

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/348098020>

# DYNAMIC LUNG FUNCTIONS DURING PREGNANCY: COMPARATIVE STUDY IN LOWER SOCIOECONOMIC RURAL FEMALES OF VADODARA CITY, GUJARAT

Article in *Annals of Tropical Medicine and Public Health* · December 2020

DOI: 10.36295/ASRO.2020.2323147

CITATIONS

0

READS

13

3 authors, including:



Jaman Mohan Harsoda

SUMANDEEP VIDYAPEETH UNIVERSITY, VADODARA, INDIA

81 PUBLICATIONS 89 CITATIONS

SEE PROFILE

Some of the authors of this publication are also working on these related projects:



PhD thesis [View project](#)

## **DYNAMIC LUNG FUNCTIONS DURING PREGNANCY: COMPARATIVE STUDY IN LOWER SOCIOECONOMIC RURAL FEMALES OF VADODARA CITY, GUJARAT**

J M Harsoda<sup>1</sup>, Dr Geetanjali Purohit<sup>2\*</sup>, Trushna Shah<sup>3</sup>

1. Prof. & Head, Physiology, SBKS MI & RC, Sumandeep Vidyapeeth Deemed to be University, Piparia, 391760, Vadodara, Gujarat.
2. Associate Professor, Physiology, Dr. MK Shah Medical College & Research Center (By Sumandeep Vidyapeeth). Ahmadabad, Gujarat,
3. Associate Professor, Biochemistry, SBKS MI & RC, Sumandeep Vidyapeeth Deemed to be University, Piparia, 391760, Vadodara, Gujarat.

### **\*CORRESPONDING AUTHOR**

### **ABSTRACT**

**CONTEXT:** Paucity in data of the dynamic respiratory functions during pregnancy is encountered and discrepancies are there in the data available. **AIM:** Present study was taken up to examine the maternal dynamic airway functions, inspiratory and expiratory both extensively in normal pregnancy in rural females. **SETTING & DESIGN:** Cross sectional comparative study was conducted after ethical approval in the department of Physiology in collaboration with department of Obstetrics & Gynecology, SBKS MIRC, SVDU. **METHOD AND MATERIALS:** Incidental and random selection led 400 females in two groups, pregnant (N=300) and nonpregnant (N=100). Expiratory and Inspiratory lung functions were studied in 300 pregnant females in three different trimesters of pregnancy, 100 studied in each group and compared with 100 nonpregnant matched control. **STATISTICAL ANALYSIS USED:** Student's unpaired Student's t-test was used for between group variations and ANOVA was applied to find out the level of significance for the variation among three trimesters. **RESULTS:** The airway functions, small and large both have shown no significant change though a little higher value in some parameters has been noted during pregnancy. Large airways functions as FEV1%, PEFR, FEF 0.2-12 and FEF25% are preserved in pregnant group. Small airway functions as FEF25-75%, FEF75-85%, Vmax50% and Vmax75% get altered during pregnancy. **CONCLUSION:** Pregnancy is a complicated and adaptive phase in terms of respiratory parameters. The maternal respiration may be compromised in the presence of smaller airway diseases. Thus, the pregnant women with respiratory diseases pose a special challenge.

**KEY WORDS:** FEV1, Large airways. Small airways, adaptation

**KEY MESSAGE:** Pregnancy is a physiological stage. Small airway disease poses special challenges as small airway functions get altered during normal pregnancy.

**How to cite this article:** Harsoda JM, Purohi G, Shah T (2020): Dynamic lung function during pregnancy: Comparative study in lower socioeconomic rural females of Vadodara city, Gujarat, Ann Trop Med & Public Health; 23(S23): SP2323147. DOI: <http://doi.org/10.36295/ASRO.2020.2323147>

## INTRODUCTION

It has long been recognized that pregnancy can alter lung functions and the natural maternal history of certain pulmonary diseases. The differential diagnosis for respiratory disease as particular symptoms and appearance of any radiographic abnormalities is followed by refinement of additional information gleaned from physical examinations, pulmonary function tests, additional imaging studies and bronchoscopic examinations.

