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RESEARCH ARTICLE

GENDER DIFFERENCES IN AIRWAY DYNAMICS IN HEALTHY NONSMOKING LIBYAN MEDICAL STUDENTS

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ABSTRACT

Some of the respiratory structures and functions vary with the gender. Only 2-3 parameters of the forced vital capacity (FVC) were studied earlier in both sexes in Libyan population. In the present study, we have measured all the parameters of forced expiratory vital capacity in homogenous age group (18-20 years) of 50 male and 58 female Libyan medical students. All the values of FVC including forced expiratory volume in 1 second (FEV_1), forced expiratory flow rates (FEF) at 0.2 to 1.2 L, 25-75% of FVC and 75-85% of FVC were found to be significantly higher in male compared to female subjects. Instantaneous expiratory flows at 75%, 50% and 25% of remaining FVC in lung ($V_{max75\%}$, $Vmax_{50\%}$ and $Vmax_{25\%}$) were found to be significantly higher in male compared to female subjects. However FEV_1% (ratio of FEV_1 to FVC) and $FEF_{25-75\%}$ / FVC ratio were significantly higher in female compared to male subjects. The differences of these dynamic respiratory functions in male and female subjects may have some influences in clinical manifestation of airway disease.

Key words: Airway dynamics, forced vital capacity, instantaneous expiratory flows.

INTRODUCTION:

It has long been recognized that some respiratory structures and functions vary with gender and the variations takes place as early as fetal life. Evidence suggests that, between 25-32 weeks of gestation, the lung of human female fetuses had greater histological maturity than those of male fetuses [1]. The female fetus have increased deflation stability index by retaining more air in their lungs during deflation [2]. Earlier work suggests that the respiratory response to hypoxic stimuli differs in different sexes and that may occur during the first week of life. This response is increased in females at the time of puberty [3]. Up to puberty pulmonary volume increases steadily in both sexes, while around puberty there is marked increase in some pulmonary indices noted in boys [4]. This may be correlated with height and body built, but not depends on their sex hormone [3]. Pubertal growth surge in lung function lags a few months behind the surge of height [5]. Being dependent on body size the lung function values leveled off in girls at the age of around 15 years and in the boys around 18 years [6], reaching maximum values (at their peak values during total life span) and from the early 20s there is a gradual decline in most pulmonary indices, the pattern may vary between the individuals [5, 7].

After the onset of puberty the reproductive life in women is much protracted, dynamic and having cyclical changes than in men. Evidence suggests that female reproductive hormone modulates some of the respiratory functions [8]. Data from both human and animal studies suggests that sex hormone may contribute to disease pathogenesis or serve as protective factors, depending on the disease involved [9, 10]. Thus gender differences are an important determinant of clinical manifestation of airway disease [11]. Till date detail study of pulmonary function, especially airways function, in young adult Libyan men and women are scanty and in most cases [6, 12, 13] predicted equation but not absolute values were given. Therefore, further studies of influence of gender on absolute values of lung and airways function in healthy nonsmoker male and female Libyan subjects of early adulthood age was undertaken in order to interpret values made in those with respiratory disease.

MATERIALS AND METHODS:

The present study on pulmonary function was carried out in the department of physiology, faculty of medicine of Garyounis University, Libya. Included in this study were age matched (age range 18-20 years) eligible consenting male and female medical students who had no

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evidence of cardiopulmonary, renal, gynecologic or any other medical disorders. All students were white and were not engaged in regular physical or sports activities. Smokers, ex-smokers and passive smokers were excluded. Subjects were also excluded if satisfactory measurements could not be taken because of lack of cooperation or an inability to perform the tests. The study group comprises of 50 male and 58 female subjects. The female subjects were studied once only irrespective of the different phases of their menstrual cycle.

