

*Tanaffos* (2005) 4(15), 19-26

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# Spirometric Standards for Healthy Iranians Dwelling in the Centre of Iran

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## ABSTRACT

**Background:** In order to determining spirometric reference values in healthy, nonsmoker adult subjects, this study was performed on populations dwelling in the centre of Iran, Kashan city. The area was selected as the representative of a less polluted area in Iran, as we intended to exclude possible effects of air pollution on spirometric values.

**Materials and Methods:** The study was performed on 550 subjects (295 Males, 255 Females) aged 17 to 82 years, randomly selected from the general population, and assessed anthropometrically for age and height by using stepwise regression analysis. The prediction equations were calculated on the basis of age and height for forced vital capacity (FVC), forced expiratory volume in one second (FEV<sub>1</sub>), and forced expiratory flow during the middle half of the FVC (FEF<sub>25-75%</sub>). Comparisons with predictions of other Caucasians studies are reported.

**Results:** A Comparative study of FVC and FEV<sub>1</sub> values of our subjects, standardized for age and height was much closer to FVC and FEV<sub>1</sub> of other studies. The prediction equations (based on age and standing height) for FVC (liters) in males:  $-5.546 + 0.065 \text{ height} - 0.027 \text{ age}$ ; and females  $-3.214 + 0.046 \text{ height} - 0.023 \text{ age}$ ; FEV<sub>1</sub> (liters) in males:  $-2.853 + 0.046 \text{ height} - 0.029 \text{ age}$ ; and females:  $-2.430 + 0.039 \text{ height} - 0.024 \text{ age}$ ; for FEF<sub>25-75%</sub> in males:  $+ 1.987 + 0.027 \text{ height} - 0.044 \text{ age}$ ; and females:  $- 0.769 + 0.037 \text{ height} - 0.033 \text{ age}$ .

**Conclusion:** A comparison between equation from the present study and other available reference data shows that our prediction values were similar to those previously reported. The present regression equations for predicted values of lung function measurements may be regarded as the definitive norms for adult population dwelling in the centre of Iran and will be useful for diagnostic and research purposes. (*Tanaffos* 2005; 4(15): 19-26)

**Key words:** Prediction equation, Reference values, Spirometry standards

## INTRODUCTION

Spirometry, which is probably the most important tool in screening for pulmonary disease, is the most frequently performed pulmonary function test. Measurements of lung function are important for the

evaluation of complete assessment of persons with respiratory disease. Correct interpretation of pulmonary function tests requires the use of appropriate reference values with which the patient's results are compared. A wide selection of published reference values and "Lower limits of normal" is available (1). Unlike many physiologic parameters, for which normal values do not vary with the

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characteristics of the particular patient, predicted values of pulmonary function depend upon age, height, gender and race. Several standard values of lung function indices for European and Americans of all ages have been established (2-4).

In 1991 the American Thoracic Society (ATS) published a listing of pulmonary function reference values and recommendations for interpretative strategies (5). The ATS statements by the ATS on standardization of spirometry (update 1994) had been reflected the changes in clinical emphasis and equipment that include: 1-The strong emphasis on the use of portable peak flow meters to monitor lung function, 2-A better understanding of the complexities of correcting spirometric values to BTPS conditions, 3-A greater appreciation of the importance of the technicians and procedures in achieving good spirometric results (6).

Unfortunately, a specific set of reference equations was not recommended; in comparison, the European Respiratory Society made specific recommendations in 1983 (1). For spirometry testing, a recent survey of pulmonary function laboratories showed about equal use of equations from the studies of Crapo (7), Morris (8), and Knudson (9) for adults, whereas most used the study of Polgar (10) for children. Recently Garcia et al. underscored the importance of using prediction equations appropriate to the origin, age and height characteristics of the subjects being studied (11).

Masjedi and Coworkers (12) in Iran had determined spirometric reference values previously among 275 healthy persons and recently it has been reported in 4 to 18 years old children (13). In another study Golshan and colleagues obtained spirometric reference values from a large randomly selected healthy nonsmoker subjects in Isfahan, Iran (14).

