

Pulmonary Function Tests and Their Associated Factors in HIV-infected Patients at Jimma Medical Center; Ethiopia: A Comparative Cross-Sectional Study

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Abstract

Background

HIV-infected persons have a greater risk of developing respiratory disorders. Poor socio-economic status, High viral load, low CD4 counts, and anti-retroviral therapy are linked with the problems. Despite its high prevalence the association between retroviral infection and pulmonary function status as well as their associated factors has not yet well established in resource-scarce countries in general and study setting in particular

Methods

A comparative cross-sectional study was conducted from September 24 to October 15 of 2020 at Jimma Medical Center among HIV-positive patients and matched control group. Data were collected using a pretested structured questionnaire administered via face-to-face interview. The collected data included Socio-demographic, respiratory, retroviral infection, and substance use related. Pulmonary function tests were also conducted using SP10 spirometer. Collected data were entered and analyzed using SPSS version 26. Independent t-test and multiple linear regressions were carried out to identify factors independently associated with the pulmonary function status of the study participants while controlling for potential confounders.

Results

One hundred ninety two HIV-positive patients and matched control individuals participated in the study. A mean pulmonary function test parameters among HIV-infected participants were FVC (l) (2.957 ± 0.792 , $p < 0.006$), FEV₁ (l) (2.289 ± 0.593 , $p < 0.001$), and PEF₁ (l) (4.258 ± 2.039 , $p < 0.001$) with a significant declined in the group. Respiratory symptom, history of pulmonary TB, duration of living with RVI, duration of treatment, and current CD4 cell count were significant predictors of pulmonary function test indices ($p < 0.05$) in HIV infected respondents.

Conclusion

A significant reduction in mean pulmonary function parameters were observed among HIV-positive participants in comparison to non-RVI participants. A strong association was observed between pulmonary function status of HIV-infected patients and current CD4 count, duration of living with RVI, duration of treatment, and history of PTB. Therefore, due consideration in screening, diagnosing, and managing noninfectious lung diseases should be given by health professionals while treating HIV-infected patients.

Introduction

Acquired immune deficiency syndrome is a syndrome caused by a retrovirus that predominantly targets and destroys CD4 T cells [1, 2]. It is a pandemic that affects 36 million people worldwide [3].

The lung is a chief target organ for retroviral infection, rendering it vulnerable to an inclusive array of infectious and noninfectious complications [4]. Innovation and provision of highly active antiretroviral treatment (HAART) for Retroviral infected patients has been a new horizon in the reduction of Acquired immune deficiency Syndrome related mortality and prolong life expectancy [5]. As a result, the spectrum of infectious and noninfectious diseases significantly altered [6].

The incidence of non-communicable diseases particularly, chronic non-infectious pulmonary diseases is dramatically increased in RVI patients in the aftermath of HAART [7]. Obstructive lung diseases (OLD) especially, chronic obstructive pulmonary diseases (COPD) and asthma are an emerging pulmonary burden [8]. Chronic lung diseases are categorized based on the pattern of anomaly detected with pulmonary function test indices.

The cause of Obstructive lung disease (OLD) in RVI patients is to date an obscure concept [8]. The prevalence of tobacco use in RVI patients is higher than the prevalence in the general USA population. Despite this fact, HIV infection is independently associated with OLD incidence and prevalence without smoking exposure. Such query highlight OLD in RVI patients is mechanistically beyond the risk factor that has been considered in the general population [5].

Recent studies try to link the physiological mechanism between pulmonary diseases and RVI deep down to the defense mechanism of the pulmonary system. HIV persistently infected alveolar macrophage-more often smaller alveolar macrophages. As a result, alveolar macrophage function altered and secretes dozen of cytokine and chemokine which calls deregulated Cytotoxic T-cells. The alveolar airspace is infiltrated with malfunctioned cytotoxic T-cells that intensify the activation and reactivation of proteases. Proteases disrupt the extracellular matrix component elastin and collagen which end up with alveolar parenchyma destruction [6]. HIV also associated with a rapid decline of muscle mass and strength of the respiratory muscle due to the chronic inflammatory process and chronic malnutrition [9]

Socio-demographic factors (age, sex), history of pulmonary tuberculosis, smoking and substance use, time of ART initiation, CD4 count, viral load, and HAART have been crudely associated with pulmonary disease development and progression in RVI patients [10].

