SPIROMETRY PROFILES AMONG PREGNANT AND NON-PREGNANT AFRICAN WOMEN

Jacktan Josephat

MSc (Physiology) Dissertation

Muhimbili University of Health and Allied Sciences

June, 2021

Muhimbili University of Health and Allied Sciences

Department of Physiology

SPIROMETRY PROFILES AMONG PREGNANT AND NON-PREGNANT AFRICAN WOMEN

By

Jacktan Josephat

A Dissertation Submitted in Partial Fulfillment of the Requirements for the Degree of Masters of Sciences (Physiology) of the Muhimbili University of Health and Allied Sciences.

June, 2021

CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled ***Spirometry Profiles among Pregnant and Non-Pregnant African Women***, in fulfillment of the requirements for the degree of Master of Science (Physiology) of Muhimbili University of Health and Allied Sciences.

_____

Dr. Alexander M. Tungu (MD, PhD)

(Supervisor)

Date: _____

_____

Dr. Fredrick Mashili (MD, PhD)

(Supervisor)

Date: _____

DECLARATION AND COPYRIGHT

I, **Jacktan Josephat**, declare that this **dissertation** is my own original work and that it has not been presented and will not be presented to any other University for a similar or any other degree award.

Signature…… Date…….....….....

ACKNOWLEDGMENT

I would like to offer my appreciation to my supervisors on this research, Dr. Alexander M. Tungu and Dr. Fredrick Mashili for their tireless effort in contributions, critique, and inputs to make this research well-expressed. I also would like to thank the Department of Physiology at Muhimbili University. With extended thanks to Mr. Elibariki Kapinda who was my research assistant. Also, fellow students Dr. Elvis Msaki and Dr. Tuntufyege Mwasanjobe for their dedication to this research together with the ethical review committee for clearing this research to be conducted. Distinct gratitude is to the University of Dodoma (UDOM) for funding my research.

I would also like to give thanks to the management of Mnazi Mmoja health center with extended appreciation to the Reproductive and Child health unit workers for their corporation and allowing the study to be conducted within their vicinity. Critical thanks goes to all women who granted their partaking in this study.

Last but not least, I would like to give great thanks to my Parents, My beautiful wife Maria, and young sister Jacklina who were understanding and positive throughout my studies.

ABSTRACT

Background: Lung function tests are done to assess the working and possible mechanical deterioration of lungs, respiratory muscles, and chest wall. Spirometry is the commonly used test. Pregnancy derives an altered physiological state due to accompanied hormonal and anatomical changes that affect the respiratory system. Despite that, spirometry is rarely done in pregnancy, and if done test results are compared against non-pregnancy references.

Objective: This study aimed at determining spirometry profiles in pregnant and non-pregnant women and describe their differences.

Methodology: This hospital-based cross-sectional study was conducted at Mnazi Mmoja antenatal clinic where pregnant women who met the inclusion criteria were randomly recruited. Also, non-pregnant women were recruited from MUHAS as controls. Lung function was assessed using a digital spirometer (EasyOne®) while adhering to standard operating procedures (SOPs) and infection prevention protocols. Data were entered and analyzed using SPSS version 23. The means of spirometry parameters of pregnant women were compared to parameters of non-pregnant women using an independent sample t-test. The level of significance was set to < 0.05 p-value.

Results: A total of 92 pregnant and 98 non-pregnant women were subjected to spirometry. Mean FVC (p <0.01), FEV1 (p <0.01), and PEF (p <0.01) of pregnant women were significantly lower than non-pregnant women.

Conclusion: Spirometry test values obtained from pregnant women were lower than those obtained from non-pregnant controls.

Recommendations: Spirometry test values of pregnant women should be carefully interpreted against non-pregnancy references otherwise can cause underestimation of their values, and hence over-hospitalization. There is also a need to evaluate the accuracy of non-pregnancy spirometry reference equations for predicting test values among pregnant women.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ATS:	American Thoracic Society
BMI:	Body Mass Index
BMJ:	British Medical Journal
CI:	Confidence Interval
ERC:	Ethical Review Committee
ERS:	European Respiratory Society
FEV1:	Forced Expiratory Volume in 1 Second
FVC:	Forced Vital Capacity
L:	Liter
ml:	milliliter
MUHAS:	Muhimbili University of Health and Allied Sciences
NHANES:	National Health and Nutrition Examination Survey
Non-preg:	non-pregnant
PEF:	Peak Expiratory Flow
SD:	Standard Deviation
SEM:	Standard Error of Mean
SOP:	Standard Operating Procedures

DEFINITION OF TERMS

FEV1:	The volume of air exhaled in the first second of FVC measurement
FVC:	The volume of air a person exhales maximally and forcefully after inhaling maximally
Gestation:	The period when a woman is carrying an embryo or fetus
Multiple pregnancies:	Carrying more than one embryo in the same pregnancy
Parity:	A number of viable births a woman had regardless of whether a child was alive or not. Nulliparous have never given birth while parous have given birth at least once.
PEF:	The person's maximum rate at which air can be forcefully exhaled after inhaling maximally
Spirometry:	The lung function test which measures the amount and rate at which air is exhaled after maximal inhalation

CHAPTER ONE

INTRODUCTION

1.1 Background

Lung function tests are investigations done to assess the ability of lungs to exchange gasses and possible mechanical deterioration of lungs, respiratory muscles, and chest wall. They are widely used to confirm and classify respiratory disorders, also to monitor respiratory response to pharmacological, environmental, and developmental changes (Behr and Furst, 2009). They include spirometry, lung volumes test, lung diffusion capacity, pulse-oximetry, arterial blood gas analysis and fraction exhaled nitric oxide test. Of these, spirometry is the commonly used lung function test (Behr and Furst, 2009). Spirometry assesses functions of lung tissue, chest wall, respiratory muscles, and airways by measuring the volume of air and the rate at which a person can exhale from lungs that are filled at their full capacity (Kevin McCarthy and Raed A Dweik, 2020). The most useful spirometry measurements are forced vital capacity (FVC), forced expiratory volume (FEV), and peak expiratory flow (PEF) (Graham *et al.*, 2019). FVC is the volume of air a person exhales maximally and forcefully after inhaling maximally. FEV1 is the volume of air exhaled in the first second of FVC measurement. PEF is a person's maximum rate at which air can be forcefully exhaled after inhaling maximally.

Interestingly, spirometry parameters vary depending on various factors like age, sex, height, weight, body position, and race or ethnic groups (Pellegrino *et al.*, 2005). Most of the parameters peak at 20-25 years before they start to decline (Talaminos Barroso *et al.*, 2018). The most affected parameters are FVC and FEV1 (Talaminos Barroso *et al.*, 2018). These parameters differ between males and females mainly due to biological and body size differences (Townsend, Miller and Prakash, 2012; Quanjer *et al.*, 2014). Also, the profile of common spirometry parameters differs

between known races of the world (Quanjer *et al.*, 2014) and varies when taken in different positions (sitting, standing, or lying) (Siva *et al.*, 2015). The influence of age, sex, body size, race, and positions are thought to be due to their relation with expiratory muscles mass and strength, chest wall compliance, airway resistance, and lung tissue elasticity (Sharma and Goodwin, 2006; Townsend, Miller and Prakash, 2012; Lalley, 2013; Quanjer *et al.*, 2014; Siva *et al.*, 2015; Lutfi, 2017; Talaminos Barroso *et al.*, 2018). A growing body of evidence shows that expiratory muscles mass and strength, chest wall compliance, airway resistance, and lung tissue elasticity appear to be influenced during pregnancy (Gilroy, Mangura and Lavietes, 1988; Smith *et al.*, 1990; Gilleard and Brown, 1996; Lapinsky *et al.*, 2014).

Even though pregnancy is not a disease, it derives an altered physiological state mostly due to accompanied hormonal changes (Yeomans and Gilstrap, 2005). Progesterone and estrogen are the main triggers and drivers of pregnancy-induced physiological changes (Weinberger *et al.*, 1980; LoMauro and Aliverti, 2015; Ku *et al.*, 2018). Progesterone serum level increases linearly and is responsible for physiological alterations while estrogen modulates the effects of progesterone by increasing receptors number and sensitivity (Weinberger *et al.*, 1980; LoMauro and Aliverti, 2015; Ku *et al.*, 2018).

Like all other organ systems, the respiratory system is influenced by and has to adapt to anatomical and physiological factors of pregnancy (Gazioglu *et al.*, 1970; Manfré Pastro *et al.*, 2017). Apparently, growing gravid mechanically interferes with lungs and respiration. The diaphragm and lungs are displaced upward (Smith *et al.*, 1990), the ribcage volume (Gilroy, Mangura and Lavietes, 1988) and chest wall compliance decreases (Lapinsky *et al.*, 2014) with uterine growth. Respiratory muscles and other abdominal muscles respond to increasing abdominal volume by increasing their separation breadth, stretch, and insertion angle (Gilleard and Brown, 1996) thereby

dipping their strength. These changes often cause nocturnal dyspnea, chest discomfort, and difficulty in breathing, especially during late pregnancy (Leighton and Fish, 2009).

Meanwhile, progesterone stimulates respiration either by directly acting on the respiratory center (Bayliss *et al.*, 1987) or by increasing metabolic activity hence oxygen demand. Estrogen modulates respiratory effects of progesterone by increasing receptor number and sensitivity expressly in the medullary respiratory center (Weinberger *et al.*, 1980; LoMauro and Aliverti, 2015; Ku *et al.*, 2018). This hyperstimulation causes an upsurge in the depth of respiration and it is the commonest cause of physiological dyspnea that normally improves with gestation aging (Tenholder and Sout-Paul, 1989; Knox, 2001).

Nevertheless, physiological and anatomical changes of pregnancy largely target to protect the fetus, yet are likely to predispose the mother to diseases or exacerbate pre-existing conditions (Ie *et al.*, 2002; Murphy, Clifton and Gibson, 2006). Immunological changes in pregnancy predispose mothers to respiratory infections (Bhatia and Bhatia, 2000; Yeomans and Gilstrap, 2005). Likewise, cardiovascular changes may increase the risk of developing pulmonary edema (Bhatia and Bhatia, 2000; Yeomans and Gilstrap, 2005) thromboembolism (Toglia and Weg, 1996) and can exacerbate asthma, especially between 24 and 36^{th} weeks of gestation (Smith *et al.*, 1990). These in turn may affect the spirometry parameters among pregnant women. For that reason, distinguishing normal physiological changes from pathological changes using spirometry was important. However, what is normal should be known to identify an abnormality.

About half of all pregnant women report respiratory infections during pregnancy (Collier *et al.*, 2009). Restriction pattern appears to be more severe in pregnancy (Lapinsky *et al.*, 2014) than in the general population (Nonato *et al.*, 2015). Despite that, lung function tests including spirometry are less frequently performed among pregnant women even among those with conditions that

affect the lungs (Zieleskiewicz *et al.*, 2014). There are no spirometry reference values for pregnant women; hence comparisons are made with the general population. This is likely to underestimate the lung function parameters among pregnant women. Therefore, evaluation of the lung function profile among the pregnant population was important. Thus, this study assessed the lung function profile among women with normal pregnancies and compared it with non-pregnant women using spirometry.

1.2 Problem statement

Pregnancy brings up anatomical and physiological changes that affect the respiratory system. The respiratory response to pregnancy ranges from mechanical to physiological changes in the lungs, respiratory muscles, and the respiratory centers(Weinberger *et al.*, 1980; Gilroy, Mangura and Lavietes, 1988; Smith *et al.*, 1990; Gilleard and Brown, 1996; Lapinsky *et al.*, 2014; LoMauro and Aliverti, 2015; Ku *et al.*, 2018). Also, respiratory conditions are common in pregnancy (Collier *et al.*, 2009) and restrictive disorders if occur during pregnancy severely affects lung function profile (Lapinsky *et al.*, 2014) than the general population (Nonato *et al.*, 2015). Respiratory disorders are associated with adverse perinatal outcomes (Schatz *et al.*, 2006; Little and Sinert, 2016; Yland *et al.*, 2020).

Despite that, spirometry is less frequently performed among pregnant women, even among those with respiratory conditions. Furthermore, there is a lack of reference values for spirometry parameters and their associated factors among pregnant in Sub Saharan Africa including Tanzania. Few studies available only involved non-pregnant African women (Knudsen *et al.*, 2011; Musafiri *et al.*, 2013; Ivanova *et al.*, 2020). Therefore, the test results among pregnant women are compared against the general population reference values. This is likely to underestimate the spirometry parameters among pregnant women, thus increasing the risk of mismanagement, particularly

among those with respiratory conditions. This study aimed at evaluating lung function in pregnant and non-pregnant women in African settings using spirometry.

1.3 Conceptual framework

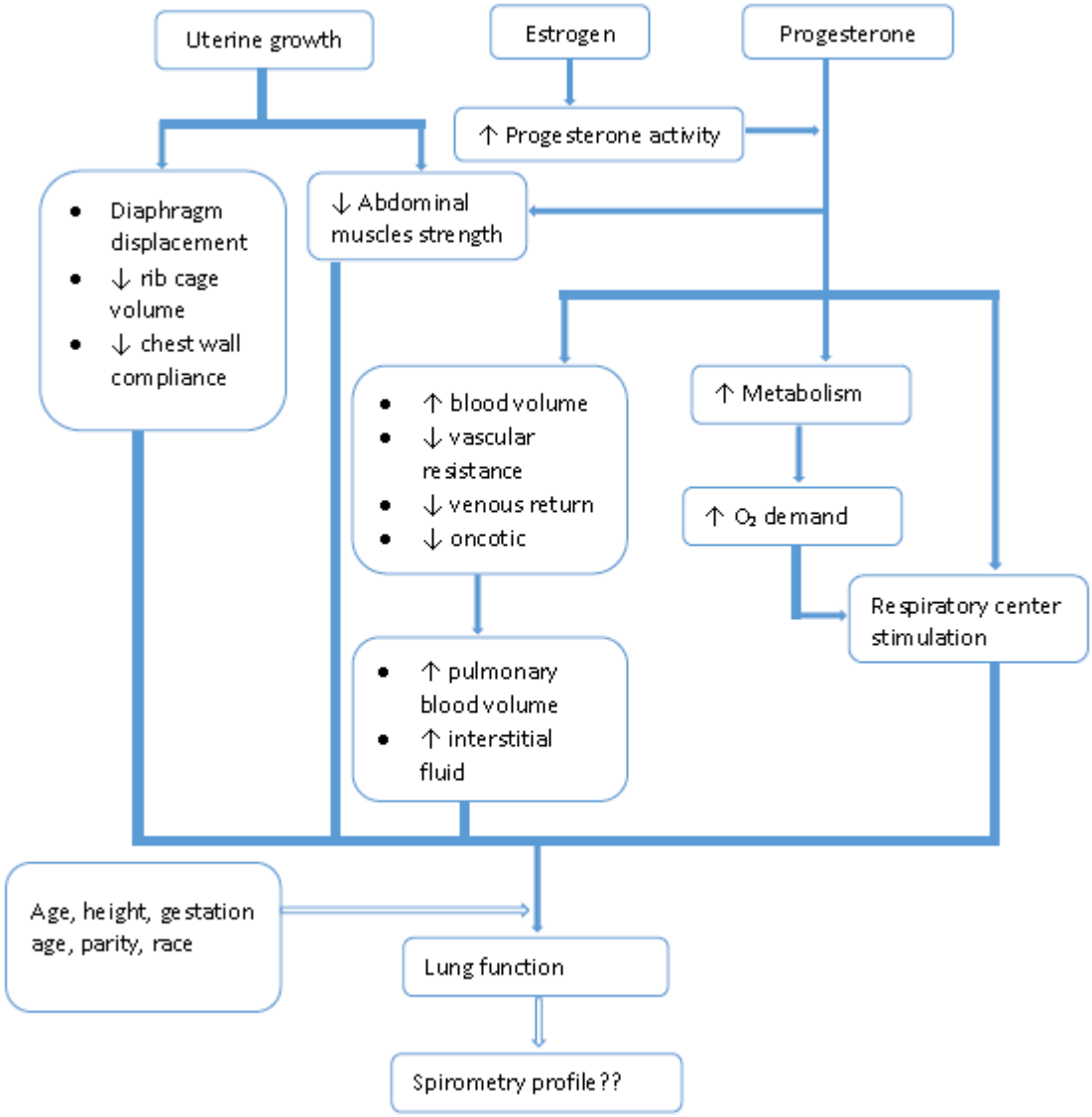

Figure 1: Conceptual framework

1.4 Rationale of the study

Interpreting spirometry tests in pregnancy against reference values generated from the general population could be inappropriate. There was a lack of studies documenting spirometry profiles and their associated factors among pregnant women in Sub-Saharan Africa including Tanzania. Consequently, interpretation of the spirometry results among pregnant women was done against reference values obtained from the non-pregnant populations which are likely to underestimate the

spirometry profiles among the pregnant women. Thus, a study documenting spirometry profiles among pregnant and compare to non-pregnant women in Sub-Saharan Africa was important.

