THE BURDEN OF RESPIRATORY SYMPTOMS AND PREVALENCE OF SPIROMETRIC ABNORMALITIES AMONG HIV INFECTED PATIENTS AT THE KENYATTA NATIONAL HOSPITAL COMPREHENSIVE CARE CENTRE

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H58/75208/2014

A STUDY DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF THE MASTERS OF MEDICINE DEGREE IN INTERNAL MEDICINE

DECLARATION

I hereby declare that this dissertation is my original work and has not been presented for any degree or research to any other institution or university.

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ACKNOWLEDGEMENT

I wish to express my sincere gratitude to the following for their contribution towards the success of this dissertation: My supervisors Dr. Jared Mecha, Dr. Loice Achieng and Professor C. F Otieno who have worked tirelessly and patiently to ensure completion of this study.

I am thankful to my Family for the unwavering support, patience and love they accorded me.

To all my friends and classmates who supported me immeasurably, I am grateful.

Finally to Almighty God for his grace and mercies.

DECLARATION OF ORIGINALITY

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DECLARATION

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DEDICATION

I dedicate this work to my loving family, George, Claire and Ian.

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LIST OF ACRONYMS AND ABBREVIATIONS

AIDS – Acquired Immune- Deficiency Syndrome

ATS – American Thoracic Society

ATS- DLD – American Thoracic Society – Division of lung disease

COPD – Chronic Obstructive Pulmonary Disease

CVA – Cardiovascular Accident

DLCO – Diffusion Lung Capacity for Carbon monoxide

EBV – Epstein bar virus

ELISA – Enzyme Linked Immunosorbent assay

ERS – European respiratory society

FVC – Forced Vital Capacity

FEV – Forced Expiratory Volume

FEV_1 – Forced expiratory volume in one second

GINA – Global Initiative for Asthma

GOLD – Global Strategy for Obstructive Lung Disease

HAART – Highly Active Anti-Retroviral Therapy

HIV – Human Immunodeficiency Virus

IL – Interleukin

ILD – Interstitial Lung Disease

IQR – Inter-quartile range

KNH – CCC – Kenyatta National Hospital Comprehensive Care Centre

LIP – Lymphoid Interstitial Pneumonitis

NASCOP – National AIDS and STI Control Program

NRTI – Nucleoside/Nucleotide Reverse Transcriptase Inhibitor

NNRTI – Non Nucleoside Reverse Transcriptase inhibitor

NSIP – None Specific Interstitial Pneumonitis

PTB – Pulmonary Tuberculosis

PFTs – Pulmonary Function Tests

PM – Particulate matter

TNF – Tumor Necrosis Factor

URTI – Upper Respiratory Tract Infection

WHO- World health organization

ABSTRACT

BACKGROUND: In recent years, attention has been drawn to the increasing prevalence of several non-infectious pulmonary complications linked to HIV infection. The prevalence and type of spirometric abnormalities, factors that alter lung function parameters and the accompanying respiratory symptoms are largely unevaluated especially in sub-Saharan Africa, which is home to two thirds of people living with HIV globally.

OBJECTIVES: This study set out to describe the burden of respiratory symptoms and to determine the prevalence and type of spirometric abnormalities among ambulatory ART- treated HIV patients on follow up at the Kenyatta National Hospital Comprehensive Care Centre (KNH-CCC).

METHODOLOGY: This was adescriptive cross sectional study carried out among ambulatory HIV infected adults on HAART on routine follow–up at the KNH Comprehensive Care Centre

DATA MANAGEMENT AND ANALYSIS: The American thoracic society – Division of lung disease (ATS-DLD) respiratory questionnaire was used to obtain demographic data and data on the respiratory symptoms. All patients underwent spirometric test as per the ATS/ERS guidelines. Data was analysed using SPSS version 21.0. Descriptive characteristics of the population were summarised as percentages for categorical data and means or medians for continuous variables. The prevalence of spirometric abnormalities and respiratory symptoms were analysed and presented as proportions with 95% confidence intervals. Pearson Chi-square test was used to check for any association between the patients' characteristics and the presence of spirometric abnormalities and respiratory symptoms.

RESULTS: This study recruited 371 ART treated patients. The study population was largely female with a mean (SD) age of 47.4 (10.3) years. The median CD4 count and viral load were 480.2 cells/ml and 0.01 copies/ml respectively. A history of previous pulmonary tuberculosis infection was present in 31% of the participants while 15% had a previous history pneumonia. The most common respiratory symptom was cough (22.4%) followed by sputum production (18.9%), breathlessness (15%), sneezing (13.5%) wheezing (12.7%) and nasal congestion (11.6%). Restrictive spirometric abnormalities were the most frequent at 11.3% (95% CI [8.1; 14.5]) obstructive at 6.2% (95% CI [3.7; 8.7]) and mixed at 1.1% (95% CI [0.0; 2.1]). A previous history of severe respiratory infection, BMI, and duration on HAART were significantly

associated with respiratory symptoms while only cigarette smoking status was significantly associated with abnormalities on spirometry.

CONCLUSION: In conclusion, we found that the most common respiratory symptoms in our study population were cough, sputum production, and breathlessness. Spirometric abnormalities of restrictive nature were the most frequent followed by obstructive then mixed. Long-term complications of recurrent pulmonary opportunistic infections, including pulmonary tuberculosis and pneumonia, are a possible cause of respiratory symptoms in these patients and could explain the predominantly restrictive spirometric abnormalities. Although our prevalence of both respiratory symptoms and spirometric abnormalities were low in comparison to other studies, our study population was relatively young. The respiratory symptoms and spirometric changes could become more clinically relevant as the HIV population on ART ages.

CHAPTER ONE

BACKGROUND

Sub-Saharan Africa bears the greatest burden of Human Immunodeficiency Virus (HIV) disease with an estimated two thirds of people living with HIV found in this region. Approximately 41% of all people living with HIV in Sub - Saharan Africa have access to anti-retroviral therapy (1).

In Kenya the prevalence of HIV/ Acquired Immune Deficiency Syndrome (AIDS) has significantly declined from 6.7% in 2003 to 5.9% in 2015(2). However, it is still ranked as one of the highest HIV burden countries in Africa. According to the World Health Organization global health observatory data, HAART coverage in the low and middle income countries increased by about 21% between the year 2012 and 2013 (3). Kenya has realized tremendous gains in HIV treatment since the roll out of free ART in 2003. There has been a decline in in AIDS related deaths by 30% between 2003 and 2015 and an 11% increase in retention to care at 5 years. Subsequently the number of people living with HIV on treatment has increased by 40% between 2013 and 2015(2). This translates into an increase in life expectancy of people living with HIV disease (4). It is therefore predicted that non- infectious HIV related complications will soon become more evident in the HIV infected population in sub-Saharan Africa.

Literature from developed countries indicates that HIV associated mortality and opportunistic infections have markedly decreased due to widespread use of HAART (5,6). Subsequently, attention has been drawn to the increasing prevalence of HIV associated non - infectious pulmonary complications including Chronic Obstructive Pulmonary Disease (COPD) , asthma pulmonary hypertension, lung cancer, Kaposi's Sarcoma, lymphoma, interstitial lung disease, and bronchiectasis (7,8)

The effects HIV virus replication, HAART use, cigarette smoking and biomass exposure compound the residual effects of recurrent infections on lung physiology. The resultant ventilatory defects, as measured by spirometry, and the accompanying respiratory symptoms are largely unevaluated especially in sub-Saharan Africa where a majority of the HIV disease burden lies (9)

LITERATURE REVIEW

PATHOPHYSIOLOGY OF PULMONARY COMPLICATIONS IN HIV

The mechanisms by which non-infectious lung disease occurs in HIV is not fully understood but could result from; recurrent opportunistic infections, cigarette smoking, uncontrolled HIV replication, biomass exposure and older age (10–12)

Recurrent infections

Bacterial pneumonia occurs throughout HIV infection but tends to develop more frequently in patients with advanced immunosuppression (13). Patients with a CD 4 + count of < 200cells /ml are at an increased risk of acquiring pneumocystis pneumonia and invasive pneumococcal pneumonia.

In the lungs, resting T lymphocytes are reservoirs for the HIV virus. During an infection activation of these T lymphocytes occurs, the HIV virus resumes replication with the production of new virus particles (13,14). This perpetuates persistence of HIV virus in the lungs and chronic inflammation with progressive airflow obstruction and reduced pulmonary compliance.

In HIV pneumocystis co-infection, there is activation of macrophages with the production of cytokines, particularly interleukin 13 (IL- 13). This causes production of matrix metaloproteases and cathepsin that degrade pulmonary collagen tissue leading to emphysematous changes.

Pulmonary function abnormalities that occur after tuberculosis infection are secondary to pulmonary fibrosis, emphysema and bronchiectasis (15). Increased prevalence of bronchiectasis in HIV infection is thought to result from frequent and severe airway bacterial and viral infections which mediate persistent inflammation and damage to bronchial walls (7)

In a prospective cohort study, HIV infected patients evaluated at one and six months following a bacterial or pneumocystis pneumonia infection were found to have a permanent decline in pulmonary function. The greatest changes in FEV1, FVC and FEV1/FVC ratio were seen in pneumocystis pneumonia patients (16). Emphysematous lung changes have also been found in HIV patients with Pneumocystis pneumonia during acute infection and at least three months after the infection (17,18)

In a cross-sectional study done in Kenya to assess the pulmonary function and health-related quality of life of patients two years post TB treatment, 29% of the study population had pulmonary impairment, out of which 23% were restrictive, 5% obstructive and 1% mixed (19). Other studies have also shown that a large percentage of fully treated and partially treated pulmonary tuberculosis patients develop permanent restrictive or airflow obstruction defects (20,21).

Immunological status

Poorly controlled HIV has been associated with worse pulmonary function and a greater decline in lung function. Patients with a high viral load have also been shown to have a poorer ventilatory function as compared to those with undetectable viral. Studies evaluating pulmonary function in HIV infection have described lower spirometry values in patients with CD4 + count of <200copies/ml (22,23).

Advancing HIV disease is associated with a decline in CD4+ count and high viremia that is responsible for persistent low-grade inflammation in the lungs. HIV virus persists in the lungs where it causes a decrease in inflammatory cytokines and impaired bronchoalveolar T lymphocytes and macrophage response(14). This eases colonization and persistence of potential pathogens that contribute to lung injury alone or in synergy with other factors.

Pulmonary endothelial cells, though not infected by HIV virus, are susceptible to apoptosis when exposed to HIV proteins (Tat and Nef) which are present in high concentrations in the lungs (14). These proteins cause dysfunction of the epithelial barrier and impair the first line defenses contributing to inability to clear infections(7)

HIV proteins induce an imbalance in both systemic and lung oxidants and antioxidants. Increased oxidative stress in the lungs alters expression of epithelial tight junction proteins hence a dysfunctional epithelial barrier (24). Increased oxidation also causes activation of matrix metaloproteases and inactivation of anti - proteases with a decreased ability of the lung to repair itself (25). This leads to areas of fibrosis and emphysema.

Excessive Inflammatory responses to HIV proteins in the lungs cause immune dysregulation with CD8+ T cell proliferation and a decline in CD4+T cells and inflammatory cytokines. CD8+ T cell lymphocytic infiltration of the pulmonary interstitium is thought to contribute to the development of HIV associated

lymphoid interstitial pneumonitis (7). LIP in HIV has also been associated with Epstein bar virus (EBV) infection. EBV infected B cells are susceptible to infection by HIV and may facilitate HIV replication in the lung leading to persistent immune activation with a low-grade asymptomatic alveolitis which may progress to LIP or NSIP (26,27).

Cigarette smoking

Patients with HIV infection and a history of cigarette smoking develop a rapid decline in pulmonary function as compared to their HIV negative counterparts matched for age, sex and smoking history (28). Tobacco smoking in HIV infected patients also causes frequent exacerbation of both asthma and COPD and affects asthma control (7)

There is a two-fold increase in the risk of bacterial pneumonia in HIV infected Smokers (29,30). Smoking leads to dysfunction of HIV infected alveolar macrophages making airway colonization and persistence of potential pathogens easier (14). In COPD cigarette smoke causes oxidative stress in the airway, epithelial damage and ciliary dysfunction leading to the impaired clearing of airway secretions. This propagates the vicious cycle of infection and inflammation leading to airway remodeling and decline in lung function (28).

Anti- retroviral therapy

An independent association between use of combination anti-retroviral therapy and air way obstruction has been reported in literature (10,31). However this association is not uniform, in a Philadelphia study a 13.6% prevalence of obstructive changes on spirometry was associated with increased age, previous history of pneumocystis infection and the number of pack years but not use of HAART(32). The biological link between ARV therapy and airway obstruction is not clear but several mechanisms have been postulated.

