ADDIS ABABA UNIVERSITY

COLLEGE OF MEDICINE AND HEALTH SCIENCES

DEPARTMENT OF MEDICAL PHYSIOLOGY

PULMONARY FUNCTION TESTS AMONG PREGNANT WOMEN OF DIFFERENT TRIMESTER IN DEBERE BERHAN REFERAL HOSPITAL, SHOA, ETHIOPIA

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A Thesis Submitted to the School of Graduate Studies of Addis Ababa University in Partial Fulfillment of the Requirements for Master of Science Degree in Medical Physiology.

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ACRONYMS AND ABBREVIATIONS

AAU - Addis Ababa University
ANC- Antenatal Care
ANOVA- Analysis of Variance
ATS - American Thoracic Society
BMI - Body Mass Index
CI -Confidence Interval
Cm- Centimeter
CO₂ – Carbon Dioxide
COPD -Chronic Obstructive Pulmonary Disease
FEF₂₅-₇₅% – Forced Expiratory Flow Rate at the Middle Part of FVC
FEV₁ - Forced Expiratory Volume in one Second
FEV₉ – Timed Forced Expiratory Volume
FEV₁₉% - FEV₁ to FVC ratio x 100
FVC - Forced Vital Capacity
L/s- Liter per Second
PaCO₂ – Partial Pressure of Carbon Dioxide
PaO₂- Partial Pressure of Oxygen
PEFR - Peak Expiratory Flow Rate
PFTs - Pulmonary Function Tests
RR- Respiratory Rate
SaO₂- Oxygen Saturation of Arterial Blood
SD - Standard Deviation
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ABSTRACT

Introduction: Pregnancy is characterized by sequence of dynamic physiological changes that impact on multiple organ system functions. The increasing size of the fetus with advancing gestation and associated hormonal changes constitute a mechanical impediment to normal process of maternal ventilation. As the uterus expands, the diaphragm is pushed up as much as 4 centimeter. Precise knowledge of the pulmonary function test parameters helps to understand and manage the course and outcome of pregnancy leading to safe delivery. It also helps to avoid misdiagnosis and unnecessary interventions.

Objective: The aim of this study was to determine the effect of normal pregnancy on pulmonary function tests among women that visit Antenatal care clinic in Debere Berhan Referral Hospital, Ethiopia.

Methods: Comparative cross-sectional study design was used in Debere Berhan referral Hospital. A total of 176 study participants were enrolled by convenience sampling technique and categorized in to four groups (those in their first, second and third trimesters, and control). Each group comprised of 44 study participants. Written consent was obtained; anthropometric data, saturation of arterial blood and pulmonary function testes were collected using height and weight measuring scales, pulse oximetry (Oxi-Max N-65), and spiropro® (Courtesy of Jaeger/Cardinal Health, Hochberg, Germany) respectively. Data was tabulated and analyzed using SPSS version 20.0 statistical software.

Results: Mean of FVC for the controls, first, second, and third trimesters were (2.59 ± 0.26, 2.13 ± 0.15, 1.93 ± 0.27, and 1.90 ± 0.11 liters) respectively. Except similar FEV1%, the mean value of FVC, FEV1, PEFR, and FEF 25-75% in pregnant group (at all three trimesters) were significantly decreased from the controls (P<0.05). Strong negative correlation was seen between SaO2 and RR (r= -0.865; P <0.01).

Conclusion: As pregnancy progressed from first to third trimester, dynamic pulmonary function tests (FVC, FEV1, FEF25-75% and PEFR) were dropped and respiratory rate increased. Thus, the results had shown tendency of obstructive pattern while pregnancy becoming advanced. Remarkable decline in SaO2 was observed in pregnant women that might be counterbalanced by raised respiratory rate.

Key words: Pregnancy, high altitude, dynamic lung volumes.
1. INTRODUCTION

1.1. Background of the Study

Pregnancy causes the physiological and anatomical changes in different body systems (Patil HJ, 2015; Teli et al., 2013; McCormack and Wise, 2009; Carlin and Alfìrevic, 2008). The physiological changes occurring in a pregnant woman are vast and widespread. These include changes in genital organs, increase in breast size, weight gain, and other systemic alterations including respiratory, cardiovascular, body water metabolism, hematological and metabolic changes (Deshpandea et al., 2013). These adaptations are necessary to meet the increased metabolic demands of the mother and the fetus.

The combination of hormonal changes and mechanical effects of the enlarging uterus lead to a change on pulmonary physiology of a mother (Patil HJ, 2015; Jadhav et al., 2013). In addition, capillary engorgement and edema of the upper airway down to the pharynx, false cords, glottis and arytenoids would happen in the time of gravidness thereby bringing a substantial change in pulmonary physiology (Heidemann and McClure, 2003).

Progressively enlarging uterus causes diaphragm position to rise up approximately 4 cm above its usual resting position that causes the lung to hold less air (Thomas, 1983). As a result, lung volumes are compromised including functional residual capacity (FRC), total lung capacity (TLC), and vital capacity (VC) (Priyadarshini and Mishra, 2014; Pandey et al., 2014). Dynamic pulmonary function tests like FVC, FEV₁, FEV₁%, and FEF_{25-75%} also decrease due to gravid state of advanced pregnancy (Patil HJ, 2015; Teli et al., 2013).

Besides the size of gravid uterus, many of the physiological changes in the respiratory system are mediated by increased progesterone levels (Heidemann and McClure, 2003). Progesterone is a known stimulant of breathing; and its level in the blood gradually rises approximately from 25 ng/ml at six weeks of gestation to 150 ng/ml at term (LoMauro and Aliverti, 2015; Teli et al., 2010). This progressive increment is responsible for raised respiratory depth and rate (Cebakulu, 2014; Yeomans and Gilstrap III, 2005). Progesterone increases tidal volume around by 200ml (from 500ml to 700ml) and minute ventilation approximately by 40%. This is by increasing sensitivity of respiratory center to carbon dioxide. Progesterone-mediated hypersensitivity to CO₂ increases the respiratory rate by 10% which attributes the raised oxygen consumption during
pregnancy (Yeomans and Gilstrap III, 2005). It also causes fall in functional residual capacity that comprises residual and expiratory reserve volume. As a consequence, alveolar ventilation increases (Carlin and Alfirevic, 2008). Total lung capacity is minimally decreased because of the reduction in residual volume (Yeomans and Gilstrap III, 2005).

Moreover, pregnancy induced elevated progesterone causes bronchial and tracheal smooth muscle relaxation. Therefore, upward displacement of diaphragm along with reduced strength of expiratory muscles may hamper forceful expiration (Jadhav et al., 2013). The increase in ventilation and associated fall in PaCO₂ occurring in pregnancy are probably due to progesterone, which may act via a number of mechanisms. Progesterone lowers the threshold and increases the sensitivity of the respiratory center to CO₂. It is also possible that progesterone acts as a primary stimulant to the respiratory center independently of any change in CO₂'s sensitivity or threshold. Not only does progesterone stimulate ventilation, but it also increases the level of carbonic anhydrase in the red blood cell. An increase in carbonic anhydrase will facilitate CO₂ transfer, and also tends to decrease PaCO₂ independently of any change in ventilation (Priyadarshini and Mishra, 2014; Heidemann and McClure, 2003; Bhatia, 2000). PaCO₂ might reaches to a mean of 20-30 mmHg in the last 12 weeks of pregnancy (Thomas, 1983) resulting in constriction of bronchial smooth muscle to conserve CO₂ (Jadhav et al., 2013). Even, progesterone accompanies reduced chest wall compliance through structural changes in ribcage and abdominal compartments (McCormack and Wise, 2009).

