



Study of pulmonary parameters like FVC and PEFR in pregnant females and its correlation with progesterone levels

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Abstract

Pregnancy is a normal physiological state accompanied by significant hormonal, mechanical and circulatory changes. Changes in respiratory physiology during pregnancy occur due to structural changes in the chest wall and abdominal compartments as a consequence of hormonal changes, enlarging uterus and elevated diaphragm. Though there are changes in certain respiratory parameters, FEV1 and PEFR are largely unaffected. It is essential that the normal physiological changes in the respiratory system have to be kept in mind to enable accurate diagnosis of respiratory impairment in pregnancy. PEFR is a simple, non-invasive, easily performable, portable, economical and reproducible tool for effective assessment of asthma control. Though PEFR has been postulated not to significantly change throughout pregnancy, there are conflicting reports from various studies on the variation of PEFR in pregnancy. Hence based on above findings the present study was planned for Study of Pulmonary Parameters like FVC and PEFR in Pregnant Females and Its Correlation with Progesterone Levels.

The present study was planned in Department of Physiology, Patna Medical College, Patna, Bihar from January 2019 to May 2019. Total 80 cases were enrolled in the present study. The 20 cases are of non-pregnant females. The 20 cases are of each 1st Trimester, 2nd Trimester and 3rd Trimester cases. FVC & PEFR was performed using Mini Wright's Peak Flow Meter and best of three recordings noted. Data analyzed using SPSS package version 21.0. Association between PEFR with Age and BMI performed using Pearson correlation.

The data generated from the present study concludes that definite alteration in pulmonary parameters during different trimesters of pregnancy. The same study involving larger population would help us more in deriving the norms on predicted values on pulmonary parameters in pregnancy.

Keywords: pregnancy, forced vital capacity, peak expiratory flow rate, progesterone, Bihar region, etc

1. Introduction

Spirometry (meaning the measuring of breath) is the most common of the pulmonary function tests (PFTs). It measures lung function, specifically the amount (volume) and/or speed (flow) of air that can be inhaled and exhaled. Spirometry is helpful in assessing breathing patterns that identify conditions such as asthma, pulmonary fibrosis, cystic fibrosis, and COPD. It is also helpful as part of a system of health surveillance, in which breathing patterns are measured over time [1]. Spirometry generates pneumotachographs, which are charts that plot the volume and flow of air coming in and out of the lungs from one inhalation and one exhalation. The basic forced volume vital capacity (FVC) test varies slightly depending on the equipment used, either closed circuit or open circuit, but should follow the ATS/ERS standardisation of spirometry.

Generally, the patient is asked to take the deepest breath they can, and then exhale into the sensor as hard as possible, for as long as possible, preferably at least 6 seconds. It is sometimes directly followed by a rapid inhalation (inspiration), in particular when assessing possible upper airway obstruction. Sometimes, the test will be preceded by a period of quiet breathing in and out from the sensor (tidal volume), or the rapid breath in (forced inspiratory part) will come before the forced exhalation. During the test, soft nose clips may be used to prevent air escaping through the nose. Filter mouthpieces may be used to prevent the spread of

microorganisms. The maneuver is highly dependent on patient cooperation and effort, and is normally repeated at least three times to ensure reproducibility. Since results are dependent on patient cooperation, FVC can only be underestimated, never overestimated. Due to the patient cooperation required, spirometry can only be used on children old enough to comprehend and follow the instructions given (6 years old or more), and only on patients who are able to understand and follow instructions — thus, this test is not suitable for patients who are unconscious, heavily sedated, or have limitations that would interfere with vigorous respiratory efforts. Other types of lung function tests are available for infants and unconscious persons. Another major limitation is the fact that many intermittent or mild asthmatics have normal spirometry between acute exacerbation, limiting spirometry's usefulness as a diagnostic. It is more useful as a monitoring tool: a sudden decrease in FEV1 or other spirometric measure in the same patient can signal worsening control, even if the raw value is still normal. Patients are encouraged to record their personal best measures.

The most common parameters measured in spirometry are Vital capacity (VC), Forced vital capacity (FVC), Forced expiratory volume (FEV) at timed intervals of 0.5, 1.0 (FEV1), 2.0, and 3.0 seconds, forced expiratory flow 25–75% (FEF 25-75) and maximal voluntary ventilation (MVV) [7], also known as maximum breathing capacity [2]. Other tests

may be performed in certain situations.