The purpose of this research was providing spirometric reference equations for the healthy non – smoker males and females dwelling in the center of Iran, Kashan city.

## MATERIALS AND METHODS

The study was conducted on a sample population of adult subjects (aged from 17 to 82 years) of both sex who were resident in Kashan and underwent spirometry. The subjects were selected randomly. Method of selection was arranged by referring to health service system of Kashan. Number of families participated in polio vaccination project was obtained. Through interviews and physical examination, 705 subjects were selected by simple random sampling and were invited to participate in this study. All adult subjects seen consecutively during 6 month periods were enrolled prospectively into the study. Spirometry was scheduled in the morning of examination. Subjects were selected for the study who were never – smoker and had no diagnostic symptoms (cough and / or phlegm on most days for 3 months per year; chest tightness; shortness of breath; wheeze; asthma; pneumonia; tuberculosis; thoracic surgery; or abnormal chest X – ray).

Anthropometric measurements included the followings: standing height without shoes with the subject's back adjacent to a vertical backboard and weight. Age was recorded to the nearest birthday. Barometric pressure and temperature were registered every morning. Variations of barometric pressure that measured by instrument of blood gas analyzer (AVL 995) were less than 5 mmHg. All subjects underwent evaluation using a spirometer (ST – 95 Fukuda, Japan). Spirometry was conducted in accordance with American Thoracic Society (ATS) recommendation (6). In this statement on spirometry,

a change in reproducibility criteria to a constant 200 ml and the extrapolated volume lower limit from 100 to 150 ml was approved. The ATS also recommended that three acceptable and reproducible maneuvers should be performed. A single technician experienced in spirometry performed all tests. The system was calibrated with a 3-liter syringe daily in the morning. The technician also performed a daily control by assessing his own lung function. The subject was sitting during the test, and a nose clip was used.

In this study we examined only one part of the recorded volume and flow values: forced vital capacity (FVC), forced expiratory volume in 1 second (FEV<sub>1</sub>), the forced expired flow from 25 to 75% of the FVC (FEF<sub>25-75%</sub>), computed from the test with the largest sum of FEV<sub>1</sub> and FVC. Stepwise multiple linear regressions of lung function on height and age were performed separately for each group of male and female subjects (6). Results for the various variables studied were expressed as mean  $\pm$  SD. Statistical significance was assumed for  $p < 0.05$ . The lower limit of normal (LLN) range was calculated as follows:

$$\text{LLN} = \text{predicted value} - 1.645 \times \text{RSD}$$

Calculations were performed using statistical SPSS software.

## RESULTS

Of the 705 subjects initially invited for interview and spirometry, 155 were excluded due to various reasons including: history of smoking, cardiopulmonary diseases and inability to provide acceptable spirometric manoeuvres. The remaining 550 subjects (295 males, 255 females) with an age range of 17 to 82 years were included in analysis

(Fig 1).

All the spirometric values (FVC, FEV<sub>1</sub> and FEF<sub>25-75%</sub>) were greater in male subjects as compared with female subjects (Table 1). Stepwise regression analyses of spirometric parameters on height and age were performed separately for men and women (Table 2). Input variables were height and comparison with other studies is presented in tables 3 and 4.