At high altitude (>2500m above sea level), PaO₂ in the atmosphere falls thereby the number of molecules of O₂ present per breath decreases that leads to hypobaric hypoxia. This would be more pronounced during pregnancy (Chawla and Saxena, 2014; San et al., 2013). At high altitude, ventilation has a positive correlation with the consumed energy cost and also, the power and endurance of respiratory muscles which have basic roles for ventilation activity (Chawla and Saxena, 2014). This has been shown by fatigue of diaphragmatic muscle that may affect breathing at high altitude. Ventilatory studies at high altitudes have shown decreased forced vital capacity (FVC), forced expiratory volume in 1 second (FEV₁), and maximal midexpiratory flow rate (FEF₂₅₋₇₅%) (Chawla and Saxena, 2014; Valizadeh et al., 2012). Therefore, the present study was designed to assess the degree of variability of pulmonary function tests of pregnant women in different gestational ages at high altitude.
1.2. Statement of the Problem
Over breathing is one of the many physiological adaptations of pregnancy which is made considerably in progress of maternal and fetal possible needs. The increase in minute ventilation that accompanies pregnancy is often perceived as shortness of breath. About 75% of pregnant women have exertional dyspnea by 30 weeks of gestation. Shortness of breath at rest or with mild exertion is so common that it is often referred to as physiologic dyspnea and is completely reversible once pregnancy is over (Deshpande et al., 2013; McCormack and Wise, 2009). Understanding of the changes is critical in distinguishing the common dyspnea that occurs during normal pregnancy from pathophysiologic states associated with cardiopulmonary diseases seen in pregnancy, and anticipating disease worsening condition during pregnancy in those women with cardiopulmonary diseases (Patil HJ, 2015).

Therefore, an accurate knowledge of the physiological changes in pulmonary functions during normal pregnancy is necessary. In Ethiopia, there is shortage of published findings on pulmonary function tests among pregnant women at altitude. Thus the present study focused on the dynamic pulmonary function tests of high altitude pregnancy at Debere Berhan, North Shoa Zone Amhara Region, Ethiopia.

1.3. Significance of the Study
Pulmonary function status of women is affected by pregnancy and the problem is assumed to be aggravated at high altitude. The body’s response to the dual stressors is determining factor for maternal as well as fetal wellbeing. Hence, knowledge of predicted changes in the respiratory system associated with pregnancy helps clinicians to prevent misdiagnosis of physiological changes as pathological.
2. LITERATURE REVIEW

2.1. Determinants and Tests of Pulmonary Function

Gender and height are the most important predictors of lung function. The third predictor, age, may be a confounding factor. Predicted values are calculated from the measurements performed in reference groups, according to height, age and gender. The study of age-dependent changes in lung function throughout the lifespan reveals distinctive differences. Lung functions decline throughout adult life, even in healthy persons (Pruthi and Multani, 2012). There is no doubt that gender and height are the most important predictors of lung function. Height linearly correlates with lung size. Other predictors for the declining of PFTs such as cigarette smoking, occupational and environmental exposures, airway hyperresponsiveness, productive cough, or malnutrition, altitude residence are indicated (Pruthi and Multani, 2012; Ostrowski and Barud, 2006; Belousova et al. 1997). The most important physiological changes associated with ageing are of respiratory system depicting the decrease in static elastic recoil of the lung, in respiratory muscle performance, and in compliance of the chest wall and respiratory system, resulting in increased work of breathing. Normal aging results in changes of pulmonary mechanics, respiratory muscle strength, gas exchange and ventilatory control. Increased rigidity of chest wall and a decrease in respiratory muscle strength with aging result in an increased closing capacity and a decreased in timed forced expiratory volumes (Pruthi and Multani, 2012). Also, the influence on lung function of waist size, weight, and body composition or muscle strength are underscored.

Pulmonary function test (PFTs) is a generic term used to indicate a series of studies or maneuvers that may be performed using standardized equipment to measure lung function. PFTs can include simple screening spirometer, formal lung volume measurement, diffusing capacity for carbon monoxide, and arterial blood gases. These studies may collectively be referred to as complete pulmonary function survey (Gildea and McCarthy, 2010). Spirometric lung function parameters are used as a diagnostic tool and to monitor the therapy efficacy or course of a disease.

Lung function tests examine the dynamic or static properties of the respiratory system in terms of a driving force (pressure) and flow. Static lung volumes are determined using methods in which airflow velocity does not play a role. It usually refers to the measurements of total lung capacity (TLC), residual volume (RV), functional residual capacity (FRC), and vital capacity (VC). The most common dynamic PFT parameters are 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% (FEF₂₅–₇₅%), peak expiratory flow rate (PEFR).

The FVC is the most commonly performed pulmonary function measurement. In the normal individual, the *total expiratory time* (TET) required to completely exhale the FVC is 4 to 6 seconds. In obstructive lung disease (e.g., chronic bronchitis), the TET increases and it has been reported greater than 10 seconds. In the normal individual, the FVC and the slow vital capacity (SVC) are usually equal. In the patient with obstructive lung disease, the SVC is often normal and the FVC is usually decreased because of air trapping. The FVC is also decreased in restrictive lung disorders (e.g., pulmonary fibrosis, adult respiratory distress syndrome, pulmonary edema). This is primarily due to the low vital capacity associated with restrictive disorders. The total expiratory time needed to exhale the FVC in restrictive disorder, however, is usually normal or even lower than normal, because the elasticity of the lung is high (low compliance) in restrictive disorders (Des Jardins, 2012).

FEVT measurement is obtained from an FVC maneuver. The most frequently used time period is 1 second. Other commonly used periods are 0.5, 2, and 3 seconds. Normally, the percentage of the total FVC exhaled during these time periods is (FEV₀.₅, 60%; FEV₁, 83%; FEV₂, 94%; and FEV₃, 97%). Patients with obstructive pulmonary disease have a decreased FEVT. Likewise, restrictive lung disease also have a decreased FEVT; primarily due to the low vital capacity associated with such disease (Des Jardins, 2012).

Under normal conditions the individuals FEV₁% should be 83% or greater. Clinically, however, an FEV₁% of 65% or more is often used as an acceptable value in older ages. Collectively, the FVC, FEV₁, and the FEV₁% are the most commonly used pulmonary function measurements to (1) determine the severity of a patient’s obstructive pulmonary disease, and (2) distinguish between an obstructive and restrictive lung disorder. The key pulmonary function differences between an obstructive and restrictive lung disorder are; in obstructive lung disorders, both the FEV₁ and the FEV₁% are decreased whereas in restrictive lung disorders, the FEV₁ is decreased, but the FEV₁% is normal or increased (Des Jardins, 2012). The significance of this ratio is twofold. First, it aids in quickly identifying persons with airway obstruction in whom the FVC is reduced. Second, the ratio is valuable for identifying the cause of a low FEV₁. In pulmonary restriction (without any associated obstruction), the FEV₁ and FVC are decreased proportionally; hence, the ratio is in the
normal range. Indeed, in some cases of pulmonary fibrosis, the ratio may increase even more because of the increased elastic recoil of such a lung (Madhani, 2004).

The FEF$_{25\%-75\%}$ is the average flow rate that occurs during the middle 50 percent of an FVC measurement. This average measurement reflects the condition of medium- to small-sized airways. The average FEF$_{25\%-75\%}$ for normal healthy men aged 20 to 30 years is about 4.5 L/sec (270 L/min), and for women of the same age, about 3.5 L/sec (210 L/min). The FEF$_{25\%-75\%}$ decreases with age and in obstructive lung disease. In obstructive lung disease, flow rates as low as 0.3 L/sec (18 L/min) have been reported (Des Jardins, 2012).