Results are usually given in both raw data (litres, litres per second) and percent predicted the test result as a percent of the "predicted values" for the patients of similar characteristics (height, age, sex, and sometimes race and weight). The interpretation of the results can vary depending on the physician and the source of the predicted values. Generally speaking, results nearest to 100% predicted are the most normal, and results over 80% are often considered normal. Multiple publications of predicted values have been published and may be calculated online based on age, sex, weight and ethnicity. However, review by a doctor is necessary for accurate diagnosis of any individual situation. A bronchodilator is also given in certain circumstances and a pre/post graph comparison is done to assess the effectiveness of the bronchodilator. See the example printout. Functional residual capacity (FRC) cannot be measured via spirometry, but it can be measured with a plethysmograph or dilution tests (for example, helium dilution test).

Asthma is a chronic inflammatory disease of the airways that is characterized by increased responsiveness of the tracheobronchial tree to multiple stimuli. It is the most common chronic condition in pregnancy [3]. The disease is episodic, being characterized by acute exacerbations intermingled with symptom-free periods. Most asthma attacks prove to be short-lived, lasting minutes to hours. Although patients appear to recover completely clinically, evidence suggests that patients with asthma develop chronic airflow limitations.

The prevalence of asthma in the general population is 4-5%. In pregnancy, the prevalence ranges from 1-4%. Asthma-related morbidity and mortality rates in pregnant women are comparable to those in the general population. The mortality rate from asthma in the United States is 2.1 persons per 100,000 [4]. Although women with mild asthma are unlikely to have problems, patients with severe asthma are at greater risk of deterioration. The deterioration risk is highest in the last portion of a pregnancy. Pregnancy has a significant effect on the respiratory physiology of a woman. While the respiratory rate and vital capacity does not change in pregnancy, tidal volume, minute ventilation (40%), and minute oxygen uptake (20%) increase, with a resultant decrease in functional residual capacity and residual volume of air as a consequence of the elevated diaphragm. In addition, airway conductance is increased and total pulmonary resistance is reduced, possibly as a result of the influence of progesterone.

The consequence of these physiologic changes is a hyperventilatory picture as a normal state of affairs in the later half of pregnancy. This results in the picture of a chronic respiratory alkalosis during pregnancy, with a decreased partial pressure of carbon dioxide (pCO₂), decreased bicarbonate, and increased pH.

A normal pCO₂ in a pregnant patient may signal impending respiratory failure. The increased minute ventilation and improved pulmonary function in pregnancy promote more efficient gas exchange from the maternal lungs to the blood. Therefore, changes in respiratory status occur more rapidly in pregnant patients than in non-pregnant patients. Asthma is characterized by inflammation of the airways, with an abnormal accumulation of eosinophils, lymphocytes, mast cells, macrophages, dendritic cells, and myofibroblasts. This leads to a reduction in airway diameter caused by smooth muscle contraction, vascular congestion, bronchial wall

Edema, and thick secretions.

Almost all anti-asthma drugs are safe to use in pregnancy and during breastfeeding. In fact, undertreatment of the pregnant patient is a frequent occurrence, because such patients are worried about medication effects on the fetus. Outpatient management of asthma is similar for the pregnant patient as it is for the nonpregnant patient. Beta-adrenergic agonists remain the mainstay of treating exacerbations and handling mild forms of asthma. Early research suggests a management algorithm for asthma in pregnancy based on fraction of exhaled nitric oxide (FE NO) and symptoms significantly reduces asthma exacerbations [5].

For moderate-persistent asthma, a beta-adrenergic agonist combined with an inhaled anti-inflammatory agent or inhaled corticosteroid is recommended for treatment. In severe asthma, oral corticosteroids and beta agonists are recommended.

Corticosteroids can be used in the acute and outpatient setting and have been shown to be relatively safe in pregnancy. The intravenous, intramuscular, and oral preparations can be used for acute exacerbations, whereas the inhaled preparations are reserved for outpatient maintenance therapy. Recent data on inhaled glucocorticoids support its relative safety although there is the potential risk for offspring endocrine and metabolic disturbances [6]. Some studies suggest the "sustained" use of systemic steroids may cause a slight increase in congenital malformation (mainly cleft lip), prematurity, low birth weight, preeclampsia, gestational diabetes, and neonatal insufficiency [8, 9, 10, 11, 12, 13]. However, randomized trials have not been performed. A longer-acting beta₂-adrenoreceptor agonist (eg, salmeterol), the bronchodilator effects of which last at least 12 hours, is an effective treatment for nocturnal asthma. Historically, methyl xanthines and oral beta agonists have been used to treat asthma. Both have been shown to be safe in pregnancy but have fallen out of favor for newer medicines and the inhaled forms, respectively.

Magnesium sulfate is another medication that is safe to use in pregnancy. It works as a smooth-muscle relaxant of the airway. Epinephrine use should be avoided in the pregnant patient. In general, epinephrine is used only in the most severe asthma exacerbations. In pregnancy, employment of the drug can lead to possible congenital malformations, fetal tachycardia, and vasoconstriction of the uteroplacental circulation. In rare cases where a systemic beta-agonist is needed, SQ use of terbutaline may be considered [7].