As peripheral airways contribute only 20-25% of total airway resistance, it is clear that considerable diseases may be present in the small airways before conventional test (FEV1) becomes significantly abnormal. FEF 25-75%. FEF25-75% is said to be a very sensitive parameter to detect airflow in peripheral airways where the diseases of chronic airflow obstruction are thought to begin.<sup>1,2</sup> FEV1 includes significant flows at higher lung volumes to reflect large airway changes in addition to small airway changes. Therefore, in absence of changes in FEV1 or FEV1%, measurement of FEF25-75%, FEF75-85% and Vmax75% in lung are more useful as a measure of small airways functional abnormality, as suggested by various studies.<sup>3,4</sup>

Present study was aimed to quantitate the changes during pregnancy for forced expiratory and inspiratory flow rates both at large and small lung volumes and expiratory and inspiratory Instantaneous flows.

## MATERIAL AND METHOD

It was a longitudinal cohort study and included the rural females of lower socioeconomic class. Study carried out in Department of Physiology, Smt. B K Shah Medical Institute and Research Center jointly with Department of OBGy, DGH, Piparia, Vadodara. This study was complied with the ethical committee guidelines of SVIEC (SVIEC/ON/MEDI/PhD/1202).

### Methodological approach of this study includes:

#### Study Population & Sample Size

Total 300 apparently healthy normal pregnant women of age 20-40 years were studied throughout the gestational period as experimental group, serially and vertically and both primi and multipara females with singleton pregnancy included. Pregnant females studied in different trimesters as follows

I trimester- 8-12 week

II trimester-13-24 week

III trimester- 25-40 week

100 non-pregnant apparently healthy women matched more or less for age, height and socioeconomic status were examined as control group. The control group was studied once.

All women were explained the purpose and importance of the study in detail and only those who were motivated enough to give their consent and volunteered were recruited. Females with Cardio-respiratory, Haemolytic and Gynaecological problems were excluded. Unsatisfactory training and recording with the instrument and neuromuscular and musculoskeletal problems that may affect the pulmonary test accuracy were also considered as exclusion.

### Interventions

Before the actual test for respiratory parameters, instrumental training was given to the participants. Four to five subjects matched with inclusion, recruited from outpatient department of OBG, brought to the respiratory laboratory set up. The spirometer was shown and procedure and duration of experiment with instrument was explained to them. In order to reduce anxiety, it was clearly pointed out that it is merely a matter of breathing ordinary air that involves no discomfort or danger. Whenever one subject was given trail, others were asked to observe. Thus each subject was demonstrated and trained to perform the test.<sup>5</sup>

On the same day after training of all recruited women were assessed for pulmonary function test, by using a digital spirometer Spiro Win+ version 3.1 (Genesis medical Systems Pvt Ltd, Made in India). The pregnant women were investigated for at least thrice (as per the ATS guidelines) for each trimester of pregnancy.<sup>6</sup> To make FVC maneuver reproducible, on each attempt subject was encouraged to make a maximum effort. A series of three determinations were made, with minimum rest of 10 minutes and highest reading was considered. Difference of more than 200 ml in parameters was excluded for consideration.

Student's unpaired Student's t-test was used for between group variations of pregnant group and non-pregnant control group. One way analysis of variance (ANOVA) was also applied to find out the level of significance for the variation among three trimesters. The alpha error was set at the 5% level.