Therefore, this study provided a spirometry profile among women which will improve our understanding of lung function of women with and without pregnancy. The description of spirometry profiles in pregnant and non-pregnant African women will be useful for reference purposes in the diagnosis and management of respiratory conditions.

1.5 Research questions

This study aimed at answering the following general question; what are the spirometry profiles and associated factors among pregnant and non-pregnant women?

The general question was addressed by answering the following specific questions.

i. What is the spirometry profile among 6-36 weeks pregnant women?
ii. What is the spirometry profile among non-pregnant women?
iii. What are the factors affecting spirometry profiles among 6-36 weeks pregnant and non-pregnant women?
iv. Is there any difference in spirometry profiles between 6-36 weeks pregnant and non-pregnant women?

1.6 Objectives

The objectives of this study were the following;

Broad objective: - to evaluate spirometry profile and associated factors among pregnant and non-pregnant African women.

Specific objectives: -

i. To describe the spirometry profile among non-pregnant women

ii. To describe the spirometry profile among 6-36 weeks pregnant women

iii. To describe the factors affecting spirometry profiles among 6-36 weeks pregnant and non-pregnant women

iv. To determine the difference in spirometry profiles between 6-36 weeks pregnant and non-pregnant women

CHAPTER TWO
LITERATURE REVIEW

2.1 Spirometry profile of non-pregnant women

Compared to men, women's respiratory system grows faster at more proportionality hence they peak earlier and have lower specific airway resistance which causes higher expiratory flow rates (Townsend, Miller and Prakash, 2012). However, women have smaller lungs and airways which give smaller peak flow volumes (Lomauro and Aliverti, 2018). Average women's spirometry profiles in the general population have been shown to vary closely in different studies. A multinational survey reported average spirometry in women to be FVC 3.39 ±0.56L which was 99.6 ±12.9% of predicted by age and height, FEV1 2.67 ±0.46 L which was 98.8 ±13.8% of predicted by age and height, and FEV1/FVC ratio of 79 ±6% (Ekström *et al.*, 2017). The study done in Tanzania reported the average spirometry profile of non-pregnant healthy women to be FVC 2.71 ±0.56L, FEV1 2.24 ± 0.51L, PEF 328.8 ±82.8L/min and FEV1/FVC 82.5 ±7% (Knudsen *et al.*, 2011). These values were very close to other values obtained from Rwanda (Musafiri et al., 2013) and Mozambique (Ivanova *et al.*, 2020).

2.2 Spirometry profile in pregnancy

Spirometry parameters show variation across different stages of pregnancy. The study done in Norway reported mean (in liters) FEV1 3.0, and PEF 4.6 (Nørregaard *et al.*, 1989). In another study, respective mean FEV1, FVC, and FEV1/FVC ratio were higher in the first trimester (3.1±0.4L, 3.6±0.5L and 87.9±5.9%) than (3.0±0.4L, 3.5±0.5 and 84±4.9%) in the last trimester while PEF means decreased (Harirah *et al.*, 2005). Most studies agree that the spirometry values in pregnancy were in the normal range of their percent predicted by age and weight (Gazioglu *et al.*, 1970; Weinberger *et al.*, 1980; Wise and Polito, 2000; Leighton and Fish, 2009; LoMauro and Aliverti, 2015). The studies from Sub-Saharan Africa including Tanzania were lacking.

2.3 Factors affecting spirometry profile

In a study involving healthy women, spirometry profile was related to their age, height, body weight and composition, and history of tobacco smoking (Hall, Heywood and Cotes, 1979; White *et al.*, 1994; Orie, 1999; Knudsen *et al.*, 2011; Musafiri *et al.*, 2013; Ivanova *et al.*, 2020). After 25 years of age, FEV and FVC decline by about 20ml per year (Rufino *et al.*, 2017) as a part of the normal aging process although can occur due to a decrease of spirometry performance with aging (Harik-Khan *et al.*, 1999). The FEV1 and FVC were predicted by height (Quanjer *et al.*, 2014) and values decreased as participants became shorter (Rufino *et al.*, 2017). Literature does not agree on the effect of weight on FEV1 and FVC because the resulting ratio is not affected by obesity (Talaminos Barroso *et al.*, 2018). While some literature reported FEV1 and FVC decrease as a person becomes more obese due to airway limitation (Rufino *et al.*, 2017), the others reported the decrease only when obesity was morbid (McCallister, Adkins and O'Brien, 2009). Percentage of fat in body composition was not found to affect FEV but in women who were smokers, values were appreciably reduced (Hall, Heywood and Cotes, 1979). Finally, spirometry profile differs significantly between known races to an extent that cannot be explained by anthropometry and skin color (Rufino *et al.*, 2017; Talaminos Barroso *et al.*, 2018).

On the other hand, during pregnancy lung function is affected by parity, gestational age, and body position (Nørregaard *et al.*, 1989; Wise and Polito, 2000; Kolarzyk, Szot and Lyszczarz, 2005; Grindheim *et al.*, 2013; Manfré Pastro *et al.*, 2017) in addition to anthropometry and behavior factors. The FVC and FVC% were found to be higher in multiparous women compared to nulliparous (Grindheim *et al.*, 2013) however they had a lower FEV1/FVC ratio in another study (Manfré Pastro *et al.*, 2017). PEF, FEV1 and FEV1/FVC ratio were lower in the third trimester than the first with more decreases observed in parous (Nørregaard *et al.*, 1989; Manfré Pastro *et*

al., 2017). However, the other studies reported contradicting findings whereby PEF, FEV1, and FVC were higher in the later trimesters than earlier (Kolarzyk, Szot and Lyszczarz, 2005). A study by Harirah found PEF to decline by 0.68L per week whereby PEF average at postpartum was 71.9% of baseline recorded at earlier weeks (Harirah *et al.*, 2005). Compared to the upright position, supine PEF and FEV1 were much decreased presumably due to airway obstruction (Nørregaard *et al.*, 1989).

2.4 Comparison of spirometry profiles between pregnant and non-pregnant women

The studies done indicate that spirometry remains in the normal ranges of non-pregnancy. The FVC, FEV1, FEV1/FVC ratio, their percent of predicted and flow curves were found to remain in the normal range as non-pregnant (Gazioglu *et al.*, 1970; Weinberger *et al.*, 1980; Wise and Polito, 2000; Leighton and Fish, 2009; LoMauro and Aliverti, 2015). This was thought to indicate that large airway resistance is not affected by pregnancy. Other studies went further by arguing that lung function improved during pregnancy (Harik-Khan *et al.*, 1999). However, the overall FVC% was higher in parous women than nulliparous and remained higher during the postpartum period suggesting a permanent increase of FVC which may affect the clinical evaluation of and management of respiratory diseases (Grindheim *et al.*, 2013).

Yet spirometry profile was shown to be more deranged in pregnancy with the respiratory disorder than the general population. In a case series of restrictive conditions in pregnancy, median FVC was only 40% of the predicted values, 50% of women had FVC less than 1 liter and 60% of them had premature delivery (Lapinsky *et al.*, 2014). While the average FVC from the general population with a restrictive pattern was 2.35±0.74 liter which was 65.5±9.4% of predicted (Nonato *et al.*, 2015). Also, lowered spirometry profiles in pregnancy were associated with gestational hypertension and prematurity (Schatz *et al.*, 2006).

CHAPTER THREE

MATERIALS AND METHODS

3.1 Study design

A cross-sectional design was used. Study participants were recruited from the antenatal clinic and the general population. Spirometry measurements and information about affecting factors were collected on the same encounter.

3.2 Study area and settings

This study was conducted at Mnazi Mmoja hospital and MUHAS in Dar es Salaam. Dar es Salaam is the largest city and industrial center of Tanzania, eastern Africa. The city's population was estimated to be 6,702,000 people by 2020.

Mnazi Mmoja is located 1.2 kilometers from the city center. The hospital has one big reproductive health center serving about 100 women every working day. This provided a large sampling frame. On the other hand, MUHAS is one of the best public universities accredited by the Tanzania Commission of Universities (TCU). The university's main campus from which non-pregnant women were recruited is located about 2.7 kilometers from the city center. During the study period, the institution was hosting 3,861 students and other non-student persons which provided a good sampling frame for random sampling.

3.3 Study population

This study involved pregnant women aged 18 to 35 years who were attending antenatal clinic services at Mnazi Mmoja hospital. This hospital was chosen among others because it receives women with uncomplicated pregnancies. Non-pregnant women of the matched group age, height, and weight range were recruited from among female persons at MUHAS.

3.4 Sample size

The sample size was calculated using a formula for cross-section studies with quantitative variables published by Charan and Biswas (Charan and Biswas, 2013) review.

Sample size = $\mathbf{Z_{1-\alpha/2}^2 SD^2 / d^2}$ where;

$Z_{1-\alpha/2}$ is a standard normal variate for a given level of significance (*p*-value)

SD is a standard deviation for a variable obtainable from the previous or pilot study

d is an acceptable margin of error set by a researcher

This study used standard deviation (7.36) for mean FEV1/FVC ratio in the second trimester from the previous study (Kolarzyk, Szot and Lyszczarz, 2005), level of significance (P-value) of probability <0.05, and marginal error was set to 1.6. The sample size was adjusted to 10% non-response. Therefore, the sample was expected to be 182 women among whom 91 would be pregnant women and the same number of non-pregnant women. Then 226 women were subjected to spirometry and 190 of them produced acceptable and repeatable measurements enough to be included in this study among whom 92 were pregnant and 98 non-pregnant women as controls.

3.5 Sample selection

A simple random sampling technique was employed to obtain pregnant women. Upon consenting to participate, those meeting all the criteria were assigned with numbers. Then 10 pregnant women were selected using a table of random numbers on each day until the total sample size was attained.

All eligible women at MUHAS who were not pregnant were welcomed to participate in this study. Convenient sampling was used to obtain non-pregnant controls in an attempt to match pregnant women group characteristics as much as it was possible. Ten women per day were scheduled for

data collection until a total sample was attained. The absence of pregnancy was confirmed using a standard urine dipstick pregnancy test before data collection. If found pregnant or fails to appear for data collection was replaced by the next woman.

3.6 Inclusion criteria

Included in this study were African decency pregnant women of age 18 to 35 years and gestational age from 6 to 36 weeks. Pregnant women below 18 were not included since their presumed immature reproductive system could influence the observed spirometry profile. Meanwhile, women with more than 35 years were not included as they are likely to experience complications related to advanced maternal age pregnancy (Carr, 1995; van Katwijk and Peeters, 1998; Correa-de-Araujo and Yoon, 2021). The first five weeks were excluded due to the difficulty of certainly diagnosing pregnancy at this gestational age (Andrea D Shields, 2017). Term pregnancy wasn't included due to safety issues related to increased intra-abdominal pressure during spirometry maneuver (Kevin McCarthy, 2020). Since first visit weight was to be used for the calculation of BMI in pregnancy instead of pre-pregnancy weight, only women who booked their first visit in the first trimester were included. Age, height, and weight group matched non-pregnant women were recruited for comparison.

3.7 Exclusion criteria

Women among whom spirometry is contraindicated (Cooper, 2011) were excluded from the study. Screening for contraindications was done on every woman before enrolment. Also, women already known to have any lung disease or any other diseases affecting lung function or exposed to tuberculosis in the past year, had lax uterus or history of mid-trimester abortion (Cooper, 2011), had a history of smoking, had multiple pregnancies, or failed to obtain any acceptable and repeatable spirometry measurement were excluded. Merely measurements without errors were

accepted. Measurements were regarded repeatable if they didn't deviate by more than 150 ml (Graham *et al.*, 2019). Women who were pregnant in the last 42 days before the day of data collection weren't used as a control to exclude the effects of previous pregnancy.

3.8 Variables

Independent variables were age, pregnancy status, parity, gestational age, height, and weight. Dependent variables were spirometry parameters which are FVC, FEV1, PEF, and FEV1/FVC ratio. All volumes and rates were measured in liters and liters per minute respectively.

3.9 Data collection method

3.9.1 Recruitment of research assistant

One experienced lab technician was recruited to assist with data collection. The training was done to accustom with data collection procedures, test troubleshooting, quality assurance, and accurate data recording. One experienced registered nurse was used to assist in the recruitment of pregnant women.

3.9.2 Data collection tools

A structured checklist adapted from validated maternal recall questionnaires was used to collect demographic information. The checklist was used to collect anthropometry and spirometry measurements.

3.9.3 Pretesting of the tools

The data collection tool was tested through a pilot test administered to 19 women who were equivalent to 10% of the total sample size which was expected. The test was based on the ability of a tool to collect information that was able to answer the research questions. Modifications of the tool were done where warranted before use for data collection.

3.9.4 Data collection process

Demographic and pregnancy information was collected by interview using a structured checklist adapted from the maternal recall questionnaire (Carter *et al.*, 2015). The absence of pregnancy was confirmed among the non-pregnant group using standard urine pregnancy test at MUHAS physiology laboratory. Height was measured in an erect standing position using the SECA stadiometer. On-date weight was measured using the SECA adult weighing machine. Participants were asked to stand with feet on a scale placed on a flat surface looking straight ahead while hands positioned at their side (Kumar *et al.*, 2014). Weight on the first visit for pregnant women was obtained from antenatal cards and was used to calculate BMI in pregnancy instead of pre-pregnancy weight as it was not available. BMI was further categorized into underweight (BMI <18.5), normal weight (BMI =18.5-24.9), overweight (BMI = 25-29.9), and obesity (BMI ≥30).

