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An Evaluative Study of Diffusing Lung Capacity in Normal young adults Aged between 16 to 29 in Mumbai Metropolitan

Authors
Dr Arjun Ramaswamy, Dr P.V. Potdar, Dr Shubham Dewedi
MGMIHS

Abstract
Pulmonary function test in the form of spirometry, measurement of lung volume including total lung capacity (TLC), functional residual capacity (FRC) , Residual volume (RV) & single breath diffusion capacity measurement were done in 100 healthy young volunteers from Mumbai metropolitan region area. Regression equations were derived for young men & women for predicting normal values of diffusion capacity (DLCO).

Introduction

Lung functions in normal healthy individual depends on, age, sex, height, ethnicity, physical activity, environmental conditions, altitude & socioeconomic status. Body weight was found to be one of the variable determining DLCO in Spanish females[1] though this remains controversial. India being amultiethnic country the criteria for normal can vary from place to place. Various geographical and climatic conditions in a vast country like India could also contributeto variation in normal values. Rapid urbanization, globalization & free market economy have caused shift of population from rural to urban areas in the form of metropolitan cities. Mumbai metropolitan area is a large urbanized conglomeratewith people from all over India.In a cosmopolitan city like this patients often have mixed ethnic background.

Various Indian authors have derived prediction formulas for distinct ethnic background population like north Indians[5] and Tamils[4]

Ideally prediction equation for each ethnic group should be prepaid with the help of large sample size & standardized equipment & fixed concentrate of inspired oxygen across a wide range of age

DLCO measurement as a part of pulmonary function test is important in evaluation of patients with emphysema, interstitial lung disease & pulmonary vascular disease.

Extrapolation of predictions equation prepared from young normal to elderly normalis not acceptable as proved by studies in normal population over the age of 70 in European[10]& American[11] populations.

Lastly methodical difference would also contribute to differences in prediction equations. Though the current methods are automated the difference in gas analysis, flow measuring devices; analogue to digital converters might influence the normal values.[12,13,14]

In a mixed ethnicity population like Mumbai where 16 major languages are spoken & 8 major

religions groups live for generations it is often a challenging to define what represents a normal or astandard. With this problem in mind we set out to find normal values for diffusion capacity for this area.

Methods

The study was approved by the institutional ethical committee.

Subject Selection – In total l00 subjects were studied which included 61 males & 39 females. Subjects were healthy students undergoing post graduate & undergraduate studies of our institute. Normals were defined as asymptomatic, non-smoker with no past history of any respiratory & cardiac illness, chest injury or operation. All subjects had normal physical examination; chest radiography & 12 lead ECG.

A written informed consent was taken from all the subjects.

Subject were tested in the morning hours between 10 am to 1 pm .PFT Lab room temperature varied between 21 to 27^0 C.Spirometry & DLCO were performed by a computer based automated system (Master lab pro – vision 4.3 from JAEGER – GERMANY).

Volume calibration was performed daily. Gas analyzer calibration was performed weekly

The test procedure was explained and demonstrated to the subject before test. Spirometry & DLCO was measured in a sitting position with nose clips &breathing through a mouthpiece of the spirometer. At least three vital capacities were obtained in each subject.DLCO was measured by single breath method DLCO–SB (modified Krogh method). Total lung capacity was measured by helium dilution method together with the measurement of DLCO – SB. Since measurement procedure of DLCO SB involves the same spirometry-breathing maneuver, after exhaling to the residual volume, the subject inhaled maximally, a gas mixture containing 0.29 % Co – 9%, Helium & 27% oxygen for the inspiratory bag of the diffusion apparatus.This is followed by breath – holding at full lung inhalation & then performing a rapid exhalation washing out dead space air followed by collection of alveolar sample in the expiratory bag. The concentration of CO& helium in the inspired & expired gas were analyzed. Inspired volume should be more than 85- 90 % of the previously measured vital capacity & inspiration was completed within 2 – 3 seconds. Breath holding time was set at 9seconds. Valsalva or miller maneuvers were avoided. Effective breath holding time was calculated using method of Jones and Mead and kept between 10 +/- 2 seconds. Expiratory maneuver was smooth, unforced & without interruption .The total exhalation time was less than 4 seconds with sample collection time less than 3 seconds. The DLCO was expressed in mill moles co/min/mm hg at standard temperature & pressure. dry. (STPD) It was corrected for hemoglobin. Correction for altitude was not requested as Mumbai metropolitan region area is sea level.