## OBSERVATION &amp; RESULTS

Table I: Expiratory Respiratory Functions in all three trimesters of pregnant female and nonpregnant female

Variables		I Trimester	II Trimester	III Trimester	Control	Statistics (ANOVA)
FVC (Ltr)	M	1.958	1.911	1.862	1.952	p>0.05, NS
	SD	0.36	0.31	0.37	0.44	
FEV0.5 (Ltr)	M	1.158	1.135	1.080	1.265	p>0.05, NS
	SD	0.36	0.39	0.41	0.29	
FEV1 (Ltr)	M	1.71	1.69	1.660	1.60	p>0.05, NS
	SD	0.35	0.31	0.35	0.35	
FEV3 (Ltr)	M	1.879	1.817	1.787	1.911	p>0.05, NS
	SD	0.431	0.39	0.34	0.44	
FEV0.5 %	M	59.43	59.56	56.93	55.35	p>0.05, NS
	SD	15.5	18.04	16.12	15.42	
FEV1 %	M	87.62	89.33	89.14	82.63	p>0.05, NS
	SD	8.29	8.69	6.89	7.22	
FEV3 %	M	96.10	92.78	95.83	95.76	p>0.05, NS
	SD	10.78	13.83	13.38	16.06	
PEFR (Ltr/sec)	M	2.93	2.79	2.77	2.933	P >0.05,NS
	SD	1.09	0.98	0.96	0.69	
FEF0.2-1.2 Ltr	M	2.405	2.395	2.284	2.554	p>0.05, NS
	SD	0.73	1.03	0.90	0.67	
FEF 25-75 %	M	2.06	2.128	2.00	2.295	p>0.05, NS
	SD	0.57	0.81	0.68	0.48	
FEF 75-85 %	M	1.156	1.164	1.13	1.178	P>0.05, NS
	SD	5.32	0.38	0.65	0.28	
FEF 25 %	M	2.688	2.731	2.63	2.796	p>0.05, NS
	SD	0.88	1.12	1.02	0.75	
FEF 50 %	M	2.249	2.299	2.22	2.488	p>0.05, NS
	SD	0.70	0.91	0.80	0.563	
FEF75 %	M	1.403	1.432	1.342	1.512	p>0.05, NS
	SD	0.37	0.46	0.46	0.32	

**Table II: Inspiratory Respiratory Functions in all three trimesters of pregnant female and nonpregnant female**

Variables		I Trimester	II Trimester	III Trimester	Control	Statistics (ANOVA)
FIVC (Ltr)	M	1.891	1.850	1.671	1.710	p>0.05, NS
	SD	0.41	0.345	0.41	0.46	
FIV0.5 (Ltrs)	M	0.905	0.882	0.822	0.903	p>0.05, NS
	SD	0.43	0.37	0.39	0.39	
FIV1 (Ltrs)	M	1.483	1.343	1.301	1.437	p>0.05, NS
	SD	0.64	0.72	0.74	0.56	
FIV3 (Ltrs)	M	1.774	1.844	0.713	1.742	P>0.05, NS
	SD	0.81	0.62	0.43	0.58	
FIV0.5 %	M	46.98	46.76	49.8	47.49	p>0.05, NS
	SD	11.7	11.2	10.2	10.6	
FIV1%	M	77.85	74.82	72.24	80.63	p>0.05, NS
	SD	10.12	11.32	12.29	11.6	
FIV3%	M	96.1	92.78	95.83	95.76	p>0.05, NS
	SD	10.78	13.83	13.38	16.06	
FIF 0.2-1.2 Ltr	M	1.761	1.613	1.710	1.848	P>0.05,NS
	SD	0.94	0.91	0.62	0.87	
FIF 50%	M	2.087	1.794	1.828	2.012	P>0.0, NS
	SD	0.84	0.717	0.62	0.83	
FIF25-75%	M	1.778	1.506	1.497	1.778	P<0.05,S
	SD	0.77	0.84	0.68	0.80	
PIFR	M	2.550	2.264	2.212	2.292	P>0.05,NS
	SD	0.846	0.58	0.51	0.77	

## DISCUSSION

Flow volume loop collating inspiratory and expiratory flows determine two different aspects of dynamic respiration, helps to differentiate between obstructive and restrictive conditions. Forced expiratory vital capacity (FEVC) is rapidly performed reproducible quantitative stratagem and factors as maintenance of the effort during test and

neuromuscular coordination predominate this phase. The terminal portion of FEVC is effort independent and predictably the most sensitive indicator of diffused obstructive bronco-pulmonary diseases.