After initiation of HAART, the viral load in bronchoalveolar lavage (BAL) fluid of more than 80% of patients' decreases to undetectable levels. There is also a consequent increase in the CD4+counts and a decrease in interferon gamma (IFN- γ) and IL- 6 levels in the alveolar space (14). The resulting immune restoration leads to an exaggerated CD4+ driven inflammatory response to residual pathogens including Cryptococcus, non-tuberculosis mycobacteria, pneumocystis and tuberculosis (33). In this situation, a severe bystander lung injury occurs even after resolving the infection. Sarcoidosis, usually characterized by a non-specific granulomatous inflammation and CD4+ alveolitis, has been reported in patients with CD4+ cell

count of >200cells/ml following initiation of HAART. It is thought to occur as a result of immune reconstitution with pulmonary CD4+ cell restoration (34)

The non- infectious HIV- associated pulmonary complications include airway disease (COPD, Asthma, bronchiectasis), interstitial lung diseases, pleural and chest wall disease, pulmonary hypertension and malignancies (7)

HIV ASSOCIATED AIRWAY DISEASE

Chronic obstructive pulmonary disease

The prevalence of COPD in people infected with HIV is high as compared to the general population but varies from place to place. A study done in The United States in 2009 reported a COPD prevalence of 8.3% in the HIV infected patients (10). A cross-sectional study carried out in Europe in HIV infected patients found a COPD prevalence of 23.1%, this is similar to 21% prevalence found by Gingo et al in USA (31). In Nigeria, a cross-sectional study that was aimed at evaluating the prevalence of COPD and associated risk factors in HIV infected adult found a prevalence of 15.4% using a post bronchodilator FEV1/FVC <0.7 (23)

COPD is the fourth leading cause of death worldwide (35). Studies have shown that Co morbid COPD in HIV is a major risk factor for hospitalization and a leading cause of respiratory failure in critically ill patients (36). It is also associated with a significantly worse physical and mental health in HIV(37)

Risk factors for COPD in the HIV infected population include low socio economic status, cigarette smoking low CD4+ T cell count and recurrent pulmonary infections (23,38–40). Higher viral loads have been independently associated with an increased prevalence of spirometric defined obstructive lung disease (23,41)

Asthma

It is estimated that 235 million people suffer from asthma worldwide but the prevalence varies widely from place to place (42). Epidemiological studies examining the relationship between asthma and HIV have described conflicting results. Gingo et al found a prevalence of 20.6% of asthma and bronchodilator reversibility among HIV infected adults. Co morbid HIV in asthma is associated with an increase in all-cause mortality(43) and poor asthma control. Risk factors for asthma in HIV infection include obesity, family

history of asthma, allergy, prior infection and absence of HAART (44). Other studies have found no association between asthma with HIV infection (45).

Bronchiectasis

The prevalence of bronchiectasis in patients infected with HIV is higher than in the general population (46). This is attributable to the high rates of recurrent and severe pulmonary infections in patients infected with HIV.

HIV ASSOCIATED INTERSTITIAL LUNG DISEASES

Interstitial lung diseases are a group of lung diseases affecting the alveolar epithelium, pulmonary capillary endothelium, basement membrane, and perivascular and peri-lymphatic tissue (47).

HIV associated interstitial lung diseases are uncommon however, lymphoid interstitial pneumonitis (LIP) is an AIDS defining illness in children under 13years (26). LIP and Non-specific interstitial pneumonitis (NSIP) were described in HIV infected patients in the pre anti -retroviral therapy era (48) and are less common in HAART era

HIV associated cryptogenic organizing pneumonia, hypersensitivity and sarcoidosis have been related to IRIS occurring after initiation of HAART (34,49)

PLEURAL INVOLVEMENT IN HIV

Two thirds of pleural disease in HIV are caused by infections and the remaining one third by non- infectious etiology including malignancies, cardiac and liver disease (50). Pleural disease commonly manifests as pleural effusion. Bacterial pneumonia accounts for about 30% and mycobacteria 8-10% of pleural effusion in hospitalized HIV patients. Pneumocystis pneumonia effusion is uncommon but has been associated with pneumothorax and pleural masses (51). Inflammation of the pleura due to the disease processes heals with scaring leading to restriction of lung expansion. The presence of fluid, air or a mass in the pleural space also results in restrictive defects on spirometry.

RESPIRATORY SYMPTOMS IN HIV INFECTION

There is an overlap in clinical presentation of respiratory disease in HIV infected people across the various pulmonary diagnoses. The symptoms include complains of cough, sputum production, dyspnea on exertion, wheeze and chest pain (7). The presentation can be acute, sub-acute or chronic in duration depending on the underlying pathology.

The overlap and variation in symptoms across various pulmonary diagnoses have been described in literature. In a large multicenter study, the likely diagnoses in the HIV infected population were COPD, bacterial pneumonia, pulmonary tuberculosis, pneumocystis pneumonia, pulmonary hypertension and pulmonary fibrosis. However, dyspnea cough and wheezing were most the common symptoms (11). In Nigerian study which evaluated the burden of respiratory symptoms among HIV positive patients not on HAART, common respiratory symptoms were a dry cough (48%), cough with sputum production (35%), breathlessness (32%) and chest pain (29%) (22). These finding were replicated in a different study but in a similar geographical region in which 17% of the respondents had a cough 11% had dyspnea and 4.5% had a wheeze.

Factors associated with increased respiratory symptoms in HIV infection are smoking, poor HIV control, and HIV infection itself (11,28). HIV Patients with respiratory symptoms generally have lower spirometry parameters than asymptomatic HIV infected patients (10,22)

PULMONARY FUNCTION TESTS

Pulmonary function tests (PFTs) are physiologic measures of respiratory function and structure. They are used to evaluate unexplained respiratory symptoms e.g. cough, dyspnea, and wheezing, for monitoring patients with a known respiratory disease such as asthma and COPD and to evaluate the effects of occupational exposures e.g. dust on the lungs (52).

The main types PFTs are spirometry, diffusion capacity for carbon monoxide (DLCO) and lung volumes (53). DLCO measures the ability of the alveolar capillary membrane to diffuse gases and lung volumes are used to demonstrate the total lung capacity. Lung volumes are most useful in diagnosing restrictive disease (54)

The influence of HIV infection on lung function is mainly due to the effects of post infectious lung disease and chronic obstructive airway disease on airflow, pulmonary compliance and diffusion capacity for carbon monoxide.(9)

Spirometry

Spirometry assesses lung function by measuring the volume of air that the patient can expel from the lungs after a maximal inspiration. The obtained values are compared with the predicted normal values for age, height, sex and ethnicity in order to determine the severity of air way obstruction (55).

The standard spirometry maneuver is a maximal forced exhalation after a maximal deep inspiration.The values which can be derived from this maneuver include;forced vital capacity (FVC), Forced expiratory volume in one second (FEV $_1$), Forced expiratory volume in six seconds (FEV$_6$) and the slow vital capacity (slow VC). The FEV$_1$/FVC ratio is calculated and expressed as a percentage. Flow volume curve can also be generated by some spirometers.

FVC is the total volume of air, in liters, that the patient can forcibly exhale in one breath expressed as a percentage of the predicted volume. FEV$_1$ refers to the volume of air that the patient is able to exhale in the first second of forced expiration expressed as a percentage of the predicted volume. FEV6 measures the volume of air that can be expired in six seconds. Using FEV6 instead of FVC may be helpful in patients with more severe airflow obstruction.

A normal spirometric pattern is defined by an FEV1 and FVC above 80% predicted FEV$_1$/FVC ratio above 0.7. Obstructive defects are defined by an FEV1 below 80% predicted, FEV$_1$/FVC ratio below 0.7 with a normal or reduced FVC (55). Restrictive defects are characterized by a normal or mildly reduced FEV1, FVC below 80% predicted and FEV$_1$/FVC ratio above 0.7 (55)

Office spirometry is recommended by the National Lung health Education Programme (NLHEP) for office use by primary care providers for patients 45years of age or older who smoke cigarettes to detect pre-clinical COPD (56). It is also recommended for patients with unexplained respiratory symptoms e.g. chronic cough, wheezing, and exertional dyspnea to detect obstructive airway disease.

Obstructive airway disease can be accurately diagnosed using spirometry alone by demonstrating a lower than predicted FEV_1/FVC ratio (57). A study evaluating the diagnostic accuracy of spirometry for diagnosing air flow obstruction in patients with asthma and COPD found a sensitivity 84% of and specificity 92% of for COPD and sensitivity 29% of and specificity of 90% for asthma (57). Restrictive lung disease is less accurately diagnosed by spirometry because a low FVC on spirometry is not specific for a restrictive impairment as it can also be seen in patients with obstruction and air trapping (58). In 1999, Aaron et al evaluated the accuracy of spirometric measurements in diagnosing restrictive lung disease. They found that a low FVC when used alone had a sensitivity of 86% and specificity 83% in detecting a true restrictive disease. The sensitivity and specificity of a combination criterion of a low FVC and a normal or greater than normal FEV1/FVC was 68% and 93% respectively (58)

In a retrospective study that evaluated the spirometric data from 8315 patients to determine the utility of spirometric measurements FVC, FEV_1 and FEV1/FVC in diagnosing pulmonary restriction as compared to lung volume measurements, the sensitivity of FVC < lower limit of normal (LLN) criteria alone to diagnose restriction was 88% and specificity of 56.8%. The sensitivity of FVC <LLN and FEV1/FVC greater than or equal to normal was 72.4% and specificity of 87.1% (59)

The prevalence of spirometric abnormalities in HIV disease ranges from 7% (10) to 35% (22,60) in different regions. Obstructive airway disease is the most evaluated lung function abnormality with a prevalence of 5.4% in a Nigerian study (23) and 6.8% in the US (10), both determined by FEV_1/FVC below 0.70. A few studies have reported restrictive defects (60) but their true prevalence is not clear.

Table 1: studies on the prevalence of respiratory symptoms and spirometric abnormalities in HIV

Author	Design	Prevalence of respiratory symptoms	Prevalence of spirometric abnormalities
Onyedum et al, 2010 (22)	Cross-sectional, 100 HAART naïve		35% had at least one spirometric abnormality
Cui et al, 2010 (28)	Cross-sectional, 116 HIV infected patients		20% had at least one spirometric abnormality
George et al, 2009 (10)	Cross-sectional, 234 HIV infected patients	31% had at least one respiratory symptom	6.8% had irreversible airflow obstruction
Gingo et al, 2010 (31)	Cross-sectional, 167 HIV infected patients	41% had at least one respiratory symptom	21% had irreversible airflow obstruction
Passos et al, 2011 (61)	Prospective cross-sectional, 86 HIV infected patients		15.8% had at least one spirometric abnormality

STUDY INSTRUMENTS

American Thoracic Society - Division of Lung Disease questionnaire 78 (ATS – DLD 78)

The ATS – DLD -78 questionnaires is a standardized respiratory disease questionnaire recommended by the American Thoracic Society for use in epidemiological studies of people aged 13 years or more. It was designed for assessing the prevalence of respiratory symptoms and disease. The questions are reproducible, valid and free of bias (61)

It has two parts. The first part consists of the minimum questions that should be asked in any survey. The second part consists of additional questions which can be included by the investigator depending on the type of the study and the nature of the population being studied (62).

The British MRC questionnaire was the first standardized respiratory questionnaire to be developed in 1960. It was meant for use as a standard questionnaire for eliciting symptoms associated with chronic bronchitis. Due to changes in the nature and hypothesis of respiratory disease, there was a perceived need for questions

that would provide more information than provided by MRC questionnaire. In 1971, the National Heart Lung Institute (NHLI) proposed the NHLI questionnaire which was a modification of MRC questionnaire (62)

In 1974, The ATS DLD questionnaire was developed by the American thoracic society together with the Division of lung disease of the NHLI. Its purpose was for use in the survey of respiratory disease in epidemiologic studies. It was built on the strength and experience of the MRC and NHLI questionnaires, adding more detailed questions on smoking history, occupational history and family health history(62).

When used to elicit respiratory symptoms, the ATS DLD questionnaire yields similar results to those obtained by the MRC questionnaire. In a study comparing the ATS DLD and the MRC questionnaire, the two questionnaires were administered by the same interviewer to 914 patients the difference in the totals for each symptom was trivial in respect to chronic cough, phlegm and breathlessness on exertion. A history of a chronic cough was elicited more by the ATS DLD questionnaire as compared to MRC questionnaire (9.8% vs. 7.6%) (63)

In another cross-sectional survey comparing the ATS-DLD, MRC and NHLI questionnaires, one of the three questionnaires was administered to the respondent either by a telephone interview or via mail. The prevalence of chronic cough and phlegm was the same for all the three questionnaires. The MRC and ATS DLD questionnaires produced similar a prevalence of chronic wheeze, asthma and hay fever. These conditions are not covered by NHLI questionnaires. When interviewer-administered, the NHLI showed a greater variability in symptomatology than either the ATS DLD or MRC questionnaires. When self-administered by mail, the ATS DLD had the lowest percentage of misunderstood questions followed by NHLI then MRC (64)

The validity of the ATS- DLD questionnaire has been documented in various studies correlating the presence of respiratory symptoms and pulmonary function tests in different populations (62(65). Currently, there is no validated questionnaire for the study of respiratory symptoms in HIV infected patients. Different questionnaires including the Modified St Georges respiratory questionnaire and structured pre-tested questionnaires have been used in different studies evaluating for the burden of respiratory symptoms in HIV infected patients.

In a cross-sectional survey of 372 textile workers in Pakistan whose objectives were to correlate obstructive spirometric lung pattern with respiratory symptoms and to validate the ATS DLD questionnaire for use among occupational workers, there was a high correlation of respiratory symptoms with reduced lung function. The specificity of the questionnaire for chronic cough, chronic phlegm, chronic wheeze and shortness of breath on exertion was 93.1%, 85.1%, 75.4% and 55.6% respectively. The sensitivity for the same symptoms was 14.2%, 23.3%, 44.8% and 45% respectively.