Statistical analysis was carried out. Data are presented as mean +/- standard deviation. Pearson's correlation analysis & univariate regression were carried out to identify significant predictor variables for DLCO, VA. Gender specific linear prediction equations were developed by simple regression analysis with DLCO value as department variable.

Results

Demographic details of all patients together & male, females separately are shown in table 1-4

Mean age of male group was 24.85 (STD – 2.064)

Mean height of male group was 169.82 cm (STD – 10.33)

Mean BMI of male group was 22.20(STD –3.83).

The corresponding values in 39 females were 24.18 yrs (STD 3.042), 164.54 (STD -10.13)& 22.41 (STD 3.98) respectively.

Spirometric data, DLCO & TLC for all 100 subjects, 61 males & 39 females are presented in table 5, 6, & 7 respectively.

The mean DLCO for male group (61) was 8.28 mmol (STD 1.158) minimum 4.04 & maximum 11.39

The mean DLCO for female group (39) was 7.78 (STD 1.71), minimum 4.30 & maximum 11.28.

Mean TLC in male group was 4.57 (STD.82) & in female group was 4.32(STD 0.95)

Mean alveolar volume in male & female group was 4.48 (STD 0.78) & 4.19 (STD 0.93) respectively.

Correlation matrix for male and female are given in table 8 & 9 respectively

Linear regression & prediction formula for DLCO in males is presented in table 10 & 11

Linear regression & prediction formula for alveolar volume in males is presented in table 12 &13.

Linear regression & prediction formula for DLCO & alveolar volumes in females are presented in Table 14 15 16 & 17respectively

Table 1: Age group and Sex wise distribution of subjects

Age group	Sex		Total
	Female	Male	
15 – 19	2	0	2
20 – 24	15	28	43
25 – 29	22	33	55
Total (%)	39	61	100

Table 2: Overall

Parameters	N	Min	Max	Mean	SD
Age (yrs)	100	16	29	24.59	2.499
Weight (kg)	100	30.00	100.00	63.0400	13.75685
Height (cms)	100	140.00	184.00	167.7600	10.52186
BMI	100	15.30	35.70	22.2820	3.87114
HB	100	11.00	18.00	14.2230	1.30669

Table 3: Male

Parameters	N	Min	Max	Mean	SD
Age (yrs)	61	21	28	24.85	2.064
Weight (kg)	61	44	90	64.89	12.22
Height (cms)	61	140	184	169.82	10.33
BMI	61	15.60	35.70	22.20	3.83
HB	61	11.0	16.0	14.34	1.09

Table 4: Female

Parameters	N	Min	Max	Mean	SD
Age (yrs)	39	16	29	24.18	3.042
Weight (kg)	39	30	100	61.51	15.91
Height (cms)	39	140	182	164.54	10.13
BMI	39	15.30	30.90	22.41	3.98
HB	39	11.0	18.0	14.04	1.59

Table 5: Spirometric, Total Lung Capacity & Diffusion Capacity values for all 100 patients

	FEV1	FVC	DLCO / SB	VA	DLCO/VA	TLC /SB
Mean	3.0159	3.5234	8.0885	4.3699	1.8509	4.47726
Std Deviation	0.5997	0.7366	1.414	0.8557	1.794	0.88211
Minimum	1.68	1.68	4.04	2.57	2.373	2.05
Maximum	4.44	5.24	11.39	6.47	1.693	6.57