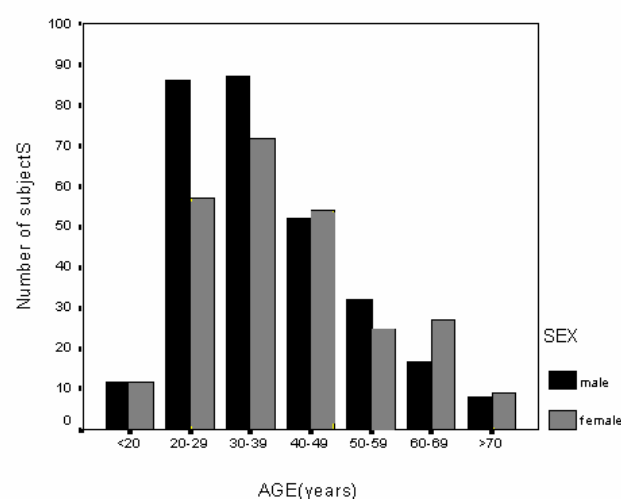


Figure 1. Age distribution in the study population

Table 1. Body measurements and spirometric data\*

Parameter	Male (n = 295)	Female (n = 255)
Age, (Yr)	37.4 (13.13)	39.7 (14.3)
Height, (cm)	169.9 (6.8)	155.9 (6.2)
FVC, (lit)	4.47 (0.81)	3.03 (0.61)
FEV <sub>1</sub> (lit)	3.94 (0.68)	2.72 (0.56)
FEF <sub>25-75%</sub> (L/S)	4.92 (1.09)	3.59 (0.87)

\* Values are mean  $\pm$  (SD)

**Table 2.** Regression equations for prediction of normal lung function in adult Kashan population, dwelling in the centre of Iran.

Variable	Equation	r <sup>2</sup>	SEE	p. value
<b>Male</b>				
FVC	0.062271H-0.027131A-5.086	0.68	0.47	0.001
Lower limit of normal	0.062271H-0.027131A-5.165			
FEV1	0.043822H-0.028801A-2.425	0.73	0.40	<0.001
Lower limit of normal	0.043822H-0.028801A-2.491			
FEF 25-75%	0.026752H-0.043170A+2.008	0.37	0.65	<0.001
Lower limit of normal	0.026752H-0.043170A+1.902			
<b>Female</b>				
FVC	0.046167H-0.022557A-3.274	0.73	0.38	<0.001
Lower limit of normal	0.046167H-0.022557A-3.337			
FEV1	0.039489H-0.023593A-2.498	0.79	0.35	<0.001
Lower limit of normal	0.039489H-0.023593A-2.556			
FEF 25-75%	0.036296H-0.034202A-0.694	0.49	0.57	<0.001
Lower limit of normal	0.036296H-0.034202A-0.787			

FVC: forced vital capacity; FEV1: forced vital capacity in one second; FEF25-75%: expiratory flow from 25 to 75% of the vital capacity; H: Height in cm; A: age in years; r<sup>2</sup>: regression coefficient; SEE: standard error of the estimate

**Table 3.** Predicted values for FEV<sub>1</sub> and FVC derived from Selected Studies of Nonsmoking Caucasian Men\*.

First Author, Year (Ref)	Age Range (Yr)	Number Studied	FEV <sub>1</sub> <sup>†</sup> for Ht 1.75 m, Age 45 Yr	Regression <i>Coefficient</i>		RSD OR SEE	FVC <sup>†</sup> for Ht 1.75 m, Age 45 Yr	Regression <i>Coefficient</i>		RSD OR SEE
				Ht	Age			Ht	Age	
Morris, 1971 (8)	20-84	517	3.63	3.62	-0.032	0.55	4.84	5.83	-0.025	0.74
Cherniak, 1972 (37)	15-79	870	3.74	3.59	-0.023	NR	4.52	4.76	-0.014	NR
Quanjier, 1983 (1)	21-64	186	3.59	4.05	-0.031	0.43	4.51	6.11	-0.032	0.64
Crapo, 1981 (7)	15-91	125	3.96	4.14	-0.024	0.49	4.89	6.00	-0.021	0.57
Knudson, 1983 (9)	25-84	86	3.81	6.65	-0.029	0.52	4.64	8.44	-0.030	0.64
Dockery, 1985 (27)	25-74	624	3.78	Equation* non – linear		0.40	4.72	Equation* non – linear		0.47
Roca, 1986 (36)	20-70	443	3.95	4.99	-0.021	0.44	5.15	6.78	-0.015	0.53
Paoletti, 1986 (30)	26-64	59	3.83	4.94	-0.027	0.48	5.06	7.24	-0.027	0.58
Miller, 1986 (32)	18-85	176	3.94	5.66	-0.023	0.41	4.84	7.74	-0.021	0.51
Masjedi, 1988 (12)	17-65	167	3.82	4.60	-0.045	NR	4.77	5.68	-0.039	NR
Golshan, 2003 (14)	21-82	1302	3.99	4.53	-0.026	0.43	4.66	5.65	-0.025	0.53
Present study	17-82	295	3.95	4.38	-0.029	0.40	4.59	6.23	-0.027	0.47

\* Predicted FEV<sub>1</sub> or FVC = Predicted value for Ht 1.75 m, Age 45 + Ht Coefficient × (Ht – 1.75) + Age Coefficient × (Age – 45).