Spirometry was done using a computerized EasyOne® Diagnostic spirometer in a sitting position without a nose clip. Test mode was set to DIAGNOSTIC, predicted reference was set to NHANES III, and select value was set to BEST VALUE. Women were coached for correct maneuvers using protocols adapted from NHANES 2011 spirometry examination manual (Center for Health Statistics, 2011) and synchronized with ATS and ERS spirometry standardization 2019 update (Graham *et al.*, 2019). They were instructed to elevate the chin, straight the neck, then take a deep breath to fill the lungs. Then place a mouthpiece in the mouth between teeth and above the tongue before blowing up as fast and forcefully as possible until when asked to stop after a minimum of six seconds. At least three acceptable and reproducible measurements according to ATS and ERS technical update (Graham *et al.*, 2019) were measured but the best value was recorded. Measurements were recorded on a checklist as continuous variables. Every participant and personnel washed and sanitized their hands before touching the mouthpiece and spirometer while

stayed at least one meter apart without facing each other directly. The participants were instructed about how to unwrap and insert mouthpiece onto the spirometer on their own. Mouthpieces were discarded after use and the spirometer was properly sanitized before use by another participant.

3.10 Investigation tools and validity and reliability

The validity and reliability of the EasyOne® spirometer made by Switzerland's NDD Medical Technologies Company had been established by previous studies. In one study, when tested against a laboratory-based spirometer using waveforms generator with standard American Thoracic Society (ATS) waveforms, EasyOne® handheld spirometer produced valid and reliable results hence it was recommended for research use (Barr *et al.*, 2009). In this study, errors were assessed through the evaluation of both the volume-time curve and flow-volume curve. Only measurements free of errors were acceptable. Measurements were considered reproducible if they don't diverge by more than 150 ml (Graham *et al.*, 2019). For the sake of quality assurance, assessment of acceptability and repeatability measurements was done by personnel who did not conduct the given test. The spirometer was calibrated as per manufacturer-recommended procedures. The standard operating procedures (SOP) were prepared and used to guide all steps.

SECA weighing scale and stadiometer were calibrated using standard weight and height respectively. Measurements were done on a flat surface while standing with feet, their hands at the side, and instructed to look straight ahead (Kumar *et al.*, 2014).

3.11 Data management and analysis

Data were entered using SPSS version 23. Normality of spirometry test values was assessed and FVC, FEV1, and PEF were found to be normally distributed hence described using means while FEV1/FVC was slightly skewed to the right hence median was described. The one-way analysis of variance (ANOVA) was used to test the effect of factors on FVC, FEV1, and PEF in each group,

and Kruskal-Wallis was used to test the effect on FEV1/FVC ratio. The difference between means of predicted and measured values was analyzed using paired t-test. The means of spirometry parameters in pregnancy were compared to non-pregnant using an independent sample t-test (Leeper, no date; This and Test, 2011). Adjustments to potential confounders were done through analysis of covariance (ANCOVA). The level of significance was set to < 0.05 p-value.

3.12 Ethical consideration

Ethical clearance was obtained from MUHAS institutional review board. Permission to conduct the study was obtained from Mnazi Mmoja hospital administration via Dar es Salaam regional administrative secretary, Ilala District Administrative Secretary, and Ilala Municipal Council Executive Director. Also, permission to include MUHAS female persons as controls was obtained from the Vice-Chancellor Research Academic and Consultancy. Study protocols and objectives were revealed to women. Written informed consent was prearranged and signed by women before enrolment into the study. To maintain privacy, a pregnancy test among the non-pregnant group was conducted at the MUHAS physiology laboratory. Every participant undertook a test and received results privately. Personal identifying information was not collected and all other information collected was used for research purposes only. Women with abnormal findings were recommended for medical evaluation as per Mnazi Mmoja hospital protocol.

Generally, spirometry is considered safe during pregnancy as no complications have been reported (Cooper, 2011). However, several safety precautions were taken to avoid potential complications related to the spirometry maneuver. Women among whom spirometry was contraindicated were excluded. All women who meet inclusion were screened for contraindications using a tool adapted from NHANES 2011 procedure manual, ATS/ERS 2019 update, and BMJ updates on spirometry contraindications (Center for Health Statistics, 2011; Cooper, 2011; Graham *et al.*, 2019). Also,

spirometry was done in a seating position as a precaution against potential lightheadedness due to exertion during the spirometry maneuver.

3.13 Dissemination of the results

Firstly, study findings shall be presented to the Department of Physiology. Then, hard and soft copies will be produced for deposition into department and university repositories. Likewise, the publication will be done in a reputable peer-reviewed journal. Also, findings and discussions shall be presented at different local and international conferences.

CHAPTER FOUR

RESULTS

A total of 969 pregnant women who visited Mnazi Mmoja hospital during the study period were invited to participate in the study (Figure 2). Out of 969; 449 pregnant women were eligible to participate while 520 were not eligible based on exclusion and inclusion criteria. A total of 119 participants were randomly selected from the 449 eligible participants. Among the selected pregnant participants; 92 (77.3%) produced acceptable spirometry tests while 27 had unacceptable spirometry tests. A total of 107 eligible non-pregnant women were invited to participate among whom 98 (91.6%) produced acceptable spirometry tests while 9 had unacceptable spirometry tests.

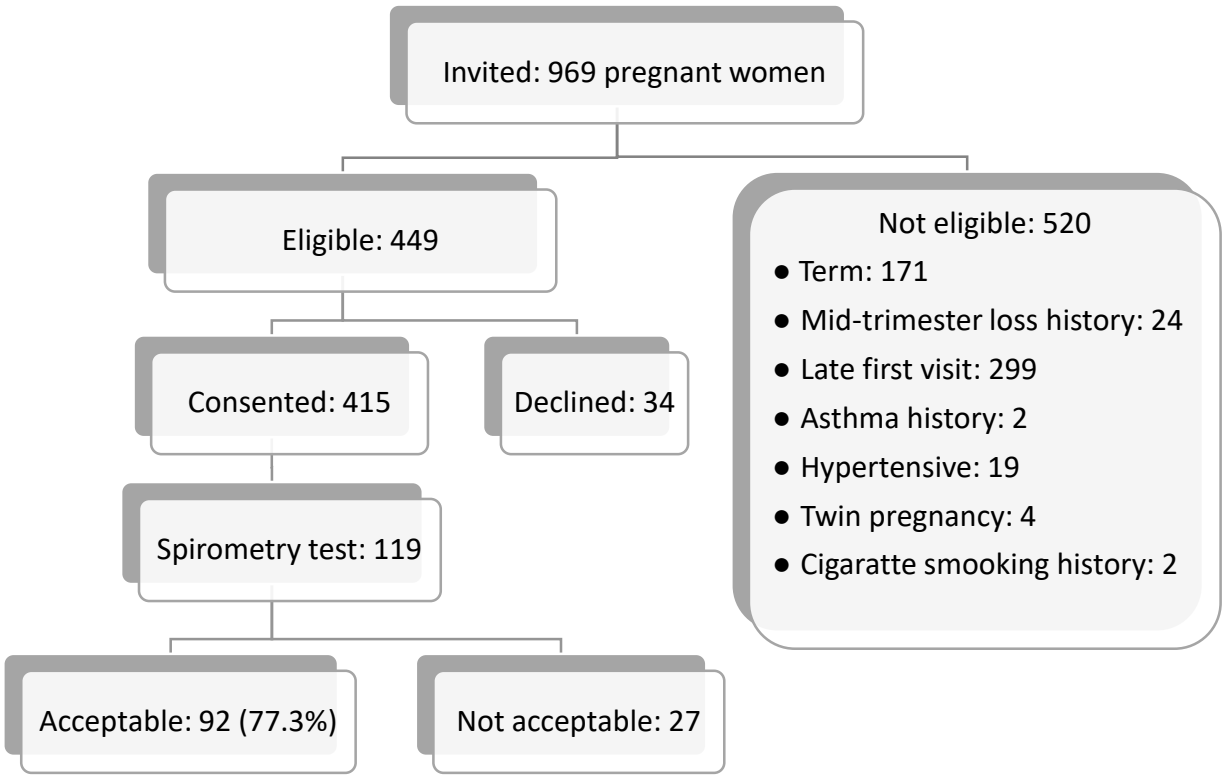

Figure 2: Schematic for recruitment of pregnant participants

4.1 Description of characteristics of participants

The mean age of study participants was 27 years (SD = 5). Their mean height was 157.4 centimeters (SD = 6.7) ranging from 135 cm to 173 cm tall. The mean weight was 67 Kg (SD = 14.2) ranging from 47 to 117 Kg. Among all participants, 46.7% were overweight or obese while 7.6% were underweight.

Table 1: Characteristics of participants (n = 190)

		Pregnant		Non-pregnant		
		Frequency (%)	Mean ± SD	Frequency (%)	Mean ± SD	*p*- value
Age	18-19	2 (24)		7 (7.1)		
	20-24	24 (25.5)		48 (48.7)		
	25-29	25 (27.5)		20 (20.4)		
	30-35	41 (44.6)		23 (23.7)		
	Total	92	28 ± 5	98	26 ± 5	0.040
Height	135-139	1 (1.1)		0		
	140-149	11 (11.8)		11 (11.2)		
	150-159	51 (55.3)		43 (43.9)		
	160-169	29 (31.7)		40 (40.8)		
	170-179	0		4 (4.1)		
	Total	92	156.3 ± 6.4	98	158.5 ± 6.8	0.290
Weight	41-50	6 (6.0)		20 (20.4)		
	51-60	16 (17.5)		28 (28.6)		
	61-70	24 (26.5)		24 (24.5)		
	71-80	23 (24.4)		15 (15.3)		
	81-90	15 (16.7)		8 (8.2)		
	91-110	8 (6.3)		3 (3.1)		
	Total	92	70.9 ± 13.8	98	62.6 ± 13.5	0.011
BMI	Underweight	6 (6.4)		9 (8.7)		
	Normal	37 (40.3)		50 (50.8)		
	Overweight	30 (33.0)		16 (16.7)		
	Obese	19 (20.3)		23 (23.7)		
	Total	92	25.8 ± 4.8	98	25.0 ± 5.4	0.131
Parity	0	32 (34.8)		57 (58.2)		
	1	32 (34.8)		16 (16.3)		
	2	14 (15.2)		12 (12.2)		
	3	12 (13)		6 (6.1)		
	4	2 (2.2)		7 (7.1)		
	Total	92		98		0.006
Gestation age	first trimester	7 (7.6)				
	second trimester	31 (34.0)				
	third trimester	54 (58.4)				
	Total	92	25.3 ± 7.9			

p -value for characteristic difference between pregnant and non-pregnant women

Of all participants, 52.4% had previously given birth at least once. Among pregnant participants, 7% were in their first trimester while 58.4% were in the third semester. There was a significant difference between age, weight, and parity of pregnant and non-pregnant women (

Table 1).

4.2 Description of spirometry test values of participants

Spirometry test values of FVC (in liters), FEV1 (liters), PEF (in liters/minute), and their respective percentage predicted were normally distributed in a study sample except FEV1/FVC (in %) ratio (Figure 3).

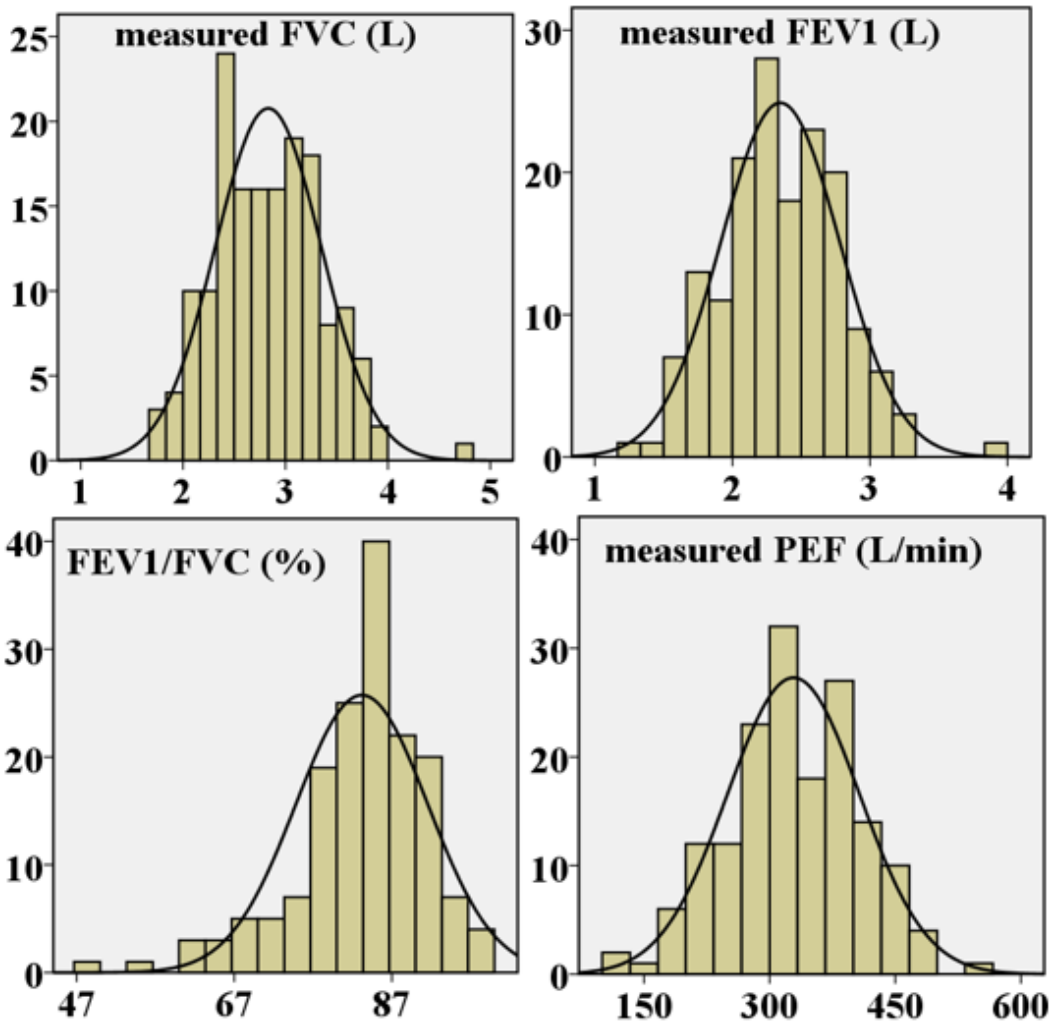

Figure 3: Histogram describing the distribution of spirometry test values of participants (n = 190)

The mean FVC for all participants was 2.8 L (SD = 0.52) which was 94.9% (SD = 16.3) of the values predicted by age and height. Their mean FEV1 was 2.4 L (SD = 0.43) which was 90% (SD = 14.5) of predicted. The Median FEV1/FVC ratio was 84.3% (48.8-99.8). The mean PEF was 329.3 L/min (SD = 78.5) L/min which was 84.2% (SD = 19.8) of predicted (Table 2).

