



Prevalence of cardiovascular comorbidity and associated factors among patients with COPD At St. Paul's Hospital Millennium Medical College (SPHMMC) and Tikur Anbessa Specialized Hospital (TASH), Five Years Review

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Research submitted to the department of Internal Medicine, St. Paul's Hospital Millennium Medical College in partial fulfillment of the requirement for specialty certificate in Internal Medicine.

October, 2022

ADDIS ABABA, ETHIOPIA

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LIST OF ABBREVIATIONS

CI: Confidence Interval

COPD: Chronic Pulmonary Obstructive Disease

CVD: Cardiovascular diseases

DC: Data Collectors

ECG: Electrocardiogram

ECHO: Echocardiography

FEV1: Forced Expiratory Volume in the first second

FVC: Forced Vital Capacity

GOLD: The Global Initiative for Chronic Obstructive Lung Disease

HMIS: Health Management Information System

MRN: Movement Reference Number

NCD: Non communicative disease

OR: Odds Ratio

PAD: Peripheral Arterial Disease

PI: Principal Investigator

SD: Standard Deviation

SPHMMC: St. Paul's Hospital Millennium Medical College

SPSS: Statistical Package for Social Sciences

TASH: Tikur Anbessa Specialized Hospital

WHO: World Health Organization

ABSTRACT

Introduction: Chronic obstructive pulmonary disease (COPD) is a disease state characterized by persistent respiratory symptoms and airway limitation that is not fully reversible. It is the third leading cause of death worldwide, causing 3.23 million deaths in 2019. Nearly 90% of COPD deaths in those under 70 years of age occur in low- and middle-income countries. Patients with COPD experience different complications. Cardiovascular diseases are the leading cause of death in such patients.

Objectives: The objective of the study was to assess the Prevalence of cardiovascular comorbidity and associated factors among patients with COPD at St. Paul's Hospital Millennium Medical College (SPHMMC) and Tikur Anbessa Specialized Hospital (TASH)

Method: An institution based cross-sectional study was conducted on 132 COPD patients, who fulfilled the inclusion criteria at St. Paul's Hospital, Millennium Medical College and Tikur Anbessa Specialized Hospital. A structured questionnaire in the English language with components of demographic data, symptoms and sign, ECG, echocardiography, and spirometry reports of COPD was used to collect data. And the data was analyzed using the statical package for social science (SPSS) version 26.0. Means, standard deviations, and percentages computed, and logistic regression model used to assess various variable relationships at a significant level of P value 0.05.

Result: The study revealed that the majority of the patients were non-smokers and the mean number of pack years for smokers was 13.5. The majority of the patients lived in urban areas (77.3%) and had no occupational risk (84.1%). Cardiovascular disease was observed in 73 (55.3%). After adjusting other variables using multivariate binary logistic regression age above 75 years, 5.343(95% CI, 1.66-17.57), previous smoker, 6.952(95% CI, 1.531-31.57), COPD severity stage 3, 16.86 (95% CI, 7.289-16.520) and COPD stage 2, 9.158(95% CI, 7.72-15.2692) were significantly associated with cardiovascular comorbidity.

Conclusion: The prevalence of cardiovascular comorbidity is very high (55.3%) in patient with COPD and pulmonary hypertension, arterial hypertension, ischemic heart disease, arrhythmia, ischemic stroke and heart failure are prevalent in this study.

Key words: COPD, cardiovascular comorbidity, risk of COPD, ECG, ECHO, GOLD

1. Introduction

1.1 Background of the study

Chronic obstructive pulmonary disease (COPD) is a slowly progressive disease that results in airflow obstruction(1).It is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases and influenced by host factors including abnormal lung development(2). It is the third leading cause of death worldwide, causing 3.23 million deaths in 2019. Nearly 90% of COPD deaths in those under 70 years of age occur in low- and middle-income countries(3). Globally, the COPD burden is projected to increase in coming decades because of continued exposure to COPD risk factors and aging of the population(4)

The most common symptoms of COPD include dyspnea, cough and/or sputum production. The main risk factor for COPD is tobacco smoking but other environmental exposures such as biomass fuel exposure and air pollution may contribute. Besides exposures, host factors predispose individuals to develop COPD. These include genetic abnormalities, abnormal lung development and accelerated aging(5).

COPD should be considered in any patients with chronic productive cough and a history of risk factors to the disease. Spirometry is needed for diagnosis. It is managed by different bronchodilators and anti-inflammatory agents(6).

COPD patients experienced significant concomitant diseases which impacted the disease progression and contributed to the overall morbidity and mortality(1). Cardio-vascular diseases (CVDs) are one of the most significant and important co-morbidities in these patients. Common pathogenic mechanisms are systemic inflammation, oxidative stress, extracellular matrix destruction and drugs used for treatment. Additionally, they share risk factors such as tobacco smoking and sedentary lifestyle which will contribute for cardiovascular diseases comorbidity in such patients Large studies have also shown that airflow limitation is an independent risk factor for CVD, proving that COPD has significant systemic consequences(5).

According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD), the five most common CVDs that should always be considered in these patients are arterial hypertension, ischemic heart disease, chronic congestive heart failure, rhythm disorders, and peripheral vascular disease (PVD) (1). Patients with COPD should periodically be monitored for symptoms of ischemic heart disease, especially in more severe stages, as the risk of myocardial impairment during an acute exacerbation is increased in patients manifesting both diseases(6). The annual incidence rate of heart failure in patients with COPD is 3–4% and is a significant and independent mortality factor. Undiagnosed heart failure can accompany acute exacerbation. Cardiac arrhythmias are another common co-morbidity of COPD, with atrial fibrillation having the most direct impact on FEV1 values(7).

1.2 Statement of the problem

Chronic obstructive pulmonary disease is one of the top three causes of death in the world. It is the third leading cause of death worldwide, causing 3.23 million deaths in 2019. Nearly 90% of COPD deaths in those under 70 years of age occur in low- and middle-income countries (3). COPD is a major cause of chronic morbidity and mortality around the world. The results of different meta-analyses confirmed that the diagnosis of cardiovascular disease is strongly associated with the diagnosis of COPD. Major cardiovascular diseases (ischemic heart disease, cardiac dysrhythmia, heart failure, diseases of the pulmonary circulation, and artery diseases) are increased by up to five times in patients with COPD (5). And CVD is the leading cause of mortality worldwide, responsible for 31% of all deaths and accounting for 18 million deaths annually. COPD is a recognized risk factor for CVD(8). Few studies in Ethiopia have been done focusing on the prevalence and risk factors of COPD, but to our knowledge, little is known about the prevalence of cardiovascular comorbidity in patients with COPD.