In a cross sectional study carried out in the US, Bateman et al used the ATS- DLD respiratory questionnaire to evaluate for respiratory symptoms among a cohort 327 HIV infected patients without a history of HIV related pulmonary complications and a group of controls with a similar age and smoking history. Respiratory symptoms including dyspnea (41.6% vs. 7.7%), cough (40% vs. 25%), and phlegm production (41.9% vs. 23.1%) were more common than in the HIV-negative group. Current and previous history of cigarette smoking was the greatest predictors of respiratory symptoms in the HIV infected patients (66).

In a study done in Baltimore to determine the impact of HIV and obstructive lung disease on respiratory symptoms in intravenous drug users, the ATS – DLD respiratory questionnaire was self-administered by 974 participants of whom 228 were HIV infected. Respiratory symptoms were common in neither individuals with obstructive lung disease nor HIV. Wheezing was the most frequent at 34.5%, followed by phlegm at 29.5% and Cough at 25.5%. HIV infection was not associated with increasing cough, phlegm or wheezing (67)

The ATS has approved and recommended the ATS-DLD respiratory questionnaire for use in epidemiologic surveys. It retains most of the original questions on respiratory symptoms contained in the British MRC questionnaire and has additional validated questions on, smoking, pulmonary tuberculosis and type of home fuel, which are important variables in this study. For the purpose of this study, the ATS – DLD questionnaire has been modified to include two additional questions from the pre-validated supplementary questions. The modified questionnaire has been translated into the Swahili language. The Swahili version was administered to a group of ten randomly selected individuals and found to produce similar answers to the English version. The questionnaire will be interviewer administered in Swahili or English languages depending on the language best understood by the respondent.

JUSTIFICATION

Since the onset of the HIV pandemic, the lungs have been one of the major sites of complications. Up to 70% of HIV infected patients develop pulmonary complications in the course of the disease, mainly of infectious in etiology. HIV related mortality and morbidity in sub-Saharan Africa is still dominated by opportunistic infections. Due to increased availability of HAART, HIV infected patients are living longer to experience the residual effects of respiratory infections and HIV virus replication in the lungs.

HIV associated non-infectious pulmonary complications are a major cause of hospitalization, adverse health related quality of life and respiratory failure in the HIV population. HIV comorbidity in asthma has been linked with increased all-cause mortality and is associated with poor asthma control.

Data from developed countries indicate an increasing prevalence of chronic lung disease in people infected with HIV. Despite the high burden of HIV/AIDS in Sub Saharan Africa, the effects of HIV replication and opportunistic infections on lung function as measured by spirometric tests are not well known. The prevalence and nature of respiratory symptoms that accompany these diseases are also unevaluated.

Knowledge gained from this study will increase clinician awareness of the presence and presentation of chronic lung disease in HIV infected patients and therefore ensure proper diagnostic evaluation and treatment. It will also add to the scientific knowledge that seeks to determine whether HIV patients are at a sufficient risk to benefit from routine spirometry as screening tests to detect chronic lung diseases.

RESEARCH QUESTION

What is the prevalence and pattern of respiratory symptoms and spirometric abnormalities among HIV positive patients on follow up at KNH-CCC?

OBJECTIVES

BROAD OBJECTIVES

To describe the burden of respiratory symptoms and to determine the prevalence and type of spirometric abnormalities among ambulatory ART- treated HIV patients on follow up at the Kenyatta National Hospital Comprehensive Care Centre (KNH-CCC).

SPECIFIC OBJECTIVES

Primary objectives

1. To determine the prevalence of respiratory symptoms among ambulatory HIV infected patients presenting at Kenyatta national hospital Comprehensive Care Centre
2. To document the nature of respiratory symptoms among ambulatory HIV infected patients presenting at Kenyatta national hospital Comprehensive Care Centre
3. To determine the prevalence of spirometric abnormalities among ambulatory HIV infected patients on follow up at Kenyatta national hospital Comprehensive Care Centre
4. To describe the types of spirometric abnormalities among ambulatory HIV infected patients on follow up at Kenyatta national hospital Comprehensive Care Centre

Secondary objectives

1. To correlate selected patient factors such as smoking status, previous severe respiratory tract infections, CD4+ T lymphocyte count, viral load and duration and type of combination anti-retroviral therapy with the presence of any spirometric abnormality and respiratory symptom.

METHODOLOGY

Study design: This was a descriptive cross sectional study

Study site: The study wascarried out at the Kenyatta National Hospital - Comprehensive Care Centre (KNH-CCC).

Study population: ambulatoryadult HIV infected patients on HAART presenting at The KNH-CCC for routine follow-up.

Sample size:

Sample size was determined using Fischer's formulae for prevalence studies.

$$n = \frac{Z^2 \times P\,(1\text{-}P)}{d^2}$$

n – Sample size

Z – 1.96 (95% confidence interval)

P – Estimated prevalence of spirometric abnormalities = 35% from Onyedum et al, Nigeria (22)

d – Margin of error (precision error) = ±5 %

Substituting into the formula,

n = 350

A minimum of 350 patients was required to estimate prevalence of spirometric abnormalities within 5 % margin of error.

Case definition: Patients with a documented laboratory diagnosis of HIV disease using Enzyme - linked immunosorbent assay (ELISA) and on HAART for not less than six months

Inclusion criteria

1. Ambulatory patients attending KNH-CCC and on HAART for at least 6 months

2. Age ≥18 years

Exclusion criteria

1. Patients on intensive treatment for pulmonary tuberculosis or suspected to have active pulmonary tuberculosis

2. Pregnant patients

3. Patients with a contraindication to spirometry (*Appendix 5*) or patients unable to perform spirometry for any reason

DEFINITION OF STUDY VARIABLES

a) **Independent variables**

- Age in years

- Sex –male or female

- Weight was expressed in kilograms

- Height was expressed in centimeters

- BMI – the body mass index will be calculated from the height and weight and expressed in kg/m^2

- **Smoking status**was categorized as current, ever or never smokers. Current smokers were patients who have smoked one cigarette a day for one year or 20 packs of cigarette in their lifetime and currently smoke cigarettes every day or some days. Ever smokers were patients who have smoked at least one cigarette a day for one year or 20 packs of cigarette in their lifetime, but stopped smoking more than one month before the date of the study. Never smokers were patients who have never smoked at all who have smoked fewer smoked 1 cigarette a day for one year or 20 packs of cigarette in their lifetime.

- **CD4+ T lymphocyte cell count** was defined as the absolute serum CD 4+ T lymphocyte cell count expressed in cells per microliter. Current CD4+ was the most recent CD4 count recorded for the patient. Nadir and highest CD4 counts were as recorded in the electronic

medical register. The CD4 count categories were stratified into >500 cells/µl, 351-499 cells/µl, 200-350 cells/µl, and < 200 cells/µl

- **HIV Viral load-** The most recent viral load (any) recorded, irrespective of the duration,was considered.They were expressed in absolute copies per milliliter and stratifiedas<1000 copies/ml, 1001-10000 copies/ml, >10001 copies/ml

- **Duration since HAART initiation**was defined in months or years from the date of HAART initiation. The nature of HAART (1st line or 2nd line treatment) was as captured in the patients' medical records. Firstline treatment is the initial regimen consisting of two NRTIs and one NNRTI, second line treatment is the salvage regimen used in patients with a persistent detectable viral load despite ART. It consists of at least three drugs from two classes of anti-retroviral agents.

- Past history of pulmonary tuberculosis infection-, this referred to patients who report a previous history of confirmed sputum positive tuberculosis or radiological or clinical suspicion of tuberculosis and completed six months of treatment.

b) **Dependent variables**

- FVC.
- FEV_1/FVC ratio.
- Any one respiratory symptom such as phlegm production, cough with phlegm production, wheezing and breathlessness.

Primary outcomes

1. Presence or absence of any spirometric abnormality
   - An obstructive spirometry defect is defined by an FEV_1 below 80% predicted and FEV1/FVC ratio below 0.7. with a normal or reduced FVC
   - A restrictive spirometry defect is defined by an FVC below 80% predicted and FEV1/FVC ratio above 0.7 with a normal or mildly reduced FEV_1
   - A mixed spirometric defect is defined by an FVC below 80 with FEV_1/FVC ratio of < 0.7

2. Presence or absence of any respiratory symptom; including cough, phlegm production, cough with phlegm production, wheezing, breathlessness, sneezing and nasal congestion.

Secondary outcomes

1. Association of respiratory symptoms to spirometric abnormalities.

2. Association of selected patient factors (history of smoking, previous history of severe respiratory tract infections, immunological status (as determined by CD4+ T lymphocyte count), viral load, type and duration of combination anti-retroviral therapy) with specific spirometry abnormalities and respiratory symptoms

Patient recruitment procedure

Patients were recruited through simple random sampling. The investigatorssampled twenty patients from the adult and youth daily appointments register on each day of the data collection. Patients who had any of the exclusion criteria e.g. ongoing upper respiratory tract infection, physical limitations, acute illnesses and debilitating oral sores/lesions or were unable to perform the spirometry procedure due to any reason were excluded. The Investigators explained the purpose and procedure of the study to the participants and obtained a written informed consent. Data collection was done after the clinicians reviewed the patients. The PI and research assistants kept track of the patients' movements to avoid losing them. The investigators repeated the sampling procedure daily until the desired sample size was achieved.

Data Collection, management and analysis

Clinical methods

The eligible participants were weighed, height measured in centimeters using a mounted heightometer and their body mass index calculated from the height and weight measurements.

An interviewer-administered respiratory questionnaire (ATS – DLD 78 questionnaire) was used to obtain data on the socio-demographic data, respiratory symptoms, previous severe respiratory infections, cigarette smoking status and history of biomass exposure. Information on the duration and type (1st or 2nd line) of HAART, CD4 count and viral load were obtained from the patients' electronic medical records and by self-report.

Spirometry

At the end of the interviews**,** Pre-bronchodilator Spirometry tests were performed using portable spirometers (Spiro lab III MIR and vitalograph alpha touch) with the assistance of a trained research assistant according to the European Respiratory Society (ERS) guidelines *(Appendix 5)*.

Measurements were done with the patients sitting with a nasal clip in place. The spirometry maneuvers were repeated until three acceptable and reproducible tests were obtained. The best FEV1, FVC and FEV1/FVC ratio of at least three acceptable maneuvers were used for analysis.

Spirometry measured airflow abnormalities were defined as follows; an obstructive pattern was defined by a normal or reduced FVC, FEV1 <80% with an FEV1/FVC <0.7, a restrictive defect was defined by FVC <80% predicted, FEV1/FVC >0.7, and mixed defect by FVC <80% predicted and FEV1/FVC <0.7.Spirometric measurements for each patient were transferred and stored to an attached computer

Data management and analysis

Data analysis was done using SPSS version 21.0. Descriptive characteristics of the population were summarised as percentages for categorical data and means or medians for continuous variables. The prevalence of spirometric abnormalities and respiratory symptoms were analysed and presented as proportions with 95% confidence intervals. Pearson/Fisher's Exact Chi-square tests for association was used to check for an association between the patients' characteristics (biomass exposure, history of smoking, history of severe respiratory tract infection, BMI, duration since initiation of HAART, current CD4 count and viral load) and the presence spirometricS abnormalities and respiratory symptoms.

ETHICAL CONSIDERATIONS

This study was carried out after approval by the Department of Clinical Medicine and Therapeutics, University of Nairobi and the KNH / UON Research and Ethics committee.

The patients were informed about the study and given a detailed explanation of the nature of the study and spirometric test to be done. They were assured that participation would be voluntary and that medical attention would not be denied if they were to decline participation in the study. The participants then signed the consent form following full explanation and acceptance.

Patients found to have respiratory symptoms or spirometric abnormalities werereferred to KNH chest clinic for further evaluation and management by a respiratory physician. A copy of the spirometry results was placed in the patients' file in CCC.

Confidentiality was strictly maintained and all data gathered is securely stored and can only be revealed to relevant authorities upon a need to know basis.

CHAPTER FOUR

RESULTS

Four hundred and twenty nine (429) participants were enrolled into the study after meeting the inclusion criteria. 17 participants filled the questionnaire but did not have the spirometric test done (7 were lost to the researchers while 10 quoted time constraints). 412 participants had both the respiratory questionnaire and spirometric test done. Spirometric tests from 41 participants were excluded from the analysis because they did not meet the ATS/ERS acceptability, repeatability and reproducibility criteria. Data from 371 participants were analyzed. Of the 371, 18 participantsdid not have either CD4 count or viral load in their electronic medical records.