Table 2: Summary of spirometry test values of participants (n = 190)

		Pregnant	Non-pregnant			
		Mean ± SD		t-value	df	*p* -value
FVC (L)	predicted	2.9 ± 0.28	3.1 ± 0.32			
	measured	2.7 ± 0.54	2.9 ± 0.48	-3.041	189	0.006
	FVC%	92.9 ± 18.6	96.3 ± 13.4	-1.431	167	0.179
FEV1 (L)	predicted	2.6 ± 0.22	2.7 ± 0.3			
	measured	2.2 ± 0.42	2.5 ± 0.41	-4.512	189	0.000
	FEV1%	86.9 ± 15.1	93.1 ± 13.4	-2.990	189	0.003
PEF (L/min)	predicted	387.6 ± 23.6	397.9 ± 29.5			
	measured	303.2 ± 84.5	353.8 ± 63.6	-4.647	169	0.000
	PEF%	78.4 ± 21.8	89.7 ± 15.8	-4.100	166	0.000
		Median (Range)				
FEV1/FVC (%)		83.7 (48.8-99.8)	85.1 (65.0-98.1)			0.281

p- value for respective difference between pregnant and non-pregnant women

4.3 Factors affecting spirometry profiles

4.3.1 Age and spirometry test values

The relationship between age and spirometry profile appeared to be phasic with an increase to peak then decrease. However, the pattern was marked by earlier peak age with lower peak values in pregnant women as compared to non-pregnant women (Figure 4). The pattern was statistically significant for FVC [F (3, 88) =2.83; p =0.043] and FVC% [F (3, 88) =2.89; p =0.04] among pregnant women even after adjusting for height but not after including weight in the analysis of covariance (ANCOVA). The pattern was statistically significant for FVC [F (16, 81)

=2.44; *p* <0.01], FVC% [F (16, 81) =1, 79; *p* =0.05], FEV1 [F (16, 81) =2.53; *p* <0.01], FEV1% [F (16, 81) =1.81; *p* =0.04], PEF [F (16, 81) =2; *p* =0.02], PEF% [F (16, 81) =2.59; *p* <0.01] and FEV1/FVC (*p* =0.042) among non-pregnant women even after adjusting for height and weight.

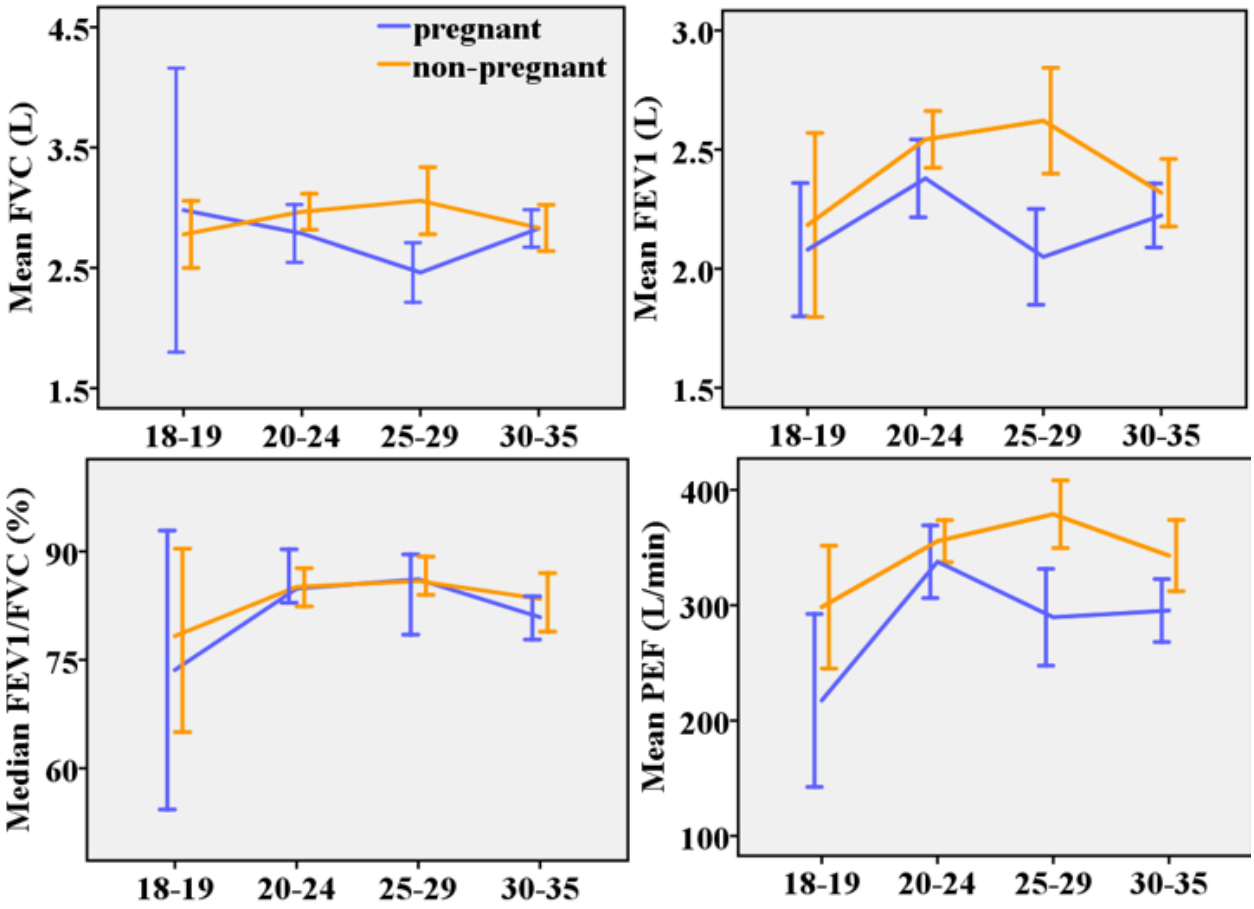

Figure 4: Plots of spirometry test values against age [n = 190, Error bar: ±2SEM (95%CI)]

4.3.2 Height and spirometry test values

Spirometry values appeared to increase as height increased (Figure 5) except for means of FVC%, FEV1%, and median FEV1/FVC of non-pregnant women which appeared to decrease as height increased. The pattern was statistically significant for FVC [F (25, 66) = 1.88; *p* = 0.02], FEV1 [F (25, 66) = 2.54; *p* < 0.01] and PEF [F (25, 66) = 1.79; *p* = 0.03] among pregnant women but was no longer significant for FVC and PEF after adjusting for weight and age. The pattern was

statistically significant for FVC [F (3, 94) =7.96; p <0.01] and FEV1 [F (3, 94) =6.65; p <0.01] among non-pregnant women even after adjusting for age and weight.

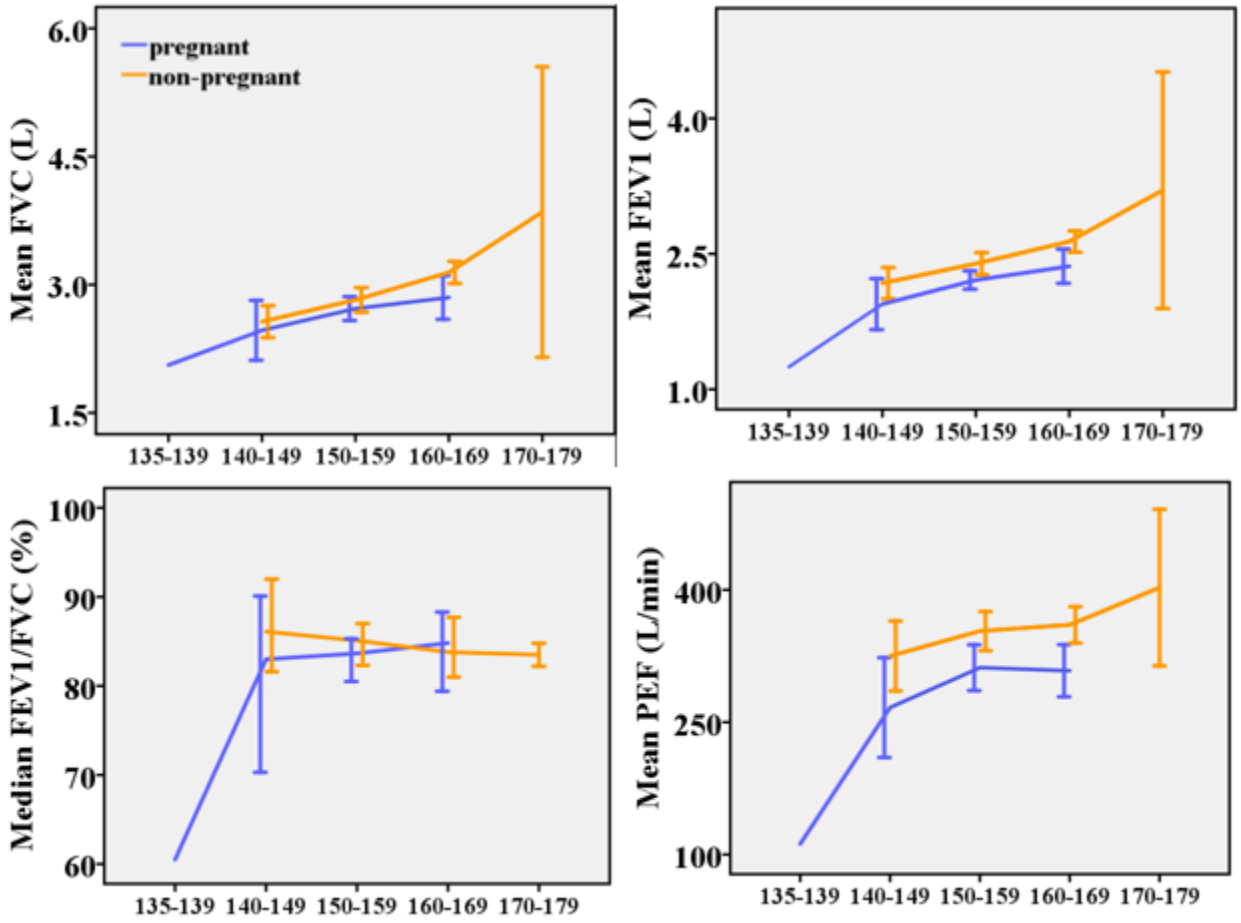

Figure 5: Plots of spirometry test values against height [n = 190, Error bar: ±2SEM (95%CI)]

4.3.3 Weight and spirometry test values

The means of FVC, FEV1, and PEF of pregnant women increased with weight until 60-70 Kg then decreased. Median FEV1/FVC of pregnant and non-pregnant women remained unchanged as weight increased (Figure 6). No pattern was statistically significant except for PEF (p =0.010) of non-pregnant women which also was no longer significant after adjusting for age and height.

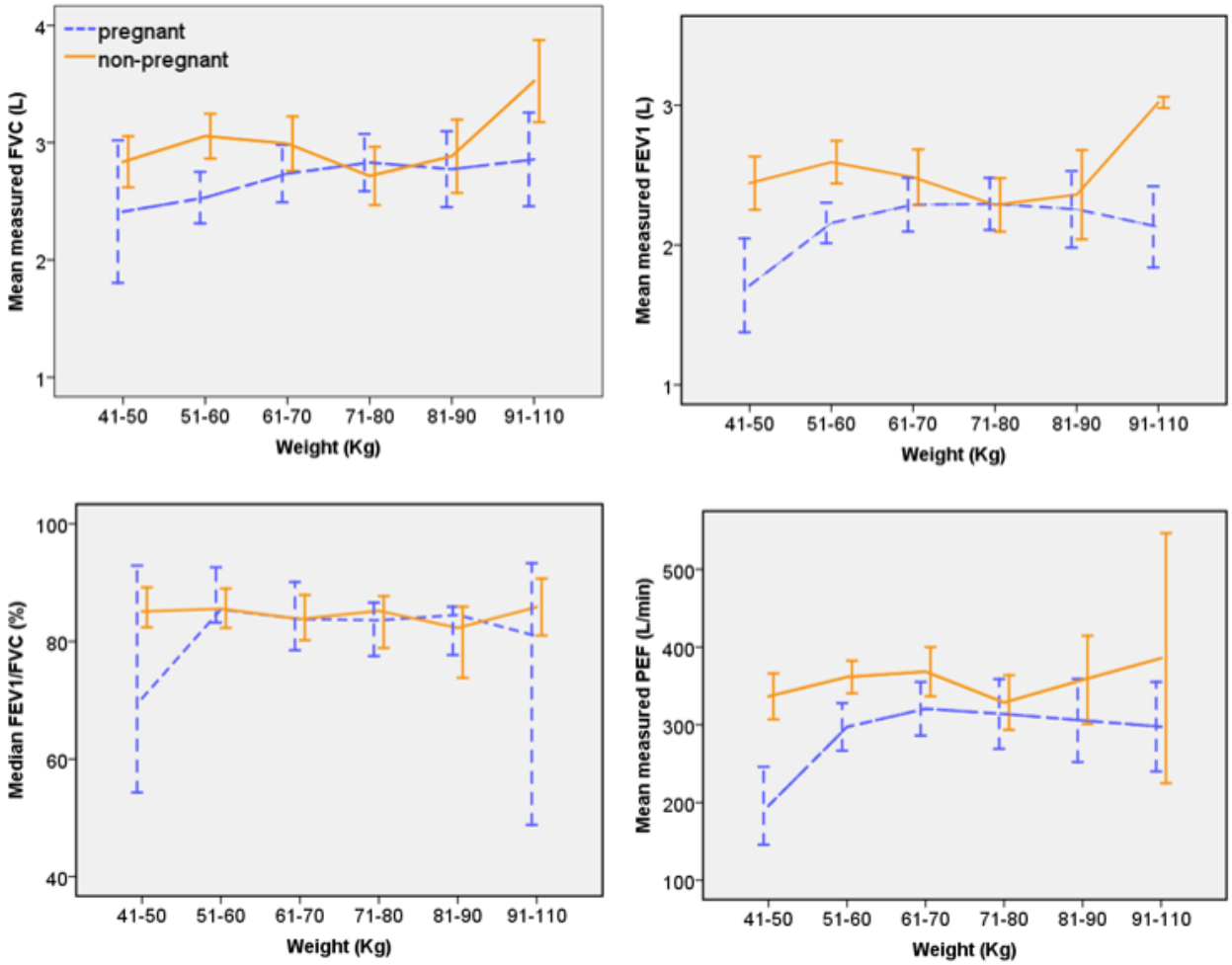

Figure 6: Plots of spirometry test values against weight [n = 190, Error bar: ±2SEM (95%CI)]

While mean spirometry test values of pregnant women increased with BMI, mean values of non-pregnant women decreased as BMI increased and medians of the FEV1/FVC ratio remained fairly unchanged (Figure 7). But all the patterns were not statistically significant.