1.3 Significance of the study

The available literature showed that COPD is one of the leading causes of death worldwide. A number of studies have reported that it has different complications. The major cause of death in such patients is cardiovascular disease.

According to National Data Management Center for health non communicable diseases is the leading cause of death in Ethiopia with an estimated rate of 554 per 100000 population. Every second an estimate of 1 Ethiopian is dying of NCD(9). Majority of these deaths resulted from Neoplasms and CVDS of which COPD accounts 7%(9). So far, little is known about the prevalence of cardiovascular comorbidity of COPD in Ethiopia. Knowing the prevalence of cardiovascular comorbidity and associated factors of for CVD in patients with COPD in our country will be very important for early detection and initiation of treatment for each cardiovascular complication. Moreover, assessing the prevalence of cardiovascular comorbidity in COPD and its associated factors will serve as an indispensable source for further studies. The gravity of the problem will be attested by this study. The results of the study can form basis for sensitizing physicians to the early screening, detection, and management of CVD complications in patients with COPD.

2.1 Literature Review

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality worldwide and its burden is increasing because of continuous exposure to different noxious stimuli. Cardio-vascular diseases (CVDs) are one of the most significant and important co-morbidities in patients with COPD(10). Currently, several observational studies suggest that the coexistence of COPD and CVD results in important adverse clinical outcomes.

In a systematic review of 25 studies from 7,322 citations in Medical Literature Analysis and Retrieval System Online (MEDLINE) to assess the prevalence of cardiovascular comorbidity in COPD, the results showed that its prevalence ranged from 28% to 70%(11–13). In this study, there was an association between the severity of airflow limitation and CVD risk.(13) There was also a systematic review and meta-analyses study on obstructive lung diseases which showed that, patients with COPD were more likely to be diagnosed with cardiovascular disease (odds ratio [OR] 2.46; 95% CI 2.02–3.00; $p < 0.0001$), including a two to five times higher risk of ischemic heart disease, cardiac dysrhythmia, heart failure, diseases of the pulmonary circulation, and diseases of the arteries including. The associations between COPD and these cardiovascular disease types and cardiovascular disease risk factors were consistent and valid across studies(12).

A retrospective observational study was done in different sites in Bulgaria which included around 426 (296 men and 130 women) patients with a spirometry diagnosis (10). The result showed that the majority of the patients had a history of smoking, with a mean pack per year of 38.16, and more than 80% of them had cardiovascular comorbidity. Hypertension was the most common cardiovascular comorbidity of COPD, accounting for 88% of men and 89% of women. According to this study, the prevalence of heart failure was 39% and that of ischemic heart disease was 33% in women. The prevalence of arrhythmia was 6%, and there was no gender difference. From sub group analysis, the most frequent comorbidities were hypertension, heart failure, and ischemic heart diseases, and they had a strong association with the severity of the diseases that was assessed by GOLD ABCD. A similar study was conducted in Bulgaria to assess the prevalence of co-morbidities among 338 COPD patients. The mean prevalence of cardiovascular disease was 73.5%. The commonest cardiovascular comorbidity was hypertension, 70.4%, followed by congestive heart failure, 47.4%, and ischemic heart disease, 37.5%. And arrhythmia, 12.6%. The

cardiovascular prevalence was high in patients with severe disease which was assessed by GOLD staging(14).

A study was done in Saskatchewan(15), Canada with the aim of assessing the prevalence and mortality of cardiovascular diseases in patients with COPD compared with non-COPD. The prevalence of CVD was higher in the COPD group, including a higher risk for arrhythmia 1.76 (CI: 1.64– 1.89), angina 1.61 (CI: 1.47–1.76), acute myocardial infarction 1.61 (CI: 1.43–1.81), congestive heart failure 3.84(CI: 3.56–4.14), stroke 1.11 (CI: 1.02–1.21), and pulmonary embolism 5.46 (CI: 4.25–7.02). The risk of hospitalization due to each cardiovascular cause was elevated in the COPD group. The risk ratio for cardiovascular mortality was 2.07 (CI: 1.82–2.36) and all-cause mortality was 2.82 (CI: 2.61–3.05).

Another case control study was done in the United Kingdom which compared COPD-free patients to COPD patients and the risks of developing an incident cardiovascular disease were assessed(4). Most cardiovascular diseases were more prevalent among COPD patients than among the comparison group of COPD-free patients. The relative risk estimates of developing an incident diagnosis of cardiac arrhythmia (OR 1.19, 95% CI 0.98–1.43), deep vein thrombosis (OR 1.35, 95% CI 0.97–1.89), pulmonary embolism (OR 2.51, 95% CI 1.62–3.87), myocardial infarction (OR 1.40, 95% CI 1.13–1.73), or stroke (OR 1.13, 95% CI 0.92–1.38), tended to be increased for patients with COPD as compared to COPD-free controls.

A retrospective analysis was done in Germany which compared the prevalence of comorbidities in patients with COPD and non-COPD patients. It showed that cardiovascular comorbidities were the most frequent, with over 70% of COPD patients having essential primary hypertension, and congestive heart failure was close to 20% in the COPD group, and had the strongest odds ratio of the cardio-related comorbidities. When compared to non-COPD, COPD patients were 2.345 times more likely to have congestive heart failure. Acute and recurrent myocardial infarction (coronary heart disease) also exhibited odds ratios close to two(5).

As per a prospective observational study done in India on 100 patients with COPD, 60% of the patients had CVD. Common CVDs were ischemic heart disease (21%), congestive heart failure (20%), stroke (5%), and arrhythmias (3%). The prevalence of CVD among patients with stages 1

and 2 COPD was 44.4%, stage 3 COPD was 61.5% and stage 4 COPD was 66.7% ($P=0.298$). Patients with COPD and CVD had a lower BMI as compared with those without CVD (13).