Spirometric tests were conducted with a wedge bellow spirometer, Vitalograph (Vitalograph Medical Instruments Ltd., Buckingham, England). Details of methods, concerning the measurements of forced expiratory spirometry with similar instrument were reported earlier [14]. In brief, the specific measurements of forced expiratory spirogram included forced vital capacity (FVC), forced expiratory volume in first one second (FEV_1), FEV_1 expressed as a percentage of FVC ($FEV_{1\%}$), maximum forced expiratory flow rate at 0.2 lit. to 1.2 lit. of FVC ($FEF_{0.2\text{-}1.2\ L}$), maximum mid expiratory flow rate at 25% to 75% of FVC ($FEF_{25\text{-}75\%}$), maximum end expiratory flow rate at 75% to 85% of FVC ($FEF_{75\text{-}85\%}$), and instantaneous flow (V_{max}) at 75%, 50% and 25% of remaining FVC. The ratio of $FEF_{25\text{-}75\%}$ to FVC was calculated. The expiratory efforts, with nose clipped, were maintained in most trials for 6 seconds. The best effort of three values within 5% or 100 ml of each other was used for analysis. The maximum FVC and FEV_1 were recorded, and flow rates were calculated from the curve with the greatest sum of FVC and FEV_1. All values were corrected for body temperature and pressure saturated with water vapor.

The experiment was carried out under similar environmental conditions during the morning hours. Room temperature was between 18-20^{0}C. On the day of the experiment, the subjects were asked to come to the laboratory without any exertion. On arrival their height and weight were recorded. Weight was recorded to the nearest 0.1 kg, and heights were recorded to the nearest 0.5 cm. Body mass index (BMI) was calculated (weight divided by height squared). During the study, each subject was given adequate demonstration of precisely how the tests (spirometry) were to be performed and proper execution of spirometry was demanded on each attempt. To make spirometry more reproducible on each attempt, the subject was encouraged to make a maximum effort.

For each of the spirometric tests in both male and female subjects, the difference between the means ±SD was evaluated with the unpaired Student's t-test. The alpha error for a significant test was set at 5% level ($p<0.5$). The percentage difference between the groups was assessed for each of the spirometric tests.

RESULTS:

Characteristics of the subjects included in the study are shown in Table 1. Male subjects of similar age were taller and had a greater mean body weight and body mass index (BMI) than the female counterpart. None of the subjects in this study were obese.

Table 2 show spirometric data in male and female subjects. Mean FVC and FEV_1 were greater ($p<0.001$) in male as compared to female subjects, 26.3% and 23.7% respectively. However, the FEV_1% was 4.2% more ($p<0.001$) in female than in male subjects.

Similarly, all the forced expiratory flow rates, $FEF_{0.2\text{-}1.2}$, $FEF_{25\text{-}75\%}$ and $FEF_{75\text{-}85\%}$, were significantly higher, 17.7% ($p<0.001$), 10.3% ($p<0.001$) and 13.4% ($p<0.01$) respectively, in male compared to female subjects. But the ratio of $FEF_{25\text{-}75\%}$ to FVC was 16.6% more ($p<0.05$) in female compared to male subjects.

The instantaneous flows (V_{max} at 75, 50 and 25 percent of remaining FVC) were significantly higher, 18.7% ($p<0.001$), 10.6% ($p<0.01$) and 13.6% ($p<0.01$) respectively, in male subjects as compared to female subjects.

Table 1: Physical characteristics of the subjects.

Variable	Male (n = 50)	Female (n = 58)	P – value
Age (year)	18.92 ± 0.695	18.88 ± 0.422	NS
Height (cm)	173.68 ± 6.908	164.31 ± 6.272	< 0.001
Weight (kg)	69.72 ± 9.829	58.24 ± 8.712	< 0.001
BMI (kg/m^2)	23.09 ± 2.680	21.52 ± 2.804	< 0.01

Data are presented as mean ± SD. NS = Not Significant. BMI = Body Mass Index.

Table 2: Spirometric data in male and female subjects.