Table 6: Males

Pulmonary Function (Male)	Minimum	Maximum	Mean	Std. Deviation
FEV1	2.30	4.44	3.1784	.5597
FVC	2.74	5.24	3.6649	.6158
DLCO/ SB	4.04	11.39	8.2841	1.1581
VA	3.11	6.47	4.4839	.7852
DLCO / VA	1.53	3.25	1.9036	.2348
TLC / SB	2.05	6.57	4.5720	.8253

Table 7: Females

Pulmonary Function	Minimum	Maximum	Mean	Std. Deviation
FEV1	1.68	4.17	2.7618	.5777
FVC	1.68	4.69	3.3021	.8558
DLCO/ SB	4.30	11.28	7.7826	1.7132
VA	2.57	6.11	4.1915	.9384
DLCO / VA	1.43	7.68	2.0174	.9564
TLC / SB	2.65	6.24	4.3290	.9563

Table 8: Correlation Matrix for Male (Number – 61)

		Age	Wt	Ht	FEV1	FVC	DLCO	VA	TLC
FEV1	R	.199	.324*	.485**					
	P- value	.124	.011	.000					
FVC	R	.369**	.355**	.495**	.924**				
	P- value	.003	.005	.000	.000				
DLCO SB	R	.108	.160	.358**	.747**	.717**			
	P- value	.408	.218	.005	.000	.000			
VA	R	.209	.159	.462**	.838**	.856**	.797**		
	P- value	.106	.220	.000	.000	.000	.000		
TLC – SB	R	.171	.215	.492**	.801**	.822**	.727**	.923**	1.000
	P- value	.189	.096	.000	.000	.000	.000	.000	

** Correlation is significant at 0.01 level (2-tailed).i.e. P<0.01
* Correlation is significant at 0.05 level (2-tailed). i.e. P<0.05
Here Correlation Coefficient = r

Table 9: Correlation Matrix for Female (Number – 39)

		Age	Wt	Ht	FEV1	FVC	DLCO	VA	TLC
FEV1	R	.253	.445**	.351*					
	P- value	.121	.005	.029					
FVC	R	.243	.510**	.433**	.924**				
	P- value	.137	.001	.006	.000				
DLCO SB	R	.308	.422**	.374*	.767**	.831**			
	P- value	.056	.007	.019	.000	.000			
VA	R	.262	.500**	.423**	.847**	.933**	.894**		
	P- value	.107	.001	.007	.000	.000	.000		
TLC - SB	R	.280	.526**	.444**	.847**	.934**	.893**	1.000**	1.000
	P- value	.084	.001	.005	.000	.000	.000	.000	

** Correlation is significant at 0.01 level (2-tailed).i.e. P<0.01
*Correlation is significant at 0.05 level (2-tailed). i.e. P<0.05
Here Correlation Coefficient = r

FEV1 and FVC are statistically significant at 5% level i.e., P<0.05, It shows that the pulmonary function of male has significant difference from female patients. But other parameters like DLCO/SB , VA , DLCO/VA and TLC/SB are not statistically significant at 5% level that means there is no difference between males and females of their pulmonary function.

Table 10: Linear Regression for Male – DLCO

Linear Regression Analysis: Dependent Variable DLCO and it depends on independent variables Age, Height and weight

Model					
Linear Regression	R	R^2	F Test	P – value	Significant at 5 % level
DLCO with Age ,Ht& Wt	0.364	0.132	2.899*	0.043	Yes

Table: 11 Prediction formula of DLCO (Male)

Parameters	Equation	Adjusted R^2	St. Error of Estimate
DLCO	0.616+0.036xAge-0.003xWt+0.041xHt	0.087	1.1067

Table: 12 Linear Regression Analysis: Dependent variable VA (Males)

Model					
Linear Regression	R	R^2	F Test	P – value	Significant at 5 % level
VA with Age , Ht & Wt	0.497	0.247	6.236	0.001	Yes

Table: 13 Prediction formulas VA (Males)

Parameters	Equation	Adjusted R^2	St. Error of Estimate
VA	-3.067+0.064xAge- 0.008xWt+0.038xHt	0.207	0.6990