A prospective cross-sectional study was conducted in India to confirm various cardiovascular manifestations in COPD patients. In this study, a total of 37% of males and 4% of females were found to have cardiovascular complications. Cardiovascular manifestations were most commonly observed in the very severe stage of COPD (71.05%). In mild cases, no patient was diagnosed with cardiovascular manifestations, whereas 10.5% of patients with moderate disease and 38.7% patients with severe disease stage had CVD. The majority of the patients (48.5%) were in the age group of 60-70 years, out of which 20.5% had cardiovascular complications. Likewise, 14% out of 37% of patients were having cardiovascular complications in the age group of 50-60 years, and 6.5% out of a total of 29, or 14.5%, were having cardiovascular complications in their 40-50 year old age group(16).

A hospital-based cross-section study done in the same country indicated that there is a significant relationship between COPD and the presence of comorbid HTN and CVD (37.25% and 13.93%, respectively). It was also found that subjects with advanced COPD were more likely to have HTN (OR 1.6, 95% CI 1.4–1.9), and CVD (OR 2.5, 95% CI 1.9–3.0)(17).

Different studies have been done in Africa to assess the risk factors and CV morbidity in patients with COPD. One of the studies is done in Egypt. In this hospital-based study, a total of 100 patients with COPD were included, and of these, 60% of the patients had CVD. Common CVDs were ischemic heart disease (21%), congestive heart failure (20%), stroke (5%), and arrhythmias (3%). The prevalence of CVD among patients with stages 1 and 2 COPD was 44.4%, stage 3 COPD it was 61.5% and in stage 4 COPD was 66.7%. Significant risk factors for CVD were serum BNP levels, dyslipidemia, and systemic hypertension. In this study, patients with COPD and CVD had a lower BMI as compared with those without CVD(18).

Another cross-sectional study conducted in Egypt on 50 participants assessed the association between the severity of COPD and Arterial disease assessed by carotid IMT(19). In this study, there is a strong association between the severity of COPD and increased intima-media thickness

(IMT) on ultrasound imaging (in mild COPD, the mean SD IMT value was 1.00.2, moderate it was 1.50.2 and in severe COPD, it was 1.750.05 (P 0.001).

A literature search was conducted in sub-Saharan Africa(20). In this review, the prevalence of COPD was 22.2% in men and 16.7% in women, which is by far the highest prevalence. This is due to high levels of prior tuberculosis and occupational exposures and smoking habits. Three billion people and up to 90% of rural households in developing countries still rely on unprocessed biomass fuels for cooking and heating, which has a similar effect to tobacco smoking.

There is also a case-control study in Kenya which enrolled 31 cases and 65 controls, age greater than 35 years of women. Cases were defined as women at least 35 years old with isolated right heart failure (IRHF). Control subjects were similarly aged volunteers without IRHF. In this study among women of western Kenya, lower kitchen ventilation, airflow limitation, HIV, and occupational dust exposure were associated with IRHF.(21)

In our country, A community-based cross-sectional study was conducted in the Abeshge district, Southern Ethiopia. In this study, a total of 779 adults participated and the prevalence of COPD was 17.8%. The risk factors that influence the development of COPD are age, exposure to biomass smoke, cigarette smoking, and poor kitchen ventilation(22).

Another cross-sectional study was conducted to evaluate the prevalence of Chronic Obstructive Pulmonary Disease in patients successfully treated for pulmonary tuberculosis seen at Tikur Anbessa Specialized Hospital, Ethiopia. A total of 99 patients were included, and forty-one of 99 (41.4%) of the study participants had post-bronchodilator FEV1/FVC 70%. This is higher than expected and shows that risk factors for COPD in our country go beyond cigarette smoking(23).

2.2 Conceptual framework

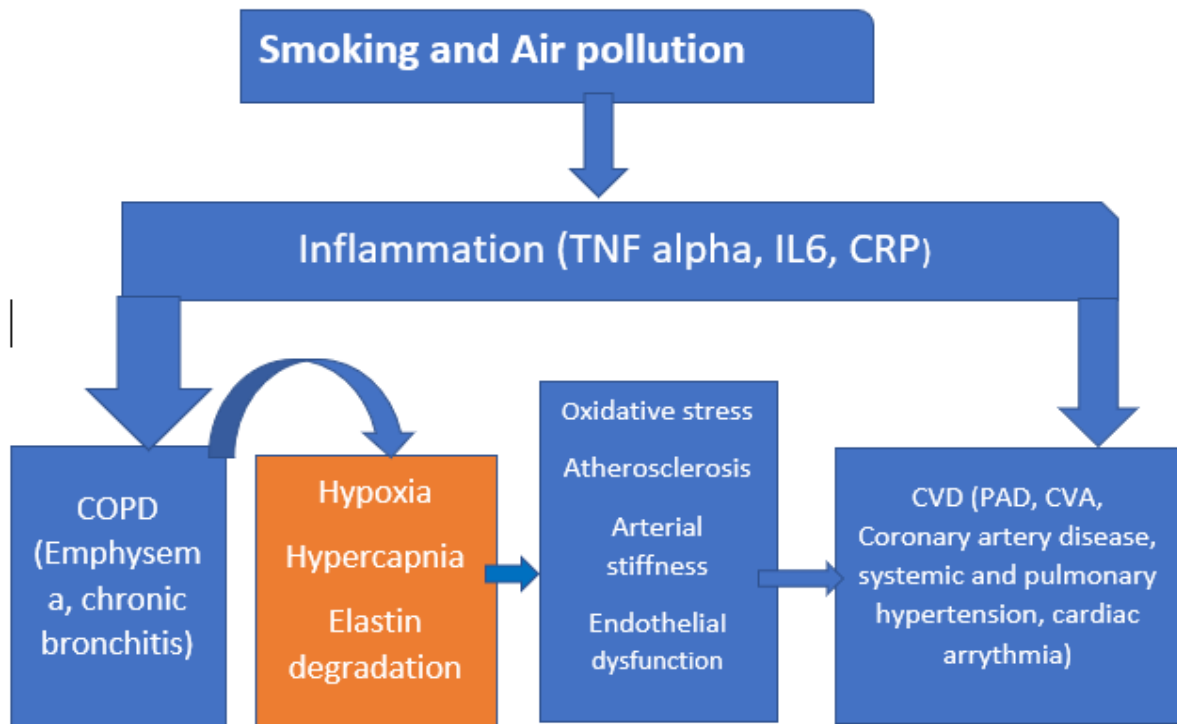


Figure 1 Conceptual framework showing the possible linkage between COPD and CVD

3. Objectives

3.1. General Objective

To assess the prevalence of cardiovascular comorbidity and associated factors of COPD among patients on follow up at SPHMMC and TASH from January 2016 to December 2021 G.C

3.2. Specific Objectives

1. To assess the prevalence of cardiovascular comorbidity in patients with COPD
2. To identify associated factors of cardiovascular comorbidity in COPD patients
3. To assess correlation between the severity of COPD and cardiovascular comorbidity

4. Methods and Materials

4.1. Study Design

An Institution-based cross-sectional, retrospective study was conducted among patients with COPD having follow-up at St. Paul's Hospital, Millennium Medical College, and Tikur Anbessa Specialized Hospital.