Despite these facts, the screening, diagnosing, and managing of noninfectious chronic lung diseases by interpreting pulmonary function test indices has been underemphasized in people living with HIV AIDS [5]. Despite the emergent of the RVI outbreak in Ethiopia, to date, scarce data is found to associate RVI and pulmonary function tests pattern.

In this regard, this study will fill this gap by determining pulmonary function tests and associated factors among RVI patients, and data from this study will be an input to establish a routine pulmonary function test platform for PLWH.

Methods And Materials

Study area

This study was conducted in Jimma University Medical Center (JUMC), from September 24 to October 15 of 2020. JUMC is located in Jimma city 352 km southwest of Addis Ababa. It provides services for approximately 15,000 inpatient, 160,000 outpatient attendants, 11,000 emergency cases, and 4500 deliveries in a year for patients coming to the hospital from the catchment population of about 15 million people. Currently, 3029 RVI patients are registered and receive service at in ART clinic

Study design

An institution-based comparative cross-sectional study design was used for this study

Source population

The source population was, all RVI patients enrolled in ART clinic for chronic follow up and age-sex matched RVI negative attendants who came to JUMC as a caregiver for their cognate and relatives aged > 18 years.

Study population

All selected RVI patients who visited ART clinic and age-sex matched RVI negative attendants, age > 18 years during the data collection time.

Participant's eligibility criteria

All RVI patients aged > 18 years, and who had regular chronic follow up in ART clinic, HAART treatment for > 6 months, complete personal information, and clinical profile were recruited into the study.

RVI patients who had diagnosed with chronic co-morbidities (hypertension, DM, cancer, PCP, ILD, oral candidiasis, chest deformity, asthma, COPD), pregnancy, < 6 months of HAART TX, severe illness, history of retinal detachment, abdominal surgery < 3 months, chest /abdominal surgery < 3 months, presume COVID -19 as well as.

Similar exclusion criteria's were used for a comparison group

Sample size determination and sampling technique

The sample size was calculated using the double proportion population formula by taking a proportion of obstructive lung diseases among RVI patients ($P_1 = 10\%$) and non RVI respondents ($P_2 = 3\%$) taken from a study done in a rural part of South Africa [10]. The confidence interval, level of significance, and power of a study was 95%, 5%, and 90% respectively. After considering the 10% non-response rate, the total sample sizes were 192 (96 for a study group and 96 for a comparison group). During the time of data collection, both RVI patients and RVI negative respondents were chosen using a consecutive sampling technique.

Data collection procedure

Data were collected using an interviewer-administered structured questionnaire. It had five distinct parts, socio-demographic characteristics, Respiratory related questionnaire, substance use, anthropometry, and spirometer measurements. RVI related questionnaires were reviewed from study participant medical records. Respiratory-related questionnaires were adapted from ST. George's Respiratory Questionnaire and medical research council's committee (MRC) on environmental and Occupational Health.

Informed and consented respondents from the comparison group were had HIV tests using a rapid HIV diagnostic kit. The procedure and result interpretation was based on the Ethiopian health and nutrition research institute (EHNRE)[11]. Weight was measured after the study respondents were barefoot and wear light cloth using a digital weight scale. Height was measured using a stadiometer after the respondents were in a standing position, barefooted and the shoulder was in normal alignment.

Pulmonary function testing procedure

The pulmonary function tests were measured using (CONTEC MEDICAL SYSTEMS CO., LTD, China) SP10 digital spirometer. The procedure, precaution, acceptability, reproducibility, and interpretation of the spirometer output were based on the CDC-National Health and Nutrition Examination Survey of respiratory health, and research article [12].

Infection control

The body of the spirometer and turbine was cleaned using 70% isopropyl alcohol at the end of each procedure. The data collectors were worn N-95 facemask after demonstrating the maneuver for study respondents and powder-free disposable gloves. Each study participant was having their mouthpiece with a bacterial viral filter which was discarded by themselves at the end of the procedure. In line with COVID-19 prevention, all preventive measure and recommendation emanate from World Health Organization was kept in practice.

