sectionally determined annual change in spirometry. *Am Rev Respir Dis* 1982; 125: 544–548.
12. Xu X, Laird N, Dockery DW, Schouten JP, Rijcken B, Weiss ST. Age, period, and cohort effects on pulmonary function in a 24-year longitudinal study. *Am J Epidemiol* 1995; 141: 554–566.

13. Bandyopadhyay A, Dalui R, Pal S, Bhattacharjee I, Goswami B, Roy AS. Pulmonary function in young females of Kolkata, India – Revisited. PhysiolInt 2016; 103: 191–201.
14. Jones AY, Dean E, Lam PK, Lo SK. Discordance between lung function of Chinese university students and 20-year-old established norms. *Chest* 2005; 28: 1297–1303.
15. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates RA, et al. Standardisation of spirometry. *Eur Respir J* 2005; 26: 319–338.
16. Chaurasia A, Harel O. Using AIC in Multiple Linear Regression framework with Multiply Imputed Data. Health serv outcomes res methodol 2012; 12(2-3): 219–233. doi:10.1007/s10742-012-0088-8.
17. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; 1: 307–310
18. Wagner NL, Beckett, WS, Steinberg R. Using spirometry results in occupational medicine and research: Common errors and good practice in statistical analysis and reporting. *Ind J Occuenviron Med* 2006; 10(1): 5–14.
19. Chhabra SK, Kumar R, Gupta U, Rahman M, Dash DJ. Prediction equations for spirometry in adults from northern India. *Indian J Chest Dis Allied Sci* 2014; 56: 221–229.
20. Quanjer PH, Stocks J, Cole TJ, Hall GL, Stanojevic S. Influence of secular trends and sample size on reference equations for lung function tests. *Eur Respir J* 2011; 37: 658–664.
21. Quanjer PH, Stanojevic S, Cole TJ et al. Multi-ethnic reference values for spirometry for 3–95 year age range: the global lung function 2012 equations. *Eurrespirj* 2012; 40(6): 1324–134.