The PEFR reflects initial flows originating from the large airways during the first part of an FVC maneuver (the effort-dependent portion of the FVC). Thus, the greater the patient effort, the higher the PEFR value. The PEFR decreases with age and in obstructive lung disease (Des Jardins, 2012).

### 2.2. Pregnancy and Pulmonary Function

The mean value of FVC in third trimester was significantly decreased while compared with control groups (Patil HJ, 2015; Priyadarshini and Mishra, 2014; Jadhav et al., 2013; Sodhi et al., 2010). Likewise, Panchal (2014), reported highly significant decrease of FVC in third trimester than controls. Another study (Grindheim et al., 2012), however, found significant increase in FVC after 14–16 weeks of gestation. A study by Priyadarshini and Mishra (2014), confirmed significant decrease of FVC in both the first and second trimesters in relation to controls. The maximum decrease being in first trimester (Teli et al., 2010).

Other studies reported a significant decrease in FVC from first to third trimester (Teli et al., 2010). But, Jadhav et al. (2013), reported that only FVC of third trimester significantly decreases. However, insignificant variation of mean FVC was observed from first to third trimester (Priyadarshini and Mishra, 2014).

Pradhan et al. (2014), recorded slight but not statistically significant difference in mean values of FVC at 36 weeks and full term pregnancy. Insignificant decline of mean FVC was observed throughout pregnancy as compared to their postpartum period (Phatak and Kurhade, 2003). Another study reported significant fall of mean FVC in early and mid-pregnancy than postpartum period (Grindheim et al., 2012).
Different studies revealed that FEV$_1$ of third trimester pregnant women illustrated decreased mean value than non-pregnant women though it was not as much as that of FVC. Typically the decrement of FVC was more pronounced than FEV$_1$ (Patil HJ, 2015; Sodhi et al., 2010).

Supplementary studies confirmed that significant decrease of mean FEV$_1$ in all trimesters of pregnancy as compared to non-pregnant women (Priyadarshini and Mishra, 2014; Teli et al., 2013; Biswas and Kulsange, 2013; Jadhav et al., 2013; Teli et al., 2010). On the other hand, Sunyal et al., (2012), reported that FEV$_1$ decreased only in the third trimester while the first and second trimesters have not shown significant difference with controls.

Further comparison amongst trimesters have revealed that significant decrease of FEV$_1$ as gestational age increases from first to third trimester (Biswas and Kulsange, 2013). Pradhan et al., (2014), also stated increased FEV$_1$ at full term than 36 weeks of pregnancy though it was not statistically significant. On the other hand, Priyadarshini and Mishra (2014), indicated maintained mean value of FEV$_1$ from first to third trimester. FEV$_1$ of second trimester depicted insignificant decrease while compared with first trimester. In addition, no significant change was seen between FEV$_1$ of second and third trimester. Meanwhile, FEV1 of third trimester has shown a significant fall as compared to first trimester (Jadhav et al., 2013; Sunyal et al., 2012). Other study described that highly significant decrease in first trimester than third trimesters of pregnancy (Teli et al., 2013; Teli et al., 2010).

The FEV$_{1\%}$ comparison between third trimester pregnancy and non-pregnant women by Patil HJ (2015), conforms significant decrease in third trimester. Other worker reported a definite increase due to a less decrease in FEV$_1$ as compared to FVC (Sodhi et al., 2010).

Different researchers showed a significant decrease of FEV$_{1\%}$ in all trimesters of pregnancy when compared to non-pregnant control group (Teli et al., 2013; Sunyal et al., 2012; Teli et al., 2010). According to Biswas and Kulsange (2013), mean FEV$_{1\%}$ in second and third trimester of pregnancy was decreased as compared to non-pregnant women. There was, however, no statistically considerable difference seen in first trimester. In contrast, the study found a maximum decrease of FEV$_{1\%}$ in the first trimester (Teli et al., 2010). FEV$_{1\%}$ in all trimesters of pregnant women was also found to increase significantly as compared to controls (Priyadarshini and Mishra, 2014). Likewise, throughout pregnancy FEV$_{1\%}$ had keeping insignificant variation with controls (Phatak and Kurhade, 2003).
FEV$_1\%$ substantially decreases from first to third trimester of gestation (Jadhav et al., 2013; Sunyal et al., 2012). Other scholar discovered highly significant decrease in first trimester than third trimester of pregnancy (Teli et al., 2013). On the other hand, sustained FEV$_1\%$ has observed from first to third trimester of gestation (Priyadarshini and Mishra, 2014). Pradhan et al. (2014), showed slight increase of FEV$_1\%$ at term than 36 weeks of gestation though not statistically significant. Similarly, it was increased significantly after 14–16 weeks of gestation. However, early and mid-pregnancy of FEV$_1\%$ were substantially decreased while compared with the postpartum period (Grindheim et al., 2012).

FEF$_{25\%-75\%}$, at third trimester of pregnancy significantly decreases as compared to the control counterparts (Sodhi et al., 2010). Similarly, highly significant decrease of FEF$_{25\%-75\%}$, was seen in third trimester (Panchal, 2014). Other scholar confirms that slight but not statistically significant increase in term pregnancy than 36 weeks of gestation (Pradhan et al., 2014).

The finding of Teli et al. (2013), discovered that decreased mean value of FEF$_{25\%-75\%}$ in all trimesters of pregnancy when compared to control group. Moreover, highly significant decrease in first trimester than third trimester was perceived.

Panchal (2014), described highly significant decrease of mean PEFR in third trimester of pregnancy as compared to control group. Similarly, substantial decrease of PEFR was seen in third trimester (Sodhi et al., 2010). It was increased significantly after 14–16 weeks of gestation. However, significantly decreased in early and mid-pregnancy while compared with the postpartum period (Grindheim et al., 2012; Bansal et al., 2012). Other researcher states increased PEFR in term pregnant women as compared to 36 weeks of gestation (Pradhan et al., 2014).

Several studies revealed that in all stages of trimesters, mean PEFR was found to decrease as compared to non-pregnant control group (Priyadarshini and Mishra, 2014; Biswas and Kulsange, 2013; Jadhav et al., 2013; Teli et al., 2010). However, except significant decrease in third trimester, no substantial change was seen during first and second trimester of pregnancy (Deshpandea et al., 2013).

On the other hand, different scholars confirmed that a significant reduction of mean PEFR from first to third trimester and yet the maximum decrease seen in the first trimester (Priyadarshini and Mishra, 2014; Jadhav et al., 2013; Deshpandea et al., 2013; Bansal et al., 2012).
2.3. High Altitude Pregnancy and Oxygen Saturation of Arterial Blood

During pregnancy oxygen consumption increases by about around 20% from 250 to 300 ml/min. Even, at term, oxygen consumption is increased by 60% above non-pregnant values (Heidemann B, 2005). Moreover, by the third trimester, maternal basal metabolic rate is increased by 10 to 20 percent compared with that of the non-pregnant state. This is increased by an additional 10 percent in women with twin gestations. With increasing altitude, hemoglobin carries less oxygen. This occurs because the partial pressure of oxygen in ambient air inspired into the lung decreases and the amount of oxygen available for diffusion into the bloodstream decreases. The resulting hypoxemia stresses oxygen-dependent metabolic processes of pregnant women (Niraj Y and Edwin C, 2012; Shigeki F and Marie R, 2005; Phatak and Kurhade, 2003).