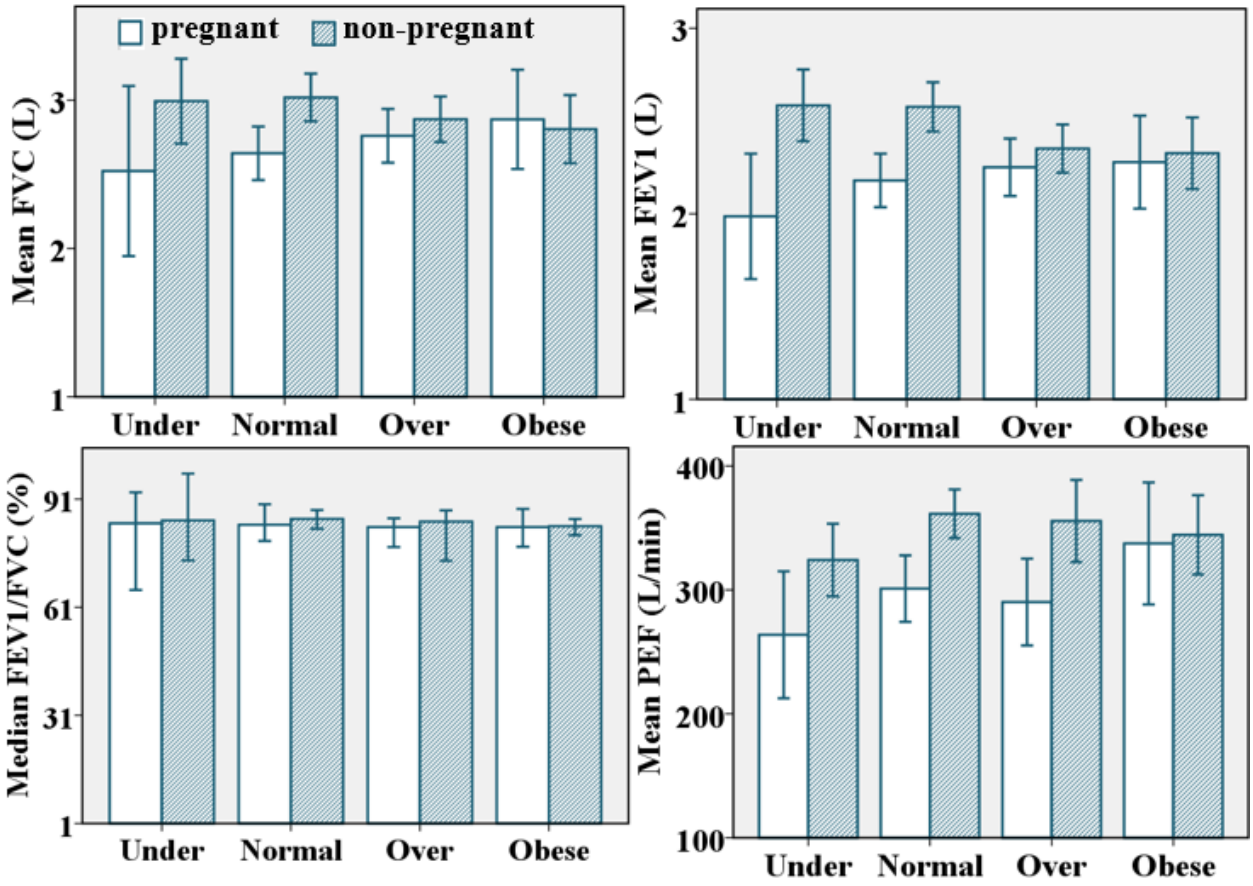

Figure 7: Plots of spirometry test values against BMI [n = 190, Error bar: ±2SEM (95%CI)]

4.3.4 Parity and spirometry test values

The mean FVC, FEV1, and PEF parous women were higher than the means of nulliparous women. Median FEV1/FVC of nulliparous women was higher than parous women (Figure 8). However, the pattern was only statistically significant for median FEV1/FVC among pregnant women (p = 0.035) and mean of FVC% [F (4, 93) =2.88; p =0.03] and FEV1% [F (4, 93) =3.89; p =0.01] among non-pregnant women and persisted when adjusted to height but disappeared when age and weight were included in the ANCOVA model.

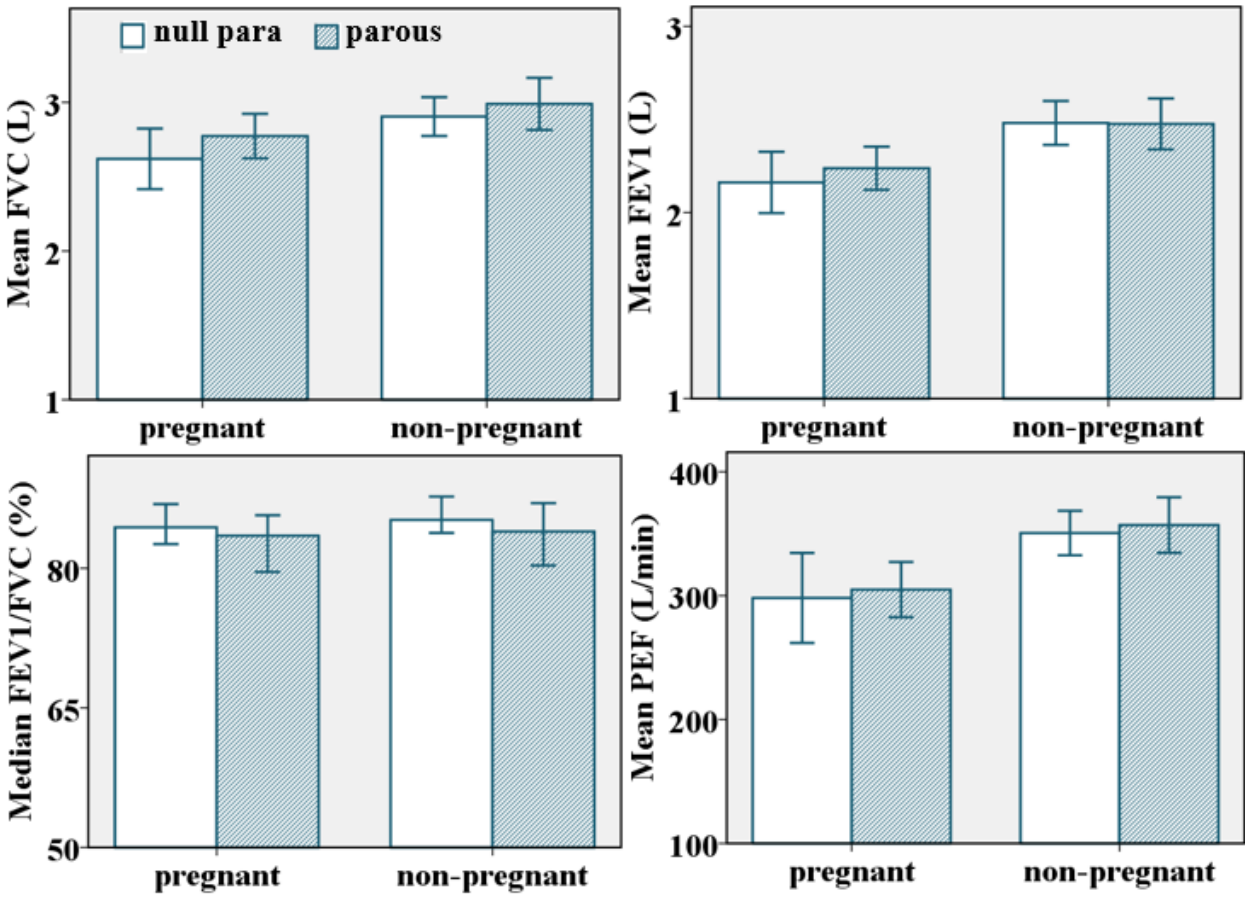

Figure 8: Plots of spirometry test values against parity [n = 190, Error bar: ±2SEM (95%CI)]

4.3.5 Gestational age and spirometry test values

The means of FVC, FEV1, PEF, and their % predicted decreased as gestational age increased. The decrease was steeper from the first to the second trimester. The median FEV1/FVC decreased just slightly as gestational age increased (Figure 9). This pattern was statistically significant for FVC [F (2, 89) =4.03; p =0.02], FVC% [F (2, 89) =6.81; p <0.01], FEV1 [F (2, 89) =3.15; p =0.048] and FEV1% [F (2, 89) =5.91; p <0.01] even after adjusting for maternal age, height and weight.

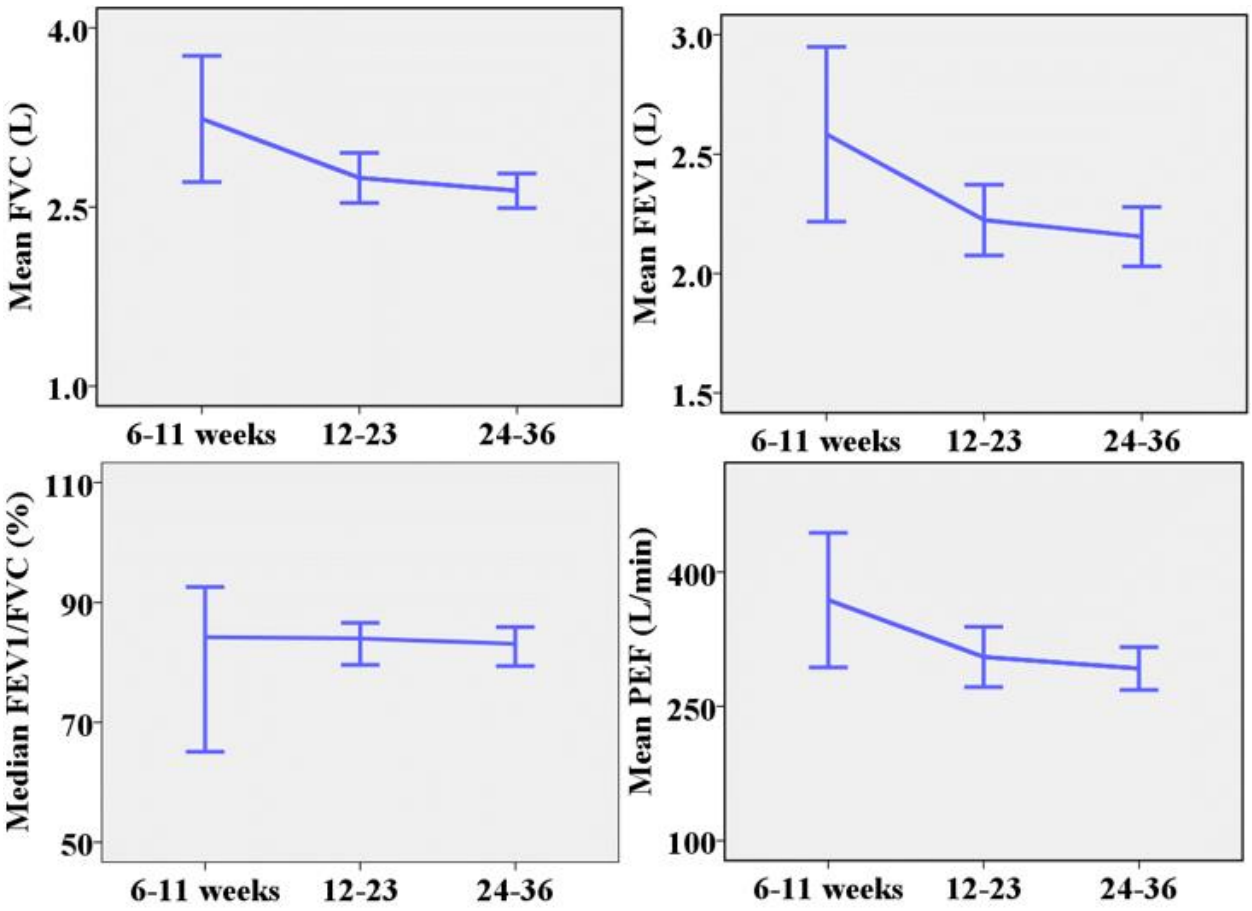

Figure 9: Plots of spirometry test values against gestational age [n = 92, Error bar: ±2SEM (95%CI)]

4.4 Difference between pregnant and non-pregnant spirometry test values

The measured FVC [t (91) = -3.97; p <0.001], FEV1 [t (91) = -8.39; p <0.001] and PEF [t (91) = -9.69; p <0.001] among pregnant women as well as FVC [t (97) = -2.86; p =0.001], FEV1 [t (97) = -5.17; p <0.001] and PEF [t (97) = -7.12; p <0.001] among non-pregnant women were significantly lower than values predicted based on age and height.

Meanwhile, the mean FVC [t (189) = -3.04; p =0.006], FEV1 [t (189) = -4.51; p <0.01], FEV1% [t (189) = -2.99; p =0.003], PEF [t (169.5) = -4.65; p <0.001] and PEF% [t (165.9) = -4.1; p <0.01] of pregnant women were significantly lower than non-pregnant mean values even after adjusting for age, weight and parity (Table 2).

CHAPTER FIVE

DISCUSSION

The respiratory system is affected by anatomical and physiological changes associated with pregnancy. This was the base of our hypothesis that spirometry profiles of pregnant women are different from those predicted by their age and height if they were not pregnant. Therefore this study was designed to examine the profiles of lung function of pregnant African women using spirometry and compare them to profiles of non-pregnant women. In this study, FVC, FEV1, and PEF values of pregnant and non-pregnant women were lower than the values predicted by their age and height. Also, FVC, FEV1, and PEF values of pregnant women were lower than values of non-pregnant women.

We report mean spirometry test values in pregnant women which are lower than means reported in Brazilians (Manfré Pastro *et al.*, 2017). The non-pregnant means of FVC, FEV1, PEF and their % predicted in this study are comparable to values reported from other studies done in Tanzania (Knudsen *et al.*, 2011), Rwanda (Musafiri *et al.*, 2013) and Mozambique (Ivanova *et al.*, 2020). Our values were slightly higher than the other studies because of the age difference as the mean age of non-pregnant women was less than 30 years in this while it was more than 35 in the other studies. Also, the values of non-pregnant women in this study were lower than values recorded in Europeans and Australians (Ekström *et al.*, 2017), Asians (Al Ghobain, 2012a), and Scandinavians (Johannessen *et al.*, 2006) but FEV1/FVC ratio was higher. Like ours, other studies have reported lower spirometry profiles in African decency which could not be explained by anthropometric and skin color differences alone (Braun, 2015; Talaminos Barroso *et al.*, 2018). A portion of this could be explained by lower seating height and socio-economic status which were reported to relate with lower values. Even so, the values are considered normal since the prognosis has not been different

(Harik-Khan *et al.*, 2001; Whitrow and Harding, 2008; Van Sickle, Magzamen and Mullahy, 2011; Burney and Hooper, 2012). In addition to ethnic differences, we found lower values probably because we did not administer a bronchodilator prior to spirometry unlike in the previous studies.