4.2. Study Area

Ethiopia, officially the Federal Democratic Republic of Ethiopia, is a country in the horn of Africa. It shares borders with countries like Eritrea, Djibouti, Somalia, Sudan, South Sudan and Kenya. With up to 110 million inhabitants, Ethiopia is the most populous landlocked country in the world and the second most populous nation in the African continent(11).

The study was conducted in the two of the largest hospitals of the country, namely SPHMMC and TASH. They are located in the heart of Addis Ababa, the capital city of Ethiopia. Both of them are referral hospitals serving more than 5 million for each. They are now the main teaching hospital for both clinical and preclinical training of most medical disciplines. They are also tertiary hospitals where specialized clinical services that are not available in other public or private institutions are given.

4.3 Study period

The study conducted from May 2021 to September 2022

4.4 Population

4.4.1 Source population

All COPD patients who are/ were on active follow-up in adult chest clinic of SPHMMC and TASH from January 1,2017- September 31, 2022

4.4.2 Study population

All spirometric confirmed COPD patient on follow-up in adult chest clinic of SPHMMC and TASH from January 1,2017- September 31, 2022 who fulfill the inclusion criteria

4.4.3.1 Inclusion criteria

- Patients with COPD who fulfill spirometric criteria for COPD diagnosis and on active follow up
- Had ECG and Echocardiography documentation

4.4.3.2 Exclusion criteria

- Those with non-conclusive spirometry result
- Those with no ECG and ECHO
- Those with non-reproducible spirometry

4.5 Sample size determination and sampling technique

All charts of COPD patients having active follow-up from January 1, 2016 to December 20, 2021 were reviewed. All charts that fulfill the inclusion criteria was included. Upon chart review, confirmed COPD patients on active follow up in St. Paul's Hospital, Millennium Medical College and Tikur Anbessa Specialized Hospital selected. We found 132 patients with COPD who fulfill our inclusion criteria.

4.6 Study variables

4.6.1 Dependent variables

- Cardiovascular disease in COPD

4.6.2. Independent variables

- Age
- Sex
- Occupation
- Smoking status
- Second hand smoke
- Chronic cough
- Sputum
- Wheeze
- Dyspnea
- Duration of follow-up
- GOLD stage

4.7 Data collection procedure

4.7.1 Data collection tool

The patients' charts were retrieved from the hospital's Archives room by using HMIS documentation as a guide to identify patients who have COPD as one of their diagnoses. After finding the charts, data about patients' demographics, clinical signs and symptoms of COPD and CVD, spirometry results, ECG and ECHO findings were collected by using a structured questionnaire.

4.7.2 Data collectors

Internal medicine residents were involved in data collection. Prior to data collection, the residents were trained on how to fill the questionnaire and followed closely for completeness and validity of the data by the investigator. The checklist pre-tested with 5% of the total sample size to check its variability and was assessed for its clarity, length and completeness.

4.7.3 Data collection technique

The data collected inside the hospital's card room during the study period. Incompletely filled questionnaires was refilled by the responsible residents.

4.8 Data processing and analysis

After the completeness of all the information on the questioners was checked, cleaned, coded, and entered using EPI DATA, then analyzed with the Statistical Package of Social Sciences (SPSS) for Windows. Categorical data analyzed as frequencies with percentages and continuous data analyzed as means with standard deviations. A simple binary logistic regression model used to calculate odd ratios (ORs) with 95% confidence interval (CI) to assess which demographic data and risk factors for cardiovascular comorbidity development. A P value < 0.05 was used to determine statistical significance. The results presented by the use of charts, tables, and texts.

4.9 Operational definitions

- ✓ **Confirmed COPD:** patients with confirmed irreversible spirometry result of FEV1/FVC of <0.7
- ✓ **Cardiovascular comorbidity:** at least one of CVD in patients with COPD which can be Ischemic heart disease, HTN, arrhythmia, peripheral vascular disease, ischemic stroke, pulmonary hypertension and heart failure(2)
- ✓ **Ischemic heart diseases:** clinically considered and started treatment for stable angina or patients with past history acute coronary syndrome or diagnosis made by ECG, ECHO, stress test or coronary angiography
- ✓ **Hypertension:** any blood pressure records greater than or equal to 130/85 mmHG at least two times or patients normal blood pressure if they are on medication or single measurement which is $\geq 180/110$ mmHg(24)
- ✓ **Arrhythmia:** is a rhythm is not sinus, documented or seen on ECG(25)
- ✓ **Peripheral vascular diseases:** diagnosis made by clinically, Ankle Branchial Index (ABI) or imaging (Doppler ultrasound or angiography)

- ✓ **Ischemic stroke:** documented diagnosis by clinically or imaging
- ✓ **Pulmonary hypertension:** Diagnosis by echocardiography or chest CT scan
- ✓ **Urban:** The one who live in city or town
- ✓ **Rural:** The one who live outside of city or town
- ✓ **Active follow up:** Patient who have follow up at least two times per year
- ✓ **Polycythemia:** hematocrit greater than 45% for female and 48% for male

4.10 Ethical consideration

Ethical clearance was obtained from Institutional Review Board of SPHMMC and TASH. All information that was obtained from the individual record is treated confidential. We use card numbers of the patient only to retrieve data. Information obtained was used only for the study purpose.

