



St. Paul Hospital Millennium Medical College

Graduate Study Program

Prevalence of Pulmonary Hypertension and associated factors at St. Paul Hospital Millennium Medical College

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Addis Ababa, Ethiopia

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List of Acronyms

SPHMMC - Saint Paul Hospital Millennium Medical College

PVR – Pulmonary Vascular Resistance

HTN – Hypertension

DM – Diabetes Mellitus

PAH – Pulmonary Arterial Hypertension

HHD – Hypertensive Heart Disease

CRVHD – Chronic Rheumatic Valvular Heart Disease

DCMP – Dilated Cardiomyopathy

IHD – Ischemic Heart Disease

Deg VHD – Degenerative Valvular Heart Disease

HIV – Human Immunodeficiency Virus

PTB – Pulmonary Tuberculosis

ILD – Interstitial Lung disease

COPD – Chronic Obstructive Pulmonary Disease.

OPD - Outpatient Department

PH – Pulmonary Hypertension

PHLHD – Pulmonary Hypertension due to Left Heart Disease.

SSA - Sub-Saharan Africa

LMIC - Low-to-middle income Countries

CTD – Connective Tissue Disease

SLE – Systemic Lupus Erythematosus

RVI – Retroviral Infection

RA - Rheumatic Arthritis

CLD – Chronic Liver Disease.

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Abstract

Background: Pulmonary Hypertension is a substantial global health issue. It is by no means rare, affects all age groups and associated with increased mortality. It is a pathologic condition that occurs due to many underlying conditions. Many of the known risk factors are endemic in Ethiopia. Despite this, data on prevalence and causes of Pulmonary Hypertension are scarce in Africa and non-existent in Ethiopia. Knowing the burden and etiologies of pulmonary HTN will help establish preventive and therapeutic strategies.

Objectives: The main objective of this study is to assess the prevalence & associated factors of pulmonary hypertension at St. Paul Hospital Millennium Medical College.

Methods: Institution based, analytic cross sectional study conducted by including adult patients with echocardiographic findings of Pulmonary Hypertension. A PASP value ≥ 35 mmHg was considered as pulmonary hypertension. Patients with different or inconsistent echocardiographic finding were excluded. Sample size was determined by single population proportion formula considering 50% prevalence of Pulmonary HTN, with the assumption of 95% confidence interval(CI), 5% margin of error & 10% non-response rate to get a final sample size of 343 and systematic sampling technique was used. Approval from the Institution Review Board was obtained. A structured questionnaire was used to collect data on sociodemographic and associated factors. After data was collected, it was entered and analyzed with SPSS 25. Descriptive statistics of categorical variables was presented by frequencies and percentage and mean with standard deviations was estimated for continuous variables. Bi-variable and multivariable regression analysis were used to test for associations between independent variables and pulmonary hypertension.

Results: Data was obtained for a total of 315 patients with 92% response rate. Pulmonary Hypertension was found in 98 (31.1%) of the patients with a mean age of $49.41 \pm$ SD of 18.167. Majority (57.1%) of the patients are between 31-60yrs of age, the peak age is 31-40yrs (27.6%) and 68(69.4%) are female. Majority of patients 76(77.6%) have moderate to severe pulmonary hypertension and 23 (23.5%) patients have right ventricular systolic dysfunction. Of these 56(57.1%) patients are NYHA Class III patients. Cardiac conditions account for the majority of the cases (65.3%), followed by lung conditions (24.5%), chronic thromboembolism(7.1%), Pulmonary Arterial Hypertension(2%) and others(1%). The major causes of pulmonary hypertension are HHD (21.4%), CRVHD(18.4%), DCMP(14.3%), COPD(13.3%) and Thromboembolism(6.1%). The associated factors are female gender ($P=0.01$), COPD($P=0.001$), Thromboembolism($P=0.008$), DCMP($P=0.001$) and CRVHD($P=0.001$), HHD(0.001). However, bronchial asthma, ILD and IHD were not significantly associated with pulmonary hypertension.

Conclusion: Generally, pulmonary hypertension is common in patients visiting cardiac and chest clinics of St. Paul Hospital Millennium Medical College and it occurred at an earlier with a peak age of 31-40yrs and female gender is one of the determining factors. Majority of patients are Class III patients and have moderate to severe pulmonary hypertension. The leading causes are cardiac and lung conditions, the major ones being HHD, CRVHD, DCMP, COPD and Thromboembolism. Further study is needed to describe the mortality and outcome of pulmonary hypertension.