Earlier studies have reported FVC to be either minimally increased, decreased, or unchanged during pregnancy compared with the nonpregnant state; on an average, there is no significant change.<sup>7-13</sup> No change in FVC and FEV1 may be explained by the mechanical alterations and their disadvantage to the respiratory apparatus induced by advancing pregnancy is well compensated by decrease in airway resistance and improved airway conductance due to smooth muscle relaxation produced by progesterone, corticosteroids and relaxin.<sup>7,14-16</sup> Various studies depicted that despite the progressively diminishing abdominal compliance maintenance of VC and FVC is attributed to the augmentation of rib cage volume displacement, relative mobility of thoracic cage and unimpaired diaphragmatic movements.<sup>14,15,17</sup> Few studies reported a fall from early to mid pregnancy in FVC due to restrictive effect of enlarging uterus, which wanes at term due to attunement, proving that gestation having accommodative change.<sup>7,18</sup>

FEV0.5% and FEV1% are essential to access ventilatory capacity and ability of bellows to ventilate but less reliant on the nascent period of the expiration that is influenced by subject's cooperation.<sup>18</sup> FEV0.5% and FEV1% with advancing pregnancy is not much affected, as velocity of air breathed out is optimal in initial phase of expiration. Moreover FEV1% ( $88.69 \pm 7.79$  vs  $82.62 \pm 7.22$ ,  $p < 0.001$ ) and FEV0.5% ( $58.59 \pm 16.5$  vs  $55.35 \pm 15.42$ ,  $p < 0.05$ ) in pregnant group were found to be significantly increased when compared with nonpregnant control.

A number of studies reviewed showed increase in FEV1% from nonpregnant to pregnant state.<sup>12,14</sup> On the contrary other studies also find a place in literature with no change<sup>14,19</sup> and decrease<sup>7,17</sup> during pregnancy. The values of these parameters suggests that dysfunction of expiratory muscle is not there during pregnancy and mechanical properties of respiratory system remain normal due to altered configuration affecting elastic recoil of chest and intra-thoracic diameter. Overall rates of gas flow, average as well as maximum, during expiration are little altered in pregnancy. Pressure required to achieve flow rates is inadequate in pregnancy than nonpregnant state, compensated by decreased airway resistance and augmented cross sectional area of airway due to relaxation of smooth muscles in airways by Relaxin.<sup>20</sup> Progesterone is known to increase P adrenergic activity that causes bronchodilatation may also be one of the contributing factor.<sup>21</sup>

Lack of change in PEFR suggest that the shortening of the thorax by the upward displacement of the diaphragm is compensated by an increase in other dimensions as transverse diameters, coastal angle and lower thoracic perimeters.<sup>17,22</sup> Despite the upward displacement of the diaphragm by the gravid uterus, diaphragm excursion actually increases by 2 cm compared with the non-pregnant state.<sup>7,23</sup> Studies reported that expiratory flow that reflect larger airway caliber and smaller airway caliber are also remain unchanged during pregnancy and increased diaphragmatic excursion and preserved respiratory muscle strength are the important adaptations, that accompanies pregnancy.<sup>11,18</sup> Progesterone may have a local pulmonary effect, which results in bronchodilatation and improvement

in gas exchange. The low results of PEFr may be because of the low socio-economic status and poor nutrition of the subjects as most of the subjects are from rural areas.<sup>24</sup>

Most Indian studies reported that PEFr value decreased with advance pregnancy due to the gravid uterus, attributed to the lesser force of contraction of main expiratory muscles (anterior abdominal and internal intercostals muscles) of the pregnant females as PEFr is largely effort dependent.<sup>23,25</sup> Also inadequate nutrition due to morning sickness and altered eating habits can further cause muscle weakness leading to decreased PEFr in pregnant females.<sup>26</sup> Some studies done in Indian population show that the vital capacity and PEFr tend to increase in the later stage of pregnancy discussed bronchodilatation secondary to progesterone and improvement in gas exchange as main contributory factors. Study conducted in Oslo university hospital in 2012 shown that PEFr increased significantly during healthy pregnancies, and should be interpreted cautiously in pregnant women with impaired lung function test.