Table – 14: Linear Regression for Female – DLCO

Linear Regression Analysis: Dependent Variable DLCO and it depends on independent variables Age, Height and weight

Model					
Linear Regression	R	R^2	F Test	P – value	Significant at 5 % level
DLCO with Age ,Ht& Wt	0.432	.186	2.670	0.063	No

Table 15: Prediction formula of DLCO (Females)

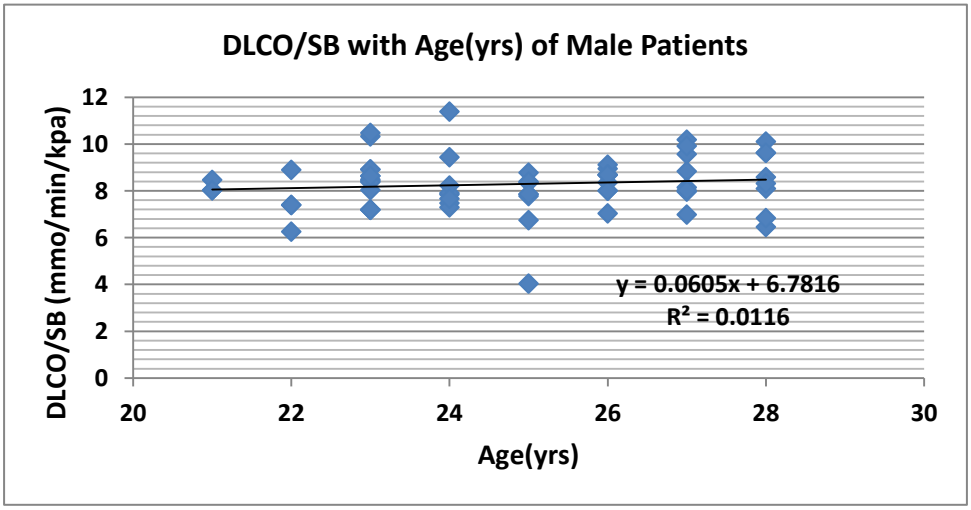
Parameters	Equation	Adjusted R^2	St. Error of Estimate
DLCO	1.759+0.043xAge-0.030xWt+0.018xHt	0.116	1.6103

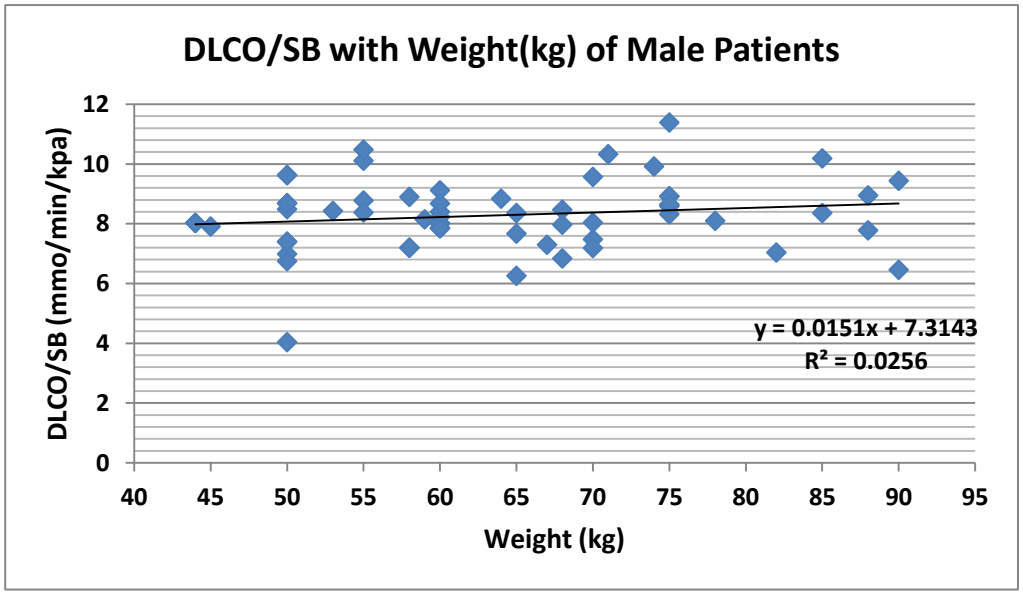
Table: 16 Linear Regression Analysis: Dependent Variable VA (Females)