1. Introduction

1.1 Background

Pulmonary hypertension (PH) is a hemodynamic and pathophysiological condition characterized by abnormally elevated pressures in the pulmonary vasculature. It is defined by a mean pulmonary artery pressure at rest of 25 mm Hg or more and PVR ≥ 3 WU, measured by right heart catheterization(1,2).

Cardiac catheterization is widely considered the 'gold standard' for the diagnosis of pulmonary hypertension. However, its routine use is limited due to its invasive nature, inherent complications and incurring cost. Transthoracic doppler echocardiography is a non-invasive tool used in clinical practice for screening and monitoring of PH progression. Although some studies describe under- or overestimation of pulmonary arterial pressures by echocardiography, a meta-analysis has shown it to have good sensitivity (87%), reasonable specificity(79%) and a correlation of 0.9 with invasively acquired measurements(3,4,5).

In echocardiograms, the pulmonary artery systolic pressure is the most frequently used parameter. The estimation of systolic PAP is made based on the peak tricuspid re-gurgitation velocity (TRV) taking into account the right atrial pressure (RAP) as described by the simplified Bernoulli equation. A PASP value of greater than or equal to 35 mm Hg is considered Pulmonary Hypertension and classified as mild(35-50 mm Hg), moderate(50-70mm Hg) and Severe(>70mm Hg) (2,3). Pulmonary Hypertension is also defined based on CT scan as an increased PA diameter (≥ 29 mm) and main pulmonary artery to ascending aorta diameter ratio (≥ 1.0) or segmental artery to bronchus ratio >1 in three or four lobes on chest CT scan(6,7).

According to WHO pulmonary hypertension is divided into five groups based on pathophysiological, clinical, and therapeutic considerations: Pulmonary Arterial Hypertension; pulmonary hypertension due to left-sided heart disease; pulmonary hypertension due to lung disease or hypoxia; chronic thromboembolic pulmonary hypertension; and pulmonary hypertension with unclear or multifactorial mechanisms(8).

The WHO also describes four functional classifications which describe the severity of Pulmonary Hypertension. These are Class I (asymptomatic), Class II (symptomatic at ordinary activities), Class III (symptomatic at subordinary activities) and Class IV (symptomatic at rest). This classification is clinically important during management and follow up of patients(9).

1.2. Statement of Problem

Pulmonary hypertension is a substantial global health issue. It is a devastating, progressive disease leading to right heart failure and death.. All age groups are affected with rapidly growing importance in elderly people, particularly in countries with ageing populations. The underlying etiology of PH could vary from region to region. In almost all parts of the world, left-sided heart and lung diseases have become the most frequent causes of pulmonary hypertension. Although left ventricular heart disease is the most common cause globally, the main contributing risk factors in LMICs are chronic infectious diseases especially human immunodeficiency virus (HIV) and schistosomiasis(10).

The exact global burden of PH remains unknown. Present estimates suggest a pulmonary HTN prevalence of about 1% of global population, which increases up to 10% in individuals aged more than 65yrs. Additionally, the increasing age of populations worldwide is leading to a marked change in the distribution and phenotypes of patients presenting with pulmonary hypertension. It is estimated that about 80% of patients with PH live in LMICs where PH is known to be highly associated with CHD, rheumatic heart disease, schistosomiasis and HIV(15). Despite these risk factors for PH, LHD still remains the dominant risk factor for PH (PH-LHD), followed by chronic lung disease and hypoxia (PH-LD) in both LMICs and high-income countries (HICs). Contrary to what is observed in HICs where PH is predominant in the elderly above the ages of 65 years, it is very common in younger individuals in LMIC. The high prevalence of PH-LHD in LMICs is expected due to a higher prevalence of uncontrolled hypertension which is also a principal cause of heart failure according to the sub-Saharan acute heart failure (THESUS-HF) study, a study conducted in nine African countries (11,19).

The development of PH is almost invariably associated with worsening of symptoms & increased mortality, independent of the underlying disease. Mortality of PH is high in both LMICs and HICs. A South African study identified PH as one of the commonest causes of death accounting for 31% of total cardiovascular deaths(16). A 5-year mortality rate of 26% was recorded in a Swiss cohort of PAH, CTEPH and PH-LD patients (27). Similar mortality rates have been recorded in SSA in a short observational period of only 6 month (18,26). In PAPUCO, it is found a high 6-month mortality of 21% in adults associated with functional limitations at time of presentation(13). A study in Cameroon reported 6-month mortality rates of 28% (31).