The combination of high altitude and the increased oxygen consumption diminishes the oxygen reserve of the mother and subsequently increases the hypoxic risk to both the mother and the fetus. This hypoxic condition presumptively increases respiratory rate of pregnant women (Shigeki F and Marie R, 2005).

There was statistically significant gradual decrease in SaO$_2$ from first to third trimester as compared to control (Niraj Y and Edwin C, 2012; Fadel et al, 1979). But, Haile and Abebe (2016), ascribed that there was increased arterial O$_2$ saturation as pregnancy progresses. Richlin and his colleagues (1998), found that maternal SaO$_2$ was around 97% throughout pregnancy for healthy, non-smoking women residing at sea level. Another complementary study also indicated that oxygen saturation value did not change appreciably during the course of normal pregnancy (Van Hook JW et al., 1996).

There was statistically very significant increase of respiratory rate from first to third trimester of pregnancy as compared to control (Teli et al., 2010). In addition, Panchal (2014), revealed that increased respiratory rate for pregnant women as compared to normal non – pregnant women. Heidemann B (2005), testified that an increase of respiratory rate by 10% during pregnancy. Yet again, marginal increase of RR was brought by other study (Deshpande et al., 2013). However, unchanged respiratory rate was reported throughout pregnancy (Shailaja Y and Srikanth S, 2013).
3. OBJECTIVES

3.1. General Objective
To assess the effect of normal pregnancy on pulmonary function tests at high altitude (2840m above sea level, 720 mmHG barometric pressure) in Debere Berhan referral Hospital.

3.2. Specific Objectives
1. To determine the pulmonary function tests in three trimesters of pregnancy.
2. To determine the effect of mild hypoxia in oxygen saturation of arterial blood (SaO\textsubscript{2}) of pregnant women.
3. To compare the pulmonary function tests and SaO\textsubscript{2} values of pregnant and non-pregnant women.
4. METHODS AND MATERIALS

4.1. Study Area
This study was carried out at Debre Berhan Referral Hospital. Debere Berhan is located in the North Shoa Zone of the Amhara Region, about 130 kilometers North East of Addis Ababa at average altitude of 2,840 meters above sea level.

4.2. Study Period
The study was conducted from January to March 2016.

4.3. Study Design
Comparative cross sectional study design was employed to assess the effect of normal pregnancy on pulmonary function outcomes among pregnant women who visited ANC clinic in Debere Berhan Referral Hospital. Non-pregnant women who came for family planning service were taken as controls. Totally, 176 study participants were recruited and divided equally into four groups, each comprising of 44 women. The groups include those in their first, second, and third trimesters, and also the non-pregnant women as controls.

4.4. Source Population
All pregnant and non-pregnant women in Debere Berhan town, North Shoa Zone, Amara region, Ethiopia.

4.5. Study Population
All pregnant women who visited ANC clinic of Debere Berhan referral Hospital and non-pregnant women who visited family planning clinic from January up to March 2016.

4.6. Eligibility Criteria

4.6.1. Inclusion Criteria
Apparently healthy pregnant women who volunteered to participate in the study. Non-pregnant women that came for utilization of either of any family planning service were included.

4.6.2. Exclusion Criteria
Those participants who had history of smoking, general debility, recurrent or persistent expectoration, asthma or recurrent bronchitis, occupational exposure to lung toxins, having diabetes mellitus, any current or past cardiovascular or respiratory disorder and with sign of any bone deformity of the thoracic cage were excluded from the study.
4.7. Sample Size Determination

Assumptions: $\alpha$ (two-sided) = 0.05; power = 0.80; effect size = 3; SD = 8.7 liter (percent predicted).

The following formula for sample size calculation was used to determine the number of study participants.

$$n = \frac{2SD^2 (Z_{\alpha/2} + Z_{\beta})^2}{d^2}$$

Where;
- $n$ = the required minimum sample size
- $SD$ = standard deviation from previous studies = 8.7
- $d$ = effect size = Size of the association/difference/effect we expect/wish to be present in the sample = 3
- A level of significance, $\alpha = 5\%$, and power of 80% ($\beta = 20\%$) would be applied
- $Z_{\alpha/2}$ depends on desired significance level, at $\alpha = 0.05$, $Z_{\alpha/2} = 1.96$
- $Z_{\beta}$ depends on desired power, at $\beta = 20\%$, $z_{\beta} = 0.84$

According to the above equation: $n = 132$

By using equal proportion allocation, 132 was divided into three equal parts for each trimester and that brought the share to 44. Another 44 non-pregnant women also recruited for comparison. Accordingly, 132 pregnant women and 44 non-pregnant women were involved in this study. In total, 176 individuals participated in the study.
4.8. Sampling Procedures

All women who were visiting ANC and family planning clinic of Debere Berhan referral Hospital

All women that were fulfilling inclusion criteria

Those women who fulfilled inclusion criteria were conveniently selected

A total of 176 Study participants were involved in the study including controls
4.9. Study Variables

4.9.1. Dependent Variables
Dependent variable includes BMI, respiratory rate and SaO₂ of study participants. In addition, dynamic pulmonary function tests (FVC, FEV₁, FEV₁₁₀, FEF₂₅ - ₇₅%, and PEFR) were dependent variables of this study.

4.9.2. Independent Variables
Age, weight, height, and gestational age of study participants were independent variables.

4.10. Operational Definition

First Trimester: Designates gestational age from 1-12 weeks.
Second Trimester: Designates gestational age from 13-26 weeks.
Third Trimester: Designates gestational age from 27-40+ weeks.
Control: Non-pregnant women they came for utilization of family planning service.
Moderate Altitude: it is an elevation between 1500-2500m above sea level.
High Altitude: it is an elevation of greater than 2500m above sea level.
FVC: The volume of air that can forcibly be blown out after maximum inspiration.
FEV₁: timed forced expiratory volume
FEV₁₁₀: This is the speed of air forcibly expelled from the lungs in the first one second from maximal inspiration.
FEV₁₁₀%: The percentage of the FVC expired in the first one second of maximal forced expiration following full inspiration.
FEF₂₅ - ₇₅%: Indicates expiratory flow in the middle portion of the FVC.
PEFR: The highest flow achieved from maximal lung inflation and forced expiration.

4.11. Data Collection Tools and Process
Semi structured questionnaire was prepared with slight modification to meet the objectives of this study. The English version of the questionnaire was translated to local language (Amharic). Data was collected by trained health workers with direct supervision of the principal investigator. Height and weight measuring scale, spiropro® (Courtesy of Jaeger/Cardinal Health, Hochberg, Germany), and pulse oximetery (Oxi-Max N-65) were used. The height was taken in centimeters (nearest to 0.1 cm) without shoes, feet together, standing as tall as possible with the eyes level and looking straight ahead, and using an accurate measuring device. Weight also measured in kilograms.
(nearest to 0.1 kg) of subject wearing light clothing and bare footed on weighing scale. The PFTs were measured with spirometer in accordance with recommendations of the American Thoracic Society (ATS) at room temperature by the same investigator to ensure its validity. Before each measurement the spirometer was calibrated. Following receipt of consent, the study participants rested for 15 minutes before measurements and the investigator informed study participants about the whole procedure and allowed to do multiple trials before the start of the experiment in order to familiarize the subjects with the test procedures. The study participants were asked to sit comfortably in a chair. After appropriate placement of nose clip, they were instructed to seal the lips around the sterile mouthpiece. The study participant was asked to breathe in maximally and then forcefully expire the air, as fast and as far as possible. Each participant performed the test at least three times, as per the requirement of ATS so that at least two of the maneuvers were reproducible. In some cases, the tests were made more than three times, when the participant failed to produce the reliable value. Maternal SaO\textsubscript{2} also measured in sitting position at the dominant index finger. Respiratory rate was recorded by inspection and palpation of chest and abdomen.