A case-control study by Gidaya *et al* investigated associations between use of β -2-adrenergic receptor (B2AR) agonist drugs during pregnancy and risk for autism spectrum disorders by using Denmark's health and population registers. The study found that B2AR agonist exposure during pregnancy may be associated with an increased risk for ASD however any intervention must be balanced against benefits of indicated medication use by pregnant women [8-9].

The key to treating asthma in the pregnant patient is to frequently assess the patient, the severity of the attack, and the response to treatment. Hypoxia, acidosis, unequal breath sounds, pneumothorax, and atypical features serve as warning signs of severe exacerbations.

Inhaled beta₂-agonists are the mainstay of treatment. The beta₂-agonist, inhaled and/or subcutaneous, is typically given in 3 doses over 60-90 minutes. Beta-adrenergic blocking agents should be avoided owing to bronchospastic effect. The early use of systemic steroids has been shown to reduce the

length of stay in the ED and the admission rate; the effect of steroids is seen within 4-6 hours of the institution of therapy. Supply supplemental oxygen to maintain oxygen saturation higher than 95%. Intravenous fluids can help to loosen and clear secretions. Fetal monitoring becomes important after 20 weeks of gestation in severe cases. Tranquilizers and sedatives should be avoided because of their respiratory depressant effect. Antihistamines are not useful in the treatment of asthma. Mucolytic agents increase bronchospasm.

Less than 1% of all asthmatic patients require mechanical ventilation. Asthmatic patients have higher complication rates from mechanical ventilation. Increased airway resistance may result in extremely high peak airway pressures, barotraumas, and hemodynamic impairment. Mucous plugging is common, increasing airway resistance, atelectasis, and the incidence of secondary pneumonia. Paradoxical increases in bronchospasm may occur from aggravation by the endotracheal tube. Typical ventilator settings may lead to stacked breaths and increased airway pressures. Decrease the ratio of the duration of inspiration to the duration of expiration (I:E ratio), and set a low respiratory rate to allow for adequate expiration.

Pregnancy is a normal physiological state accompanied by significant hormonal, mechanical and circulatory changes. Changes in respiratory physiology during pregnancy occur due to structural changes in the chest wall and abdominal compartments as a consequence of hormonal changes, enlarging uterus and elevated diaphragm. Though there are changes in certain respiratory parameters, FEV1 and PEFR are largely unaffected. It is essential that the normal physiological changes in the respiratory system have to be kept in mind to enable accurate diagnosis of respiratory impairment in pregnancy. PEFR is a simple, non-invasive, easily performable, portable, economical and reproducible tool for effective assessment of asthma control. Though PEFR has been postulated not to significantly change throughout pregnancy, there are conflicting reports from various studies on the variation of PEFR in pregnancy. Hence based on above findings the present study was planned for

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Methodology

The present study was planned in Department of Physiology, Patna Medical College, Patna, Bihar from January 2019 to May 2019. Total 80 cases were enrolled in the present study. The 20 cases are of non-pregnant females. The 20 cases are of each 1st Trimester, 2nd Trimester and 3rd Trimester cases. FVC & PEFR was performed using Mini Wright Peak Flow Meter and best of three recordings noted. Data analyzed using SPSS package version 21.0. Association between PEFR with Age and BMI performed using Pearson correlation.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Inclusion Criteria- Age group- 16-30 yrs and cases of Primigravida or multigravida.

Exclusion Criteria- respiratory or cardiovascular diseases, anaemia, multiple pregnancy, hydramnios & those on chronic therapy for any other ailment were excluded from the study

Results and Discussion

Pulmonary impairment during pregnancy has been associated with adverse outcomes including Low birth weight, IUGR, Gestational Hypertension and Pre term deliveries. It is hence necessary to monitor lung function during pregnancy to ensure optimal and safe outcomes. The course of Bronchial Asthma during pregnancy may remain stable, worsen or improve [10]. Since PEFR is a simple, portable and reproducible tool compared to spirometry, it can be used for assessment of asthma control in pregnancy. However, though PEFR is postulated to be largely unchanged during pregnancy, there are conflicting data on the variation of PEFR in different trimesters and ethnic groups [11-15].