Interestingly, a phasic relationship between age and spirometry test values of non-pregnant women was noted. There was an increase to a peak, followed by a decrease in spirometric values. A similar pattern was observed in pregnant women for FEV1/FVC, PEF, and PEF%. However, the peak age for FVC, FEV1, and PEF was earlier with lower values in pregnant women. The spirometry test values have been known to increase with age then peak around 25 years before starting to decline (Harik-Khan *et al.*, 1999; Johannessen *et al.*, 2006; Rufino *et al.*, 2017; Talaminos Barroso *et al.*, 2018). This is thought to occur as a part of the aging process. After peak age, pulmonary elastic recoil decrease with age due to progressive loss of lung tissue elasticity and increase of chest wall stiffness resulting in the decline of lung function (Frank, Mead and Ferris, 1957; Pierce and Hocott, 1960; Turner, Mead and Wohl, 1968; Niewoehner and Kleinerman, 1974; Babb and Rodarte, 2000). Also, it could be partly due to a decrease in spirometry performance with aging. Hence, age has been an important factor in spirometry test values predicting equations. Pregnancy factors could have influenced the pattern observed among pregnant women in our study.

Similar to previous studies, FVC, FEV1, and PEF of both pregnant and non-pregnant women increased with height (Johannessen *et al.*, 2006; Knudsen *et al.*, 2011; Musafiri *et al.*, 2013). Height also has been an important factor in spirometry prediction equations together with age (Ip *et al.*, 2006; Aggarwal, Gupta and Jindal, 2007; Stanojevic *et al.*, 2008; Knudsen *et al.*, 2011; Quanjer, Hall, *et al.*, 2012; Quanjer, Stanojevic, *et al.*, 2012; Rufino *et al.*, 2017; Graham *et al.*, 2019; Wang *et al.*, 2020). However, FVC% and FEV1% decreased as height increased. This could mean that as height increased participants were more likely to have lower than expected FVC and

FEV1 values but also it could be a reference equation over predicting expected values. Reference values have been reported to over predict spirometry test values in different populations (Ip *et al.*, 2006; Quanjer, Hall, *et al.*, 2012; Wang *et al.*, 2020). Other studies have found a difference in prediction even when references were derived from a closely related population such that abnormal findings in one reference were deemed normal by the other (Aggarwal, Gupta and Jindal, 2007). There was no significant relationship between height and FEV1/FVC in pregnant and non-pregnant women. This was in line with other studies (Johannessen *et al.*, 2006) and it could be due to the equal effect of height on FEV1 and FVC.

FVC, FEV1, and PEF of pregnant women increased with weight, peaked at 61-70Kg then decreased. Non-pregnant women's values decreased when women were becoming overweight and obese. Despite such a pattern, neither weight nor BMI appeared to statistically significantly affect FVC, FEV1, or PEF in neither pregnant nor non-pregnant women after adjusting for age and height. This has been found by several other studies (Knudsen *et al.*, 2011; Grindheim *et al.*, 2012, 2013; Musafiri *et al.*, 2013). However other studies have demonstrated a negative effect of the increasing waist to hip ratio (WHR) and weight gain on FEV1 and FVC (Chen, Horne and Dosman, 1993; Al Ghobain, 2012b). This could be for the reason that quantification of body mass and its index is not specific to the distribution of body composition while fats in hips, thighs, gluteal regions, and breasts are less likely to affect lungs, diaphragm, and chest wall mechanics (Al Ghobain, 2012a). While this study was limited to FVC, FEV1, and PEF, other studies have found an inverse relationship between increasing BMI and vital capacity, total lung capacity, and functional residual capacity (Jones and Nzekwu, 2006; Mehari *et al.*, 2015).

The mean FVC, FVC% FEV1%, PEF, and PEF% were higher in parous than nulliparous and first birth showed the greatest effect on the pattern in both pregnant and non-pregnant. Despite that,

only FVC% and FEV1% were statistically significantly related to parity in non-pregnant women and the relationship disappeared after adjusting for age, height, and weight. Similar results were found in a longitudinal study that involved pregnant women (Manfré Pastro *et al.*, 2017). However, other studies found a significant adjusted positive effect of parity on spirometry test values (Harik-Khan *et al.*, 1999; Grindheim *et al.*, 2012). It has been postulated that the hormonal effects of pregnancy to compensate for mechanical changes and maintain lung function persists even after the uterus have returned to its small size (Wise and Polito, 2000; Grindheim *et al.*, 2012). The median FEV1/FVC ratio was lower in parous than nulliparous in both pregnant and non-pregnant women but was statistically significant only in pregnant women after adjusting for age, height, and weight. Similar findings have been presented by other studies (Manfré Pastro *et al.*, 2017). This could be due to disproportionate changes between FVC and FEV1.

Spirometry test values decreased as gestation age advanced. This is in line with other studies conducted previously (Nørregaard *et al.*, 1989; Harirah *et al.*, 2005; Manfré Pastro *et al.*, 2017). This decline has been attributed to the limited maternal effort as gestation advances due to an increase of maternal weight, uterine enlargement, and a degree of pulmonary edema (Brancazio, Laifer, and Schwartz, 1997). However, spirometry test values have been observed to remain within normal limits (Weinberger *et al.*, 1980; LoMauro and Aliverti, 2015). Other studies have reported values that increased during pregnancy and persisted to the postpartum period (Kolarzyk, Szot and Lyszczarz, 2005; Grindheim *et al.*, 2012, 2013). But those studies concentrated on whether spirometry test values were normal as compared to a known range or not. In our study, we compared absolute values and their % of predicted values of pregnant women at different gestational periods.

FVC, FEV1, and PEF values of pregnant women were significantly lower than values predicted by age and height if they were not pregnant. The observation was similar for non-pregnant women. The other study that was done in Tanzania also reported a similar finding (Rębacz-Maron, 2018). This suggests that the reference equation derived from non-African settings could have over-predicted expected values. Also, the other study done on young men in Tanzania concluded that spirometry reference equations developed from non-African populations tended to overpredict measurements of black Africans (Rębacz-Maron, 2018). Likewise, it has been noticed by other studies in which reference values over-predicted expected values (Ip *et al.*, 2006; Quanjer, Hall, *et al.*, 2012; Wang *et al.*, 2020).

Nevertheless, when compared to non-pregnant women; FVC, FEV1, and PEF of pregnant women were significantly lower even after adjusting for age, weight, and parity. This could be explained by ribcage and volume displacement long known to take place during pregnancy (Weinberger *et al.*, 1980; Gilroy, Mangura and Lavietes, 1988; Gilleard and Brown, 1996; Tarun Madappa and Zab Mosenifar, 2011). However, Le Merre et al discussed that changes during pregnancy do not cause significant respiratory functional changes since mechanical effects are balanced by hormonal factors (Le Merre and Préfaut, 1988). Unlike other studies which compared pregnant values against the established normal range, this study compared values of pregnant women against values of non-pregnant women.

STRENGTHS AND LIMITATIONS

Study strengths

i. To our knowledge, this is the first study on lung function conducted among pregnant women using spirometry in the African setting.

ii. Spirometry test values of pregnant women were compared against values of non-pregnant women rather than comparing against the established normal range of values

iii. This study was able to adhere to standard operating procedures and infection prevention protocol

Study limitations

i. Non-pregnant healthy women were likely to hesitate to participate in the study as they would feel a lack of need for tests. This could have limited ability to match the characteristics of pregnant women. There was a significant difference between the characteristics of pregnant and non-pregnant women. To minimize the effect, the comparisons between the two groups were adjusted by age, weight, and parity.

ii. Most pregnant women didn't have their pre-pregnancy weight which was required to obtain BMI in pregnancy. The weight on the first visit was used instead. To suit that only women who booked their first visit in their first trimester were included in a study. Also, many potential participants hesitated to participate worrying that they were tested for the Coronavirus. This could have influenced the nature of pregnant women who participated in this study.

iii. Our study was limited to spirometry, therefore, could not explain other observations which would be well explained by other lung function testing methods such as measuring static lung volumes. Also, we did not quantify hormonal effects on lung function by hormonal assay.

iv. Pregnant women were obtained by random sampling while non-pregnant controls were obtained consecutively. This could have affected our comparisons between the two groups.

CONCLUSION

Spirometry test values of pregnant women decreases as gestational age advance and they are lower than profiles predicted by their age and height if they were not pregnant. Moreover, spirometry profiles of pregnant women are lower than the profiles obtained from non-pregnant controls. Spirometry profiles of pregnant women and non-pregnant African women vary according to their age, height, and parity. Weight and BMI does not affect the spirometry profile of pregnant and non-pregnant women.

RECOMMENDATIONS

This study recommends the use of spirometry in pregnancy to assess lung function. However, spirometry test values of pregnant women should be carefully interpreted against non-pregnant references otherwise can cause underestimation of pregnant values and over-hospitalization. There is also a need to evaluate the accuracy of non-pregnant spirometry reference equations in predicting pregnant test values.

The relationship between spirometry test values and age is phasic, therefore non-linear models should be considered for calculating predicted values of young African women. Also, there is a need of evaluating the suitability of various reference equations in predicting spirometry test values of young African women. Weight and BMI may not be suitable for studying the effect of body composition on lung function hence other measures should be considered.

REFERENCES

Aggarwal, A. N., Gupta, D. and Jindal, S. K. (2007) 'Comparison of Indian reference equations for spirometry interpretation', *Respirology*. John Wiley & Sons, Ltd, 12(5), pp. 763–768. doi: 10.1111/j.1440-1843.2007.01123.x.

Andrea D Shields (2017) *Pregnancy Diagnosis: Overview, History and Physical Examination, Laboratory Evaluation, Medscape*. Available at: https://emedicine.medscape.com/article/262591-overview#showall (Accessed: 11 January 2021).

Babb, T. G. and Rodarte, J. R. (2000) *Mechanism of reduced maximal expiratory flow with aging*. Available at: http://www.jap.org (Accessed: 24 June 2021).

Barr, R. G. *et al.* (2009) 'Reproducibility and validity of a handheld spirometer', *Respiratory Care*. NIH Public Access, 53(4), pp. 433–441. Available at: /pmc/articles/PMC3595551/?report=abstract (Accessed: 7 November 2020).

Bayliss, D. A. *et al.* (1987) 'Progesterone stimulates respiration through a central nervous system steroid receptor-mediated mechanism in cat', *Proceedings of the National Academy of Sciences of the United States of America*. National Academy of Sciences, 84(21), pp. 7788–7792. doi: 10.1073/pnas.84.21.7788.

Behr, J. and Furst, D. E. (2009) 'Pulmonary function tests', in *Rheumatology*. doi: 10.1093/rheumatology/ken313.

Bhatia, P. and Bhatia, K. (2000) 'Pregnancy and the lungs', *Postgraduate Medical Journal*. The Fellowship of Postgraduate Medicine, pp. 683–689. doi: 10.1136/pmj.76.901.683.

Brancazio, L., Laifer, S. and Schwartz, T. (1997) 'Peak expiratory flow rate in normal pregnancy', *Obstetrics & Gynecology*. Ovid Technologies (Wolters Kluwer Health), 89(3), pp. 383–386. doi: 10.1016/s0029-7844(96)00512-1.

Braun, L. (2015) 'Race, ethnicity and lung function: A brief history', *Canadian Journal of Respiratory Therapy*. Canadian Society of Respiratory Therapists, pp. 99–101. Available at: /pmc/articles/PMC4631137/ (Accessed: 28 June 2021).

Burney, P. G. J. and Hooper, R. L. (2012) 'The use of ethnically specific norms for ventilatory function in African-American and white populations', *International Journal of Epidemiology*,

41(3), pp. 782–790. doi: 10.1093/ije/dys011.

Carr, S. R. (1995) ‘High Risk Pregnancy: Management Options’, *JAMA*. American Medical Association, 273(3), pp. 259–260. doi: 10.1001/JAMA.1995.03520270095051.

Carter, E. B. *et al.* (2015) ‘Pregnancy Complications as Markers for Subsequent Maternal Cardiovascular Disease: Validation of a Maternal Recall Questionnaire’, *Journal of Women’s Health*, 24(9), pp. 702–712. doi: 10.1089/jwh.2014.4953.

Center for Health Statistics, N. (2011) *Respiratory Health Spirometry Procedures Manual*.

Charan, J. and Biswas, T. (2013) ‘How to calculate sample size for different study designs in medical research?’, *Indian Journal of Psychological Medicine*. Indian Psychiatric Society South Zonal Branch, pp. 121–126. doi: 10.4103/0253-7176.116232.

Chen, Y., Horne, S. L. and Dosman, J. A. (1993) ‘Body weight and weight gain related to pulmonary function decline in adults: A six year follow up study’, *Thorax*, 48(4), pp. 375–380. doi: 10.1136/thx.48.4.375.

Collier, S. A. *et al.* (2009) ‘Prevalence of self-reported infection during pregnancy among control mothers in the National Birth Defects Prevention Study’, *Birth Defects Research Part A: Clinical and Molecular Teratology*. John Wiley & Sons, Ltd, 85(3), pp. 193–201. doi: 10.1002/bdra.20540.

Cooper, B. G. (2011) ‘An update on contraindications for lung function testing’, *Thorax*, 66, pp. 714–723. doi: 10.1136/thx.2010.139881.

Correa-de-Araujo, R. and Yoon, S. S. (Sarah) (2021) ‘Clinical Outcomes in High-Risk Pregnancies Due to Advanced Maternal Age’, *https://home.liebertpub.com/jwh*. Mary Ann Liebert, Inc., publishers 140 Huguenot Street, 3rd Floor New Rochelle, NY 10801 USA , 30(2), pp. 160–167. doi: 10.1089/JWH.2020.8860.

Ekström, M. *et al.* (2017) ‘Absolute values of lung function explain the sex difference in breathlessness in the general population’, *The European respiratory journal*. European Respiratory Society, 49(5), p. 1602047. doi: 10.1183/13993003.02047-2016.

Frank, N. R., Mead, J. and Ferris, B. G. (1957) ‘The mechanical behavior of the lungs in healthy

elderly persons', *The Journal of clinical investigation*. American Society for Clinical Investigation, 36(12), pp. 1680–1687. doi: 10.1172/JCI103569.

Gazioglu, K. *et al.* (1970) 'Pulmonary function during pregnancy in normal women and in patients with cardiopulmonary disease.', *Thorax*, 25(4), pp. 445–450. doi: 10.1136/thx.25.4.445.

Al Ghobain, M. (2012a) 'The effect of obesity on spirometry tests among healthy non-smoking adults', *BMC Pulmonary Medicine*. BioMed Central, 12(1), pp. 1–5. doi: 10.1186/1471-2466-12-10.

Al Ghobain, M. (2012b) 'The effect of obesity on spirometry tests among healthy non-smoking adults', *BMC Pulmonary Medicine*. BMC Pulm Med, 12. doi: 10.1186/1471-2466-12-10.

Gilleard, W. L. and Brown, J. M. M. (1996) 'Structure and function of the abdominal muscles in primigravid subjects during pregnancy and the immediate postbirth period', *Physical Therapy*. American Physical Therapy Association, 76(7), pp. 750–762. doi: 10.1093/ptj/76.7.750.

Gilroy, R. J., Mangura, B. T. and Lavietes, M. H. (1988) *Rib Cage and Abdominal Volume Displacements during Breathing in Pregnancy1-3*.