4.11 Dissemination of results

The results of this study will first be presented to the Internal medicine and public health departments during the research defense presentation. It will also be submitted to the hospital's cardiology and pulmonology units. Attempts will be made to publish the study in peer-reviewed journals and make presentations in scientific conferences.

5. RESULT

5.1 Socio- Demographic characteristics

A total of 132 patients, 80 from SPMMC and 52 from TASH were included in this retrospective cross-sectional study of which 90 were men and 42 were women. The average age in the study was 63 ± 12.1 years. The majority of the patients are non-smokers and the mean number of pack ears for smokers was 13.5. The majority of the patients lived in urban areas (77.3%) and had no occupational risk (84.1%) (table 1).

Table 1 Socio-demographic characteristics of patients with COPD, SPHMMC and TASH, Addis Ababa, Ethiopia, 2022

Variables	Subgroup	Value (132)	Percent (100%)
Sex	Male	90	68.2
	Female	42	31.8
10-years age groups	Below 30	2	1.5
	30-39	7	5.3
	40-49	14	10.6
	50-59	33	25.0
	60-69	44	33.3
	70-79	26	19.7
	Above 80	6	4.5
Marital Status of the patient	Married	93	70.5
	Single	6	4.5
	Divorced	10	7.6
	Widowed	23	17.4
Occupation of the Patient	Farmer	20	15.2
	Factory Worker	15	11.4
	Construction Worker	6	4.5
	Others	91	68.9
Residency	Urban	102	77.3
	Rural	30	22.0

5.2 Exposure risk of patient with COPD

The majority of the patients had no documented occupational risks; 84.1% and 82 (62.1%) patients had never smoked, respectively, while 20 (15.2%) were current smokers. Only 42 (31.8%) patients had biofuel exposure, and only 8 (6.1%) were second-hand smokers (Table 2).

Table 2 Exposure risk of patients with COPD, SPHMMC and TASH, Addis Ababa, Ethiopia, 2022

Variables	Subgroup	Value (132)	Percent (100%)
Occupational risk	Had No risk	111	84.1
	Had a risk	21	15.9
Smoking status	Never smoked	72	54.5
	Previously smoker	44	33.3
	Current smoker	16	12.1
Biofuel Exposure	Yes	42	31.8
	No	90	68.2
Second hand smoker	Yes	8	6.1
	No	124	93.9

5.3 Clinical characteristics and CVD co-morbidities

At the time of their initial presentation, nearly all COPD patients (98.5%) had a chronic cough that was accompanied by sputum production (95.5%) and dyspnea (65.9%). Only 21.2% of patients exhibited symptoms of heart failure, while 99.2% of those who had been examined had wheezing findings with a heart failure sign 19.7%. (Table 3).

The severity of airflow limitation tool was used to assess the severity of COPD. The majority of the patients were at GOLD stage 3 (43.9%) and GOLD stage 2 (30.3%). Only a small number of the patients had acute exacerbations that required admission (19.7%). More than 80% of the patients had a chest CT scan and the most common reported abnormality was emphysema (84.1%) (table 3).

The majority of the patients did not have morbidity (90.2%). The most frequently observed associated morbidity was diabetes mellitus, in 7 (5.3%) followed by chronic kidney disease (1.5%), retroviral infection (1.5%) and others (2.3%) (table 3).

Cardiovascular disease was observed in 73 (55.3%). The commonest cardiovascular disease was pulmonary hypertension, which accounted for 41 (31.1%), followed by diastolic heart failure, at 38 (28.8%) and hypertension (28%). Arrhythmias were reported in 12 (9.1%) of the COPD patients, of which atrial fibrillation is the most common (6.1%). There were around 5 (3.8%) ischemic strokes documented (figure 1).

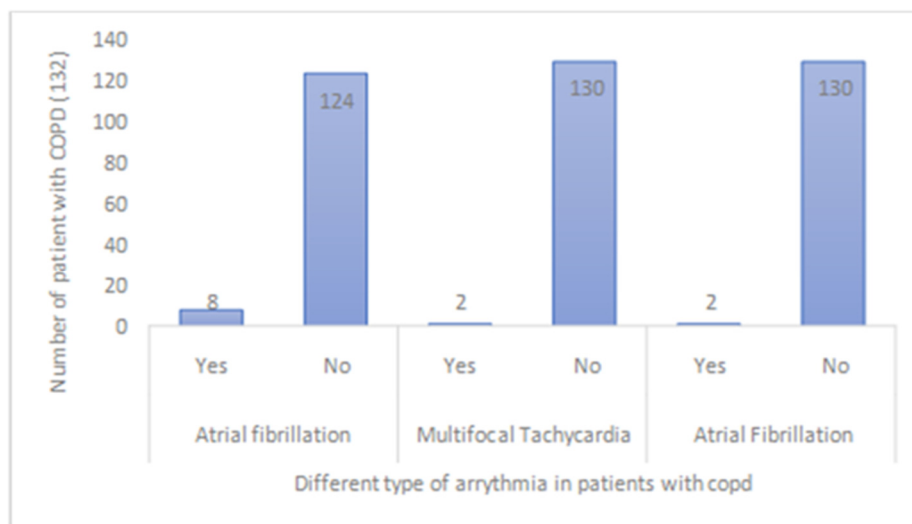


Figure 2: Frequency of Arrhythmias in of patients with COPD, SPHMMC and TASH, Addis Ababa, Ethiopia, 2022

Table 3 Clinical characteristics of patients with COPD, SPHMMC and TASH, Addis Ababa, Ethiopia, 2022

Category	Subgroup	Value (132)	Percent (100%)
Comorbidity	Yes	13	9.8
	Has no comorbidity	119	90.2
DM	Yes	7	5.3
	No	125	94.7
CKD	Yes	2	1.5
	No	130	98.5
Retroviral infection	Yes	2	1.5
	No	130	98.5
Others morbidity	Yes	3	2.3
	No	129	97.7
Chronic cough	Yes	130	98.5
	No	2	1.5
Sputum production	Yes	126	95.5
	No	6	4.5
Shortness of breath	Yes	87	65.9
	No	45	34.1
Heart failure symptom	Yes	28	21.2
	No	104	78.8
Admission for AE	Yes	26	19.7
	No	106	80.3
Wheeze	Yes	131	99.2
	No	1	0.8
Decrease air entry	Yes	73	55.3
	No	59	44.7
Heart failure sign	Yes	26	19.7
	No	106	80.3
Medication used	Aminophylline	0	0
	SABA only	59	44.7
	ICS and LABA	73	55.3
COPD severity	Stage 1	13	9.8
	Stage 2	40	30.3
	Stage 3	58	43.9
	stage 4	21	15.9
Chest CT scan Finding	Has no chest CT scan	16	12.1
	Emphysematous	111	84.1
	Fibrosis	4	3.0
	Others	1	0.8