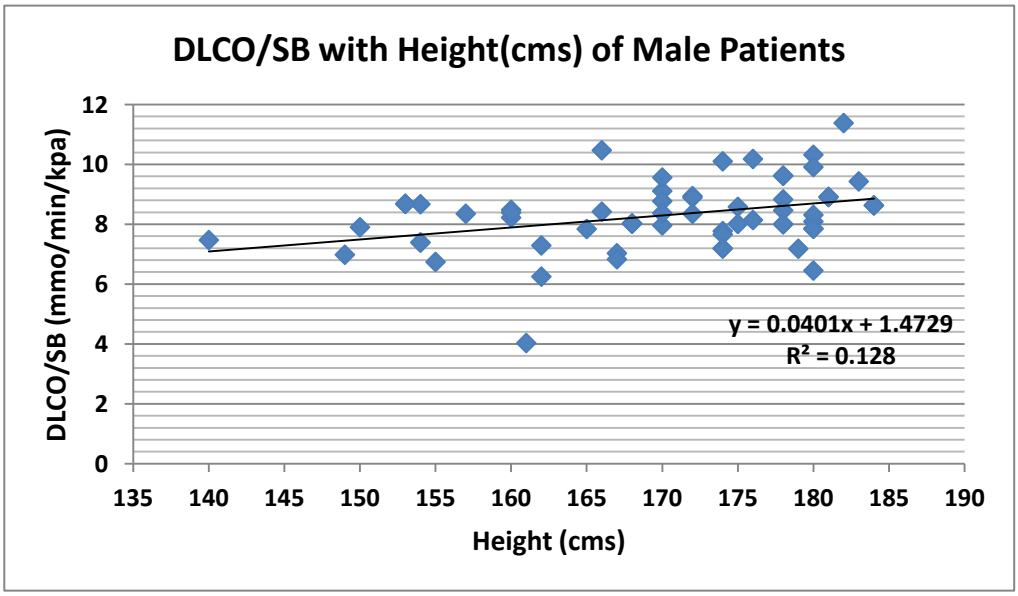
Model					
Linear Regression	R	R^2	F Test	P – value	Significant at 5 % level
VA with Age , Ht & Wt	0.506	0.256	4.009	0.015	Yes

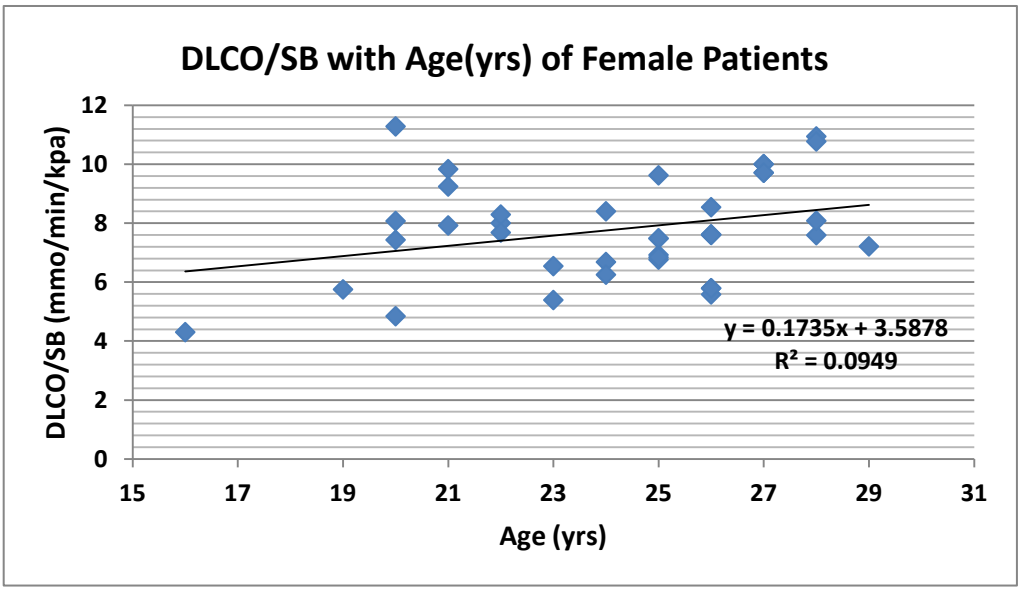
Table: 17 Prediction formulas VA (Females)