Large airways functioning can also be detected by the spirometry parameters viz FEF0.2-1.2 and Vmax25%. The little changes were observed in the parameters. Therefore, from the above observation, it is seen that the large airway function during pregnancy almost remains unaffected. Similar observations were reported by other researchers too.<sup>17,19,27,28</sup> Our findings in healthy subjects demonstrate that large airways function may be compensated by smooth muscle relaxation due to progesterone. However there exists a controversy regarding the changes in airways resistance in pregnancy measured during quiet respiration. Variability has been shown as increased<sup>29,30</sup>, decreased<sup>31</sup> or unchanged throughout pregnancy.<sup>10</sup> Enlarged gravid uterus causing upward displacement of diaphragm in pregnant women tends to increase the flow resistance of airways by reduction in FRC.<sup>29</sup> Similarly reduced PaCO<sub>2</sub> during pregnancy leads to increase in airways resistance<sup>30</sup> secondary to bronchial smooth muscle constriction. Since in this study we have not found any significant change in large airway function by assessing PEFr, FEV<sub>1</sub>, FEF0.2–1.2 and FEF25% therefore, there may be a mechanism operating in pregnancy leading to dilate the bronchi due to Progesterone.<sup>20</sup> Even increase in P adrenergic activity in large airways may have caused bronchodilatation and decrease airway resistance as reported by Raz et al.<sup>21</sup>

Unlike larger airway functions, dysfunction in peripheral or smaller airways is tedious to detect at earlier by the standard methods for assessment of airways function. It is now possible to investigate the function of these peripheral or smaller airways with the use of measurements such as FEF25-75% (MMEFR), FEF75-85%, Vmax50% and Vmax75%. It is noted that the first 25% of FVC maneuver is totally effort dependent while terminal phase not involves neuromuscular factors. Therefore MMEFR believed to be more important and more sensitive tests as they are relatively effort independent portion of FVC maneuver.<sup>32-33</sup>

FEF25-75% is mid portion i.e. 25% to 75% of the FVC, is reliable indicator of diffused obstructive pulmonary disorders and also reported to reduce in restrictive condition. So far studies reviewed have found unalteration in this parameter<sup>11,17,19</sup> and our results are similar to above studies. Thus, the peripheral airway functions remain unaffected



during pregnancy, inspite of compressed lung bases and increased angulations of bronchi.<sup>31</sup> Increase in airways cross sectional areas may lead to such findings, postulated by some studies which may be due to increase in the cross sectional area of respiratory smooth muscles secondary to progesterone.<sup>15</sup> Woolcock et al, 1969<sup>34</sup> suggested that P adrenergic activity of progesterone is more marked in peripheral airways as opposed to large airways and causes easy flow of air. It would seem likely that the constancy of large and small airways function in pregnancy is a balance between factors tending to increase and those tending to decrease airways resistance.<sup>35</sup>

In addition to FEF25-75%, the other functions independent to effort and are important to detect small airway patency, particularly in airways with a diameter <2 mm, are FEF75-85%, Vmax50% and Vmax75%. The mean difference calculated statistically between groups in each parameter was found to be significantly ( $P < 0.05$ ) lower in pregnant group as compared to control group. 25% reduction in FEF75-85% is considered to be clinically abnormal however the sensitivity of FEF25-75% to dysfunction is not necessarily greater within and between individual variability.<sup>36,37</sup>