Graham, B. L. *et al.* (2019) 'Standardization of spirometry 2019 update an official American Thoracic Society and European Respiratory Society technical statement', *American Journal of Respiratory and Critical Care Medicine*. American Thoracic Society, pp. E70–E88. doi: 10.1164/rccm.201908-1590ST.

Grindheim, G. *et al.* (2012) 'Changes in pulmonary function during pregnancy: a longitudinal cohort study', *BJOG: An International Journal of Obstetrics & Gynaecology*. John Wiley & Sons, Ltd, 119(1), pp. 94–101. doi: 10.1111/j.1471-0528.2011.03158.x.

Grindheim, G. *et al.* (2013) 'Changes in Pulmonary Function During Pregnancy', *Obstetric Anesthesia Digest*. Ovid Technologies (Wolters Kluwer Health), 33(1), p. 34. doi: 10.1097/01.aoa.0000426095.57478.f4.

Hall, A. M., Heywood, C. and Cotes, J. E. (1979) 'Lung function in healthy British women', *Thorax*, 34, pp. 359–365. doi: 10.1136/thx.34.3.359.

Harik-Khan, R. *et al.* (1999) 'The effect of gestational parity on FEV1 in a group of healthy

volunteer women', *Respiratory Medicine*. W.B. Saunders Ltd, 93(6), pp. 382–388. doi: 10.1053/rmed.1999.0572.

Harik-Khan, R. I. *et al.* (2001) 'The effect of anthropometric and socioeconomic factors on the racial difference lung function', *American Journal of Respiratory and Critical Care Medicine*. American Lung Association, 164(9), pp. 1647–1654. doi: 10.1164/ajrccm.164.9.2106075.

Harirah, H. M. *et al.* (2005) 'Effect of gestational age and position on peak expiratory flow rate: A longitudinal study', *Obstetrics and Gynecology*, 105(2), pp. 372–376. doi: 10.1097/01.AOG.0000152303.80103.69.

Ie, S. *et al.* (2002) 'Respiratory complications of pregnancy', *Obstetrical and Gynecological Survey*, pp. 39–46. doi: 10.1097/00006254-200201000-00022.

Ip, M. S. M. *et al.* (2006) 'Updated spirometric reference values for adult Chinese in Hong Kong and implications on clinical utilization', *Chest*. American College of Chest Physicians, 129(2), pp. 384–392. doi: 10.1378/chest.129.2.384.

Ivanova, O. *et al.* (2020) 'Lung function testing and prediction equations in adult population from maputo, Mozambique', *International Journal of Environmental Research and Public Health*. MDPI AG, 17(12), pp. 1–11. doi: 10.3390/IJERPH17124535.

Johannessen, A. *et al.* (2006) 'Post-bronchodilator spirometry reference values in adults and implications for disease management', *American Journal of Respiratory and Critical Care Medicine*. American Thoracic Society, 173(12), pp. 1316–1325. doi: 10.1164/rccm.200601-023OC.

Jones, R. L. and Nzekwu, M. M. U. (2006) 'The effects of body mass index on lung volumes', *Chest*. American College of Chest Physicians, 130(3), pp. 827–833. doi: 10.1378/chest.130.3.827.

van Katwijk, C. and Peeters, L. (1998) 'Clinical aspects of pregnancy after the age of 35 years: a review of the literature', *Human Reproduction Update*. Oxford Academic, 4(2), pp. 185–194. doi: 10.1093/HUMUPD/4.2.185.

Kevin McCarthy (2020) *Pulmonary Function Testing: Spirometry, Lung Volumes Determination, Diffusing Capacity of Lung for Carbon Monoxide, Medscape*. Available at:

http://emedicine.medscape.com/article/303239-overview (Accessed: 11 January 2021).

Kevin McCarthy and Raed A Dweik (2020) *Pulmonary Function Testing: Spirometry, Lung Volume Determination, Diffusing Capacity of Lung for Carbon Monoxide*, *medscape*. Available at: https://emedicine.medscape.com/article/303239-overview (Accessed: 8 September 2020).

Knox, A. J. (2001) 'Respiratory diseases in pregnancy: Introduction', *Thorax*, p. 324. doi: 10.1136/thorax.56.4.324.

Knudsen, T. M. *et al.* (2011) 'Predictive equations for spirometric reference values in a healthy adult suburban population in Tanzania', *Tanzania Journal of Health Research*, 13(3), pp. 214–223. doi: 10.4314/thrb.v13i3.64540.

Kolarzyk, E., Szot, W. M. and Lyszczarz, J. (2005) 'Lung function and breathing regulation parameters during pregnancy', *Archives of Gynecology and Obstetrics*. Springer, 272(1), pp. 53–58. doi: 10.1007/s00404-004-0691-1.

Ku, C. W. *et al.* (2018) 'Serum progesterone distribution in normal pregnancies compared to pregnancies complicated by threatened miscarriage from 5 to 13 weeks gestation: a prospective cohort study', *BMC Pregnancy and Childbirth*. BioMed Central Ltd., 18(1), p. 360. doi: 10.1186/s12884-018-2002-z.

Kumar, S. N. S. *et al.* (2014) 'Reliability, agreement, and validity of digital weighing scale with MatScan in limb load measurement', *Journal of Rehabilitation Research and Development*. Rehabilitation Research and Development Service, 51(4), pp. 591–598. doi: 10.1682/JRRD.2013.07.0166.

Lalley, P. M. (2013) 'The aging respiratory system-Pulmonary structure, function and neural control', *Respiratory Physiology and Neurobiology*. Elsevier, pp. 199–210. doi: 10.1016/j.resp.2013.03.012.

Lapinsky, S. E. *et al.* (2014) 'Restrictive lung disease in pregnancy', *Chest*. American College of Chest Physicians, 145(2), pp. 394–398. doi: 10.1378/chest.13-0587.

Leeper, J. (no date) *Choosing the Correct Statistical Test in SAS, Stata, SPSS and R, UCLA: Statistical Consulting Group*. Available at: https://stats.idre.ucla.edu/other/mult-pkg/whatstat/ (Accessed: 9 September 2020).

Leighton, B. M. and Fish, J. E. (2009) ‘Pulmonary Disease in Pregnancy’, *The Global Library of Women’s Medicine*. Sapiens Publishing, LTD. doi: 10.3843/GLOWM.10170.

Little, M. and Sinert, R. (2016) *Asthma in Pregnancy: Risks and Prevalence, Pathophysiologic Mechanisms, Asthma Differentials, Drugs & Diseases: Emergency Medicine*. Available at: https://emedicine.medscape.com/article/796274-overview (Accessed: 4 March 2021).

Lomauro, A. and Aliverti, A. (2018) ‘Sex differences in respiratory function’, *Breathe*. European Respiratory Society, 14(2), pp. 131–140. doi: 10.1183/20734735.000318.

LoMauro, A. and Aliverti, A. (2015) ‘Respiratory physiology of pregnancy’, *Breathe*. European Respiratory Society, pp. 297–301. doi: 10.1183/20734735.008615.

Lutfi, M. F. (2017) ‘The physiological basis and clinical significance of lung volume measurements’, *Multidisciplinary Respiratory Medicine*. BioMed Central Ltd., p. 3. doi: 10.1186/s40248-017-0084-5.

Manfré Pastro, L. D. *et al.* (2017) ‘Longitudinal study of lung function in pregnant women: Influence of parity and smoking luciana’, *Clinics*. Universidade de Sao Paulo, 72(10), pp. 595–599. doi: 10.6061/clinics/2017(10)02.

McCallister, J. W., Adkins, E. J. and O’Brien, J. M. (2009) ‘Obesity and Acute Lung Injury’, *Clinics in Chest Medicine*. Elsevier, pp. 495–508. doi: 10.1016/j.ccm.2009.05.008.

Mehari, A. *et al.* (2015) ‘Obesity and pulmonary function in African Americans’, *PLoS ONE*. Public Library of Science, 10(10). doi: 10.1371/journal.pone.0140610.

Le Merre, C. and Préfaut, C. (1988) ‘[Pregnancy and the respiratory function].’, *Revue des maladies respiratoires*, 5(3), pp. 249–54. Available at: http://www.ncbi.nlm.nih.gov/pubmed/3041498 (Accessed: 8 August 2020).

Murphy, V. E., Clifton, V. L. and Gibson, P. G. (2006) ‘Asthma exacerbations during pregnancy: Incidence and association with adverse pregnancy outcomes’, *Thorax*. BMJ Publishing Group Ltd, pp. 169–176. doi: 10.1136/thx.2005.049718.

Musafiri, S. *et al.* (2013) ‘Spirometric reference values for an east-African population’, *Respiration*. Respiration, 85(4), pp. 297–304. doi: 10.1159/000337256.

Niewoehner, D. E. and Kleinerman, J. (1974) ‘Morphologic basis of pulmonary resistance in the human lung and effects of aging’, *Journal of Applied Physiology*, 36(4), pp. 412–418. doi: 10.1152/jappl.1974.36.4.412.

Nonato, N. L. *et al.* (2015) ‘Occurrence of respiratory symptoms in persons with restrictive ventilatory impairment compared with persons with chronic obstructive pulmonary disease: The PLATINO study’, *Chronic Respiratory Disease*. SAGE Publications Ltd, 12(3), pp. 264–273. doi: 10.1177/1479972315588004.

Nørregaard, O. *et al.* (1989) ‘Lung function and postural changes during pregnancy’, *Respiratory Medicine*, 83(6), pp. 467–470. doi: 10.1016/S0954-6111(89)80127-1.

Orie, N. N. (1999) ‘Comparison of normal respiratory function values in young Kenyans with those of other Africans and Caucasians’, *East African Medical Journal*, 76(1), pp. 31–34.

Pellegrino, R. *et al.* (2005) ‘Interpretative strategies for lung function tests’, *European Respiratory Journal*, 26(5), pp. 948–968. doi: 10.1183/09031936.05.00035205.

Pierce, J. A. and Hocott, J. B. (1960) ‘Studies on the collagen and elastin content of the human lung.’, *The Journal of clinical investigation*. American Society for Clinical Investigation, 39(1), pp. 8–14. doi: 10.1172/JCI104030.

Quanjer, P. H., Hall, G. L., *et al.* (2012) ‘Age- and height-based prediction bias in spirometry reference equations’, *European Respiratory Journal*. European Respiratory Society, 40(1), pp. 190–197. doi: 10.1183/09031936.00161011.

Quanjer, P. H., Stanojevic, S., *et al.* (2012) ‘Multi-ethnic reference values for spirometry for the 3-95-yr age range: The global lung function 2012 equations’, *European Respiratory Journal*. European Respiratory Society, 40(6), pp. 1324–1343. doi: 10.1183/09031936.00080312.

Quanjer, P. H. *et al.* (2014) ‘All-age relationship between arm span and height in different ethnic groups’, *European Respiratory Journal*. European Respiratory Society, 44(4), pp. 905–912. doi: 10.1183/09031936.00054014.

Rębacz-Maron, E. (2018) ‘The multi-ethnic global lung initiative 2012 and Third National Health and Nutrition Examination Survey reference values do not reflect spirometric measurements in Black boys and men from Tanzania’, *Clinical Physiology and Functional*

Imaging. Blackwell Publishing Ltd, 38(1), pp. 76–86. doi: 10.1111/cpf.12386.

Rufino, R. *et al.* (2017) 'Spirometry reference values in the Brazilian population', *Brazilian Journal of Medical and Biological Research*. Associacao Brasileira de Divulgacao Cientifica, 50(3). doi: 10.1590/1414-431X20175700.

Schatz, M. *et al.* (2006) 'Spirometry is related to perinatal outcomes in pregnant women with asthma', *American Journal of Obstetrics and Gynecology*. Mosby, 194(1), pp. 120–126. doi: 10.1016/j.ajog.2005.06.028.

Sharma, G. and Goodwin, J. (2006) 'Effect of aging on respiratory system physiology and immunology.', *Clinical interventions in aging*. Dove Press, pp. 253–260. doi: 10.2147/ciia.2006.1.3.253.

Van Sickle, D., Magzamen, S. and Mullahy, J. (2011) 'Understanding socioeconomic and racial differences in adult lung function', *American Journal of Respiratory and Critical Care Medicine*, 184(5), pp. 521–527. doi: 10.1164/rccm.201012-2095OC.

Siva, N. *et al.* (2015) 'Effect of Different Postures on Peak Expiratory Flow Rate and Peak Inspiratory Flow Rate on Healthy Individuals', *~ 42 ~ International Journal of Physical Education, Sports and Health*, 1(3). Available at: www.kheljournal.com (Accessed: 17 December 2020).

Smith, J. L. *et al.* (1990) 'Adult respiratory distress syndrome during pregnancy and immediately postpartum', *Western Journal of Medicine*, 153(5), pp. 508–510.

Stanojevic, S. *et al.* (2008) 'Reference ranges for spirometry across all ages: A new approach', *American Journal of Respiratory and Critical Care Medicine*. American Thoracic Society, 177(3), pp. 253–260. doi: 10.1164/rccm.200708-1248OC.

Talaminos Barroso, A. *et al.* (2018) 'Factors Affecting Lung Function: A Review of the Literature', *Archivos de Bronconeumología (English Edition)*. Elsevier BV, 54(6), pp. 327–332. doi: 10.1016/j.arbr.2018.04.003.

Tarun Madappa and Zab Mosenifar (2011) *Pulmonary Disease and Pregnancy: Alterations in Pulmonary Physiology During Pregnancy, Alterations in Cardiac Physiology During Pregnancy, Dyspnea During Pregnancy*. Available at:

https://emedicine.medscape.com/article/303852-overview (Accessed: 10 September 2020).

Tenholder, M. F. and Sout-Paul, J. E. (1989) 'Dyspnea in pregnancy', *Chest*. Elsevier B.V., 96(2), pp. 381–389. Available at: https://go.gale.com/ps/i.do?p=AONE&sw=w&issn=00123692&v=2.1&it=r&id=GALE%7CA12682700&sid=googleScholar&linkaccess=fulltext (Accessed: 12 October 2020).

This, I. and Test, C. S. (2011) 'What statistical analysis should I use ? Statistical analyses using SPSS', pp. 1–23. Available at: https://stats.idre.ucla.edu/spss/whatstat/what-statistical-analysis-should-i-usestatistical-analyses-using-spss/ (Accessed: 9 September 2020).

Toglia, M. R. and Weg, J. G. (1996) 'Venous thromboembolism during pregnancy', *New England Journal of Medicine*, pp. 108–114. doi: 10.1056/NEJM199607113350207.

Townsend, E. A., Miller, V. M. and Prakash, Y. S. (2012) 'Sex differences and sex steroids in lung health and disease', *Endocrine Reviews*. Oxford Academic, pp. 1–47. doi: 10.1210/er.2010-0031.

Turner, J. M., Mead, J. and Wohl, M. E. (1968) 'Elasticity of human lungs in relation to age.', *Journal of applied physiology*, 25(6), pp. 664–671. doi: 10.1152/jappl.1968.25.6.664.