Fig 1. Study flow chart

520 patients sampled

91 excluded (19 on HAART for <Mo, 12 on intensive phase anti TB, 2 oral lesions, 2 CVA, 27 URTI, 3 acute illness, 17 did not consent, 9 missed clinic)

429 enrolled into the study

17 dropped out

412 had both respiratory questionnaire and spirometry done

41 spirometries did not meet ATS/ERS criteria

Data from 371 patients analyzed
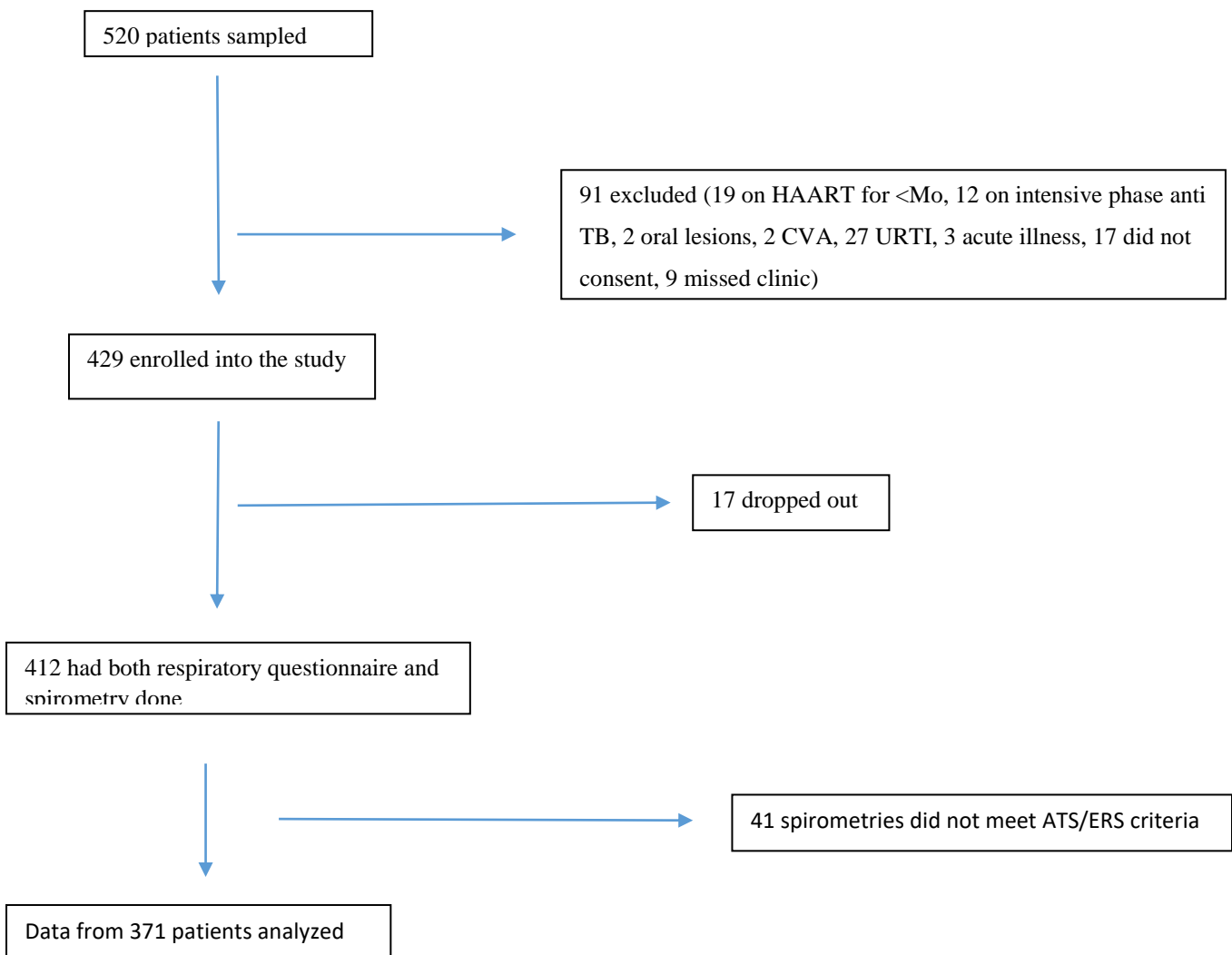
Socio-demographic and clinical characteristics

The study participants were largely female (60.1%) with a mean (SD) age of 44.7 years (10.3).Slightly more than half of the participants 201 (54.2%) were either overweight or obese. A history of biomass exposure was present in 42.9% of the participants. Previous, current and never-smokers were 14.0%, 2.7% and 83.3% respectively. The median (IQR) duration on HAART was 7.0 years (3.0-10), 83.0%) had a viral load less than 1000 copies/ml with while 74.3% had an undetectable viral load (Lower limit of HIV viral load quantification 20 copies/m). Among the patients who reported a previous severe respiratory infection, 31.5% had a previous history of pulmonary tuberculosis, 15.4% reported a history of bacterial pneumonia.

The socio-demographic and clinical characteristics are summarized in **table 2** and **table 3** below

Table 2: Socio-demographic and clinical characteristics

Variable	Category	Frequency	Proportion (%)
Gender (n=371)	Female	223	60.1
Marital status	Married	224	60.4
(n=371)	Single	65	17.5
	Separated	45	12.1
	Widowed	30	8.1
	Divorced	7	1.9
Level of Education	Secondary	124	33.4
(n=371)	Primary	116	31.3
	Tertiary	102	27.5
	None	29	7.8
BMI (n=371)	Underweight(<18.5)	18	4.9
	Normal (18.5-24.9)	**152**	**41.0**
	Overweight (25.0– 29.9)	106	28.6
	Obese (>30)	95	25.6
Biomass exposure	**Yes**	**159**	**42.9**
	No	212	57.1
Smoking	Never smokers	309	83.3
	Ever smokers	52	14.0
	Current smokers	10	2.7

Previous severe respiratory infection (n=371)	None	221	59.6
	Pulmonary TB	93	25.1
	Bacterial pneumonia	33	8.9
	PTB and bacterial Pneumonia	24	6.5
HAART regimen (n=371)	First line	325	87.6
	Second line	45	12.1
	Third line	1	0.3
Current CD4 count (cells/ml) (n=353)	>500	182	49.1
	351-499	79	21.3
	200-350	61	16.4
	<200	49	13.2
Viral load (copies/ml) (n=358)	<1000	308	83.0
	1000 – 10,000	13	3.5
	>10,000	50	13.5

Table 3: Median duration on HAART, CD4+ count and viral load

Variable	N	Median	IQR	Lowest	Highest
Duration on HAART(years)	371	7.0	3.0-10.0	0.5	30.0
Nadir CD4 (cells/µl)	353	234.0	97.0-374.0	4.0	1379.0
Highest CD4 (cells/µl)	353	567.8	406.0-757.9	4.0	2481.0
Current CD4 (cells/µl)	353	480.3	307.7-675.8	4.0	1404.5
Current Viral load (copies/ml)	358	0.01	0.01-20.00	0.01	849355.00

Respiratory symptoms

The overall prevalence of any respiratory symptoms was 42.9% 95% CI [37.0; 47.1]. The most common symptoms were cough (22.4%), sputum production (18.9%) and breathlessness (15.1%) as summarized in table 4

Table 4: The prevalence of respiratory symptoms

Variable	Frequency	Proportion (%)	[95% CI]
Any respiratory symptom	159	42.9	[37.0; 47.1]
Specific respiratory symptoms			
Cough	83	22.4	[18.1; 26.6]
Sputum production	70	18.9	[15.0; 23.2]
Breathlessness	56	15.1	[11.5; 18.7]
Wheezing chest	47	12.7	[9.3; 16.1]
Sneezing	50	13.5	[10.0; 17.0]
Nasal congestion	43	11.6	[8.3; 14.9]

Spirometric abnormalities

The prevalence of spirometric abnormalities among patients in this study was 18.6% (69/371) with 95% CI [14.6%; 22.6%]. Among the 69 patients with spirometric abnormalities, restrictive was the most frequent (42/69; 60.9%), followed by obstructive (23/69; 33.3%) and mixed (4/69; 5.8%).

Table 5: The prevalence of spirometric abnormalities

Variable	Frequency	Proportion (%)	[95% CI]
Any spirometric abnormality present (n=371)	69	18.6	[14.6; 22.6]
Restrictive	42	11.3	[8.1; 14.5]
Obstructive	23	6.2	[3.7; 8.7]
Mixed	4	1.1	[0.0; 2.1]

Association between patient characteristics and Spirometric abnormalities

Pearson/Fisher's Exact (*) Chi-square tests for association was done to check for association between the patients' characteristics (biomass exposure, history of smoking, history of severe respiratory tract infection, BMI, duration since initiation of HAART, current CD4 count and viral load) and the presence spirometric abnormalities. Only the patient's history of smoking was found to be significantly (Pearson chi-square=11.637; P-value=0.003) associated with having a spirometric abnormality.

Table 6: Association between patients' characteristics and spirometric abnormalities

Variable	Category	Spirometric abnormalities Absent	Spirometric abnormalities Present	Pearson Chi-sq.	P-value
Biomass Exposure	Yes	134	25	1.519	0.218
	No	168	44		
Smoking Status	Never smoked	255	54	**11.637**	**0.003**
	Ever smoked	43	9		
	Current smoker	4	6		
History of severe Respiratory infection	Yes	120	36	3.566	0.059
	No	182	33		
BMI	Underweight	12	6	5.452	0.142
	Normal	120	32		
	Overweight	87	19		
	Obese	83	12		
Duration since HAART initiation	<12.5 years	271	65	1.312	0.252
	≥12.5 years	31	4		
HAART Regimen	First line	266	59	0.661	0.626*
	Second line	35	10		
	Third line	1	0		
Current CD4 Count	>500	147	35	1.813	0.612
	351-499	62	17		
	200-350	50	11		
	<200	43	6		
Current Viral load	<1000	248	60	3.140	0.235*
	1000-10,000	13	0		
	>10,000	41	9		
Any respiratory Symptoms	Present	125	34	1.426	0.232
	Absent	117	35		

Association between patients' characteristics and respiratory symptoms

Pearson chi-square test of association was used to check for association between specific patient characteristics and the presence of respiratory symptoms. History of severe respiratory infection (p-value=0.038), BMI (p-value=0.036) and duration since initiation of HAART (p-value=0.012) were found to be significantly associated with a patient having/not having respiratory symptoms.

Table 7: Association between patient characteristics and respiratory symptoms

Variable	Category	No respiratory symptomsn=211	Respiratory symptoms n=159	Pearson Chi-sq.	P-value
Biomass Exposure	No	120	92	0.059	0.809
	Yes	92	67		
Smoking Status	Never smoked	175	134	2.080	0.353
	Ever smoked	33	19		
	Current smoker	4	6		
History of severe Respiratory infection	No	135	85	**4.313**	**0.038**
	Yes	76	74		
BMI	Underweight	8	10	**8.569**	**0.036**
	Normal	92	60		
	Overweight	68	38		
	Obese	44	51		
Duration since HAART initiation	<12.5 years	199	137	**6.312**	**0.012**
	≥12.5 years	13	22		
HAART Regimen	First line	190	135	0.431	0.511
	Second line	20	24		
	Third line**	1	0		
Current CD4 Count	>500	102	80	4.872	0.181
	351-499	40	39		
	200-350	42	19		
	<200	28	21		
Current Viral load	<1000	184	124	5.016	0.081
	1000-10,000	6	7		
	>10,000	22	28		

Regression analysis

A multiple logistic model was fitted to evaluate the effect of various factors on the odds of a patient having spirometric abnormalities/respiratory symptoms (table 8 and 9). Only the current viral load of the patient was found significant. Adjusting for the effect of other covariates in the model, a patients with a viral load of less than 1000 copies/ml had 51% reduced odds on having respiratory symptoms compared to a patient with a viral load of 1000 copies/ml and above (OR=0.49, P-value=0.015).

None of the predictors in the model had a significant effect on the odds of a patient having spirometry abnormality. However, an obese patient had a 79% decreased odds (OR=0.21, p-value=0.15) of having

spirometric abnormalities relative to an underweight patient adjusting for the effect of other covariates.

Overall, BMI had no significant effect on the odds of patient having spirometric abnormalities

Table 8: Regression analysis: Effect of covariates on the odds of having spirometric abnormalities

Variable	Category	Odds Ratio (OR)	[95% CI OR]	P-value
Current CD4 count	≥500 cells (Ref)			
	351-499 cells	1.04	[0.53; 2.04]	0.919
	≤350 cells	0.71	[0.36; 1.42]	0.333
Biomass Exposure	No (Ref)			
	Yes	0.66	[0.37; 1.17]	0.155
HAART regimen	First line (Ref)			
	Second line	1.44	[0.65; 3.20]	0.366
Current viral load	≥1000 copies			
	<1000 copies	1.62	[0.72; 3.66]	0.245
Smoking status	Current/ever smoked (Ref)			
	Never smoked	0.76	[0.38; 1.51]	0.427
BMI	Underweight (Ref)			
	Normal weight	0.42	[0.14; 1.28]	0.125
	Overweight	0.33	[0.10; 1.08]	0.068
	Obese	0.21	[0.06; 0.73]	0.015*
Respiratory symptoms	None(Ref)			
	Present	1.50	[0.06; 0.73]	0.153
Age		1.02	[0.99; 1.05]	0.180

Table 9: Regression analysis: Effect of covariates on the odds of having respiratory symptoms

Variable	Category	Odds Ratio (OR)	[95% CI OR]	P-value
Current CD4 count	≥500 cells (Ref)			
	351-499 cells	1.33	[0.76; 2.31]	0.316
	≤350 cells	0.65	[0.38; 1.10]	0.109
Biomass Exposure	No (Ref)			
	Yes	1.05	[0.67; 1.63]	0.847
HAART regimen	First line (Ref)			
	Second line	1.66	[0.86; 3.21]	0.129
Current viral load	≥1000 copies			
	<1000 copies	0.49	[0.27; 0.87]	0.015*
Smoking status	Current/ever smoked (Ref)			
	Never smoked	0.99	[0.54; 1.81]	0.986
BMI	Underweight (Ref)			
	Normal weight	0.56	[0.20; 1.58]	0.271
	Overweight	0.49	[0.17; 1.45]	0.200
	Obese	1.08	[0.36; 3.25]	0.894
Spirometry	Normal (Ref)			
	Abnormal	1.50	[0.86; 2.60]	0.152
Age		0.99	[0.97; 1.02]	0.768

Patients excluded from data analysis

Of the 58 patients who were sampled but excluded from the analysis, 67.2% were female, 82.7% never smokers, 10.3% ever smokers, 5.1% never smoked, 19% had a previous history of pneumonia while 39.6% had previous history of pulmonary tuberculosis. The prevalence of a cough was 6.9%, sputum production 5.2%, wheezing 6.9%, breathlessness 6.9%, sneezing 10.3, and nasal congestion 5.2%.