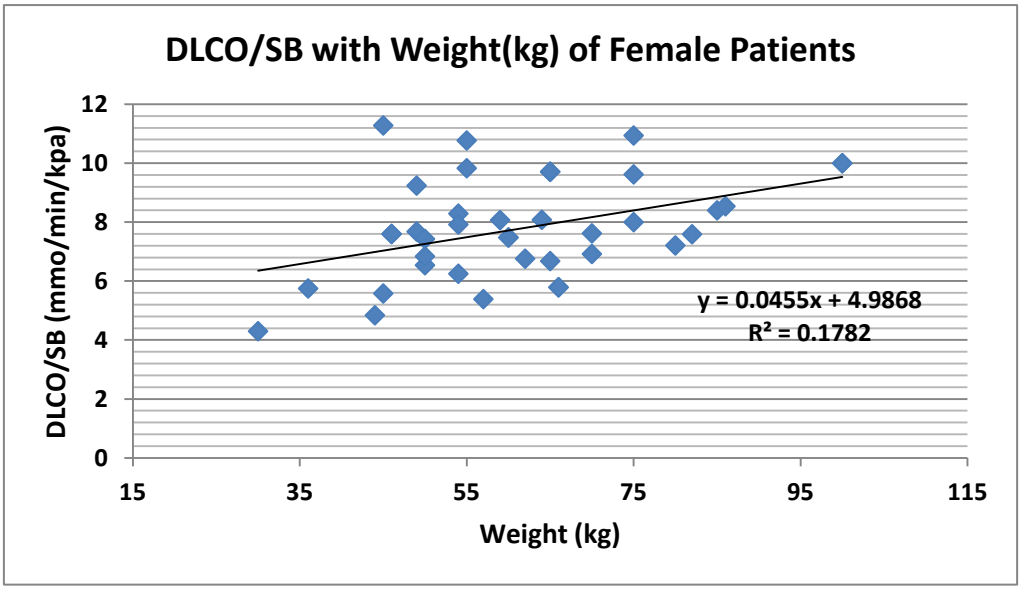
Parameters	Equation	Adjusted R^2	St. Error of Estimate
VA	1.889-0.023xAge+0.028xWt+0.0066xHt	0.802	0.297