Instrument calibration

The calibration of the instrument was based on SP-10 pocket spirometer user Manuel which was prepared by the manufacturer. Under the calibration interface verification was checked for pre-calibration with a 3L syringe.

Spirometer examination was done in a quiet room in a sitting position by qualified personnel. The procedure was done in the morning between 8:00 AM to 12:00 AM daily at room temperature. Participants' ID, age, sex, weight, height, race, and smoking status was feed into SP10 spirometer for each participant before the maneuver. A very explicit instruction was delivered to the study participants until a common understanding was grounded for spirometer examination. Well thought of the purpose of the study, emphasize the need for extra effort from them to get a maximal result, avoidance of tight clothing and denture was encouraged.

Maneuver

The study participant was sitting upright with chin elevated and neck extended slightly, Feet flat on the ground with uncrossed leg and Hold their nostrils tightly by left/right thumb and index fingers. Then take a big deep breath and fill their lung with air and Hold the spirometer, place the mouthpiece into the mouth above the tongue and between the teeth. The respondent Blast out the air as hard and as fast as possible. Keep blowing out for the first 6 seconds to empty the lung. The procedure was repeated until three acceptable and reproducible measurement was obtained for a maximum of eight attempts. The procedure was stopped and rescheduled if a respondent was unable to produce an acceptable and repeatable spirometer output after eight attempts.

Data were collected by four BSc nurse professionals who had previous experience in data collection.

Operational definition

Respiratory symptom – Saint George respiratory questionnaire score >24 is considered a prevalent respiratory symptom

Alcohol taking – drinking ≥ 2 bottles of beer per drinking session for males and ≥ 1 bottle of beer per drinking session for females ≥ 3 sessions/week within 1 month before the study.

Khat chewer – chewing ≥ 1 bundle of khat leaves per chewing session ≥ 3 days/week with 1 month before the study.

Data analysis procedure

The collected data were clean, coded, and entered into epidata manager (v.4.6.0.2), EpiData Entry Client (v.4.6.0.2), and export into SPSS version 26 for data analysis.

Using SPSS, continuous variables were summarized as mean and standard deviation using descriptive statistics. Categorical variables were summarized as frequency and percentage using cross-tabulation.

An Independent T-test was used for the comparison of the mean of pulmonary function test indices between RVI and non-RVI study respondents. The assumption of independent sample t-test was checked using Shapiro–Wilk and Levine’s tests.

A simple linear regression was employed to determine the factors which predict pulmonary function tests indices of RVI respondents. Variables that were significant predictors of PFTs in simple linear regression were entered into multiple linear regression.

Multiple linear regression analysis were utilized to obtain the best fit linear combination of sex, weight, BMI, respiratory symptom, history of pulmonary TB, duration of RVI, duration of treatment, current CD4 cell count, alcohol taking, and khat chewing which were significant in simple linear regression.

The assumption of multiple linear regression (linearity, normality, homoscedasticity, outliers, and multicollinearity) was checked and met. Normality was checked using histogram, P-P, and Q-Q plot.

Multicollinearity was checked using variance inflation factors (VIF) and VIF >5 shows an association between predictor variables. Recruited variables in multiple linear regressions which had a P-value of ≤ 0.05 were said to be a significant predictor of pulmonary function.

Data quality management

To assure the clarity of the questionnaire pretest was done on 5% of the study respondents in shanen gibe hospital. Training for data collectors and supervisor were given for two consecutive days about the purpose of the study, interview, measurement technique, and ethical issues by the principal investigator. Questionnaires were translated to Afan Oromo and Amharic language and retranslated back to English for consistency purposes by language experts.

Results

Socio-demographic characteristics of the respondents

One hundred and ninety two respondents (96 = RVI and 96 = non RVI) were recruited in the study. Of them 65% were females. The mean age of RVI and non-RVI respondents were 37.56 (SD = \pm 7.017) and 36.06 (SD = \pm 7.20) respectively. Regards to the level of education, 3.1% and 4.7% of RVI respondents and 7.3 and 15.1% of non-RVI respondents were unable to read and write and above diploma respectively (table 1)

Table 1: Socio-demographic characteristics of RVI and non-RVI respondents in Jimma town, Southwest Ethiopia, 2020.