Table 1: Basic Details

Group of Females	Non Pregnant	1 st Trimester	2 nd Trimester	3 rd Trimester
No. of Cases	20	20	20	20
Age in years	19-23	20-24	21-25	21-24
Height in cm	154.5-160.3	152.4-159.7	151.5-162.8	153.3-163.7
Weight in Kg	45-58	49-56	63-67	65-73
BMI (kg/m ²)	19.3-23.7	21.1-23.9	21.5-26.8	25.4-30.1

Table 2: Pulmonary function parameters

Group of Females	Non Pregnant	1 st Trimester	2 nd Trimester	3 rd Trimester
No. of Cases	20	20	20	20
FVC (% predicted)	91-105	65-94	81-94	72-99
PEFR (% predicted)	72-82	46-70	49 - 62	51-62
Progesterone	6.2-22.3	31.2-47.5	49.4-58.9	62.7-77.6

FVC: Forced vital capacity PEFR: Peak Expiratory Flow Rate

Residual volume may decrease slightly during pregnancy but the changes are not consistent. The major changes due to the decrease of functional residual capacity is the decrease in the expiratory reserve volume. These alterations in lung volumes are measurable at 16 to 24 weeks of gestation and progresses until term. The increase in diameter of thoracic cage and preserved respiratory muscle function allow the vital capacity

to remain unchanged, and total lung capacity decreases only minimally by term. Several measurements of the vital capacity can therefore be used to follow the patient with respiratory disease during pregnancy. Measurements of airflow are also not significantly affected by pregnancy. Lung compliance don't appear to be influenced by pregnancy, but chest wall and total respiratory compliance are reduced in the

third trimester because of chest wall changes and increased abdominal pressure.

A significant increase in the respiratory minute ventilation occurs beginning in the first trimester and reaching 10 to 20% above the base line, and term ventilation increases by 50 to 70%. Hyperventilation is due to both increase in metabolic carbon-dioxide production (which increases drive due to the gestation period), as well as increase in the respiratory drive due to the elevated serum progesterone level. The effects of progesterone manifests soon after conception and the degree of hyperventilation correlates with the serum progesterone levels. Progesterone may act either as a direct respiratory stimulant or by changing the sensitivity of the respiratory center to carbon-dioxide. The augmented ventilation is the result of an increase in tidal volume to about 30 to 35%, due to increased rib cage volume displacement.

Pradhan *et al* [16] studied all the pulmonary function parameters were increased except PEFr in group II as compared to group I but this was not statistically significant. The PEFr was increased in group II as compared to group I and this was statistically significant. Conclusion: The PEFr was increased significantly in 36 weeks pregnancies, and should be interpreted carefully in pregnant women.

Neeraj *et al* [17] study was conducted on 100 pregnant women in third trimester of uncomplicated pregnancy (Test group) and 100 age-matched non-pregnant women (Control group) in the age group of 25 to 35 years. Pulmonary function test parameters FVC, FEV1, PEFr and FEF25-75% recorded using Medspiror. All parameters except FEV1/ FVC ratio were found to decline in the Test group as compared to the Control group. This study validates the physiological changes in pulmonary function brought by pregnancy and highlights the need to compile expected and accepted alterations in predicted values of PFT in comparison with the non-gravid states for safer outcome of the pregnancy.

A decrease in FVC, FEV1 & PEFr in pregnancy was observed by Neeraj Candy S *et al* [18] and our study do not correlate with this study. A non-significant increase in FEV1 and significant increase in VC was observed in our study. Decline in PEFr during the third trimester of pregnancy was observed by Hemant Deshpande *et al* [19] correlates with our study.

Chinko *et al* [20] found that Peak expiratory flow rate was found to be significantly lower among the pregnant females compared to the control PEFr was also significantly decreased with increased gestational age ($p < 0.05$), similar study was also done by Rasheed *et al* [21].

There are several studies and reviews of the pregnancy on respiratory function and physiology in health and disease. During pregnancy, there is a 20% increase in oxygen consumption and 15 % rise in the metabolic rate achieved through a 40-50% increase in the resting minute ventilation. The mild respiratory alkalosis seen during normal pregnancy is due to the effect of progesterone causing hyperventilation. Though dramatic physical and hormonal changes occur leading to decreases in chest wall compliance, FRC, minute ventilation and ERV, PEFr and other measures of airway function like FEV1, FEV1/FVC are postulated to largely remain unchanged as airway mechanics and diaphragmatic function are unaltered [22-23].

Enlargement of gravid uterus may cause restrictive effect. Reported reduction in alveolar partial pressure of carbon dioxide in pregnancy [24-25] is associated with bronchial smooth muscle constriction and can cause obstruction in

airway function [26]. Low partial pressure of carbon dioxide has been shown to have direct effect on smooth muscle causing constriction in bronchial muscle strips [27]. Also increased airway angulation at the lung base as occurs in pregnancy can alter airway function. Airway resistance is dependent on lung volume, a reduction in the latter causing an increase in the former [28]. Increased intrapulmonary blood volume as occurs in pregnancy would also tend to reduce airway caliber and increase resistance [29].

Conclusion

The data generated from the present study concludes that definite alteration in pulmonary parameters during different trimesters of pregnancy. The same study involving larger population would help us more in deriving the norms on predicted values on pulmonary parameters in pregnancy.

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