CHAPTER FIVE

DISCUSSION

Pulmonary complications are an important cause of morbidity and mortality among HIV infected patients. Due to the widespread availability of ART and resultant longevity of HIV patients, non-infectious pulmonary disorders associated with HIV infection, antiretroviral treatment, recurrent respiratory infection, cigarette smoking and biomass fuel exposure have become a concern. In this study,we analyzed data from a relatively young population of HIV infected adults with a mean (SD) age of 44.7 (10.3) years, who had used ART for a minimumduration of six months. Majority of the participants had a well-controlled HIV disease.

Using an interviewer-administered ATS-DLD questionnaire, the occurrence of respiratory symptoms was common in this population of ART treated patients with well-controlled disease. The most frequent respiratory symptoms were cough (22.4%), sputum production (18.9%), breathlessness (15.1%) and sneezing (13.5%). The most common Spirometric abnormality was a restrictive pattern followed by obstructive then mixed. An FEV1/FVC ratio of <0.7 was used to diagnose airway obstruction as opposed to lower limit of normal which has been used in some studies. We did not do a post-bronchodilator spirometric test, due to resource constrains, and therefore made no distinction between reversible and non-reversible airway obstruction. Generally,the prevalence of both respiratory symptoms and spirometric abnormalities were low in comparison to other studies. However, our study population was relatively youngand the respiratory symptoms and spirometric changes could become more clinically relevant as the HIV population on ART ages.

Our observations of the pattern of Occurrence of respiratory symptoms were similar to that found in other studies in both ART treated and Non- ART treated HIV infected patients(22,68,69). The frequencies of specific respiratory symptoms were comparable to that by George et al who reported 23% cough and 16% dyspnea among ART- treated HIV patients(10). However, we reported lower frequencies of specific respiratory symptoms in comparison to studies done in Non-ART treated patients (22,68). In previous studies, a previous history of pneumonia, pulmonary tuberculosis, cigarette smoking low CD4+ count and high plasma viral load were associated with increased respiratory symptoms (10,68,69). We found none of these factors to be significantly associated with respiratory symptoms except a history of previous severe respiratory tract infection (pneumonia/PTB). Slightly more than half of the participants with respiratory

symptoms reported a previous history of severe respiratory tract infection (**table 4**). In addition, BMI was also significantly associated with the presence or absence of respiratory symptoms, 55.9% of patients with respiratory symptoms were either overweight or obese.

Although we did not have ART naive controls, our findings could suggest that treatment with ART reduces the occurrence of respiratory symptoms in HIV patients. This is likely due to the attenuation of HIV mediated chronic airway inflammation as a result viral suppression. After starting ART, the viral load in BAL of more than 80% of patients decrease to undetectable levels(70), this significantly decreases pulmonary inflammatory response minimizing lung injury and colonization by opportunistic pathogens (7,14). While IRIS occurring after initiation of ART could be a risk factor for respiratory symptoms(33), a majority of our study population had been on ART beyond the duration within which IRIS typically occurs(71) and the symptoms evaluated were chronic rather than acute.

Findings of a significant association between a previoussevere respiratory tract infection (PTB/pneumonia) with the presence or absence of respiratory symptoms suggest the presence of underlying undiagnosed chronic respiratory diseases resulting as complications of recurrent respiratory tract infections.Pulmonary tuberculosis has been associated with several long term complications including bronchiectasis, various forms of pulmonary aspergillosis, lung fibrosis, and COPD which can cause persistence of symptoms even after successful treatment PTB (72,73). Emphysematous lung changes and permanent decline in pulmonary function have been described in patients treated for pneumocystis pneumonia and severe bacterial pneumonia (16,17), however, it was not possible to ascertain how many of our patients had previously suffered bacterial, pneumocystis or viral pneumonia due to reliance on self-report and unavailability of proper medical records.

Extrapolation from existing data on the relationship between asthma and HIV suggests a probable contribution of allergic airway disease including asthma and airway hyper-responsiveness (44,74) to the etiology of sneezing, nasal congestion and wheeze. However, diagnosis of these diseases was beyond the scope of our study. Slightly more than half of our study population had either obesity or overweight and this was significantly associated with the presence or absence of respiratory symptoms. Studies in non- HIV populations have found increased reporting of dyspnea and wheezing at rest or on exertion in obese patients as compared to individuals with a normal BMI(75), besides, obesity is a defined risk factor for asthma in HIV disease (43).

The prevalence of spirometric abnormalities of 18.6% is similar to that of a study done in Spain which found a 17% prevalence of airflow limitation in HIV infected participants on treatment with well-controlled disease (69). Similar studies done in Africa looked at ART naïve patients and reported a higher prevalence of spirometric abnormalities (27, 73). Drummond et al in the USA found an association between airflow obstruction and high viral load suggesting a role of HIV in the pathogenesis of obstructive pulmonary disease (76). Although achievement of relatively good viral suppression through ART in our study population could have attenuated the chronic inflammatory effects of viral replication in the lungs and preserved lung function, other studies have associated use of ART with obstructive lung disease and increased respiratory symptoms in HIV infected patients because of IRIS and autoimmunity phenomenon. However, we found neither the duration of ART nor the markers of HIV control to be significantly associated with the presence or absence of spirometric abnormalities.

Findings of predominantly a restrictive spirometric pattern agrees with that of studies in sub Saharan Africa countries with high TB burden (22,77). Approximately 40-60% of patients treated for pulmonary tuberculosis suffer sequelae of obstructive, restrictive or mixed patterns of lung disease despite successful treatment(72,73). In a cross - sectional study done in Kenya to assess the pulmonary function of patients two years after PTB treatment, 23% had a restrictive pulmonary impairment and only 5% were obstructive(19). In this study, the relationship between a previous respiratory infections and spirometric abnormalities was tending towards an influence, however, the figures were not statistically significant (P=0.059). It is possible that the large proportion of participants with previous pulmonary tuberculosis infection was the driving factor for the predominantly restrictive spirometric pattern seen.

Our estimates of obstructive spirometric abnormalities of 6.2% were lower than 21% and 27% reported by Gingo and Drummond et al in the USA(31,78). Both studies were done among patients with a higher smoking prevalence compared to our study population. In a population of patients with a similar smoking exposure, Pefura et al in Cameroon reported a lower prevalence of 2.2% and 5.2% using a fixed FEV1/FVC ratio of 0.7 and FEV1/FVC < lower limit of normal respectively(79). Cigarette smoking is a well-documented risk factor for obstructive lung disease. Its association with a reduction in FEV1/FVC ratio in both HIV and non- HIV infected people has been demonstrated in various studies carried out in developed countries where the intensity and prevalence of smoking are higher than in our population (31,41,78,80). We found smoking status to be significantly associated with the presence or absence of spirometric

abnormalities. However, the observation of a majority (54/69) of the participants with spirometric abnormalities being non-smokers could be because we had only a small proportion of ever and current smokers (16.7%) as compared to studies which found smoking to be an independent risk factor for obstructive airflow defects. Pefura et al did a post-bronchodilator spirometry to establish a diagnosis of COPD while we only did pre-bronchodilator spirometry. Our study also had a higher proportion of patients with a previous history of pulmonary tuberculosis (25.1% vs. 11.9%); these could explain why this study picked a slightly higher percentage of obstructive defects as compares to the Cameroon study.

We did not find an association between biomass exposure and occurrence of spirometric abnormalities despite a large proportion of participants having used biomass fuel. Biomass smoke associated indoor air pollution is influenced by ventilation, pollutant concentration and time spent by an individual in that environment (exposure hour- years) (81). Unfortunately, this study did not set out to measure these variables.There is an increased frequency of respiratory symptoms and disease in wood rather than charcoal fuel users due to its association with a higher respirable particulate matter (PM 10), carbon monoxide, nitrogen and sulfur oxides and other constituents which are known to be toxic or irritants to the respiratory system(82,83). Considering the nature of housing in the urban and peri- urban areas of Kenya (84) , the participants in this study were more likely to have been using charcoal as opposed to wood fuel for cooking. Being a young urban population it is possible that the duration and intensity of exposure was not sufficient to cause measurable disease, however it is reasonable to anticipate biomass attributable chronic respiratory diseases as the population ages.

Conclusion

In conclusion, we found that the most common respiratory symptoms in our study population were cough, sputum production, and breathlessness. Spirometric abnormalities of restrictivenaturewere the most frequent followed by obstructive then mixed. Long-term complications of recurrent pulmonary opportunistic infections, including pulmonary tuberculosis and pneumonia, are a possible cause of respiratory symptoms in these patients and could explain the predominantly restrictive spirometric abnormalities.

Strengths and Limitations

This is the first study of this nature to be done in Kenya and the large sample size used in this study allowed for correlations.

This study had several limitations. Lack of healthy controls and /or Non ART treated HIV infected controls limited interpretation of our findings. CD4 cell count and serum HIV RNA levels were not done prospectively and therefore it was not possible to look at the effects of disease progression on lung function. A proportion (4.8%) of the study population had missing data on CD4+ count and viral load due to improper documentation. The study had set out to document the proportion of patients with PCP in addition to bacterial pneumonia and tuberculosis but this was not possible due to lack of documentation on the patients' medical records and recall bias

Recommendations

We recommend a larger prospective case control study to look at the effects of HIV disease progression and recurrent respiratory tract infectionson respiratory symptoms and progression of lung function in our population of patients with a low prevalence and intensity of cigarette smoking.

Besides monitoring patients for viral suppression, measures forprompt case finding and immediate treatment ofrespiratory tract infection should be intensified to mitigate against the effects of these diseases on lung function.

Interventions for weight reduction should be prioritized in this population in order to reduce the respiratory morbidity associated with obesity and overweight.

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APPENDIX 1: PATIENT INFORMATION

Introduction

My name is Dr. Juliet Akoth Ooko. I am a postgraduate student of internal medicine at the University of Nairobi. The purpose of this statement is to inform you about a research study that I am carrying out. I am doing a study on the prevalence of spirometry abnormalities at Kenyatta National Hospital Comprehensive Care Centre (KNH-CCC). The purpose of this study is to determine how many people have respiratory symptoms and spirometry abnormalities among HIV positive ambulatory patients on follow up at Kenyatta national hospital CCC.

A spirometer is a machine that helps the doctor to analyze how well your lungs are working.

Procedures to be followed in the study

Participation in this study is voluntary. Should you accept to participate, the following is a summary of what the study involves:

1. Obtaining information such as age, gender, marital status, and level of education

   NOTE: your name and hospital identification number will not be included in this information for your privacy

2. Obtaining information on your respiratory symptoms e.g. cough and wheezing.

3. Obtaining information regarding your HIV diagnosis. The information you give will be verified from your medical records.

4. Spirometry test using a portable spirometer to generate your lung function parameters will then be performed. You will be asked to blow into a spirometer machine via a disposable mouthpiece.

5. This will take about 25 to 30 minutes of your time

Risks and costs incurred

There are minimal risks for participating in this study. You may feel minimal strain on your chest while undertaking the spirometry procedure. The investigators will cover the cost of the spirometric test. You will however receive a copy of the spirometricresults that will be placed in your file.

Your rights as a participant

Your participation in this research is voluntary and in the event that you refuse to participate in this study, your treatment will not be affected. If you choose to participate and not answer certain questions, you are free to do so. You are free to terminate the interview and withdraw from the study at any time. You are free to ask questions before signing the consent form.

Assurance of confidentiality

All your responses as well as your results will remain confidential. Your individual responses will be stored in a locked place under my control and will only be seen by my statistician and I.

Benefits to you as a participant

There will be no direct benefits to you as a participant. Your primary health physician will be informed of any findings relevant to your medical care and a copy of the spirometry result will be put in your file. The results obtained from this study will help improve clinical decision making and improve patient care in this facility. The information will also assist in development of expert clinical guidelines on screening for chronic lung diseases in HIV.

Compensation

Participants will not receive any monetary compensation for participating in this study.

Contacts

If you have any questions, please do not hesitate to ask. Clarifications may also be sought from:

Dr Juliet Akoth Ooko

P.O BOX 2681

Machakos

TEL: 0703-830396

The Secretary

KNH/UoN Ethics and Review Committee

Tel 2726300 Ext: 44102

I Request you to sin the attached consent form

APPENDIX 2: CONSENT FORM

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research.

Print Name of Participant/ Next of kin   ……………………..

Signature / Left thumbprint of subject   ………………………

 Date   ………………………

Investigator's statement:

I, the Principal Investigator, have fully informed the research participant on the purpose and implication of this study.