4.12. Data Quality Control
In order to assure the quality of the data, the following measures were undertaken. Training has been given to data collectors about the objective of the study, data collection procedures, and relevance of the study prior to actual data collection. The PI was actively involved in supervising data collection and checking completeness of the questionnaire on daily basis. The collected data was reviewed before data entry. The spirometer was regularly checked for ambient conditions (temperature of 17-20°C, 65-74% humidity, and barometric pressure of 1018-1025 hpa).

4.13. Data Processing and Analysis
Data was coded, entered and cleaned after checking for completeness and consistencies. SPSS version 20.0 statistical software package was used for analysis. Data entry was made by the principal investigator. Mean ± SD of all study groups were compared for statistical significance by independent “t” test and ANOVA. Inter-group comparison was done for Respiratory rate, oxygen saturation of arterial blood, and PFTs of the study participants. Statistical significance was preset at P< 0.05.
4.14. Ethical Consideration
This study was carried out after obtaining ethical approval from the department of medical Physiology, Addis Ababa University; and permission from Debere Berhan referral Hospital. Each study participants were briefed about the objective of this study. Accordingly, volunteered participants who fulfilled the inclusion criteria were included in this study. Throughout data collection process respondent’s privacy was kept confidential by using codes rather than names. Personal data was used only for the stated objectives.
5. RESULT

5.1. Characteristics of Study Participants
A total of 176 study participants were involved in this study. Out of these, 132 were pregnant women correspondingly allocated to each trimester and the rest were 44 controls. Anthropometric measurements, respiratory rate, oxygen saturation of arterial blood and dynamic pulmonary function tests were measured for all 176 respondents.

Figure 1 Illustrates the mean age of study participants for each trimester and controls. Mean age for the first, second and, third trimester and control were $24.41 \pm 2.34$, $25.02 \pm 2.31$, $25.07 \pm 3.17$ and $24.36 \pm 1.57$ years respectively. There were no significant difference seen in between groups.

![Figure 1: Mean age of study participants in Debre Berhan referral Hospital, January to March 2016.](image-url)
As shown in table 1 below, the mean height revealed significant difference ($P < 0.05$) between pregnant women in their third trimester and controls. Whereas, in their first and second trimester kept insignificant variation. In each trimester, the mean weight increased significantly as compared to control group ($P < 0.05$). Mean BMI in the first trimester was not increased significantly from controls. But, it was substantially augmented in second and third trimesters ($P < 0.05$). BMI across all study groups lied with in normal range.

*Table 1: Comparison of mean anthropometric measurements of study participants in Debre Berhan Referral Hospital, January to March 2016.*

<table>
<thead>
<tr>
<th>Gestational age</th>
<th>Height (m)</th>
<th>Weight (kg)</th>
<th>BMI (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trimester 1</td>
<td>1.57 ± 0.01 (P= 0.76)</td>
<td>58.57 ± 3.81 (P= 0.000*)</td>
<td>19.77 ± 1.02 (P= 0.533)</td>
</tr>
<tr>
<td>(n= 44)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trimester 2</td>
<td>1.58 ± 0.02 (P= 0.96)</td>
<td>60.80 ± 3.82 (P= 0.000*)</td>
<td>20.87 ± 1.08 (P= 0.000*)</td>
</tr>
<tr>
<td>(n= 44)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trimester 3</td>
<td>1.59 ± 0.03 (P= 0.000*)</td>
<td>66.02 ± 3.87 (P= 0.000*)</td>
<td>21.69 ± 1.22 (P= 0.000*)</td>
</tr>
<tr>
<td>(n= 44)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>1.58 ± 0.02</td>
<td>55.43 ± 4.27</td>
<td>20.03 ± 1.08</td>
</tr>
<tr>
<td>(n= 44)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Indicates that it was statistically significant when compared with control ($p < 0.05$)
5.2. Arterial Blood Oxygen Saturation and Respiratory Rate

From table 2 below, the mean respiratory rate and arterial blood oxygen saturation of all study participants were presented. Mean respiratory rate was significantly increased in all trimesters as compared to the control group. In similar fashion, mean arterial blood oxygen saturation had shown significant decrease as gestational age increases (P < 0.05).

*Table 2: Mean of arterial blood oxygen saturation and respiratory rate of study participants in Debre Berhan referral Hospital, January to March 2016.*

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Gestational age</th>
<th>Mean ± SD</th>
<th>P - Value</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>RR (breath/minute)</td>
<td>Trimester 1 (n = 44)</td>
<td>17.77 ± 1.93</td>
<td>0.032 *</td>
<td>13.66 ± 1.08</td>
</tr>
<tr>
<td></td>
<td>Trimester 2 (n = 44)</td>
<td>19.80 ± 1.29</td>
<td>0.012 *</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Trimester 3 (n = 44)</td>
<td>21.50 ± 1.44</td>
<td>0.000 *</td>
<td></td>
</tr>
<tr>
<td>SaO₂ (%)</td>
<td>Trimester 1 (n = 44)</td>
<td>95.50 ± 1.50</td>
<td>0.021 *</td>
<td>97.14 ± 1.81</td>
</tr>
<tr>
<td></td>
<td>Trimester 2 (n = 44)</td>
<td>94.23 ± 1.13</td>
<td>0.011 *</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Trimester 3 (n = 44)</td>
<td>91.23 ± 1.14</td>
<td>0.000 *</td>
<td></td>
</tr>
</tbody>
</table>

* Indicates that it was statistically significant when compared with control (p< 0.05)
The line graph below demonstrates mean respiratory rate and arterial blood oxygen saturation of study participants by their group. Mean respiratory rate in control group was lower than in pregnant women. And, it was increased significantly as gestational age advances. However, arterial blood oxygen saturation significantly drops as gestational age upsurges.

* Indicates that it was statistically significant when compared with control (P < 0.05)

Figure 2: Mean respiratory rate and arterial blood oxygen saturation of study participants in Debre Berhan referral Hospital, January to March 2016.
Mean arterial blood oxygen saturation was significantly related with respiratory rate of study participants (p<0.001). Pearson’s test revealed strong negative correlation between these variables (r = - 0.865).

Figure 3: Correlation between mean arterial blood oxygen saturation and respiratory rate of study participants in Debre Berhan referral Hospital, January to March 2016.
### 5.3. Dynamic Pulmonary Function Tests

PFT parameters were compared among cases and controls. Moreover, all the parameters were compared between first and second trimesters, second and third trimesters, first and third trimesters. Mean values for PFT parameters in non-pregnant controls were higher than those subjects in all the three trimesters except FEV$_1$% had a relatively similar value (table 3).