Parameters	Male (n = 50)	Female (n = 58)	% difference from male	P - value
FVC (L)	4.56 ± 0.569	3.36 ± 0.423	- 26.3	< 0.001
FEV_1(L)	4.04 ± 0.539	3.08 ± 0.351	- 23.7	< 0.001
FEV_1%	88.82 ± 5.15	91.90 ± 4.206	+ 4.2	< 0.001
$FEF_{0.2-1.2}$ (L/sec)	7.28 ± 1.848	5.99 ± 1.259	- 17.7	< 0.001
$FEF_{25-75\%}$ (L/sec)	4.25 ± 0.652	3.81 ± 0.609	- 10.3	< 0.001
$FEF_{25-75\%}$ /FVC	0.95 ± 0.158	1.14 ± 0.206	+ 16.6	< 0.001
$FEF_{75-85\%}$ (L/sec)	2.23 ± 0.673	1.93 ± 0.488	- 13.4	< 0.01
$V_{max75\%}$ (L/sec)	6.82 ± 1.718	5.54 ± 1.092	- 18.7	< 0.001
$V_{max50\%}$ (L/sec)	4.72 ± 0.853	4.22 ± 0.746	- 10.6	< 0.01
$V_{max25\%}$ (L/sec)	2.78 ± 0.748	2.40 ± 0.633	- 13.6	< 0.01

Data are presented as mean ± SD.

DISCUSSION:

The pulmonary function test is an important investigative method in clinical medicine. Normally the pulmonary function varies with different ethnic groups, socioeconomic status, age, body size, exercise, smoking habits etc. In the present study, a narrow age range (18-20 years) of subjects were selected from both male and female nonsmoking groups of same socioeconomic status in order to minimize the effect of these variables on respiratory function and allow a more direct evaluation of differences, if at all, due to gender. We have selected the age range of 18-20 years because pulmonary functions reach maximum values around this period and then start declining with the increase of age [5-7]. Earlier studies in Libyan population were limited to measure few parameters of the forced expiratory vital capacity test [6, 12, 13]. Present study has covered almost all the spectrum of forced expiratory vital capacity maneuver. We have expressed all the parameters in terms of absolute values. The comparison with normal absolute values may influence decisions which have important implications both on individual and on health care system. Even the values can be easier to apply in the field studies.

Our results reveal the difference between male and female student for all the lung function indices. The absolute values of all the volumes and flow rates were found in general, to be higher in age matched males. However, volume adjusted flow rates, FEV_1 to FVC ratio and $FEF_{25-75\%}$ to FVC ratio were found to be higher in females compared to males and is consistent with the trend of results reported earlier [15]. The values of FVC, FEV_1 and flow rates in male subjects are in close agreement with the previously reported study in Libyan men [12]. However, absolute values of lung function in Libyan women were not reported earlier. The greater body built including the thoracic and lung size and the greater muscular effort may be the prime determinants of higher FVC observed in male subjects [11, 16, 17]. Forced expiratory volume in one second evaluates the flow resistive properties of both large and small airways, which was about 23% less in females. The lower flow rates at large lung volumes, such as $FEF_{0.2-1.2L}$ and $V_{max75\%}$ in female students might have caused by either decrease in large airways function or a decrease in effort, inasmuch as these flows are largely effort dependent. Although our subjects performed tests using maximum effort, a decrease in expiratory muscle power in female subjects cannot be entirely ruled out. Small airways function as indicated by $FEF_{25-75\%}$ and $V_{max50\%}$ and most peripheral airways function indicated by $FEF_{75-85\%}$ and $V_{max25\%}$ were found to be 10% (p<0.001) and 13% (p<0.001) lower in female compared to male subjects. Normally these tests, the flow rates at lower lung volume, have a wide normal range; but trend of changes in one subject can show narrow range of variability [18]. However, these parameters of FVC maneuver and flow volume curve evaluate peripheral airways where disease of chronic airflow obstruction are thought to originate [19]. Our all subjects were in normal and good health during this study. Even in past (at least last six months before the test) they did not suffer from any cardio-respiratory illness.

Therefore, it is not the disease, but possibly the size of the airways are responsible for this lower small airway function observed in female subjects compared to male. It is evident that airway sizes including lungs are small in young women compared with the young men [9].