	RVI positive(n=96) mean ± SD	RVI negative(n=96) mean ± SD
Demographic characteristics		
Age	37.56 ±7.017	36.06 ±7.20
Sex	Number (%)	Number (%)
Female	63 (65.6)	63 (65.6)
Male	33 (34.4)	33 (34.4)
Level of education		Number (%)
Unable read &write	6 (3.1)	14 (7.3)
Primary	46 (24)	31 (16.1)
Secondary	35 (18.2)	22 (11.5)
Diploma and above	9 (4.7)	29 (15.1)
Occupational status		
Govt employer	30 (31.2)	50 (52.1)
Own business	28 (30.4)	32 (34.7)
Daily laborer	25 (26)	11 (11.5)
Unemployed	13 (13.5)	3 (3.1)

Anthropometry, medical history, and substance use-related characteristics of respondents

The mean height of RVI and non-RVI respondents were 1.63(SD=±0.868) and 1.65(SD=±0.110) respectively. The mean weight of RVI and non-RVI respondents were 59.4(SD=±11.812) and 56.91(SD=±9.881) respectively. Similarly, the mean BMI of RVI and non-RVI respondents were 21.85(SD=±3.573) and 21.49(SD=±7.634) respectively. 6.8% and 2.6% of RVI and non-RVI respondents have reported a history of TB respectively.

Twenty-five percent of RVI respondents were former smokers and one percent of non-RVI respondents were current smokers. The proportions of khat chewing and alcohol taking in RVI and non-RVI respondents were (9.4% vs 11.5%) and (11.5% vs 8.3%) respectively (Table 2).

Table 2 Anthropometric, medical history, and Substance use-related characteristics of RVI and non-RVI respondents in Jimma town, southwest Ethiopia, 2020.

Variables	RVI positive(n=96)	RVI negative(n=96)
	mean ± SD	mean ± SD
Height (meter)	1.63±0.868	1.65±0.110
Weight (kg)	56.9±9.9	59.42±11.812
BMI (kg/m ²)	21.85±3.573	21.49±7.634
Medical history	Number (%)	Number (%)
History of PTB	13(6.8)	5 (2.6)
History of pneumonia	2(1)	1 (0.5)
Smoking status		
Current smoker	-	2 (2.2)
Former smoker	25 (26)	-
Never smoker	71 (74)	94 (97.8)
No of cigarette/day	-	9.5 ± 3.5
Alcohol taking	11(11.5)	8 (8.3)
Khat chewing	9 (9.4)	11(11.5)

RVI related characteristics of the respondents

The mean duration of RVI was 7.98 years (SD±4.641) and the mean duration of treatment was 7.15 years (SD± 4.635) in RVI respondents. The mean of current CD4 counts and current viral loads were 659 cells/mm³ (SD±465.53) and 247.32 copies/ml (SD±1036.38) respectively. Using the medication adherence rating scale (MARS score), 33.3% of the RVI respondents were poor adherence (Table 3).

Table 3: RVI related characteristics

Parameter	RVI pts. mean \pm SD
Duration of RVI (yrs.)	7.98 (4.641)
Duration of Rx (yrs.)	7.15 (4.635)
Current CD4 count (cells/mm ³)	659 (465.53)
Current viral load (copies/ml)	247.32 (1036.38)
Drug adherence	Number (%)
High adherence	5 (5.2)
Moderate adherence	59 (61.5)
Low adherence	32 (33.3)

RVI- retroviral infection, RX-treatment, CD4 – a cluster of differentiation 4

Comparison of mean of pulmonary function tests among RVI and non-RVI respondents

The current study showed that the mean of FVC (l) was significantly reduced in RVI respondents (2.957 \pm 0.792) as compared to non-RVI respondents (3.268 \pm 0.765, p0.006). Similarly, the presented study reveals that the mean of FEV1 (l) (2.289 \pm 0.593, p<0.0013), and PEF (l/s) (4.258 \pm 2.039, p< 0.001) were significantly declined in RVI respondents as compared to non-RVI respondents.

Conversely, the mean score of FEV1/FVC (85.44 \pm 45.508, p0.622) and FEF₂₅₋₇₅ (l/s) (3.135 \pm 2.135, p0.733) were had no significant difference between RVI respondents and non-RVI respondents (table 4).