*Table 3: Comparison of mean PFTs between pregnant women and non-pregnant controls in Debre Berhan referral Hospital, January to March 2016.*

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Gestational age</th>
<th>Mean ± SD</th>
<th>P - Value</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (L)</td>
<td>1$_a$ (n = 44)</td>
<td>2.13 ± 0.15</td>
<td>0.000 *</td>
<td>2.59 ± 0.26</td>
</tr>
<tr>
<td></td>
<td>2$_a$ (n = 44)</td>
<td>1.93 ± 0.27</td>
<td>0.000 *</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3$_a$ (n = 44)</td>
<td>1.90 ± 0.11</td>
<td>0.000 *</td>
<td></td>
</tr>
<tr>
<td>FEV$_1$ (L)</td>
<td>1$_a$ (n = 44)</td>
<td>1.87 ± 0.08</td>
<td>0.000 *</td>
<td>2.29 ± 0.22</td>
</tr>
<tr>
<td></td>
<td>2$_a$ (n = 44)</td>
<td>1.73 ± 0.22</td>
<td>0.000 *</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3$_a$ (n = 44)</td>
<td>1.60 ± 0.07</td>
<td>0.000 *</td>
<td></td>
</tr>
<tr>
<td>FEV$_1$% (%)</td>
<td>1$_a$ (n = 44)</td>
<td>86.50 ± 4.10</td>
<td>0.984</td>
<td>86.73 ± 3.70</td>
</tr>
<tr>
<td></td>
<td>2$_a$ (n = 44)</td>
<td>86.11 ± 3.99</td>
<td>0.592</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3$_a$ (n = 44)</td>
<td>86.73 ± 3.49</td>
<td>0.988</td>
<td></td>
</tr>
<tr>
<td>FEF$_{25-75}$% (L/s)</td>
<td>1$_a$ (n = 44)</td>
<td>1.80 ± 0.06</td>
<td>0.000 *</td>
<td>2.07 ± 0.11</td>
</tr>
<tr>
<td></td>
<td>2$_a$ (n = 44)</td>
<td>1.74 ± 0.22</td>
<td>0.000 *</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3$_a$ (n = 44)</td>
<td>1.59 ± 0.12</td>
<td>0.000 *</td>
<td></td>
</tr>
<tr>
<td>PEFR (L/s)</td>
<td>1$_a$ (n = 44)</td>
<td>4.30 ± 0.58</td>
<td>0.000 *</td>
<td>4.75 ± 0.38</td>
</tr>
<tr>
<td></td>
<td>2$_a$ (n = 44)</td>
<td>4.43 ± 0.52</td>
<td>0.000 *</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3$_a$ (n = 44)</td>
<td>3.78 ± 0.34</td>
<td>0.000 *</td>
<td></td>
</tr>
</tbody>
</table>

*Indicates that it was statistically significant when compared with control (p< 0.05)

1$_a$: first trimester  
2$_a$: second trimester  
3$_a$: third trimester
As presented in Table 4, the comparison of mean PFTs between first and second trimester of pregnant women. The measurements of FEV\textsubscript{1\%}, FEF\textsubscript{25-75\%}, and PEFR did not show considerable difference. Meanwhile, FVC and FEV\textsubscript{1} had greater mean value in first trimester than second trimester (P<0.05).

*Table 4: Comparison of mean PFTs between first and second trimester of pregnant women in Debre Berhan referral Hospital, January to March 2016.*

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Trimester 1 (n=44)</th>
<th>Trimester 2 (n=44)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (L)</td>
<td>2.13 ± 0.15</td>
<td>1.93 ± 0.27</td>
<td>0.011 *</td>
</tr>
<tr>
<td>FEV\textsubscript{1} (L)</td>
<td>1.87 ± 0.08</td>
<td>1.73 ± 0.22</td>
<td>0.000 *</td>
</tr>
<tr>
<td>FEV\textsubscript{1%} (%)</td>
<td>86.50 ± 4.10</td>
<td>86.11 ± 3.99</td>
<td>0.944</td>
</tr>
<tr>
<td>FEF\textsubscript{25-75%} (L/s)</td>
<td>1.80 ± 0.06</td>
<td>1.74 ± 0.22</td>
<td>0.102</td>
</tr>
<tr>
<td>PEFR (L/s)</td>
<td>4.30 ± 0.58</td>
<td>4.43 ± 0.52</td>
<td>0.325</td>
</tr>
</tbody>
</table>

* Indicates that it was statistically significant when the two trimesters were compared (p< 0.05)
In order to observe the degree of decline in mean PFTs as gestation progresses, we made further comparison between the first and third trimester pregnant women. As shown in the table below (table 5), all PFT parameters, except FEV₁%, in the third trimester were significantly lower than those who were in their first trimester.

Table 5: Comparison of mean PFTs between first and third trimester of pregnant women in Debre Berhan referral Hospital, January to March 2016.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Trimester 1 (n=44)</th>
<th>Trimester 3 (n=44)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (L)</td>
<td>2.13 ± 0.15</td>
<td>1.90 ± 0.11</td>
<td>0.000*</td>
</tr>
<tr>
<td>FEV₁ (L)</td>
<td>1.87 ± 0.08</td>
<td>1.60 ± 0.07</td>
<td>0.000*</td>
</tr>
<tr>
<td>FEV₁% (%)</td>
<td>86.50 ± 4.10</td>
<td>86.73 ± 3.49</td>
<td>0.985</td>
</tr>
<tr>
<td>FEF₂₅-₇₅% (L/s)</td>
<td>1.80 ± 0.06</td>
<td>1.59 ± 0.12</td>
<td>0.000*</td>
</tr>
<tr>
<td>PEFR (L/s)</td>
<td>4.30 ± 0.58</td>
<td>3.78 ± 0.34</td>
<td>0.000*</td>
</tr>
</tbody>
</table>

* Indicates that it was statistically significant when the two trimesters were compared (p < 0.05)
Table 6 indicates the comparison of mean PFTs between the second and third trimester pregnancy. The mean of FVC and FEV$_1\%$ have disclosed insignificant difference between these trimesters with P-value of greater than 0.05. On the other hand, FEV$_1$, FEF$_{25-75\%}$, and PEFR have decreased significantly in the third trimester.

Table 6: Comparison of mean PFTs between second and third trimester of pregnant women in Debre Berhan referral Hospital, January to March 2016.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Trimester 2 (n=44)</th>
<th>Trimester 3 (n=44)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (L)</td>
<td>1.93 ± 0.27</td>
<td>1.90 ± 0.11</td>
<td>0.759</td>
</tr>
<tr>
<td>FEV$_1$ (L)</td>
<td>1.73 ± 0.22</td>
<td>1.60 ± 0.07</td>
<td>0.021 *</td>
</tr>
<tr>
<td>FEV$_1%$ (%)</td>
<td>86.11 ± 3.99</td>
<td>86.73 ± 3.49</td>
<td>0.633</td>
</tr>
<tr>
<td>FEF$_{25-75%}$ (L/s)</td>
<td>1.74 ± 0.22</td>
<td>1.59 ± 0.12</td>
<td>0.013 *</td>
</tr>
<tr>
<td>PEFR (L/s)</td>
<td>4.43 ± 0.52</td>
<td>3.78 ± 0.34</td>
<td>0.011 *</td>
</tr>
</tbody>
</table>

* Indicates that it was statistically significant when the two trimesters were compared (p < 0.05)
As indicated from the graph (figure 4), all parameters had shown a decreasing pattern as gestation progressed from the first to third trimester (p<0.05).

* Indicates that it was statistically significant when compared with control (P<0.05)

**Figure 4: Comparison of mean PFTs between pregnant women and non-pregnant controls in Debre Berhan referral Hospital, January to March 2016.**
As presented below (figure 5), mean BMI was significantly associated with FVC of study participants (p<0.001). These variables had shown negative correlation with Pearson’s test ($r = -0.427$).

*Figure 5: Correlation between mean FVC and BMI of study participants in Debre Berhan referral Hospital, January to March 2016.*
The mean BMI and PEFR were significantly related as indicated by figure 6 below (p<0.001). Moreover, Pearson’s test (r = -0.865) revealed strong negative correlation between aforementioned variables.