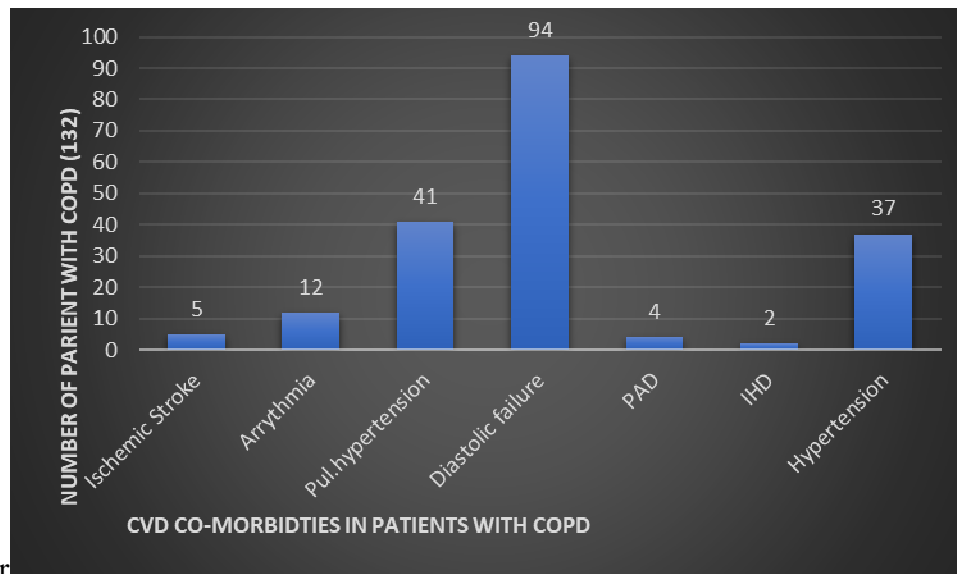


Figure 3: Cardiovascular comorbidities in of patients with COPD, SPHMMC and TASH, Addis Ababa, Ethiopia, 2022

5.4 Electrocardiogram and Echocardiography finding Results

At least 31.8% of patients with COPD had ECG abnormalities in which right axis deviation was accompanied by 21.2%, P pulmonale 12.1%, right ventricular hypertrophy 6.8%, poor progression of R wave 6%, atrial fibrillation 6.1%, MAT 1.5%, and atrial flutter 1.5%. Upon echocardiography examination, 31.1% of patients had pulmonary hypertension and diastolic heart failure, of which the majority were grade 1(25.8%). 11.4% of patients had a feature of right-side heart failure with a TAPSE less than 17 and an increased right atrial dimension. None of the patients had heart failure with a reduced ejection fraction (table 4).

Table 4 ECG and Echocardiography finding of patients with COPD, SPHMMC and TASH, Addis Ababa, Ethiopia, 2022

Category	Subgroup	Value (132)	Percent (100%)
Cardiovascular diseases	Present	73	55.3
	Absent	59	44.7
Stroke history	Yes	5	3.8
	No	127	96.2
PAD	Yes	4	3.0
	No	128	97.0
ECG finding	Normal	90	68.2
	Abnormal	42	31.8
Right Axis Deviation	Yes	28	21.2
	No	104	78.8
P pulmonale	Yes	16	12.1
	No	116	87.9
Right ventricular hypertrophy	Yes	9	6.8
	No	123	93.2
Poor progression of R wave	Yes	8	6
	No	124	94
Left ventricular hypertrophy	Yes	3	2.3
	No	129	97.7
Atrial fibrillation	Yes	8	6.1
	No	124	93.9
Multifocal Atrial Tachycardia	Yes	2	1.5
	No	130	98.5
Atrial flutter	Yes	2	1.5
	No	130	98.5
RBBB	Yes	0	0
	No	132	100

LBBB	Yes	2	1.5
	No	130	98.5
Left Ventricular Dimension	Normal	131	99.2
	Increase	1	0.8
Left ventricular hypertrophy	Yes	11	8.3
	No	121	91.7
Right atrial dimension	Normal	111	84.1
	Increase	21	15.9
Ejection fraction	Preserved	132	100
	Reduced	0	0
TAPSE	Greater than 17	117	88.6
	Less than 17	15	11.4
Pulmonary Hypertension	Yes	41	31.1
	NO	91	68.9
Diastolic heart failure	NO	94	71.2
	Grade 1	34	25.8
	Grade 2	3	2.3
	Grade 3	1	0.8
Wall motion abnormality	Yes	2	1.5
	NO	130	98.5

5.5 Factors associated with cardiovascular diseases

A logistic regression was used to ascertain the effect of different independent variables on cardiovascular diseases in COPD. In bivariate logistic regression analysis, age, severity stages, comorbidity, admission history for acute exacerbation and the presence or absence of polycythemia were associated with CVD comorbidity with a P value <0.2. Multivariable binary logistic regression model was applied to identify factors associate for cardiovascular comorbidity in patients with COPD (table 3).

After adjusting other variables using multivariate binary logistic regression age above 75 years, 5.343(95% CI, 1.66-17.57), previous smoker, 6.952(95% CI, 1.531-31.57), COPD severity stage 3, 16.86 (95% CI, 7.289-16.520) and COPD stage 2, 9.158(95% CI, 7.72-15.2692) were significantly associated with cardiovascular comorbidity. Patients whose age were above 75 years had more than fivefold increase risk of cardiovascular comorbidity compared with patient whose age was between 40 years and 75 years, 5.343 (95% CI, 1.626-17.557) (table 3).

Patients stage 3 COPD had sixteen times increase risk of cardiovascular comorbidity compared with stage 2 16.86 (95% CI, 7.289-16.520). Similarly risk of cardiovascular comorbidity was ninefold higher in COPD stage 2 as compared with stage 1 COPD 9.158(95% CI, 7.72-15.269). The risk of cardiovascular comorbidity was higher in a patient who had polycythemia as compared with pt with normal hematocrit level 32.4 (95% CI, 12 -87.0) (table 3).