Table 4: Comparison of mean of pulmonary function test indices in RVI and non-RVI participants in Jimma town, southwest Ethiopia, 2020.

PFT indices	RVI pts (n=96) mean ±SD	Non-RVI pts (n=96) mean ±SD	p-value
Height (m)	1.64±0.09	1.65±0.11	0.29
Weight (kg)	56.9±9.9	59±11.8	0.11
BMI (kg/m ²)	21.85±3.7	21.5±7.6	0.67
FVC(l)	2.957±0.792	3.268±0.765	0.006*
FVC (%)	67.352±19.121	75.729±18.873	0.003*
FEV1(l)	2.289±0.593	2.723±0.742	<0.001*
FEV1 (%)	61.76±16.04	77.104±19.194	0.001*
FEV1/FVC	85.44±45.508	90.917±42.508	0.622
FEF ₂₅₋₇₅ (l/s)	3.135±5.247	3.325±1.411	0.733
PEFR(l/s)	3.325±1.411	4.258 ± 2.039	0.001*
PEFR (%)	50.145±23.329	67.968±25.222	0.001*

Independent sample t-test,*significant p-value, BMI-body mass index, FVC-forced vital capacity, FEV1-force expiratory volume in 1second, FEF₂₅₋₇₅ – mid forced expiratory flow, PEFR –peak expiratory flow rate, l/s-liter per seconds.

Predictor of pulmonary function test among RVI respondents

Simple linear regression presenting predictors of PFTs among RVI respondents

A simple linear regression was employed to determine the factors which predict FVC (l), FEV_{1s} (l), FEV₁/FVC, FEF₂₅₋₇₅ (l/s), and PEFR (l/s) of RVI respondents. As result, a simple linear regression model revealed a significant association between the PFTs and sex (male being used as reference), weight, BMI, respiratory symptom (SGRQ>0 being used as reference), history of pulmonary TB (yes being used as reference), duration of RVI, duration of treatment, current CD4 cell count, alcohol taking (yes being used as reference) and khat chewing (yes being used as reference).

Conversely, age, height, current viral load, history of pneumonia, drug adherence, type of treatment regimen, and history of smoking were not statistically significant predictors of pulmonary function tests among RVI patients.

Multiple linear regression model presenting predictors of PFTs among RVI respondents

Multiple linear regression analysis was utilized to obtain the best fit linear combination of sex, weight, BMI, respiratory symptom, history of pulmonary TB, duration of RVI, duration of treatment, current CD4 cell count, alcohol taking, and khat chewing which were significant in simple linear regression ($p < 0.05$). Being a male has 0.761 liters greater FVC (l) than being a female. Similarly being a male has 0.69 liters greater of FEV_{1s} (l) than being a female.

Having frequent respiratory symptoms decreases FVC (l) by 0.38 liters compared to devoid of respiratory symptoms. Respondents who reported respiratory symptom decreases FEV_{1s} (l) by 0.378 liters compared to devoid of respiratory symptom. Similarly, having frequent respiratory symptoms decreases PEFr by 0.94(l/s) compared to devoid of respiratory symptoms.

Participants who reported a history of pulmonary TB decreases FVC (l) by 0.551 liters compared to those who never report it. Equivalently, participants who report a history of TB was had FEF₂₅₋₇₅ of 0.9 l/s less compared to respondents who never reports.

A unit increment in the duration of RVI results in 0.084 liters decline of FEV_{1s} ($\beta = -0.084$, $p = 0.03$) when the history of pulmonary tuberculosis holds constant. A unit increment in the duration of treatment results in 0.088 liters declines in FEV_{1s} (l) ($\beta = -0.088$, $p = 0.045$). Similarly, this finding revealed that a unit increase in current CD4 cell counts results in an increment of 0.01 liters of PEFr (l/s) ($\beta = 0.01$, $p = 0.03$)

Respondents who reported alcohol taking history decreases FEF₂₅₋₇₅ (l/s) by 0.05 liters compared to non-alcoholic RVI respondents ($\beta = -0.05$, $p = 0.011$). Similarly, 1 liter of PEFr (l/s) was lowered in alcohol-taking RVI study participants than non-alcoholic participants ($\beta = -1$, $p = 0.011$). Khat chewer RVI participants had a 1.36 l/s lower PEFr (l/s) than non-khat chewer RVI participants. Lastly, a unit increase in weight results in 0.175 liters declines in PEFr (l/s).