† Predicted value for Ht = 1.75 m, Age = 45 Yr.

\*FEV<sub>1</sub> = Ht<sup>2</sup> (1.541 – 4.06 × 10<sup>-3</sup> Age – 6.14 × 10<sup>-5</sup> Age<sup>2</sup>);

FVC = Ht<sup>2</sup> (1.75-1.35 × 10<sup>-4</sup> Age – 1.01 × 10<sup>-4</sup> Age<sup>2</sup>).

RSD = residual standard deviation; SEE = standard error of the estimate;

NR = not reported

**Table 4.** Predicted values for FEV1 and FVC derived from Selected Studies of Nonsmoking Caucasian Women\*.

First Author, Year (Ref)	Age Range (Yr)	Number Studied	FEV <sub>1</sub> <sup>†</sup> for Ht 1.65 m, Age 45 Yr	Regression		RSD OR SEE	FVC <sup>†</sup> for Ht 1.65 m, Age 45 Yr	Regression		RSD OR SEE
				Coefficient	Ht Age			Coefficient	Ht Age	
Morris, 1971 (8)	20-84	471	2.72	3.50-0.025		0.47	3.54	4.53 -0.024		0.52
Cherniak, 1972 (37)	15-79	452	2.87	2.37-0.019		NR	3.36	3.08 -0.015		NR
Quanjor, 1983 (1)	21-64	514	2.71	3.17-0.031		0.35	3.39	4.64 -0.027		0.42
Crapo, 1981 (7)	15-84	126	2.92	3.42-0.026		0.33	3.54	4.91 -0.022		0.39
Knudson, 1983 (9)	20-87	204	2.79	3.09-0.020		0.39	3.36	4.27 -0.017		0.49
Dockery, 1985 (27)	25-74	1830	2.79	Equation* non – linear		0.40	3.41	Equation* non – linear		0.47
Roca, 1986 (36)	20-70	427	2.87	3.17-0.025		0.31	3.72	4.54 -0.021		0.40
Paoletti, 1986 (30)	21-64	313	2.84	2.43-0.020		0.29	3.78	4.12 -0.015		0.39
Miller, 1986 (32)	18-82	193	2.91	2.68-0.025		0.33	3.59	4.14 -0.023		0.45
Masjedi, 1988 (12)	18-65	108	2.76	3.12-0.032		NR	3.34	3.51 -0.028		NR
Golshan, 2003 (14)	21-80	1110	2.99	3.72 -0.024		0.30	3.47	4.70 -0.025		0.38
Present study	17-82	255	2.96	3.95 -0.024		0.35	3.33	4.62 -0.023		0.38

\* Predicted FEV<sub>1</sub> or FVC = Predicted value + for Ht 1.65 m , Age 45 + Ht Coefficient × (Ht – 1.65) + Age Coefficient × (Age – 45).

† Predicted value for Ht = 1.65 m, Age = 45 Yr.

\*FEV<sub>1</sub> = Ht<sup>2</sup> (1.332 – 4.06 × 10<sup>-3</sup> Age – 6.14 × 10<sup>-5</sup> Age<sup>2</sup>);

FVC = Ht<sup>2</sup> (1.463-1.35 × 10<sup>-4</sup> Age –1.01 × 10<sup>-4</sup> Age<sup>2</sup>).

RSD = residual standard deviation; SEE = standard error of the estimate;

NR = not reported

## DISCUSSION

Several factors, such as age and anthropometric parameters have been found to influence the normal lung function values in males and females. In practice, this is usually done by a computer using linear regression equations (reference equations) for calculation of "predicted values," as determined by published studies of large number of healthy individuals (15). It is a common practice for the result of lung function tests to be interpreted in relation to reference values, and in terms of whether or not they are considered to be within the "normal" range (1, 16, 17).