Wang, W. T. *et al.* (2020) 'Spirometric reference values in heathy Chinese adults in Taiwan: The secular changes and comparison with other Asian populations', *Journal of the Formosan Medical Association*. Elsevier B.V., 119(1P2), pp. 290–299. doi: 10.1016/j.jfma.2019.05.015.

Weinberger, S. E. *et al.* (1980) 'Pregnancy and the lung.', *The American review of respiratory disease*, 121(3), pp. 559–81. doi: 10.1164/arrd.1980.121.3.559.

White, N. W. *et al.* (1994) 'Review and analysis of variation between spirometric values reported in 29 studies of healthy African adults', *American Journal of Respiratory and Critical Care Medicine*. American Thoracic Society, 150(2), pp. 348–355. doi: 10.1164/AJRCCM.150.2.8049814.

Whitrow, M. J. and Harding, S. (2008) 'Ethnic differences in adolescent lung function: Anthropometric, socioeconomic, and psychosocial factors', *American Journal of Respiratory and Critical Care Medicine*, 177(11), pp. 1262–1267. doi: 10.1164/rccm.200706-867OC.

Wise, R. A. and Polito, A. J. (2000) ‘Respiratory physiologic changes in pregnancy’, *Immunology and Allergy Clinics of North America*. W.B. Saunders, 20(4), pp. 663–672. doi: 10.1016/S0889-8561(05)70175-2.

Yeomans, E. R. and Gilstrap, L. C. (2005) ‘Physiologic changes in pregnancy and their impact on critical care’, *Critical Care Medicine*. Lippincott Williams and Wilkins, pp. S256–S258. doi: 10.1097/01.CCM.0000183540.69405.90.

Yland, J. J. *et al.* (2020) ‘Perinatal Outcomes Associated with Maternal Asthma and Its Severity and Control During Pregnancy’, *Journal of Allergy and Clinical Immunology: In Practice*. American Academy of Allergy, Asthma and Immunology, 8(6), pp. 1928-1937.e3. doi: 10.1016/j.jaip.2020.01.016.

Zieleskiewicz, L. *et al.* (2014) ‘Lung ultrasound predicts interstitial syndrome and hemodynamic profile in parturients with severe preeclampsia’, *Anesthesiology*. Lippincott Williams and Wilkins, 120(4), pp. 906–914. doi: 10.1097/ALN.0000000000000102.

APPENDICES

Appendix I: Data collection tool

Data collection tool for **Spirometry profiles among pregnant and non-pregnant African women**

ID: …… **Date: …….**

A: Pregnancy Status

A01: 1. Pregnant ( ) 2. Non-pregnant ( )

B: Demographic Characteristics and Anthropometry

B01: Age in years…… B02: Bodyweight in Kg ……..

B03: Height in cm …… B04: BMI in Kg/m^2 …….

C: Pregnancy Information

C01: Parity …….. C02: Gestational Age in weeks ……

D: Spirometry

Parameter	Expected	Measured	Percent predicted
FVC	D01:	D02:	D03:
FEV1	D04:	D05:	D06:
FEV1/FVC		D07:	
PEF	D08:	D09:	D10:

Appendix II: Informed consent form (English version)

Consent to participate in the study of Spirometry profiles among pregnant and non-pregnant African women

Name: ……..…… Age: …….

Dear Madam

I am Jacktan Josephat, a postgraduate student in the Department of Physiology at the Muhimbili University of Health and Allied Sciences (MUHAS). I am researching Lung function Profiles in pregnant and non-pregnant African women. I hereby, kindly request your participation.

Purpose of the study: to evaluate lung function profile in pregnant and non-pregnant African women.

How to participate: - women willing to participate will be screened for contraindications, given a short interview, measured height and weight then subjected to a non-invasive test for lung function after signing informed consent.

Confidentiality: - personal information won't be collected and information collected will be used for study purposes only

Costs: - you will incur no cost of participation

Benefits: - participants will be offered a free spirometry test. Also, information obtained from this study will help to understand lung function and generate reference profiles for African women.

Voluntary participation and the right to withdraw from the study: - you have the right to withdraw from this study anytime you feel you want to do so. Whatever your decision, it won't affect your rights to care and treatment in any way.

Risks: - generally there is no risk associated with height and weight measurements. Spirometry is also safe and painless however it may cause little dizziness or shortness of breath after performing the test. Because the spirometry test requires some exertion, it may not be safe if you have heart problems or painful ears. Also if you had recent abdominal, open chest, eye, or head surgery or at term pregnancy. Therefore, you should not participate in this study if you have any of those.

Investigators statement: - I the investigator, have educated the participant on the purpose and applications of the study.

Signed: …….. Date: …….

If you have any question you may contact through the following

P.O Box 395, Dodoma

Mobile Phone: +255 764 784 055

In case of any information regarding your rights as a participant please contact

The Chairperson of the Research and Publication committee

Muhimbili University of Health and Allied Sciences (MUHAS)

P.O Box 65001, Dar es Salaam

Telephone (+255) 022-2152489

Participant's statement

I am willing to participate in this study on lung function in pregnant and non-pregnant African women. I am doing this with a full understanding of the purposes and procedures of this study including spirometry, height, and weight measurements which have been explained to me by Jacktan Josephat.

Signature of participant ……

Signature of witness …….

Date …….

Appendix III: Informed consent form (Kiswahili version)

Idhini ya kushiriki katika utafiti wa wasifu wa ufanyaji kazi wa mapafu kwa wanawake wajawazito na wasio wajawazito wa Kiafrika

Jina: …….. …… Umri: …….

Mpendwa mama,

Mimi ni Jacktan Josephat mwanafunzi wa uzamili katika Idara ya Fiziolojia katika Chuo Kikuu cha Afya na Sayansi Shirikishi Muhimbili (MUHAS). Ninafanya utafiti juu ya wasifu wa ufanyaji kazi wa mapafu kwa wanawake wajawazito na wasio wajawazito wa Kiafrika. Kwa hivyo, ninaomba ushiriki wako.

Kusudi la utafiti: kutathmini wasifu wa ufanyaji kazi wa mapafu kwa wanawake wajawazito na wasio wajawazito wa Kiafrika.

Jinsi ya kushiriki: - wanawake walio tayari kushiriki watachunguzwa kujua iwapo kipimo kitawafaa, watafanyiwa mahojiano mafupi, watapimwa urefu na uzito kisha kufanyiwa kipimo cha ufanyaji kazi wa mapafu baada ya kusaini idhini ya kushiriki.

Usiri: - habari za kibinafsi hazitakusanywa na habari zitakazokusanywa zitatumika kwa kusudi la utafiti tu

Gharama: - hautalipa gharama yoyote ya ushiriki

Faida: - mshiriki atafanyiwa kipimo wa ufanyaji kazi wa mapafu bure. Pia, taarifa zitakazopatikana kutokana na utafiti huu zitasaidia kuelewa utendaji wa mapafu na kutoa wasifu wa rejea kwa wanawake wa Kiafrika.

Kushiriki kwa hiari na haki ya kujiodoa kwenye utafiti: - una haki ya kujiondoa kwenye utafiti huu wakati wowote ukipenda kufanya hivyo. Uamuzi wako wowote hautaathiri haki yako ya huduma na matibabu kwa namna yoyote ile.

Hatari: - kwa ujumla hakuna hatari inayohusishwa na vipimo vya urefu na uzito. Kipimo cha ufanyaji kazi wa mapafu pia ni salama na haina maumivu lakini kinaweza kusababisha kujihisi kizunguzungu kidogo au kuishiwa pumzi kidogo baada ya kufanya kipimo. Pia, kwa sababu kipimo hicho kinahitaji kupuliza kwa nguvu, kinaweza kuwa si salama ikiwa una tatizo la moyo au maumivu ya sikio. Pia kama ulifanyiwa upasuaji wa hivi karibuni wa tumbo, kifua, macho au kichwani au wakati wa ujauzito uliofikia umri wa kujifungua. Ikiwa una moja ya sababu hizo haupaswi kushiriki katika utafiti huu.

Kauli ya mtafiti: - Mimi mtafiti nimemfundisha mshiriki juu ya kusudi na matumizi ya utafiti huu.

Imesainiwa: …….. Tarehe: …….

Ikiwa una swali lolote unaweza kuwasiliana nami kupitia:

S.L.P 395, Dodoma

Simu ya Mkononi: +255 764 784 055

Ikiwa kuna swali lolote kuhusu haki yako kama mshiriki tafadhali wasiliana na:

Mwenyekiti wa kamati ya Utafiti na Uchapishaji

Chuo Kikuu cha Afya na Sayansi Shirikishi Muhimbili (MUHAS)

S.L.P 65001, Dar es Salaam

Simu (+255) 022-2152489

Kauli ya mshiriki

Nimehiari kushiriki katika utafiti huu juu ya ufanyaji kazi wa mapafu kwa wanawake wajawazito na wasio wajawazito wa Kiafrika. Ninafanya hivyo nikiwa nafahamu kusudi na taratibu za utafiti huu ikiwa ni pamoja na kipimo cha ufanyaji kazi wa mapafu, vipimo vya urefu na uzito kama ambavyo nimefafanuliwa na Jacktan Josephat**.**

Saini ya mshiriki ……

Saini ya shahidi …….

Tarehe ……

Appendix IV: Standard operating procedures (Center for Health Statistics, 2011; Graham *et al.*, 2019; Kevin McCarthy, 2020)

1. Asses for spirometry safety exclusions. Ask the following questions and exclude if she has any criteria in a specified period.
    a. Do you have diarrhea or any bowel urgency?
    b. Do you have painful ear conditions? YES/NO
    c. Have you ever had eye surgery? (exclude cosmetic surgery on eyelids or skin around the eyes) YES/NO
    d. Was the eye surgery in the last 3 months? YES/NO
    e. Have you ever had open chest or abdominal surgery? YES/NO
    f. Was the open chest or abdominal surgery in the last 3 months? YES/NO
    g. Did you or anyone in your household have tuberculosis in the past year? YES/NO
    h. Has a doctor or any health professional told you that you have a heart problem? YES/NO
    i. Has a doctor or any health professional told you that you have an eye problem? YES/NO
    j. Has a doctor or any health professional told you that you had a stroke? YES/NO
    k. Did this stroke happen in the last 3 months? YES/NO
    l. In the past month have you coughed blood? YES/NO
    m. Has a doctor or any health professional told you that you have a hypertensive disorder? YES/NO
    n. Have you ever had convulsions or seizures in the last 3 months? YES/NO
    o. Has a doctor or any health professional told you that you have a lax cervix? YES/NO
    p. Have you ever had an abortion? YES/NO

q. Did a doctor or any health professional tell you that you had a lax cervix? YES/NO

2. Spirometry test procedures.

a. Instructions and preparation

i. Repeat the purpose of the examination and emphasize the need for extra effort for maximum results

ii. Ask participants to loosen any tight clothing and remove unsecured dentures if any.

iii. Prepare all equipment and kits in place

iv. Have the participant seat straight on the office chair.

v. Have the participant elevate chin and extend neck slightly

vi. Have the participant hold the hose rather than filter

vii. Demonstrate trial exhalation using your mouthpiece. Instruct as follows

- "Take a big deep breath to fill your lungs"
- "Put your mouthpiece between teeth and on top of the tongue. Lightly bite the mouthpiece. Snugly seal your lips around the mouthpiece"
- "Blast out air as hard and fast as you can"
- "Keep blowing out the air until I tell you to stop"

viii. **NOTE:** exhalation for a minimum of 6 seconds is required

ix. As the participant stops, instruct her to direct the mouthpiece away from her face

x. Review the procedure and correct any problems for the next trial

b. Assess for acceptability and repeatability

i. Consider spirogram acceptable if there is evidence of

- No hesitation or false start on the part of the participant
- The volume of back-extrapolation (Vext) is less than 0.5% of FVC

- No coughing during the maneuver
- No glottis closure, mouthpiece obstruction, or leaks
- The visible plateau in the volume-time curve
- Maneuver lasting for at least 6 seconds

ii. Consider spirometry test reproducible if

- The two largest FVC do not differ by more than 150 ml
- The two largest FEV1 do not differ by more than 150 ml

Appendix V: Ethical clearance

UNITED REPUBLIC OF TANZANIA
MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY
MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES
OFFICE OF THE DIRECTOR - RESEARCH AND PUBLICATIONS

Ref. No.DA.282/298/01.C/ Date: 25/03/2021

MUHAS-REC-03-2021-536

Jacktan Josephat
MSc in Physiology,
School of Medicine
MUHAS

RE: APPROVAL FOR ETHICAL CLEARANCE FOR A STUDY TITLED: Lung Function Profiles among Pregnant and Non-pregnant African Women

Reference is made to the above heading.

I am pleased to inform you that the Chairman has on behalf of the University Senate, approved ethical clearance of the above-mentioned study, on recommendations of the Senate Research and Publications Committee meeting accordance with MUHAS research policy and Tanzania regulations governing human and animal subjects research.

APPROVAL DATE: 25/03/2021
EXPIRATION DATE OF APPROVAL: 24/03/2022

STUDY DESCRIPTION:
Purpose:
The purpose of this observational cross section study is to evaluate lung function profile and associated determinants among pregnant and non-pregnant women

The approved protocol and procedures for this study is attached and stamped with this letter, and can be found in the link provided: https://irb.muhas.ac.tz/storage/Certificates/Certificate%20-%20479.pdf and in the MUHAS archives.

The PI is required to:

1. Submit bi-annual progress reports and final report upon completion of the study.
2. Report to the IRB any unanticipated problem involving risks to subjects or others including adverse events where applicable.
3. Apply for renewal of approval of ethical clearance one (1) month prior its expiration if the study is not completed at the end of this ethical approval. You may not continue with any research activity beyond the expiration date without the approval of the IRB. Failure to receive approval for continuation before the expiration date will result in automatic termination of the approval for this study on the expiration date.
4. Obtain IRB amendment (s) approval for any changes to any aspect of this study before they can be implemented.
5. Data security is ultimately the responsibility of the investigator.
6. Apply for and obtain data transfer agreement (DTA) from NIMR if data will be transferred to a foreign country.
7. Apply for and obtain material transfer agreement (MTA) from NIMR, if research materials (samples) will be shipped to a foreign country,
8. Any researcher, who contravenes or fail to comply with these conditions, shall be guilty of an offence and shall be liable on conviction to a fine as per NIMR Act No. 23 of 1979, PART III section 10 (2)
9. The PI is required to ensure that the findings of the study are disseminated to relevant stake holders.
10. PI is required to be versed with necessary laws and regulatory policies that govern research in Tanzania. Some guidance is available on our website https://drp.muhas.ac.tz/.

Dr. Bruno Sunguya
Chairman, MUHAS Research and Ethics Committee

Muhimbili University of Health and Allied Sciences
DIRECTOR
Research & Publications
Box 65001

Cc: Director of Postgraduate Studies

9 United Nations Road; Upanga West; P.O. Box 65001, Dar Es Salaam: Tel. G/Line: +255-22-2150302/6; Ext. 1038; Direct Line:+255-22-2152489;Telefax:+255-22-2152489;E-mail:drp@muhas.ac.tz;Web:https://www.muhas.ac.tz