Signed ....   Date   ……………….......

APPENDIX 3: STUDY PROFORMA

PARTICIPANTS STUDY NUMBER _____

PART A: SOCIODEMOGRAPHIC CHARACTERISTICS

1) Age ☐ Years

2) Sex ☐ Male ☐ Female

3) Marital status

    a) Single ☐

    b) Married ☐

    c) Seperated ☐

    d) Divorced ☐

4) Level of education

    a) None ☐

    b) Primary ☐

    c) Secondary ☐

    d) Tertiary ☐

PART B: ANTHROPOMETRIC MEASURES (Fill in the values)

    1. Height (cm) ☐

    2. Weight (Kg) ☐

    3. BMI ☐

PART C: RESPIRATORY SYMPTOMS (tick where appropriate)

    1. Cough ☐ Yes ☐ No

    2. Sputum production ☐ Yes ☐ No

    3. Wheezing ☐ Yes ☐ No

    4. Breathlessness Y☐ N☐

    5. Sneezing ☐ Yes ☐ No

    6. Nasal congestion ☐ Yes ☐ No

PART D: PREVIOUS SEVERE RESPIRATORY TRACT INFECTION (tick where appropriate)

1. Pulmonary Tuberculosis

2. Pneumocystis pneumonia ☐

3. Bacterial Pneumonia ☐

4. Others ☐

PART E: CIGARETTE SMOKING STATUS (Tick where appropriate)

1. Current smoker ☐

2. Ever smoked ☐

3. Never smoked ☐

PART F: BIOMAS EXPOSURE

☐ **Yes**   ☐ **No**

PART G: HIV DIAGNOSIS (fill in)

1) Duratin since initiation of HAART   M☐s   Years ☐

   a) First line (Yes/No)

   b) Second line (Yes/No)

2) Nadir CD4 + count ☐

3) Highest CD4+ count ☐

4) Current CD4+ count ☐ cells/µl

5) Current Viral load ☐ copies/ml

PART H: SPIROMETRY FINDINGS

1) **FVC** ☐

2) **FEV** ☐

3) **FEV$_1$** ☐

TYPE OF SPIROMETRIC ABNORMALITY
☐ OBSTRUCTIVE
☐ RESTRICTIVE
☐ MIXED

4) FEV$_1$/FVC ratio

Filled by ………………………………………… (PI or Research assistant)

Date …………….   Time …………..   Sign ………….

APPENDIX 4

American Thoracic Society and National Heart & Lung Institute - Division of Lung

Disease Respiratory Questionnaire

ATS-DLD-78-A

ADULT QUESTIONNAIRE - SELF COMPLETION (for

those 13 years of age and older)

Thank you for your willingness to participate. You were selected by a scientific sampling procedure, and
your cooperation is very important to the success of this study. This is a questionnaire you are asked to fill

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out. Please answer the questions as frankly and accurately as possible. ALL INFORMATION OBTAINED

IN THE STUDY WILL BE KEPT CONFIDENTIAL AND USED FOR MEDICAL RESEARCH ONLY.

Your personal physician will be informed about the test results if you desire.

IDENTIFICATION

IDENTIFICATION NUMBER: #####

NAME:_____ _____ ___

        (Last)   (First)   (MI)

STREET _____

CITY _____ STATE ____ ZIP _____

PHONE NUMBER: (   ) _____-_____

INTERVIEWER: ###

DATE: _____

        MO   DAY   YR

1. BIRTHDATE: _____ ____ _____

                              Month Day Year

2. Place of Birth: _____

3. Sex: 1. Male ____

                                    2. Female ____

4. What is your marital status? 1. Single ____

                                    2. Married ____

                                    3. Widowed ____

                                    4. Separated/Divorced ____

5. Race: 1. White ____

                                    2. Black ____

                                    3. Oriental ____

                                    4. Other ____

                                    5. Widowed ____

                                    6. Separated/Divorced ____

What is the highest grade completed in school? _____

   (For example: 12 years is completion of high school)

                                    SYMPTOMS

These questions pertain mainly to your chest. Please answer yes or no if possible. If a question does not appear to be applicable to you, check the does not apply space. If you are in doubt about whether your answer is yes or no, record no.

COUGH

7A. Do you usually have a cough?   1. Yes ___ 2. No ___

(Count a cough with first smoke or on first going out-of-doors. Exclude clearing of throat.)[If no, skip to question 7C.]

B. Do you usually cough as much as 4 to 6 times a   1. Yes ___ 2. No ___

day, 4 or more days out of the week?

C. Do you usually cough at all on getting up, or   1. Yes ___ 2. No ___

first thing in the morning?

D. Do you usually cough at all during the rest   1. Yes ___ 2. No ___

of the day or at night?

IF YES TO ANY OF THE ABOVE (7A,7B,7C, OR 7D), ANSWER THE FOLLOWING:

IF NO TO ALL, CHECK DOES NOT APPLY AND SKIP TO 8A.

E. Do you usually cough like this on most days for   1. Yes ___ 2. No ___

   5 consecutive months or more during the year?

                                                                    8. Does not apply __

F. For how many years have you had this cough?   _____

                                                                    Number of years

                                                                    88. Does not apply __

PHLEGM

8A. Do you usually bring up phlegm from your chest?   1. Yes ___ 2. No ___

    (Count phlegm with the first smoke or on first

going out-of-doors. Exclude phlegm from the

nose. Count swallowed phlegm)

[If no, skip to 8C.]

B. Do you usually bring up phlegm like this as   1. Yes ___ 2. No ___

much as twice a day, 4 or more days out of the

week?

  D. Do you usually bring up phlegm at all during   1. Yes ___ 2. No ___

    the rest of the day or at night?

IF YES TO ANY OF THE ABOVE (8A, B, C, OR D),

ANSWER THE FOLLOWING:

IF NO TO ALL, CHECK DOES NOT APPLY AND SKIP TO 9A.

  E. Do you bring up phlegm like this on most days   1. Yes ___ 2. No ___

    for 3 consecutive months or more during the

    year?   8. Does not apply __

  F. For how many years have you had trouble with   _____

    phlegm?   Number of years

                                                88. Does not apply __

EPISODES OF COUGH AND PHLEGM

9A. Have you had periods or episodes of (in-   1. Yes ___ 2. No ___

    creased*) cough and phelgm lasting for 3

    weeks or more each year?

    *(For individuals who usually have cough and/or

    phlegm)

      IF YES TO 9A:

B. For how long have you had at least 1 such

    episode per year?

                         _____

                               Number of years

                           88. Does not apply __

WHEEZING

10A. Does your chest ever sound wheezy or whistling:

        1. When you have a cold?   1. Yes ___ 2. No ___

        2. Occaisonally apart from colds?   1. Yes ___ 2. No ___

        3. Most days or nights?   1. Yes ___ 2. No ___

     IF YES TO 1, 2, OR 3 IN 10A:

 B. For how many years has this been present? No of years   8. Does not apply

11A. Have you ever had an ATTACK of wheezing that   1. Yes ___ 2. No ___

    has made you feel short of breath?

      IF YES TO 11A:

 B. How old were you when you had your first   _____ Age in years

    such attack?   88. Does not apply __

 C. Have you had 2 or more such episodes?   1. Yes ___ 2. No ___

 D. Have you ever required medicine or treatment   1. Yes ___ 2. No ___

    for the(se) attack(s)?   8. Does not apply __

BREATHLESSNESS

If disabled by walking by any condition other than heart or lung

disease, please describe and proceed to question 14A

    Nature of

condition(s):_____

_____

13A. Are you troubled by shortness of breath when hurrying on the

level or walking up a slight hill?

1. Yes ___ 2. No ___ 8.Does not apply

IF YES TO 13A:

B. Do you have to walk slower than people of your age on level

because of breathlessness?

1. Yes ___ 2. No ___ 8.Does not apply

C. Do you ever have to stop for breath when walking at your own

pace on the level?

1. Yes ___ 2. No ___ 8.Does not apply

D. Do you ever have to stop for breath after walking about 100 yards

(or after a few minutes) on the level?

1. Yes ___ 2. No ___ 8.Does not apply

E. Are you too breathless to leave the house or breathless on dressing

or undressing?

1. Yes ___ 2. No ___ 8.Does not apply

CHEST COLDS AND CHEST ILLNESSES

14A. If you get a cold, does it usually go to your	1. Yes ___ 2. No ___
chest? (Usually means more than 1/2 the time)	8. Don't get colds__
15A. During the past 3 years, have you had any	1. Yes ___ 2. No ___

chest illnesses that have kept you off work, in-

doors at home, or in bed?

    IF YES TO 15A:

B. Did you produce phlegm with any of these   1. Yes ___ 2. No ___

chest illnesses?   8. Does not apply __

C. In the last 3 years, how many such illnesses,   _____Number of illnesses

with (increased) phlegm, did you have which   _____No such illnesses

lasted a week or more?   _____Does not apply

PAST ILLNESSES

16. Did you have any lung trouble before the age   1. Yes ___ 2. No ___

of 16?

17. Have you ever had any of the following:

1A. Attacks of Bronchitis?   1. Yes ___ 2. No ___

IF YES TO 1A:

B. Was it confirmed by a doctor?   1. Yes ___ 2. No ___

                                    8. Does not apply ___

C. At what age was your first attack?   _____ Age in years

                                  88. Does not apply __

2A. Pneumonia (include bronchopneumonia)?   1. Yes ___ 2. No ___

IF YES TO 2A:

B. Was it confirmed by a doctor?   1. Yes ___ 2. No ___

                                  8. Does not apply ___

C. At what age did you first have it?   _____ Age in years

3A. Hayfever?

1. Yes ___ 2. No ___

IF YES TO 3A:

B. Was it confirmed by a doctor?

1. Yes ___ 2. No ___

8. Does not apply ___

C. At what age did it start?

_____ Age in years

88. Does not apply ___

18A. Have you ever had chronic bronchitis?

1. Yes ___ 2. No ___

IF YES TO 18A:

B. Do you still have it?

1. Yes ___ 2. No ___

8. Does not apply ___

C. Was it confirmed by a doctor?

1. Yes ___ 2. No ___

8. Does not apply ___

D. At what age did it start?

_____ Age in years

88. Does not apply ___

19A. Have you ever had emphysema?

1. Yes ___ 2. No ___

IF YES TO 19A:

B. Do you still have it?

1. Yes ___ 2. No ___

8. Does not apply ___

C. Was it confirmed by a doctor?

1. Yes ___ 2. No ___

8. Does not apply ___

D. At what age did it start?   _____ Age in years

88. Does not apply __

20A. Have you ever had asthma?   1. Yes ___ 2. No ___

IF YES TO 20A:

B. Do you still have it?   1. Yes ___ 2. No ___

8. Does not apply ___

C. Was it confirmed by a doctor?   1. Yes ___ 2. No ___

8. Does not apply ___

D. At what age did it start?   _____ Age in years

88. Does not apply __

E. If you no longer have it, at what age did it   _____ Age stopped

stop?   88. Does not apply __

21. Have you ever had:s

A. Any other chest illnesses?   1. Yes ___ 2. No ___

If yes, please specify _____

B. Any chest operations?   1. Yes ___ 2. No ___

If yes, please specify _____

C. Any chest injuries?   1. Yes ___ 2. No ___

If yes, please specify _____

22A. Has doctor ever told you that you had heart

trouble?   1. Yes ___ 2. No ___

IF YES to 22A:

B. Have you ever had treatment for heart trouble   1. Yes ___ 2. No ___

in the past 10 years?   8. Does not apply ___

23A. Has a doctor ever told you that you have high   1. Yes ___ 2. No ___

blood pressure?

IF YES to 23A:

B. Have you had any treatment for high blood   1. Yes ___ 2. No ___

pressure (hypertension) in the past 10 years?   8. Does not apply __

OCCUPATIONAL HISTORY

24A. Have you ever worked full time (30 hours per   1. Yes ___ 2. No ___

    week or more) for 6 months or more?

    IF YES to 24A:

    B. Have you ever worked for a year or more in   1. Yes ___ 2. No ___

      any dusty job?   8. Does not apply ___

      Specify job/industry: _____ Total years worked __

      Was dust exposure 1. Mild ___   2. Moderate ___   3. Severe ___ ?

    C. Have you ever been exposed to gas or chemical   1. Yes ___ 2. No ___

      fumes in your work?   8. Does not apply ___

      Specify job/industry: _____ Total years worked __

      Was dust exposure 1. Mild ___   2. Moderate ___   3. Severe ___ ?

D. What has been your usual occupation or job -- the one you have

worked at the longest?

1. Job-occupation: _____

2. Number of years employed in this occupation:_____

3. Position-job title: _____

4. Business, field, or industry: _____

TOBACCO SMOKING

25A. Have you ever smoked cigarettes? (NO means   1. Yes ___ 2. No ___

less than 20 packs of cigarettes or 12 oz. of

tobacco in a lifetime or less than 1 cigarette a

day for 1 year.