A reduced Vmax75% with other small airway functions are strongly suggestive of early small airway disease even though the subjects were asymptomatic at the time of recruitment. Although a direct airway resistance and elastic recoil pressure or lung compliance were not measured, it is assumed that the observed decrease in flow rates at low lung volume is caused by increased resistance to flow rather than a decrease in driving force. Alteration in lung recoil in during pregnancy cannot be entirely ruled out; however in normal pregnant women lung elastic recoil should not be altered because lung compliance reported to remain unchanged compared with the postpartum period.<sup>38</sup> In contrast to normal pregnancy, in pregnancy with respiratory abnormalities the contribution of small airway resistance to total airway resistance is normally expected to increase at lower lung volumes, even if FEV1 would not have been clinically abnormal. Their findings are comparable to those obtained by Das et al. (1991), found a significant reduction in small airway functions in smoker group to that of nonsmokers and discussed the effects of smoking as well as passive smoking on these parameters.<sup>14</sup>

The physiological changes associated with pregnancy tend to preserve the lung compliance against gross mechanical opposing forces, but in control group with same socioeconomic status obviates this protective change and the preexisting elastic recoil pressure may dominate which might have been reflected as a decrease in flow rates observed in pregnant group. Thus above findings of lung function confirm the existence of airways obstruction prior to pregnancy and indicate that the broncho-dilatation brought about by increased level of progesterone in pregnancy, especially near term may not be sufficient to overcome the deleterious effect in airways function. Maintenance of normal lung function in pregnancy is important for maternal gas exchange across the alveolar-capillary membrane and thus also on the maternal oxygen saturation.

FIVC follows the same pattern as that of FEVC and no change is observed in pregnancy compared to the nonpregnant group. The fall has been found within the experimental group and the maximum fall has been found in

the III trimester, but within physiological limit. Restrictive effect of gravid uterus may give fall in FIVC during late pregnancy and may become significant when collating with restrictive pulmonary diseases in pregnant female. FIVC is less than FEVC during pregnancy suggesting the degree of restriction being more for inspiratory maneuver. Study reported the fall in mid pregnancy.<sup>39</sup> Searching through the literature the author insignificant rise during luteal phase has mention in literature without any rationale.<sup>40</sup>

The normal values of FIV1% with advancing gestation is not be much affected as velocity of air breathed is optimal in initial phase of inspiration. This is because cross sectional area is augmented as airway resistance decreases by progesterone and relaxin causing free inflow of more air with effort.<sup>41</sup> Moreover more amount of air is inspired in initial phase of inspiration and end inspiratory volume is affected by restrictive element produced by fetal growth.

FIF 0.2-1.2 ltr/sec showed insignificant changes during pregnancy and found to be lesser when compare to the nonpregnant control, but within physiological limit. Unaltered maximum mid inspiratory flow rates in spite of the growing fetus shows another adaptation of pregnant state. This may be due to the peripheral effect of the progesterone. The FIF25-75% is normally at least equal to and usually greater than FEF25-75%. Since inspiratory flow is more conditional on effort than is expiratory flow, a fall in FIF25-75% is usually more sensitive to respiratory muscle dysfunction or a suboptimal effort than is FEF25-75%. The strength of respiratory muscles decreases as long as the relaxing effect of progesterone on muscles persist and discomfort experienced in late pregnancy.<sup>39</sup> Pregnancy affects FIF25-75%- When airway resistance is high a disproportionate fall in FIF25-75% relative to FEF25-75% suggests an extrathoracic site of airway obstruction.

The PIFR found to be altered insignificantly during pregnancy and when compared with the nonpregnant control. In 2000 Rajesh CS et al studied the inspiratory parameters during different phases of menstrual cycle and explains the role off progesterone, known to cause hyperventilation and hypercapnia in the luteal phase of a normal menstrual cycle and found the PIFR better in luteal phase of menstrual cycle but not significantly.<sup>40</sup>

## CONCLUSION

Pregnancy is adaptive phase in terms of dynamic respiratory parameters. Management of obstetric patients requires comprehensive knowledge of physiological changes that accompany pregnancy, and awareness of these changes is vitally important in managing pregnancies with pre-existing medical conditions. However, any proposed alterations to existing management protocols should only occur after an appropriate period of robust validation and assessment in pregnant populations.

The maternal respiration may be compromised in the presence of smaller airway diseases. Small airways with low flow rates that may be occluded even during the tidal breathing. Pregnancy with underlying pulmonary disease not only experience the effects of normal mechanical and biochemical events, but may also find the natural course of pulmonary disease altered.