Figure 6: Correlation between mean PEFR and BMI of study participants in Debre Berhan referral Hospital, January to March 2016.
6. DISCUSSION

6.1. Characteristics of Study Participants
The age and height range of study participants lied between 19- 32 years and 1.51- 1.72 meters respectively. There was no statistically significant difference (P>0.05) in mean age and height of pregnant women and controls. This is in accordance with previous findings (Patil HJ, 2015; Panchal, 2014; Priyadarshini and Mishra, 2014; Jadhav et al., 2013; Sodhi et al., 2010; Phatak and Kurhade, 2003). Therefore, possible variation in indices of PFTs due to age and height would not be a factor for this study. The difference in mean weight and BMI was statistically significant between pregnant women and control groups. As gestational age increased from first to third trimester, the mean of two variables were increased significantly as indicated by table 1 (P<0.05). Patil HJ (2015), was reflected similar finding. This might be because of the normal weight gain, and uterine enlargement which occur in pregnancy.

6.2. Respiratory Rate and Oxygen Saturation in Arterial Blood
In this study, the mean respiratory rate was significantly increased from first trimester to third trimester which is in agreement with several studies (Haile and Abebe, 2016; Panchal, 2014; Teli et al., 2010). Likewise, mean respiratory rate of the control group was markedly lower than all the three trimesters (P< 0.05; Table 1, Figure 3). In line with this finding, Heidemann (2005), revealed a 10 % increase of RR during pregnancy. Borderline increment of respiratory rate was also reported in another study (Deshpandea et al., 2013). The observed substantial raise of RR during pregnancy might be due to the presence of high level of progesterone which can stimulate the breathing center in the brain. Progesterone gradually increases during the course of pregnancy from 25 ng/ml at 6 weeks’ of gestation to 150 ng/ml at term. Progesterone acts as trigger of the primary respiratory center by increasing the sensitivity of the respiratory center to carbon dioxide (LoMauro and Aliverti, 2015; Teli et al., 2010).

This study found a strong negative correlation between RR and SaO₂ (P< 0.001; r = - 0.865). This can possibly be due to the considerable reduction in partial pressure of oxygen in Debere Berhan as compared to sea level which can trigger a compensatory rise in respiratory rate. Furthermore, gestational hyperventilation is attributed to upward displacement of diaphragm, hypervolemia, increased cardiac output, and increased demand of growing fetus (Panchal, 2014). Shailaja Y. and Srikanth S. (2013), however, reported no change in respiratory rate during the course of
pregnancy. This is probably, because, sometimes increase in ventilation occurs without an increase in respiratory rate; and accomplished mainly by a rise in tidal volume only. The mean arterial blood oxygen saturation substantially drops while gestational age increases; the mean $\text{SaO}_2$ in control group was significantly higher than each trimesters as well ($p<0.05$; Table 1 and Figure 3). Previous studies have shown similar finding (Niraj Y and Edwin C, 2012; Fadel et al., 1979). However, increased $\text{SaO}_2$ with advanced gestation was reported by others (Haile and Abebe, 2016). Different from these findings, unchanged mean $\text{SaO}_2$ ($\sim 97\%$) was described across pregnancy for healthy, non-smoking women residing at sea level (Richlin S et al., 1998; Van Hook JW et al., 1996). The reduced $\text{SaO}_2$ for Debere Berhan pregnant women might be due to diminished partial pressure of oxygen which reduces alveolar oxygen tension. Other possible reason could also due to increment of, maternal plasma volume by 45 %, and red blood cell mass by 20–30 % during pregnancy. In the meantime, this disproportionate increment of plasma volume with red blood cell mass might cause arterial oxygen to be dissolved more and then unable to detected by pulseoxymetry easily (Branch and Wong, 2014).

6.3. Changes in Indices of Dynamic PFTs
Mean $\text{FEV}_1$ of all trimesters were found to be significantly decreased from the control. Previous independent studies support our finding (Priyadarshini and Mishra, 2014; Teli et al., 2013; Biswas and Kulsange, 2013; Jadhav et al., 2013; Teli et al., 2010). In other study, however, $\text{FEV}_1$ was found to be lower only in the third trimester while it was showing insignificant difference in the first and second trimester (Sunyal et al., 2012). Our study found insignificant difference in mean $\text{FEV}_{1\%}$ between pregnant and non-pregnant control groups which is in consistent with a study by Phatak and Kurhade (2003). The plausible explanation for insignificant change of $\text{FEV}_{1\%}$, might be relaxation of smooth muscles provided that pregnancy hormones (progesterone, corticosteroids and relaxin) all have some degree of Broncho dilating effect. Thus the mechanical disadvantage to the respiratory apparatus induced by advancing pregnancy is compensated by decrease in airway resistance and an improved airway conductance. Unlike our results, substantial decline of $\text{FEV}_{1\%}$ was reported by numerous studies (Teli et al., 2013; Sunyal et al., 2012; Teli et al., 2010). Priyadarshini and Mishra (2014), also stated raised $\text{FEV}_{1\%}$ in all trimesters as compared to non-pregnant counterparts. According to Biswas and Kulsange (2013), mean $\text{FEV}_{1\%}$ in the second and third trimester was slightly decreased as compared to non-pregnant women but was not statistically considerable in the first
trimester. In conformity with findings by Priyadarshini and Mishra’s, control’s mean FVC was lower than from the second and first trimesters. Again, in favor of our finding, FVC in the third trimester significantly declines while compared with the control (Priyadarshini and Mishra, 2014; Jadhav et al., 2013; Sodhi et al., 2010). Patil HJ (2015), also observed significant decrease of FEV1% only in the third trimester. Another study, however, documented a maximal decrease in FVC and FEV1% in the first trimester (Teli et al., 2010).

The current study implied significant decrease of mean FEF25-75% in all the trimesters of pregnancy as compared to the control group. Teli et al. (2013), also reported similar finding. Moreover, mean FVC, FEV1 and FEF25%-75% in the third trimester significantly decreases from the control (Patil HJ, 2015; Panchal, 2014; Sodhi et al., 2010). In contrast to our results, the decrement in FVC was more prominent than FEV1. But, our finding revealed that persistent mean FEV1% throughout pregnancy. This might be due to a proportional decrease of FEV1 and FVC so that the ratio of FEV1/FVC was appeared like unity. Sodhi et al. (2010), however, described a definite increase of FEV1% due to less drop in FEV1 as compared to FVC. Priyadarshini and Mishra (2014), have found sustained mean value of FVC, FEV1, and FEV1% from first to third trimester.

We found a significant reduction of mean FVC as gestational age increases which coincides with the finding of Teli and his colleagues (Teli et al., 2010). The decrease in FVC is attributable to the mechanical pressure of enlarging gravid uterus, elevating the diaphragm and restricting the movements of lungs that hampers the forceful expiration.

In line with ours, studies reported a significant fall in FEV1 of third trimester as compared to the first trimester (Jadhav et al., 2013; Sunyal et al., 2012). However, other studies found highly significant decrease in FEV1 and FEF25-75% in the first trimester than third trimester (Teli et al., 2013; Teli et al., 2010).

We found that significantly lower mean PEFR values in pregnant women as compared to the non-pregnant control which is in agreement with several studies (Priyadarshini and Mishra, 2014; Biswas and Kulsange, 2013; Jadhav et al., 2013; Teli et al., 2010). Other finding, however, the accounted no substantial change in PEFR in the first and second trimester except that significant decrease in the third trimester (Deshpande et al., 2013). Other complementary studies, found significant decrease in PEFR only in the third trimester (Panchal, 2014; Sodhi et al., 2010). Our findings showed extensive drop of PEFR for each trimester as compared to control groups. The
decrease in mean PEFR may be attributed to lesser force of contraction of main expiratory muscles (anterior abdominal muscles and internal intercostal muscles) or could be due to mechanical effect of enlarging gravid uterus affecting vertical dimension by restricting the diaphragmatic movement.