  IF YES to 25A:

B. Do you now smoke cigarettes (as of 1 month   1. Yes ___ 2. No ___

   ago)?   8. Does not apply ___

C. How old were you when you first started reg-   ____ Age in Years

   cigarette smoking?   88.Does not apply __

D. If you have stopped smoking cigarettes com-   ____ Age stopped

   pletely, how old were you when you stopped?   Check if

                                                            still smoking ___

                                                            88.Does not apply __

E. How many cigarettes do you smoke per day now?   ___ Cigarettes/day

PULMONARY TUBERCULOSIS

17- 5A. Have you ever had pulmonary tuberculosis? 1. Yes 2. No

B. Was it confirmed by a doctor 1. Yes 2. No

HOME HEATING AND FUEL

What fuel is used most for cooking in your home?

1. Coal or coke

2. Wood

3. Utility gas

4. Bottled. Tank, or LP gas

5. Electricity

6. Fuel oil, kerosene

FAMILY HISTORY

28. Were either of your natural parents ever told by a doctor that they had

    a chronic lung condition such as:

	FATHER			MOTHER		
	1. YES	2. NO	3. DON'T KNOW	1. YES	2. NO	3. DON'T KNOW
A. Chronic brochitis?	_____	____	_____	_____	____	_____
B. Emphysema?	_____	____	_____	_____	____	_____
C. Asthma?	_____	____	_____	_____	____	_____
D. Lung cancer?	_____	____	_____	_____	____	_____

E. Other chest

   conditions?   _____   ____   _____   _____   ____   _____

29A. Is parent currently alive?

                   _____   ____   _____   _____   ____   _____

B. Please Specify:

               _____ Age if living   _____ Age if living

               _____ Age at death   _____ Age at death

               8. Don't know _____   8. Don't know _____

C. Please specify cause of death.

   _____

APPENDIX 5: ATLS-DLD-78A - NAKALA YA KISWAHILI

FOMU YA WATU WAZIMA (WALIOZIDI UMRI WA MIAKA KUMI NA TATU)

UANAOMBWA UIJAZE PEKEE YAKO.

Asante kwa kukubali kujiunga na utafiti huu.Umechaguliwa kujiunga na utafiti huu na mbinu maalumu ya kisayansi.Ushirikiano wako nasi ni muhimu sana ili utafiti huu ufaulu.

Hii ni fomu ya maswali unayoombwa ujibu.Tafadhali jibu maswali haya kikweli na kikamilifu iwezekanavyo.

Maelezo yote tutapata kwako yatawekwa siri na kutumika kwa minajili ya utafiti huu pekee yake.Daktari wako atapewa majibu yako kwa hiari yako.

VITAMBULIZI

NAMBARI YA KUJISAJILI

TAREHE _____

1. TAREHE YA KUZALIWA _____

2. PAHALI ULIPOZALIWA _____

3. Jinsia :   Kiume   kike

4. Tafadhali tueleze hali yako ya ndoa:

       a) Sijaoa/sijaolewa _____

       b) Nimeoa/nimeolewa _____

       c) Tumeachana na niliyekuwa nimeoa/niliyeolewa naye _____

       d) Nimempa bibi talaka/nimepewa talaka _____

5. Kiwango cha juu kabisa ulifika masomoni ni gani? _____

MARADHI/DALILI YA UGONJWA:

Maswali haya yafuatayo yanahoji sana hali ya kifua chako. Tafadhali jibu, ndio, Kama umeugua maradhi yaliyouliziwa. Kama hujaugua maradhi yanayouliziwa, chagua jibu lisemalo "maradhi haya sijaugua"

Kama huna uhakika umeugua maradhi ama hujaugua, jibu swali la.

KIKOHOZI

7A. Je, kawaida wewe huwa unakohoa? (Ukikohoa pindi unapovuta sigara, pindi utokapo kwenye nyumba-hii ni kukohoa-jibu ndio.Kikohozi cha kusafisha koo halihesabiwi kama kukohoa)

<div style="text-align:center">1. Ndio   2 .La</div>

B.Je, huwa unakohoa zaidi ya mara nne au sita kwa siku,ama zaidi ya siku nne kila wiki?

<div style="text-align:center">1. Ndio   2. La</div>

C. Je, huwa unakohoa pindi uamkapo ama ukiamka kutembea?

<div style="text-align:center">1. Ndio   2. La</div>

D. Je, huwa unaendelea kukohoa mchana au usiku?

<div style="text-align:center">1. Ndio   2. La</div>

KAMA JIBU LA MASWALI YOYOTE YALIYOTANGULIA NI NDIO, JIBU MASWALI YAFUATAYO. KAMA JIBU LAKO LILIKUWA LA KWA MASWALI YOTE, JIBU MASWALI YAFUATAYO, SIJAUGUA MARADHI HAYA, NA UFULULIZE HADI SWALI 8A.

E. Je, umekuwa ukikohoa hivi kwa siku nyingi kwa muda wa miezi mitano mfululizo au zaidi mwakani?

1. Ndio   2. La   8 Sijaugua maradhi haya

F. Umeugua maradhi ya kukohoa hivi miaka ngapi?

Nambari ya miaka   88 Sijaugua maradhi haya

KUTOA KIKOHOZI:

8A. Je, huwa unatoa kikohozi ukikohoa? (Kama unatoa kikohozi ukivuta sigara, ama ukitoka nje /uamkapo, ama unatoa kikohozi na kukimeza, jibu ndio. Makamasi yatokayo puani siyo kikohozi.)

<div align="center">1.   Ndio   2. La</div>

B. Unatoa kikohozi hiki zaidi ya mara 2 kwasiku, zaidi ya siku nne kwa wiki?

<div align="center">1. Ndio   2. La</div>

C. Je, huwa unatoa kikohozi pindi uamkapo ama ukitoka kitandani au nje ya nyumba yako?

<div align="center">1. Ndio   2. La</div>

D. Je, huwa unatoa kikohozi chochote mchana au usiku?

<div align="center">1. ndio   2. La</div>

 KAMA UMEJIBU SWALI LOLOTE LILILOTANGULIA NDIO, JIBU MASWALI YAFUATAYO. KAMA MAJIBU YAKO YOTE YALIKUWA LA, JAZA SEHEMU YA SIJAUGUA MARADHI HAYA,NA UFULULIZE HADI SWALI 9A.

E. Je, umekuwa ukitoa kikohozi siku nyingi katika miezi 3 mtawalia au muda mrefu zaidi mwakani?

<div align="center">1. Ndio   2. La   8. Sijaugua maradhi haya</div>

F. Umekuwa na shida ya kutoa kikohozi nyingi miaka ngapi?

<div align="center">Nambari ya miaka   88. Sijaugua maradhi haya</div>

KUKOHOA PAMOJA NA KUTOA KIKOHOZI:

9A. Je, umekuwa na vipindi vya (ongezekola) kukohoa na kutoa kikohozi zaidi ya wiki 3 kila mwaka?

<div align="center">1.   Ndio   2. La</div>

B. Umekuwa na vipindi hivi kwa muda wa miaka ngapi?

<div align="center">Nambari ya miaka   88. Sijaugua maradhi haya</div>

KUPUMUA KWA SAUTI NA KUFUNGANA KIFUA:

10 A. Kifua chako hutoa sauti ukipumua –kama sauti ya kupiga mbinja?

1. Ndio   2. La

1. Kila nikipatwa na homa   1. Ndio   2. La

2. Saa zingine ,kama sina homa   1. Ndio   2. La

3. Siku nyingi ,mchana au usiku   1. ndio   2. La

KAMA UMEJIBU NDIO KWA SWALI 10A, 1, 2 AMA 3

B. Umekuwa ukipumua na sauti na kufungana kifua miaka ngapi?

Nambari ya miaka   88. Sijaugua maradhi haya

11A. Umewahi pumua na sauti hadi ukahisi ni kama unaishiwa na pumzi?

1. Ndio   2. La

B. Ulikuwa na umri wa miaka ngapi ulipopatwa na kipindi hiki cha kwanza?

Umri wako (miaka)   88. Sijaugua maradhi haya

C. Umepata vipindi hivi vya kufungana kifua na kupumua na sauti zaidi ya mara mbili maishani?

1. Ndio   2. La

D. Umewahi hitaji matibabu /dawa kwa vipindi hivi vya kufungana kifua na kupumua na sauti?

1. Ndio   2. La

KUHEMA

12 A. Kama umekuwa huwezi fanya kazi au shughuli zako za kawaida kwa sababu ya ugonjwa mwingine isipokuwa maradhi ya moyo au mapafu ,tueleze na ufululize hadi swali 14A.

…………………………………………………………………………………………

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…………………………………………………………………………………………

13 A. Je, umepata shida ya kuhema ukitembea haraka pahali tambarare, au ukipanda mlima?

                            1.   Ndio   2. La

ENDELEA KAMA JIBU LA SWALI LILILOTANGULIA NI NDIO

B. Huwa unatemebea polepole zaidi kuliko watu wa umri wako kwa sababu unahema sana?

             1. Ndio   2. La   8 Sijaugua maradhi haya

C. Umewahi lazimika kupumzika ili uweze kupumua baada ya kutembea kwa mwendia wako wa kawaida pahali tambarare?

             1. Ndio   2. La   8 Sijaugua maradhi haya

D. Umewahi lazimika kupumzika baada ya kutembea umbali wa yadi 100 (ama baada ya dakika chache, baada ya kutembea pahali tambarare?

             1. Ndio   2. La   8. Sijaugua maradhi haya

E. Umehema kiasi ya kushindwa kutoka nyumbani kwako ama kushindwa kuvaa au kuvua nguo zako ?

             1. Ndio   2. La   8 Sijaugua maradhi haya

HOMA NA MARADHI YA KIFUA:

14 a. Je, ukipata homa/mafua-huwa unapata maradhi ya kifua? (Yaani, karibu kila mara, homa huja pamoja na maradhi ya kifua?)

             1.   Ndio   2. La   88.Sijaugua maradhi haya

15 A. Katika muda wa miaka mitatu iliyopita, umewahi kuugua maradhi ya kifua ambayo imekuzuia kufanya kazi, ikakulazimu upumzike nyumbani ama hata kitandani?

1. Ndio   2. La   88. Sijaugua maradhi haya

B. Ukiugua maradhi haya, huwa unakohoa na kutoa kikohozi?

1. Ndio   2. La   88. Sijaugua maradhi haya

C. Katikamuda wa miaka mitatu iliyopita, ni mara ngapi umepata maradhi ya kifua na kikohozi kingi uliyougua zaidi ya wiki moja?

Idadi ya maradhi   ……………………..

Sijapatwa maradhi kama haya   …………………..

Sijaugua maradhi haya kabisa   ……………..

MARADHI YA ZAMANI:

16. Uliwahi ugua maradhi ya kifua kabla ya kutimiza umri wa miaka 16?

1. Ndio   2. La

17.Umewahi kuugua magonjwa yafuatayo:

1A. Maradhi ya bronchitis (kufungana kifua ,kukohoa kwingi na kutoa kikohozi kwa muda)

1.   Ndio   2. La

KAMA JIBU LA SWALI HILI NI NDIO:

1B. Maradhi haya yalidhibitishwa na daktari?

1.   Ndio   2. La   88. Sijaugua maradhi haya kabisa

1C. Ulikuwa na umri wa miaka ngapi ulipougua mara ya kwanza?

Umri (miaka) ……………..

Sijaugua kabisa

2A.Pneumonia (homa ya mapafu),aina ya kawaida ama ya kufungana mapafu?

    1. Ndio   2. La

    KAMA JIBU LA SWALI HILI NI NDIO:

2B. Maradhi haya yalidhibitishwa na daktari?

    Ndio   2. La   88. Sijaugua maradhi haya kabisa

2C. Ulikuwa na umri wa miaka ngapi ulipougua mara ya kwanza?

    Umri (miaka) ……………..

    Sijaugua kabisa

 3.Mafua ya kila mara,tofauti na yale ya maambukizi?

        1. ndio   2. La   88. Sijaugua maradhi haya kabisa

3B. Maradhi haya yalidhibitishwa na daktari?

    Ndio   2. La   88. Sijaugua maradhi haya kabisa

3C. Ulikuwa na umri wa miaka ngapi ulipougua mara ya kwanza?

    Umri (miaka) ……………..

    Sijaugua kabisa

18.Umewahi kuugua bronchitis(kufungana kifua ,kukohoa kwingi na kutoa kikohozi kwa muda) kwa muda mrefu?

1. Ndio   2. La

B. Je,baado unaugua maradhi haya?

1. Ndio   2. La

C. Maradhi haya yalidhibitishwa na daktari?

Ndio 2. La   88. Sijaugua maradhi haya kabisa

D. Ulikuwa na umri wa miaka ngapi ulipougua mara ya kwanza?

   Umri (miaka) ……………..

Sijaugua kabisa

19. Umeugua ugonjwa wa emphysema (kuhema sana, kushindwa kupumua na kukohoa kikohozi bila kikohozi)?

B. Je, baado unaugua maradhi haya?

1. Indio   2. La

C. Maradhi haya yalidhibitishwa na daktari?

   1.Ndio 2. La   88. Sijaugua maradhi haya kabisa

D. Ulikuwa na umri wa miaka ngapi ulipougua mara ya kwanza?

   Umri (miaka) ……………..

  Sijaugua kabisa

 1. Ndio   2. La

20. Umewahi ugua ugonjwa wa pumu?(asthma)

  1. Ndio 2. La

B. Je, baado unaugua maradhi haya?

  1. Ndio   2. La

C. Maradhi haya yalidhibitishwa na daktari?

   Ndio 2. La   88. Sijaugua maradhi haya kabisa

D. Ulikuwa na umri wa miaka ngapi ulipougua mara ya kwanza?

Umri (miaka) ……………..