Author suggests more longitudinal and serial studies with hormonal assay in different trimesters to assess the relation between hormone and respiratory parameters. Organization of multidisciplinary team with coordinate approach and physiological monitoring systems should be encouraged for pregnant females. Furthermore advance technology and tools should be readily available, enabling clinicians to improve and optimize care for pregnant female, if compromised.

**ACKNOWLEDGMENT:** I acknowledge Dr T.K. Das, Ex. Professor, Physiology, SBKS MIRC for his valuable ideas and guidance. I am also thankful to the participants and department of Ob Gy, Dhiraj hospital for their support

## REFERENCES

1. Contreras G, Gutierrez M, Beroiza T, Fantin A, Oddo H, Villarroel L et al. Ventilatory drive and respiratory muscle function in pregnancy. *Am Rev Respir Dis* 1991;144:837-41
2. Coiso M, Ghezzi H, Hogg JC, Corbin R, Loveland M, Dorman J, et al. The relation between the structural changes in small airways and pulmonary function tests. *New Eng J Med* 1978 298;1277-81.
3. Corbin RP, Loveland M, Martin RR, Mecklem PT. A four year follow up study of lung mechanism in smokers. *Am Rev Respir Dis* 1979 120;293-304.
4. Morris JF, Koski A, Breese JD. Normal values and evaluation of forced end expiratory flow . *Am Rev Respir Dis* 1980;111:755-62.
5. Lal S, Ferguson A D, Campbell EJM. Forced emphysema time- a simple test for airway obstruction. *Br Med j.* 1964;1:814
6. Medical Section of the American Lung Association. 1994. Standardization of spirometry: 1994 update. *Am. J. Respir. Crit. Care Med.* 152:1107–36.
7. Cugell DW, Frank NR, Gaenster EA, Badger TL. Pulmonary function in pregnancy- A serial observation in normal women. *Am. Rev. Tubercle.* 1953;67:568-97.
8. Alaily AB, Carrol KB. Pulmonary ventilation in pregnancy *Br J Obstet Gynaecol* 1978;85(7):518–24
9. Garcia-Rio F, Pino-Garcia JM, Serrano S, et al. Comparison of helium dilution and plethysmographic lung volumes in pregnant women. *Eur Respir J* 1997;10(10):2371–5.
10. Goucher D, Rubin A, Russo N. The effect of pregnancy upon pulmonary function in normal women. *Am J Obstet Gynecol* 1956;72(5):963–9.
11. Ihrman K. A clinical and physiological study of pregnancy in a material from northern Sweden. II. Vital capacity and maximal breathing capacity during and after pregnancy. *Acta Soc Med Ups* 1960;65:147–54.
12. Milne JA, Mills RJ, Howie AD, et al. Large airways function during normal pregnancy. *Br J Obstet Gynaecol* 1977;84(6):448–51.
13. Baldwin GR, Moorthi DS, Whelton JA, et al. New lung functions and pregnancy. *Am J Obstet Gynecol* 1977;127(3):235–9.
14. Das TK, Jana H. Maternal airways function during normal pregnancy. *Indian J Med Sci.* 1991 Oct;45(10):265-8.