In line with the current study, several researchers reported progressive decline in PEFR as gestation advanced from the first to third trimester (Priyadarshini and Mishra, 2014; Jadhav et al., 2013; Deshpandea et al., 2013; Bansal et al., 2012). Maximum decrease of PEFR was documented in the first trimester which may be attributable to hormonal changes (Teli et al., 2010). However, in our case, PEFR was highly dropped in the third trimester. This is probably because, PEFR maneuver involves muscular element which is negatively affected due to downward displacement of diaphragm around full term pregnancy (Pradhan et al., 2014).

The declining of FVC, FEV$_1$ and FEF$_{25-75\%}$ in the first trimester can be attributed to morning sickness whereas in second and third trimester it may be due to mechanical pressure of enlarging gravid uterus. Elevating the diaphragm and restricting movements of lungs and thus hampering forceful expiration, it may be also due to brochoconstrictor effect of decrease alveolar Pco$_2$ on the bronchial smooth muscles. Other factors such as hormonal influences also play a role in altering and compromising the pulmonary flow parameter like FEV$_1$, PEFR and FEF$_{25-75\%}$. 


During pregnancy, mean of respiratory parameters decline as gestational age progresses from first to third trimester. Moreover, mean PFTs of each trimester were lower than the non-pregnant controls. Pulmonary function tests including FVC, FEV1, PEFR and FEF25-75% but not FEV1%, decreased significantly. Thus the present study concluded PFTs of the pregnant women would show tendency of obstructive pattern. These outcomes might arise from combination of hormonal changes and mechanical adjustments of the enlarging uterus that has a significant effect on pulmonary physiology of the pregnant mother. It was also concluded that upraised of respiratory rate when gestational age increased. On the other hand, oxygen saturation of arterial blood was declining as pregnancy advances. These alterations are compulsory to meet the increased metabolic demands of the mother and fetus. Therefore, the present study concluded that pregnancy at altitude can bring about compensatory changes to balance with the changes occurring in dynamic pulmonary function tests.
8. LIMITATION OF THE STUDY
Longitudinal studies may reveal better results with larger sample size. The study also did not consider parity, and whether the pregnancy was singleton or multiple.

9. RECOMMENDATION
Future studies need to be done with large sample size and longitudinal studies taking parity, chest size, type of pregnancy, and other socioeconomic factors into attention.
10. REFERENCES


11. ANNEXES

I. Information sheet

Good morning/afternoon, my name is ____________. I am working on behalf of Mr. Yosef Eshetie. He came from Addis Ababa University, college of health sciences, school of medicine, and department of medical physiology to conduct his MSc research entitled with “Pulmonary Function Tests Among Pregnant Women of Different Trimester in Debere Berhan Referral Hospital, Shoa, Ethiopia, 2016”. The purpose of this study is to assess the effect of normal pregnancy on pulmonary function test at high altitude.

To do so, he has got permission from his university ethical review board and this hospital administration. Your participation is very important for the outcome of the study. If so, you would like to participate on this noninvasive minor lung function test procedure and pulse oximetry measurement which may take up to 15 minutes. All the information that I will take remains confidential and you don’t need to mention your name. Hence, I kindly request you to participate in this study. All this is completely on voluntary bases and you have the right to refuse, withdraw from the study. Participation or non-participation and refusal to procedures will have no effect on your life. If you have further questions or would like to know the results of this study, please feel free to contact the principal investigator with the following address.

Yosef Eshetie
Cell phone: 0910966364
E-mail: yophy2006@gmail.com
II. Consent Form

I have obtained adequate information about the process and the objective of the study. And also, I have understood and informed about the purpose, advantage, and disadvantage of this study entitled with effect of normal pregnancy on pulmonary function test who visit Debre Berhan Referral Hospital ANC clinic. I also understood that the research imposes no risk and no complication would be provided to me and my family. I have been told that if I fill discomfort to respond to any of the question, I fill free to withdraw at any time as I wish to do so.

I have understood the information given and the participation is completely voluntary based. I have been told that my answers to the questions will not be given to anyone and not expect to write my name. Now I am giving my written consent to participate in the study voluntarily.

Could I have your permission to continue?

1. Yes
2. No, Stop

Witness: Signature _________ Date____________

Data collector:

Name __________________________ Signature __________ Date__________

Result:

1. Questionnaire completed
2. Questionnaire partially completed
3. Participant refused
4. Others (please Specify)

Checked by Supervisor:

Name __________________________ Supervisor’s Signature ___________ Date__________
የስምምነት ውስጥ የወጡ (Amharic version)

የዉስቱን በሚያካሂት ወጤት የመሆኑን ፀትር የተጠበቀ ያለበት፡፡ የነበረ የሚወሰደው የሚሆኑ ዋላማም ይርጉምና በአተገገፋስ ወርአት ከላይ የለውን የተቃው የመለካት የመሆኑን ገብቃለሁ፡፡ ከኔ የሚወሰደው የዉሸው ያ hass ያስሆ የመረጃ የተሰጥቶኛአል፡፡ የዉህ የጥናት በተጠበቀ የሚቹላይ ይው፡፡ ከወደወጡ የሚወሰደው የዉሙ ያስሆ ያስጠቀም ከሚገለጽም ይርጉም የተጠበቅ ያለበት፡፡ የግብአት ዋላማም ይርጉም የእል የማያስከትል የመሆኑን አውቁስአለሁ፡፡ የአጤና ይግል የማያስከትል የመሆኑን አውቁአለሁ፡፡ የሚሆኑ ዋላማም ይርጉም የእል የማያስከትል የመሆኑን አውቁስአለሁ፡፡ ይህ ዯንብ የሚሆኑ ዋላማም ይርጉም የእል የማያስከትል የመሆኑን አውቁስአለሁ፡፡
III. Questionnaire

Addis Ababa University  
College of Health Sciences  
Department of physiology

1. Age of participants in year_____

2. Anthropometric measurements of study participants
   - Height in meter________
   - Weight in kilogram________
   - Body mass index (BMI) in Kg/m\(^2\) _________

3. Gestational age expressed in trimester _______

4. SaO\(_2\) (%) _______________________________

5. Pulmonary function tests

<table>
<thead>
<tr>
<th>PFTs</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>RR (breath/minute)</td>
<td></td>
</tr>
<tr>
<td>FVC (liter)</td>
<td></td>
</tr>
<tr>
<td>FEV(_1) (liter)</td>
<td></td>
</tr>
<tr>
<td>FEV(_{1})% (in percent)</td>
<td></td>
</tr>
<tr>
<td>FEF(_{25-75})% (in liter/second)</td>
<td></td>
</tr>
<tr>
<td>PEFR (liter/second)</td>
<td></td>
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</tbody>
</table>
መጠይቅ (Amharic version)

አዲስ አበባ የጤና ሳይንስ ኮሌጅ የፊዚዎሎጅ ትምህርት ክፍል

1. እድሜ (በ ከመት)

2. ከአጋ የትምህርት
   - ከመት በ ከርት
   - ከልክት በ ከጤና የጤና (BMI) in Kg/m²

3. የጽንስ እድሜ በትራይሚስተር ከርክር

4. የኦክስጅን የትምህርት (SaO₂ in %)

5. የአተነፋፈስ የትምህርት

<table>
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<td>FEV₁ (liter)</td>
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<tr>
<td>FEV₁% (in percent)</td>
<td></td>
</tr>
<tr>
<td>FEF₂₅ - ₇₅% (liter/second)</td>
<td></td>
</tr>
<tr>
<td>PEFR (liter/second)</td>
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