Conversely, the present study reported that FEV₁/FVC has no significant predictors in RVI respondents ($p > 0.05$) (table 5).

Table 5: Predictors of pulmonary function tests among RVI respondents in Jimma town, southwest Ethiopia, 2020

PFT indices	Variable	B	p-value	95% CI	Adjusted R ²
FVC(l)					0.348
	Sex	0.76	0.001	0.325,1.197	
	Respiratory symptom	-0.38	0.037	-0.742,-0.23	
	PTB	-0.55	0.024	-0.955,0.068	
FEV _{1s} (l)					0.381
	Sex	0.69	0.001	0.372,1.007	
	Duration of RVI	-0.08	0.03	-0.006,0.173	
	Duration of TX	-0.09	0.045	-0.0173,-0.002	
	Respiratory symptom	-0.38	0.005	-0.440,-0.116	
FEF ₂₅₋₇₅					0.317
(l/s)	PTB	-0.9	0.009	1.177-7.98	
	Alcohol taking	-0.05	0.011	-9.371,-1.273	
	Smoking status	-2.66	0.066	-0.18,5.5	
PEFR					0.408
(l/s)	Constant	-23.5	0.013	-42.014,-5.099	
	BMI	0.54	0.009	0.142,0.944	
	Respiratory symptom	-0.94	0.037	-1.82,-0.059	
	Alcohol taking	-1	0.011	-2.979,-0.395	
	Khat chewing	-1.37	0.042	-2.742,0.011	
	Weight	-0.18	0.017	-0.3,-0.15	
	Current CD4	0.01	0.043	-0.002,0.001	

Multiple linear regression, p<0.05 taken as significant predictors, PTB-pulmonary tuberculosis, PFT-pulmonary function test.

Discussion

In the current study, the mean of FEV1 was significantly reduced in RVI study participants than non-RVI participants. This report is in concordant with a study done in a rural part of South Africa [10] and a study done in Copenhagen [13]. This observation might be due to HIV persistently infected alveolar macrophage-more often smaller alveolar macrophages. As a result, alveolar macrophage function altered

and secretes dozen of cytokine and chemokine which calls deregulated Cytotoxic T-cells. The alveolar airspace is infiltrated with malfunctioned cytotoxic T-cells that intensify the activation and reactivation of proteases. Proteases disrupt the extracellular matrix component elastin and collagen which end up with alveolar parenchyma destruction. Physiologically, the recoil force of the alveoli is significantly reduced and the compliance of alveoli enhanced and expiratory work of breathing is increased. As a result of this, pulmonary function test indices might be declined [6]

Conversely, this finding is contradicted with the research done in Amsterdam Netherlands, which reported the mean of FEV1 was not significantly different between RVI and non-RVI respondents [9]. The reason might be due to relatively high smoking status and alcohol abuse in the controls [9]. Moreover, other socio-demographic variations and methodological choices between the two groups might be perpetuating the difference.

Our findings revealed that the mean of FVC was significantly reduced in RVI study participants than non-RVI respondents. This observation is in line with a study done in Cape Town of South Africa and Amsterdam [9, 14]. This might be linked to the fact that HIV had been associated with the rapid development of sarcopenia [9]. Sarcopenia is usually a disease of geriatrics concerned with progressive loss of skeletal muscle mass and muscle strength, despite this fact, it occurs at a young age in RVI patients [15]. The reason behind this might be due to persistent chronic immune activation and inflammation. As results of this, the muscle of expiration loss their mass and strength to perform forced expiratory maneuvers which end up with reduced FVC and a high ratio of FEV1/FVC [16].

In the current study, being male was a positive predictor of FVC (l), FVC (%), FEV1 (l), and FEV1%. This finding was consistent with a study carried out in the USA[17]. The reason might be since the male has by far a bigger chest cavity, bigger lung, large diaphragm, large number of alveoli and alveoli surface area, and high recoil pressure over the same stature as female. Those physiological advantages are helpful during forced expiratory maneuvers [18]. Our observation went against a study done in South Africa and Pittsburg [10, 19]. Such discrepancy might be due to variability in sample size, substance abuse, and occupational exposure between males and females.