Table 5 Bivariate and Multivariable logistic regression analyses to Associated factors of Cardiovascular comorbidity of patients with COPD, SPHMMC and TASH, Addis Ababa, Ethiopia, 2022

Variable		Cardiovascular diseases		95% CI		P-value
		Present	Absent	COR	AOR	
Sex of the patient	Male	48	42	1.287 (0.612 - 2.703)		
	Female	25	17	1.00		
Residency	Urban	54	48	1.85(0.242-1.208)		
	Rural	18	12	1.00		
Occupation of the Patient	Farmer	13	7	0.628 (0.229 - 1.72)		
	Factory Worker	7	8	1.333(0.446 - 3.985)		
	Construction Worker	4	2	0.583 (0.1023.346)		
	Others	49	42	1.00		
Age groups	Below 40	3	6	1.00		
	40-75	46	44	2.55(1.095 - 25.985) *	5.155(0.739-35.967)	.098
	Above 75	24	9	5.33 (11.068 - 16.091) *	5.343(1.626-17.557) **	.006
Smoking status	Never smoked	29	43	1.00	1.00	
	Previously smoker	32	12	3.95(1.306 - 15.153) *	6.952(1.531-31.570) **	.012
	Current smoker	12	4	1.125 (0.303 - 4.177) *	1.736(0.356-8.478)	.495
Second hand smoker	Yes	6	4	0.392 (0.076 - 2.017)		
	No	67	57	1.00		

Polycythaemia	Yes	63	9	35(13.214-92.703) *	32.4(12 -87.0)	.0001
	No	10	50			
COPD severity	Stage 1	4	13			
	Stage 2	12	29	1.344 (6.518 - 64.26) *	9.158(7.72-15.2692) **	.0001
	Stage 3	37	16	4.833 (5.813-41.8) *	16.861(7.289-16.520) **	.0001
	stage 4	20	1	8.65(1.067-70.080) *	7.256(0.84 - 62.59)	.071
Admission for AE	Yes	21	6	3.567(1.333 - 9.549) *	.437(0.109 - 1.76)	.241
	No	52	53	1.00		
Comorbidity	Yes	16	8	1.92(1.066-7.843) *	0.39(0.102 - 1.488)	.168
	No	55	53	1.00		

*Bivariable association

** Multivariable significant

6. DISCUSSION

Cardio-vascular diseases are one of the most frequently reported co-morbidities in patients with COPD and contribute to the overall disability and mortality (26). Among them, arterial hypertension is one of the most common comorbidities, affecting 40–60% of COPD patients (27). The mechanisms by which COPD may be a risk factor for CVD are not fully understood, but it is considered that airflow limitation and particularly hyperinflation affect cardiac function and that inflammatory mediators in circulation may initiate or worsen comorbidities such as ischemic heart disease, ischemic stroke, arrhythmia, and heart failure (28,29). These were also the most frequent comorbidities present in our study, which adds support to the above-mentioned considerations. In our study, the prevalence of cardiovascular disease was 55.3%, which is consistent with the above-mentioned study.

In a systematic review of 25 studies from 7,322 citations in Medical Literature Analysis and Retrieval System Online (MEDLINE) to assess the prevalence of cardiovascular comorbidity in COPD, the results showed that its prevalence ranged from 28% to 70%, which is similar to our study (30–32). We found that cardiovascular diseases range from 1.5% for IHD to 55.3% for hypertension. It could also be due to the fact that COPD and CVD share a number of risk factors, including smoking and aging.

Our study confirms that with the advancement of COPD, the comorbidities for cardiovascular disease increase. This data is similar to the results of other studies. A prospective study conducted in Greece among 609 patients shows that the presence of cardiovascular diseases is related to higher mortality in patients with advanced COPD (27). In the above mentioned study, there was also an association between the severity of airflow limitation and CVD risk, which is consistent with our study (33).

A retrospective observational study done in Bulgaria showed that more than 80% of them had cardiovascular comorbidity, of which hypertension was the most common cardiovascular comorbidity for COPD. In this study, the most frequent comorbidities were hypertension, heart failure, and ischemic heart diseases, and they had a strong association with the severity of the diseases, which is similar to our study(34).

We observed that the prevalence of ischemic heart disease is 1.5%, and arrhythmia 9%. The ischemic heart disease finding in our study is lower than a similar study conducted in Bulgaria, 37.5%, which could be due to the low number of smokers (38%) in our study as well as a small pack year for smokers (13.5) as compared with the above study (38.2). Arrhythmia prevalence is 12.6% in this study, which is consistent with our study and there was a strong association between cardiovascular prevalence and severity of disease assessed by GOLD staging(35).

Additionally, we discovered that the prevalence of ischemic strokes is 3.8%, which is comparable to a study done in Egypt that shown that as illness severity rose, intima-media thickness (IMT) on carotid ultrasound imaging similarly increased in comparison to control (P 0.0001)(19).

In our study, there was a strong association between patients with high hematocrit levels and cardiovascular diseases, 32.4 (95% CI, 12-87.0) as compared with patients with normal hematocrit, which is similar to a study done on adverse cardiovascular events of secondary polycythemia. In this study, people with polycythemia had a higher risk of major adverse cardiovascular events than those who had a normal hematocrit (95% CI 1.13–1.61, $p < 0.001$)(36).

7. Limitations of the study

Our study is the first study performed in two institutions, and the results are considered relevant for the total COPD population in Ethiopia. As a limitation, this was done in a tertiary center where more advanced cases have been followed, which may overestimate the outcome. The data was collected retrospectively, which means it might overestimate cardiovascular disease as ECG and echocardiography are usually done for the indication and not as screening. A small sample size is another limitation of the study due to the fact that most of the patients were diagnosed clinically and did not screen for CVD.

8. Conclusion and recommendation

The prevalence of cardiovascular comorbidity is very high in patient with COPD and pulmonary hypertension, arterial hypertension, ischemic heart disease, arrhythmia, ischemic stroke and heart failure are prevalent in this study. With the progression of COPD, the number of cardio-vascular co-morbidities per patient increases. We have to screen for CVD for COPD patient who has severe spirometry finding but we have to do prospective study.