Sijaugua kabisa

Ndio   2. La

E. Kama maradhi yaliisha,yaliisha ukiwa na umri wa miaka ngapi?

Umri iliyoisha(miaka) ……………….

88. Sijaugua kabisa

21. Je, umewahi:

A. Kuugua maradhi mengine ya kifua?

                1. ndio   2. La

Kama ndio,tueleze ………………………………………………………………

B. Kufanyiwa upasuaji wowote wa kifua?

                1. ndio   2. La

Kama ndio ,tueleze …………………………………..

C. Kupata majeraha ya kifuani?

                1. ndio   2. La

Kama ndio,tueleze …………………………………

22A. Umewahi tibiwa maradhi ya moyo?

                1. Ndio   2. La

Kama jibu ni ndio,

B. Umetibiwa maradhi ya moyo katika miaka kumi iliyopita?

                1. Ndio   2 . La   88. Sijaugua maradhi haya

23 A. Umeambiwa na daktari kwamba unaugua shinikizo la damu?

    1. Ndio   2. LA

 Kama jibu lako ni ndio:

B. Umetibiwa shinikizo la damu katika miaka kumi iliyopita?

    1. Ndio   2. La

MAELEZO YA KAZI:

24 A. Umeandikwa kazi ya siku mzima, ya kuajiriwa, kibarua au ya biashara (masaa 30 kwa wiki au zaidi), zaidi ya miezi 6?

  1. Ndio   2. La

B. Je,umewahi fanya kazi kwa muda wa miaka au zaidi ya mwaka pahali palikuwa na vumbi nyingi?

  1. Ndio   2. La   88. Sijapatana na vumbi kabisa

Ilikuwa kazi ya aina gani /kiwanda gani? ………………………………………..

Ulifanya miaka ngapi? …………………….

Je, vumbi iliyokuwa unapatana nayo ilikuwa:

  1. Kidogo 2. Kiasi wastani   3. Nyingi sana

C. Je, umewahi fanya kazi penye mvuke wa kemikali au ya aina nyingine isiyo hewa ya kawaida?

  1. Ndio   2. La   88. Sijafanya kazi pahali kama hapa

Ilikuwa kazi gani/kiwanda gani? ………………………………………………………..

Ulifanya kazi huko miaka ngapi ? ………………………………………………………….

Mvuke uliopatana nao ulikuwa kiasi gani?

  1. Kidogo   2. Kiasi wastani   3. Nyingi sana

D. Kazi uliyoajirirwa ama uliofanya muda mrefu kabisa maishani mwako ilikuwa gani?

1. Aina ya kazi …………………………………………

2. Miaka uliyafanya kazi hii ……………………………

3. Ulikuwa kwenye nafasi gani ………………………..

4. Je, kazi ilikuwa ya biashara,kiwandani au ya sekta gani ya

uchumi?...

UVUTAJI SIGARA:

25 A. Umewahi kuvuta sigara? (Jibu, la,kama hujavuta zaidi ya pakiti 20 ya sigara maishani au zaidi ya

sigara moja kwa siku kwa muda wa mwaka mmoja)

                                        1. Ndio   2. La

KAMA JIBU LAKO LILIKUWA NDIO:

B. Unavuta sigara wakati huu (kutoka mwezi mmoja uliopita)?

                        1. Ndio   2. La   8 Sijavuta sigara kabisa

C. Ulikuwa na umri wa miaka ngapi ulipoanza kuvuta sigara kila mara?

                    Umri wako (miaka)   88 Sijavuta sigara

D. Kama uliacha kuvuta sigara, ulikuwa na umri wa miaka ngapi ulipoacha?

                Umri wako (miaka)   88 Sijawahi vuta sigara

E. Saa hii, unavuta sigara ngapi kwa siku?

                Nambari ya sigara kwa siku   88. Sijawahi vuta sigara:

KIFUA KIKUU (T. B.)

17 A .Umewahi tibiwa ugonjwa wa kifua kikuu?

1. Ndio   2. La

B. Ulihakikishiwa una ugonjwa wa kifua kikuu na daktari?

1. Ndio   2. La

JINSI YA KUPIKA

Kwa kawaida, huwa unatumia moto wa aina gani kupika?

1. Makaa   4.Kuni

2. Gesi ya mtungi   5. Gesi ya petroli

3. Stima   6. mafuta taa

HISTORIA YA AFYA YA FAMILIA:

28. Wazazi wako waliwahiambiwa na daktari walikuwa na maradhi ya mapafu kama:

  BABA   MAMA

 1, Ndio 2. La 3. Sijui   1. Ndio 2. La 3. Sijui

A.Bronchitis

Ya miezi mitatu au zaidi

B. Emphysema

C. Pumu

D. Saratani ya mapafu

E. Maradhi mengine ya kifua

29a.Mzazi huyu baado ako hai?

B. Tafadhali tueleze:

 Umri kama yuko hai   umri kama yuko hai

Umri alioaga dunia

8 sijui

C. Tueleze kilichosababisha kifo chake.

……………………………………………………………………………..

NISHATI YA KUPIKIA NA KUWEKA JOTO NYUMBANI

Unatumia nishati gani zaidi kupikia nyumbani kwako?

1. Makaa madini /makaa kuni

2. Kuni

3. Gesi ya mifereji kutoka kampuni

4. Gesi ya mitungi

5. Stima

6. Mafuta ya taa

APPENDIX 6

ATS/ERS TASK FORCE: STANDARDIZATION OF LUNG FUNCTION TESTING

Contraindications for performing spirometry

i. Unstable cardiovascular status

ii. Unstable angina,

iii. Recent myocardial infarction (within one month)

iv. Pulmonary embolism

v. Haemoptysis of unknown origin

vi. Recent pneumothorax

vii. Thoracic, abdominal, or cerebral aneurysms

viii. Recent thoracic, abdominal or eye surgery

ix. Acute disorders such as nausea or vomiting

x. Severe respiratory distress

xi. Physical limitations

xii. Cognitive impairment

xiii. Dementia

Assemble the following supplies:

i. Disposable/reusable supplies: mouthpieces, nose clips, flow sensors (pneumotachometers)

ii. Infection control supplies: disposable in-line bacteria filters, gloves, gowns, masks, protective eyewear ,

iii. Stadiometer for measuring height,

iv. Scales for weight,

v. Tape measure for arm span

vi. Computer/recorder supplies

vii. Barometer, thermometer and hygrometer

viii. Validated 3L-volume calibration syringe

ix. For reversibility test: Metered dose inhaler (MDI) and spacer, or small volume nebuliser with

compressed gas source and disposable nebuliser mask/mouthpiece

Preparing the Spirometer

i. Assemble the components according to the manufacturer's instructions

ii. Put in place a new in-line bacterial filter (if used), disposable mouthpiece or disinfected reusable

mouthpiece for each patient.

iii. Turn on the system to ensure adequate warm up

iv. Allow time for equilibration to room temperature for portable systems.

v. Perform a validation check (calibration check)

vi. Document the environmental data from an accurate source representative of the laboratory prior

to calibration.

vii. Check for leaks daily

viii. Check the flow sensors for holes, clogging, channel plugging, or excess moisture daily

Preparing the patient

i. Carry out infection control measures prior to testing, particularly hand washing

for both patient and personnel performing spirometry

ii. Ensure the patient is wearing clothing that enables full chest and abdominal expansion (if possible

loosen clothing).

iii. Assess patient for physical and developmental status to determine their ability to

perform the test and/or if special arrangements are required e.g. if the patient has a tracheotomy.

iv. Record the type, dosage and time taken of any inhaled or oral medication that may

alter lung function.

v. Measure and record the patient's height (barefoot) in centimetres (cm) to the nearest

cm, with feet together, heels against the wall, standing as tall and straight as possible and with the

head in the Frankfort horizontal plane (eyes level and looking ahead

vi. Measure the patient's height using an accurate measuring device, such as a stadiometer.

vii. Patients with spinal deformities and for those who cannot stand, the measurement of

arm span can be used as it closely approximates standing height

viii. Have the patient stretch their arms in opposite directions to attain the maximal distance between

the tips of the middle fingers.

ix. Measure and record the patient's weight in kilograms (kg) to the nearest 0.5kg with

indoor clothing and without shoes.

x. For safety reasons perform the test with the patient sitting comfortably in a chair with

arms and without wheels. Ensure the patient is sitting in an upright position, legs

xi. uncrossed and both feet on the floor

xii. Clearly instruct the patient in the procedure prior to the commencement of each test

and ensure that the patient understands all requirements of the test

xiii. Allow ample opportunity for the patient to ask questions or receive clarification on the test and its

requirements.

Performing test procedure

Explain and demonstrate the test maneuver to the patient, including:

i. Correct use of the mouthpiece and nose clip

ii. Correct posture with head slightly elevated

iii. Position of the mouthpiece, including tight mouth seal over the mouthpiece.

iv. Complete inhalation prior to FVC and FEV

v. Rapid and complete exhalation with maximal force for FVC and FEV

vi. Have the patient assume the correct sitting position i.e. upright posture, legs uncrossed and both feet flat on the floor.

vii. Activate the spirometer.

a)When using the open circuit method

– Attach the nose clip and instruct patient to inhale completely and rapidly until their lungs are full, place mouthpiece in mouth and close lips tightly around the mouthpiece while holding their lungs full.

– Instruct patient to exhale forcefully until no more air can be expelled.

b)When using the closed circuit method

– Attach nose clip, place mouthpiece in mouth(or assist patient in positioning themselves on the mouthpiece) and instruct patient to close lips tightly around the mouthpiece and breathe quietly for no more than 5 breaths (i.e. relaxed, 'normal' tidal breathing).

– Instruct patient to inhale completelyand rapidly until their lungs are full.

– With little or no pause at TLC (<1sec), instruct patient to exhale forcefully until no more air can be expired.

– Encourage the patient to maintain an upright posture (i.e. no bending forwards) during the manoeuvre.

– If a flow-volume "loop" is being performed (to measure forced inspiratory vital capacity) the patient will exhale rapidly and forcefully until end of test criteria are achieved, and then inhale as rapidly as possible back to TLC.

– Observe the patient at all times during the manoeuvre in case they become unsteady due to light-headedness or experience other adverse reactions, such as chest pain.

– Terminate the manoeuvre (using keyboard, mouse or special function keys as specified by the manufacturer) once the end of test criteria has been met

Determining acceptability and repeatability).

– Repeat the instructions and manoeuvres for a minimum of three manoeuvres, more if necessary, coaching vigorously until end of test criteria are met; no more than eight manoeuvres are usually required.

– Terminate the test once the acceptability and repeatability criteria have been met

Performing the VC testing

1. Explain and demonstrate the test manoeuvre to the patient, including:

a) Correct use of the mouthpiece and nose clip

b) Position of the mouthpiece, including tight mouth seal over the mouthpiece

c) Correct posture with head slightly elevated-Emphasis on complete filling and emptying of the lungs.

2. Have the patient assume correct posture and attach nose clip.

3. Activate the spirometer.

a)When using the open circuit method

-Instruct the patient to inhale completely and rapidly until their lungs are full, place the mouthpiece in the mouth and close lips tightly around the mouthpiece while holding their lungs full

-Instruct patient to exhale slowly and completely until their lungs are empty.

b)When using the closed circuit method

—Attach nose clip, place mouthpiece in mouth (or assist patient in positioning themselves on the mouthpiece) and instruct patient to close lips tightly around the mouthpiece and breathe quietly for no more than five breaths (i.e. relaxed, 'normal' tidal breathing).

—Instruct the patient to inhale completely until their lungs are full and exhale slowly and completely until their lungs are empty. This provides a measure of expiratory

vital capacity (EVC).

—Alternatively, instruct the patient to exhale completely from end-inspiration on a tidal

breath until their lungs are empty.

This provides a measure of inspiratory vital capacity (IVC).

4. Encourage the patient to "keep going" until there is no volume change observed

Determining acceptability and repeatability

5. Observe the patient at all times during the manoeuvre in case they experience light-headedness or any other adverse reactions.

6. Terminate the manoeuvre (using keyboard, mouse or special function keys as specified

by the manufacturer) once the end of test criteria have been met

Determining acceptability and repeatability

7. Repeat instructions and manoeuvres for a minimum of three manoeuvres coaching

vigorously until end of test criteria are met; with a maximum of four attempts and a rest

period of >1 minute between each manoeuvre.

8. Terminate test once acceptability and repeatability criteria are met

Determining acceptability and repeatability

Clinically useful spirograms must be acceptable and repeatable (i.e the two highest FEV,FVC and VC from three acceptable manoeuvres are in close agreement)

A spirogram is "acceptable" if the following are met:

- Start of Test Criteria begins from full inspiration has a rapid start of test
- If the manoeuvre has an obviously hesitant start then the trial should be terminated early to avoid unnecessary prolonged effort.

How to ensure repeatability between individual spirograms

- After three acceptable spirograms have been obtained, the following checks are used to assess for repeatability:
- The two largest values of FVC or VC must be within 0.150L of each other
- The two largest values of FEV must be within 0.150L of each other
- For patients with an FVC or VC of ≤1.0L the two largest FVC or VC and FEV values must be within 0.100L of each other

A minimum of three acceptable manoeuvres should be saved and utilised for analysis/interpretation