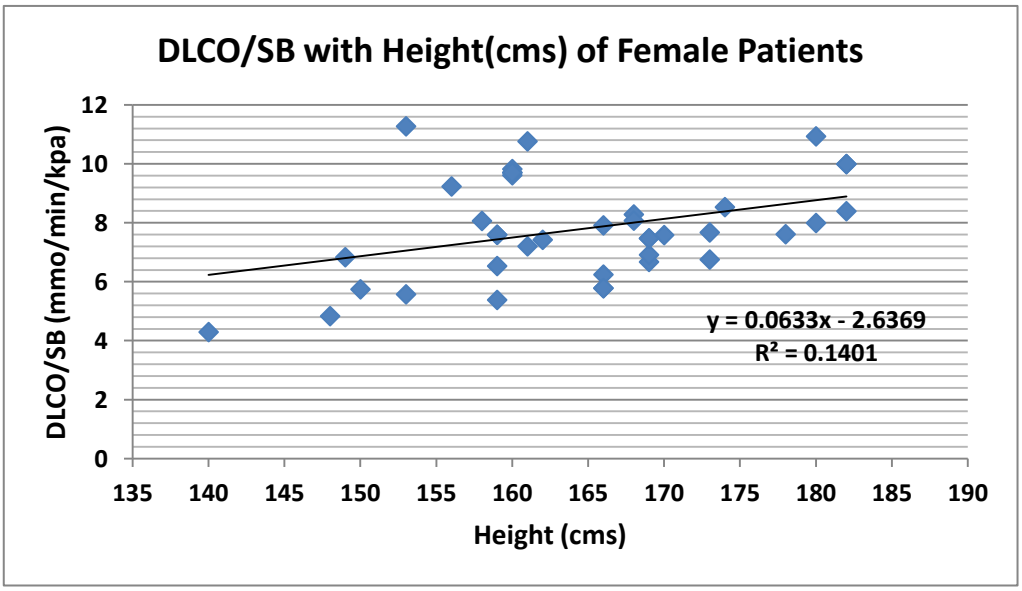



DLCO/SB with Weight(kg) of Male Patients
DLCO/SB (mmo/min/kpa)
Weight (kg)
y = 0.0151x + 7.3143
R² = 0.0256


DLCO/SB with Height(cms) of Male Patients
DLCO/SB (mmo/min/kpa)
Height (cms)
y = 0.0401x + 1.4729
R² = 0.128


DLCO/SB with Age(yrs) of Female Patients
DLCO/SB (mmo/min/kpa)
Age (yrs)
y = 0.1735x + 3.5878
R² = 0.0949





Discussion

Pulmonary function test is an important component of assessment of patients suffering from cardiopulmonary ailments. Apart from diagnostic values, PFTs are important in the evaluation of impairment and disability. Diffusion capacity is of particular importance in the assessment of patients suffering from emphysema, intestinal lung disease and pulmonary vascular disease. Diffusion capacity can be measuredby various techniques including the single breath, rebreathing and intra breathing methods. The single breathing method (DLCOsb) is most commonly used. DLCOsb is non invasive and can be repeated easily to obtain multiple measurements. Varieties of automated DLCOsb systems are available.

The ATS ERS have published standardization guidelines for DLCOsb

Careful attention to standards and clinical practice guidelines can reduce the variability in DLCOsb measurements in different laboratories.

Despite of all precautions, DLCOsb values have deferred from lab to lab even in the population of the same ethnic origin. The guidelines issued by ATS ERS recommend use of reference equations appropriate to the lab methods and patient population.

Spirometric measurements in the form of FEV1, FVC are highly dependent on ethnic group also. (Apart from height age and gender). Hence variability of diffusion capacity from one race to another is not surprising.

Results of lung function studies in normal subjects are available for south[5] north[7] and West Indian subjects. In general south Indians had lower values for spirometry compared to north Indians and Caucasians. Based on earlier studies from India and abroad we had identified age height and weight as possible predictors of DLCO.

Using our prediction formula the DLCO value of an average young male patient was compared with different Indian equations. our value of 8.266 was closest to that of Udwadiya (8.6) and lower than that of south Indian and Caucasian populations respectively.

Using our prediction formula for female with age weight and height as variables DLCO was 4.039mmol/min. This value was significantly lower as compared to the values derived from other investigators. This is not explicable easily. Compared to other investigators our study is limited by small sample size. Variability with age and height also can't be assessed satisfactorily with such a narrow range of age height and weight.

Apart from variability related to sample size, other factors in the form of procedure variations like variable Fio2, patient cooperation are also important. Reliability of smoking status was not corroborated by carboxyHb measurements.

Conclusion:

The DLCOmeasurements using our prediction formula are comparable to those of Udwadiyas[5] but significantly lower compared to those of Vijayans [4]. Taking into consideration multiethnic nature of population in metropolitan cities, we feel it is necessary to derive your own prediction formula, which is relevant to local population. In view of the small sample size we plan to check the validity of the prediction equation in a large sample size in the future.

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