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8. Annexes

8.1 ANNEX I: Information Sheet

Research Title: Assessing the prevalence of cardiovascular comorbidity and associated factors among patients with COPD At SPHMMC and TASH, FIVE YEARS REVIEW

Principal Investigator: Sintayehu Dagnaw (MD, Internal Medicine Resident)

Phone (Mobile): +251918164052

Advisors: Dr. Henoc Benti (internist, consultant cardiologist at SPMMC)

Mr. Samson Zegeye (MPH)

Sponsor: St. Paul's Hospital Millennium Medical College

8.2 ANNEX II: Data Collection, structured questionnaire

Make circle (O) or write phrases or words where necessary

Sr. No	Questions	Coding Classifications	Skip
1	MRN	_____	
2	Age	_____	
3	Sex	1. Male 2. Female	
4	Address	1. Urban 2. Rural	
5	Occupation	1. Farmer 2. Factory worker 3. Construction worker 4. Others	
6	Relationship status ¹	1. Married 2. Single 3. Divorced 4. Widowed	
7	Smoking status	1. never smoked 2. previous smoker 3. current smoker	
8	If current or previous smoker, what was the pack year(write)		
9	Is there anyone who smokes in your house?	1. Yes 2. No	
10	Exposure to biofuel combustion?	1. yes 2. No	
11.	Patient Symptoms Questions		

	Did the patient have chronic cough	1. Yes 2. No	
	Sputum production	1. Yes 2. No	
	Shortness of breath	1. Yes 2. No	
	Exercise in tolerance	1. Yes 2. No	
	Body swelling	1. Yes 2. No	
	Palpitation	1. Yes 2. No	
	Orthopnea	1. Yes 2. No	
	Paroxysmal-nocturnal dyspnea	1. Yes 2. No	
	Body weakness	1. Yes 2. No	
	Claudication	1. Yes 2. No	
	Facial deviation	1. Yes 2. No	
	Failure to communicate	1. Yes 2. No	

12.	Physical examination Questions		Skip
	was there any wheeze?	1. Yes 2. No	
	Decrease breath sound	1. Yes 2. No	
	Cyanosis	1. Yes 2. No	
	Body swelling	1. Yes 2. No	
	Any murmur	1. Yes 2. No	
	If yes type of murmur	1. Murmur of TR 2. Murmur of MR 3. Murmur AR 4. MS 5. AS	
	Jugular veinous pressure	1. Flat 2. Elevated	
	Pulse rate	1. Regular 2. Irregularly regular 3. Irregularly irregular	
13.	Any comorbidity	1. Hypertension 2. DM 3. Chronic liver disease 4. Chronic kidney diseases 5. . Retroviral infection 6. 6. Other (mention).....	
14.	Hematocrit		
15.	Chest x-ray finding suggestive of (if done)	1. Emphysematous 2. . Bronchiectasis	

		3. Fibrosis 4. . Pneumonia 5. Cardiomegaly 6. Other (mention)													
16.	Chest CT scan finding suggestive of (if done)	1. . Emphysematous 2. Bronchiectasis 3. Fibrosis 4. Pneumonia 5. Other (mention)													
17,	When did the patient first come to the follow-up clinic? Write														
18.	Total duration of follow-up in the clinic														
19.	Was the patient previously admitted to hospital?	1. Yes 2. No													
20.	If yes to the above question, how long was the duration of stay in hospital? Write														
21.	Spirometry finding pre and post bronchodilator?	<table border="1"> <thead> <tr> <th>Parameter</th><th>Prebronchodilator</th><th>Post-bronchodilator</th></tr> </thead> <tbody> <tr> <td>FEV1</td><td></td><td></td></tr> <tr> <td>FVC</td><td></td><td></td></tr> <tr> <td>FEV1/FVC ratio</td><td></td><td></td></tr> </tbody> </table>	Parameter	Prebronchodilator	Post-bronchodilator	FEV1			FVC			FEV1/FVC ratio			
Parameter	Prebronchodilator	Post-bronchodilator													
FEV1															
FVC															
FEV1/FVC ratio															
22.	GOLD stage of the pt	1. stage 1 2. Stage 2 3. Stage 3 4. Stage 4													

23.	ECG finding,	1. Normal sinus 2. Abnormal	
24.	If abnormal what is the finding		
	Right Axis Deviation	1. Yes 2. No	
	P pulmonale	1. Yes 2. No	
	Right ventricular hypertrophy	1. Yes 2. No	
	Poor progression of R wave	1. Yes 2. No	
	Left ventricular hypertrophy	1. Yes 2. No	
	Atrial fibrillation	1. Yes 2. No	
	Atrial flutter	1. Yes 2. No	
	Multifocal atrial Tachycardia	1. Yes 2. No	
	Others (mention please)		
25.	ECHO findings analysis		
	Left Ventricular Dimension		
	Left ventricular hypertrophy		
	Right atrial dimension		

	Ejection fraction		
	TAPSE	1. < 17 2. >= 17	
	Pulmonary Hypertension	1. YES 2. NO	
	Diastolic failure	1. Yes 2. No	
	If diastolic failure	1. Grade 1 2. Grade 2 3. Grade 3	
	Wall motion abnormality	1. Yes 2. No	
26.	Is there any documentation of PAD?	1. Yes 2. No	
27.	If yes, how was it diagnosis	1. Clinically 2. Arterial Doppler 3. CT angiography	
28.	what medication/s did the patient ever used?	1. SAMA and SABA 2. SABA only 3. SAMA only 4. ICS and LABA 5. ICS, LAMA and LABA	
28	Did the patient ever used aminophylline?	1. Yes 2. No	

8.3 ANNEX III: ANNEX III: Declaration

I the undersigned resident that this thesis is my original work, in partial fulfillment of the requirement for certificate of specialty in internal medicine. I also declare that it has never been presented in this or any higher institution and all the resources and materials used in the research work have duly acknowledged.

Name of the Resident: _____

Signature:_____

Date: _____

Approval of Advisors

This research work has been submitted for examination with my approval

Name of Public Health Advisor:_____

Signature:_____

Date:_____

Name of Clinical Advisor: _____

Signature:_____

Date: _____