In the present study, however, we have found that the pulmonary function in female compared to male are more in terms of flow rates in comparison to FVC. In other words, flow rates that are compensated for volume such as FEV_1% and $FEF_{25-75\%}$/FVC were found greater in female subjects. This result is consistent with other previous findings [19, 20]. This is probably due to the airway tends to grow faster than parenchymal tissue of lung in young females. The growth of airways tends to lag behind that of parenchyma in young males in a phenomenon known as dysanaptic growth, resulting in relatively narrower airways in young males than in young females [21]. Dysanapsis (low size bronchi relative to lung volume), as indicated by low $FEF_{25-75\%}$ / FVC, evaluates airway hyper responsiveness, could potentially predispose to lung pathology and is speculative to be a risk factor for developing COPD and wheezing [22, 23, 24]. Epidemiological studies have demonstrated greater small airway dysfunction in men than women [25]. Even the incidence of morbidity and mortality due to asthma are found to be less in females than in males [26]. The females probably escape from dysanapsis. It is evident that the adult female lung is the result of proportional growth of its airways in relation to lung parenchyma [21]. These dimensional advantages in female airway functions are thought to be due to not only anatomical but physiological also. The influence of their reproductive hormones, especially of estrogen and progesterone cannot be ignored. Estrogen relaxes airway smooth muscle by decreasing intracellular calcium, thus facilitating bronchodilation [27]. Several lines of evidence indicate that progesterone also improve respiratory dynamics, particularly small airways function, as small airways are rich in beta receptors [28] and progesterone have marked beta receptor activity [29].

In conclusion, the study of pulmonary function was conducted in age matched healthy male and female medical students. Although the total number of subjects in this study was limited to 108, the fact that the age, obesity, level of fitness, tobacco use and ethnicity could be ignored as variables made it simpler to identify differences between the genders. We found that absolute values of FVC, FEV_1, forced expiratory flow rates and instantaneous flows at different lung volumes were all less for female than male subjects of the same age. However, both the ratio of expiratory flow rates (FEV_1 to FVC and $FEF_{25-75\%}$ to FVC) were more in female, emphasizes the key importance of airway dynamics which is better in female compared to male subjects. Hence, gender differences in lung function could be an important determinant of the clinical manifestation of airway disease. Further studies might be performed to broaden these findings to wider age group as well as groups of different socioeconomic status and in females during their all the three phases of menstrual cycle.

REFERENCES:

1. Naeye RL, Freeman RK, Blane WA. Nutrition, sex and fetal lung maturation. Paediatric Res 1974; 8: 200-204.
2. Wetzel RC, Sylvester JT. Gender differences in hypoxic vascular response of isolated sheep lungs. J Appl Physiol (Respir Environ-Exercise Physiol) 1983; 55: 100-104.
3. Wetzel RC, Zakur HA, Sylvester JT. Effect of puberty and estradiol on hypoxic vasomotor response in isolated sheep lungs. J Appl Physiol (Respir Environ-Exercise Physiol) 1984; 56: 1199-1203.
4. Rosenthal M, Bain SH, Cramer D. Lung function in white children aged 4-19 years. I. Spirometry. Thorax 1993; 48: 794-802.
5. Wang X, Dockery D, Wypij D, et al. Pulmonary function growth velocity in children 6-18 years of age. Am Rev Respir Dis 1993; 148: 1502-1508.
6. Shamssain MH, Thompson J, Ogston SA. Forced expiratory indices in normal Libyan children aged 6-19 years. Thorax 1988; 43: 467-470.
7. Sherrill DL, Camilli A, Lebowitz MD. On the temporal relationship between lung function and somatic growth. Am Rev Respir Dis 1989; 140: 638-644.
8. Rao GS, Rajan P, Walter S. Expiratory flow rate changes during the menstrual cycle. Indian J Physiol Pharmacol 1991; 35: 74-76.
9. Carey MA, Card JW, Voltz JW, et al. It's all about sex: male-female differences in lung development and disease. Trends Endocrinol Metab 2007; 18: 308-313.
10. Stanford KI, Mickleborough TD, Ray S, Lindley LR, Koceja DM, Stager JM. Influence of menstrual cycle phase on pulmonary function in asthmatic athletes. Eur J Appl Physiol 2006; 96: 703-710.
11. Becklake MR, Kauffmann F. Gender differences in airway behavior over the human life span. Thorax 1999; 54: 1119-1138.
12. Shamssain MH. Forced expiratory indices in normal Libyan men. Thorax 1988; 43:923-925.
13. Mukhtar MS, Rao GMM, Morghom LO, Patrick JM. Spirometric standards of Libyan boys and girls. Respiration 1989; 56: 227-234.