Normal ventilatory function has come to mean the average spirometric values of a representative sample of healthy subjects drawn from the general

population. A reference population should, ideally, be representative of the general population from which the clientele of the laboratory comes.

Although a random sample of a population, as in our study is ideal, one report found that once hospital patients were excluded, the method for selecting the study sample used to generate reference values had relatively little effect on either the mean value or the range of values obtained (18).

Criteria for selecting reference values to be used in the clinical or in the epidemiologic context fall into three categories: methodologic, epidemiologic, and statistical (19). In Tables 3 and 4, the results of the present study are compared with linear model regression equations derived from published

reference equations for nonsmoking Caucasian men and women. Predicted values for men and women with age of 45 years are presented. The average heights for men and women in the present study, 175 cm and 165 cm respectively, were used. It is evident that the differences in age range, or selection criteria of the sample could explain some of the differences obtained.

The FVC and FEV1 values in our study are similar to those observed in other studies. In a recent reference value study of Golshan and colleagues performed in Isfahan (a city in about 200 kilometer distance in south of Kashan), the values of FVC and FEV1 in a male with height of 175 cm and 45 years of age were; 4.66 lit and 3.99 lit respectively (14), but in the present study it is 4.59 lit and 3.95 lit respectively (table 3). The height and age characteristics of present study are close to Golshan study. Work by Becklake and White, and the American Thoracic Society interpretative statement have summarised the sources of variation in lung function tests. These include technical variability due to instrument and procedures, and interactions between the patient, instrument and technician (20,5). Technical sources of variation can be as small as 3% when they are carefully controlled but can be overwhelming when they are not (21). To reduce technical variability, respiratory societies have emphasised standardising the instruments and procedures in lung function testing. Biological sources of variability include, but are not limited to, height, weight, age, sex and ethnic origin (20,5).

In the 1970, a number of reference equations were published based on data gathered in specific population groups such as laboratory personnel, workers in a particular industry, school populations, subjects attending a specific clinic, volunteers, and general industrial workers (21-25). Some are derived from population – based data gathered in epidemiologic studies carried out for other purposes;

in these studies reference equations are a by-product (8,26-29). Others are based on data gathered specifically for the creation of reference equations (6,30). The exact definition of a "healthy" group is difficult to agree upon (4,31). Previous studies have used many different criteria. The ATS spirometry interpretation workshop only states that subjects should be "never-smokers, free of respiratory symptoms and disease" (5).

Determination of the "Normal Range" can be used from fixed percent of predicted values. In most laboratories, FVC and FEV1 less than 80% of predicted value are considered as abnormal. The fixed value has no statistical basis in adults (32-35). Although some studies have shown that for adults of average age and height, 80% of predicted FVC and FEV1 is close to the fifth percentile, use of a fixed value will result in shorter, older subjects being more readily classified as "abnormal" (32-35), whereas taller, younger adult subjects are more likely to be erroneously classified as "normal". The practice of using 80% of predicted, as the lower limit of normal for FEF 25-75% or the instantaneous flows will also cause important errors since, for these flows, the lower limits of normal are closer to 50% predicted (8,29).

There remain many potential sources of differences in the spirometry reference equations, even from studies following the most recent ATS recommendations for spirometers, testing methods, quality assurance, and data analysis (5, 14, 36, 15). The population source, age cohort, socioeconomic and normative models are compared, some of the regressions predict spirometric values that differ by as much as 20% for volumes and 40% for flow rates (37). Even when healthy never – smokers were tested with comparable techniques and computation methods, predicted values can differ by as much as 10% for volumes and 20% for flow rates (7).

In conclusion, a comparison between equation

from the present study and other available reference data shows that the prediction values are similar to those previously reported. The subjects in the spirometry study of our research selected from different groups of people were all living in Kashan city, at altitude 950 m, with normal chest radiographs, and only 17 of the men and women were age at the 70 or older. Although all normative values include a unique set of limitation and specific applicability, the predicted values presented in this study should provide better precision in estimating lung function in men and women living in the centre of Iran.

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