In the present study, weight was a negative predictor of PEF. This might be due to increment in weight decrease chest and lung compliance which negatively affects pulmonary function parameters [20]

Similarly, our study reveals that BMI was a positive predictor of peak expiratory flow rate. This observation was in line with a study carried out in Harare of Zimbabwe [21]. The scientific argument behind this observation is HIV had been associated with chronic under-nutrition. The primary cause of under-nutrition is anorexia secondary to profoundly elevated pro-inflammatory cytokine (IL-1, 6, TNF- α) [22]. This results in inadequate energy intake coupled with energy catabolism. Entirely, respiratory muscle mass and strength are weakening and maximal expiratory pressure is weakening to achieve peak expiratory flow rate [22].

This observation went against the study done in South Africa [23]. This might be due to the variability socio-demographic and nutritional status of the participants.

The current study also reported that the duration of HAART treatment was a negative predictor of FEV1 (l) and predicted FEV1 %. This result goes inconsistent with a study done in Minneapolis of USA and Pittsburg [17, 24]. This might be due to HAART induces oxidative stress by triggering massive production of reactive oxygen species and inhibit antioxidant production in many cells of a pulmonary system [25]. The Oxidative stress-causing effect of HAART has been positively associated with increasing the duration of treatment. As remarked in the above statement oxidative stress damage airways and alveolar parenchyma. In addition to this, anorexia is an unavoidable adverse effect of HAART which is contributing factor for chronic under-nutrition. So, the strength and mass of respiratory muscle are lost to generate adequate expiratory pressure [22].

On the contrary, this finding went against the study done in Zimbabwe [21] which says early initiation of ART prevents the decline of FEV1. The reason is probably due to the difference in duration of treatment and treatment regimen.

The finding of the present study also reveals that the Duration of RVI is a negative predictor of FEV1 and FEV1%. This observation is consistent with a study carried out in Zimbabwe and Denmark [13, 26]. The reason for this observation is quite multifactorial, in the aftermath of HAART provision, RVI patients are living with a low level of viremia. This consistent low level of viremia induces persistent long-term inflammation which causes oxidative stress, disruption of mucociliary clearance mechanism, sarcopenia, airway remodeling, and undernutrition [9, 14, 21, 27]. On top of this, the duration of HIV infection is associated with the reduction of serum alpha-1-antitrypsin concentrations which are serine protease inhibitors (protect extracellular matrix of alveolar parenchyma) [28, 29]. Taken together, the duration of HIV infection on a pulmonary system is manifested as impaired pulmonary function tests and pulmonary diseases. This finding went against research carried out in South Africa which dictates that the duration of HIV has no association with the decline of pulmonary function in RVI respondents [10]. This is possibly due to variation in sample size, duration of HIV infection, and other RVI characteristics.

Current CD4 cell counts were positive predictors of pulmonary function in our findings. The finding is in line with research carried out in France [30]. The primary role of ART is viral suppression and T cell function improvement [31].

CD4 cell count increment is immunity to pulmonary function by preventing bronchial colonization, secondary inflammation, and orchestrates inflammatory response to lessen persistent viral inflammation and immune activation to airways and alveolar parenchyma [30, 32]. The finding is contradicted with a study done in the USA, Pittsburg, South Africa [10, 19, 24, 33]. This is might be due to dissimilarity in methodology, current CD4 count, current viral load, ART uses, and high smoking status.

History of TB is the negative predictor of FVC (l), FVC%, and FEF₂₅₋₇₅. This study is in line with a study done in South Africa [10, 14, 33]. The reason for such observation is in TB endemic area TB follows the

footsteps of HIV and vice versa [33]. Worldwide nearly, 30% of RVI patients estimated to have TB and 30-40% in Africa [10]. In Ethiopia, up to 52% of RVI patients estimated to have TB and vice versa [34]. Both RVI and TB are chronic inflammatory disorders which trigger persistent and consistent inflammation and immune reactivation of pulmonary defense mechanism [35].