14. Das TK, Moutquin JM, Parent JG. Effect of cigarette smoking on maternal airway function during pregnancy. Am J Obstet Gynecol 1991; 165: 675-679.

15. Premkumar K, Walter S. Exercise induced bronchial liability in men and women: A comparison. Indian J Physiol Pharmacol 1993; 37: 308-312.

16. Jacobs DR, Nelson ET, Dontas AS, Keller J, Slattery ML, Higgins M. Are race and sex differences in lung functions explained by frame size? Am Rev Respir Dis 1992; 46: 644-649.

17. Schrader PC, Quanjer PH, Olivier IC. Respiratory muscle force and ventilatory function in adolescence. Eur Respir J 1988; 1: 368-375.

18. Mirsadraee M, Forouzesh B, Roshandel E, Meshkat M, Boskabady MH. Accuracy of mid expiratory flow and dysanapsis parameters for evaluation of methacholine provocation test. Tanaffos 2009; 8: 24-30.

19. Cosio M, Ghezzo H, Hogg JC, et al. The relations between structural changes in small airways and pulmonary function tests. N Engl J Med 1978; 298: 1277-1281.

20. Parker AL, Hijleh MA, McCool FD. Ratio between forced expiratory flow between 25% and & 75% of vital capacity and FVC is determinant of airway reactivity and sensitivity to methacholine. Chest 2003; 124: 63-69.

21. Hoffstein V. Relationship between lung volumes, maximal expiratory flow, forced expiratory volume in one second, and tracheal area in normal men and women. Am Rev Respir Dis 1986; 134: 956-961.

22. Litonjua AA, Sparrow D, Weiss ST. The $FEF_{(25-75\%)}$/FVC ratio is associated with methacholine airway responsiveness. Am J Respir Crit Care Med 1999; 159: 1574-1579.

23. DeMeo DL, Carey VJ, Chapman HA, et al. Familial aggregation of $FEF_{(25-75\%)}$ and $FEF_{(25-75\%)}$/FVC in families with severe, early onset COPD. Thorax 2004; 59: 396-400.

24. Martinez FD, Morgan WJ, Wright AL, Holberg C, Taussig LM. Initial airway function is a risk factor for recurrent wheezing respiratory illness during the first three years of life. Group Health Medical Associates. Am Rev Respir Dis 1991; 143: 312-316.

25. Cohen BH, Ball AWC, Brashears S, et al. Risk factors in COPD. Am J Epidemiol 1977; 105: 223-231.

26. So SY, Ng MMT, Ip MSM, Lam WK. Rising asthma mortality in young males in Hong Kong. Resp Med 1990; 84: 1976-1985.

27. Townsent EA, Thompson MA, Pabelick CM, Prakash YS. Rapid effects of estrogen on intracellular Ca^{2+} regulation in human airway smooth muscle. Am J Physiol (Lung Cell Mol Physiol) 2010; 298: 521-530.

28. Woolcock AJ, Macklem PT, Hogg JC, Wilson NJ. Influence of autonomic nervous system on airway resistance and elastic recoil. J Appl Physiol 1969; 26: 814-818.

29. Raz S, Zeigler M, Caine M. The effect of progesterone on the adrenergic receptors of the urethra. Br J Urol 1973; 45: 131-135.