15. Singh S, Singh KC, Sabyasachi S, Kamal SN. Airway function in pregnant Indian women. *Indian J Physiol Pharmacol* 1995; 39(2): 160-62
16. Mokkalani R, Prasad EC, Venkatraman, Kaneez Fatima. Ventilatory function in pregnancy. *Indian J Physiol Pharmacol* 1991;35 (4):237-40.
17. Sternfeld B, Quesenberry CP, Eskenazi B, Newman LA. Exercise during pregnancy and pregnancy outcome. *Medicine and Science in Sports and Exercise* 1995, 27(5):634-40.
18. Pandya KD, Chandwani S, Desai CA, Dadlani AG. Study of vital Capacity and timed vital capacity in normal non-pregnant and pregnant women. *J Obs Gyn of India* 1984;36:1053-57.
19. Chhabra S1, Nangia V, Ingley KN. Changes in respiratory function tests during pregnancy. *Indian J Physiol Pharmacol*. 1988;32(1):56-60.
20. Hytten FH, Leitch I. (1971): the physiology of human pregnancy . blackwell scientific publications. Oxford London 2<sup>nd</sup> edition pg 111
21. Raz S, Zeigler M, Caine M. Effect of progesterone on the adrenergic receptors of urethra. *Br J Urol*. 1973; 45:131-35
22. Weerassekara DS, Ruberu DK, Sivayogan S. Pulmonary functions in pregnant Sri-lankan women. *Sabaragamuwa Univ Jn* 1999;2(1):57-60.
23. Turner AF. The chest radiograph in pregnancy. *Clin Obstet Gynecol* 1975; 18:65.
24. Cotes JE. Lung Function throughout Life: Determinants and Reference Values. In: Cotes JE, editor. *Lung Function: Assessment and Application in Medicine*. 5th ed. Oxford, Blackwell Scientific. 1993:445–513.
25. Quanjer PH, Borsboom GJ, Brunekreef B, Zach M, Forche G, Cotes JE et al. Spirometric reference values for white European children and adolescents: Polgar revisited. *Pediatr Pulmolol* 1995;19:135–42.
26. Benjaponpitak S, Direkwattanachai C, Kraissarin C, Sasisakulporn C. Peak expiratory flow rate values of students in Bangkok. *J Med Assoc Thai* 1999;82(Suppl):137-43.
27. Cameron SJ, Bain HH and Grant IWB. Ventilatory functions in pregnancy. *Scott Med J* 1970;15; 243
28. Gerrard GS, Littler WA, Redman CWG. Closing volume during normal pregnancy *Thorax* 1978;33:488 – 92
29. Briscoe WA, Dubois AB. The relationship between airway resistance, airway conductance and lung volume in subjects of different age and body size. *J clin. Invest*, 1958;37:1279
30. Newhouse MT, Becklake NR, Maclem PT, McGregor M. Effect of alteration in end tidal CO<sub>2</sub> tension on flow resistance. *J Appl Physiol* 1964; 19:745-49
31. Rubin A., Russo N. and Goucher D. The effect of pregnancy upon pulmonary function in normal women. *Am J Obstet and Gynec* 1956; 72:963.
32. Burton GG, Gee GN, Hodgkin JE. (1977): Respiratory care-a guide to clinical practice. JB Lippincott Co. Philadelphia.
33. Sioim NB, Hamilton LH. (1976): Respiratory Physiology. 3rd edition., CV Mosby Co. St Louis pp 40-85
34. Woolcock AJ, Vincent NJ, Macklem PT. Frequency dependence as a test for obstruction in the small airways. *J Clin Invest* 1969;48: 1097–1106

35. McFadden e. R. J. and Linden D. A. (1972): A reduction in maximum mid-expiratory flow rate: A spirographic manifestations of small airway disease. *Am J Med*, 52;725-737.
36. Morris JF, Koski A, Johnson LC. Spirometric standards for healthy non-smoking adults. *Am Rev Respir Dis* 1971;103:57–67
37. Buist AS. Test of small airways function - *Respiratory care* 1989;34(6):446-454
38. Gee JB, Packer BS, Millen JE, et al. Pulmonary mechanics during pregnancy. *J Clin Invest* 1967;46(6):945–52.
39. Pandya K. A Descriptive analysis of expiratory and inspiratory parameters of respiration during normal pregnancy: PhD theses. Vadodara, Gujarat: MS University; 2003.
40. Rajesh CS, Gupta P, Vaney N. Status of pulmonary function tests in adolescent females of Delhi. *Indian J Physiol Pharmacol*. 2000 Oct;44(4):442-8.
41. LoMauro A, Aliverti A. Respiratory physiology of pregnancy: Physiology masterclass. *Breathe*. 2015;11(4):297-301.