Similarly, a finding of the present study shows the presence of respiratory symptoms was a negative predictor of FVC (l), FVC%, FEV1 (l), FEV1%, PEFr, and PEFr%. This finding is in agreement with a study carried out in Nigeria and Baltimore [36, 37]. It is probably because HIV as a virus is associated with persistent and consistent immune-activation; HIV-activated deregulated adaptive immune response and lifetime low-grade CD8-T cells lymphocytic alveolitis might contribute to this association [37, 38].

Our finding also shows that khat chewing was a negative predictor of PEFr and predicted PEFr. The association between khat chewing and pulmonary function impairment was not elucidated very well so far. As a researcher, it can be suggested that the negative association between khat chewing and reduced pulmonary function test is probably because khat chewing could interfere with drug adherence and feeding appetite (anorexia) of RVI patients. This speculation got a fulcrum from a study done in Jimma which says –that chewers have a 4.2 times more likelihood of missing at least one dose of HAART medication than ever chewers of RVI patients [39].

Finally, the present study revealed that Alcohol taking is a negative predictor of FEF₂₅₋₇₅, PEFr, and predicted PEFr. This study is in agreement with a study done in Barcelona [40]. The general argument for this observation is Alcohol consumption is associated with increase HIV-1 replication and decrease HAART response [41]. Apart from this, alcohol consumption impairs alveolar epithelial cell surfactant production, mucociliary transport system, **Lowers Glutathione Levels, fosters oxidative injury, and acts as a respiratory depressant [40].**

As part of our strength – this paper will be the first paper that studied the effect of RVI on pulmonary function and compare it with their age-sex matched non-RVI respondents. We extensively explore the possible risk factors which affect pulmonary function including khat and alcohol uses, RVI characteristics, drug adherence, and respiratory symptom. By doing so, the current study contributes its part to the present understanding of RVI and its impact on pulmonary function. Similarly, the current study highlights possible predictors of pulmonary function in RVI patients.

Conclusion

The current study reveals pulmonary functions were significantly reduced in RVI respondents compared to age-sex matched non-RVI respondents. Sex, weight, BMI, duration of RVI, duration of HAART treatment, current CD4 cell count, khat chewing, alcohol taking, respiratory symptom, and history of TB were significant predictors of pulmonary function in RVI patients. Current viral load, type of treatment regimen, history of pneumonia, and degree of adherence had no significant association with pulmonary function of RVI participants. Based on the current results of the study, all RVI patients should be screened for

pulmonary function at their initial visits and every 2 years to detect a change in pulmonary function and all RVI patients with long duration of RVI, longer duration of RX, low CD4 cell count, history of TB and khat chewing should be screened for a pulmonary function to verify their lung function status.

Abbreviations

AAT = α 1-antitrypsin; AIDS: Acquired Immune Deficiency Syndrome; CD4:Cluster of Differentiation 4; COPD: Chronic Obstructive Lung Diseases; FEV1: Forced Expiratory Volume in the First Second; FVC: Forced Vital Capacity; PEFR: Peak Expiratory Flow Rate; HIV: Human Immune Virus; JUMC: Jimma University Medical Center; OLD: Obstructive Lung Disease; PLWH: People Living With HIV; RVI: Retro Viral Infection; TNF: Tumor Necrosis Factor.

Declarations

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Ethics approval and consent to participate

Permission to conduct the study was obtained from the Institutional Review Board of Jimma University with ethical approval number of IHRPG1/736/20. All recommendation and measures suggested by WHO was kept in practice to prevent study respondents from COVID 19 infections.

Informed written consent was obtained from all study respondents after an explicit and comprehensive explanation of the purpose and procedure of the study was given to the study respondent. The study respondents were assured that their responses will be kept confidential. All methods were carried out in accordance with relevant guidelines and regulations.

Authors' contributions

M.T, designed the study, collect the data, analyzed and interpret the result, prepare the manuscript for publication. **E.M**, review the proposal of the study, supervise the data collection, participate in data analysis and interpretation, review the manuscript, **T.G**, review the proposal of the study, supervise the data collection, participate in data analysis and interpretation. **M.A**, participate in the design of the research project and collect the data.

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Debretabor university has covered the expense of data collection, however no roles in designing the project, data analysis, and interpretation.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding authors on reasonable request.

Consent for publication

Not applicable

Competing interest

The authors declare that there is no conflict of interest

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