PH is also associated with shortened life expectancy and overall survival. For instance, pulmonary arterial hypertension (PAH) has a median survival of 2.8 years if the patient is not treated with improved treatment regimens. Following the introduction of PAH improved treatment regimens, the prognosis of PAH has improved considerably, with 1-, 3-, and 5-year survival rates of 85%, 68%, and 57%, respectively. The reasons for high mortality rates in LMICs are lack of access to health care, infrastructure and equipment to diagnose PH within the health care system, and availability of specific treatment for PH. Early diagnosis and appropriate treatment of PH are therefore paramount in order to improve its outcomes(24).

Recent advances have been made in the development of effective treatments, especially for PAH and CTEPH. Vasodilators, endothelin receptor antagonists, phosphodiesterase (PDE) inhibitors (e.g., sildenafil) and high-dose calcium channel blockers (e.g., amlodipine) are the most commonly prescribed drug, with the latter two are available in our country. CTEPH is a potentially curable disease when treated with pulmonary thromboendarterectomy (PTE)(24,25).

1.3 Rationale of the study

The epidemiological and associated factors of diseases differ from country to country and from continent to continent. It is why precise knowledge of region-specific epidemiology of PH is crucial to implement effective preventive strategies and for contextualized clinical guidelines. Data on prevalence and causes of pulmonary hypertension are scarce in Africa and non-existent in Ethiopia. Many known risk factors for PH are endemic in Ethiopia, including human immunodeficiency virus (HIV) infection, rheumatic heart disease, hypertension, chronic hepatitis B and C, tuberculosis, and schistosomiasis(35,36,37). Despite this the epidemiology of PH remains poorly described in Ethiopia. This study aims to assess the prevalence and associated factors of pulmonary hypertension. The cause of pulmonary hypertension is of critical importance as it defines subsequent treatment. So, knowing the burden and causes of pulmonary HTN will help establish preventive and therapeutic strategies and will also be an input for further researches.

2. Literature Review

About 80% of patients with pulmonary hypertension live in the developing world, where heart disease and lung disease have become the most frequent causes of pulmonary hypertension, but other disorders such as schistosomiasis, HIV, or sickle cell disease continue to play an important part. Hence, in industrialised countries, pulmonary hypertension affects mainly elderly people whereas mostly young people are diagnosed in the developing world (10,13).

A population-based study of 3381 participants in Rotterdam, Netherlands, reported echocardiographic signs suggestive of pulmonary hypertension in 2.6% of the overall population. The prevalence of echocardiographic signs of possible pulmonary hypertension was higher in older individuals (8.3% in those older than 85 years compared with 0.8% in those aged between 65 years and 70 years). Factors independently associated with higher ePASP were older age, higher BMI, left ventricular diastolic dysfunction, COPD and systemic hypertension(12).

A population based study done in Armadale, in western Australia, 32% had pulmonary hypertension with left heart disease being the commonest cause(68%), 9% respiratory causes, 2% had CTEPH, 2.7% had multifactorial causes, and 15% had no known cause for PH. The 2.7 % of patients were found to have PAH after confirmed by RHC. The mean time to death from diagnosis was 4yrs. Risk of death increased with PHTN severity. Severe pulmonary hypertension shortened lifespan by an average of 1.1yrs compared with mild pulmonary hypertension. Those with PHTN from left heart disease had the worst prognosis and those with idiopathic PAH receiving disease-specific management had the best prognosis(82% survival at the end of study)(21).

A review on PH in Africa, findings showed that the prevalence of PH varies widely across different population: 9.8% in patients presenting with cardio-respiratory complaints, 10% in HIV-infected patients, 32.9% in patients with heart failure, 23.2% in patients on hemodialysis, 12.9% in patients with RHD, 37% to 53% in patients with sickle cell disease 62.7% in patients with chronic obstructive pulmonary disease; 25.4% in patients with systemic lupus erythematosus; 68.7% in patients with cardiac surgery; and 7.4% in patients with systemic sclerosis(13,22).

A study on Pulmonary hypertension in low- and middle-income countries with focus on sub-Saharan Africa showed that PH is a common clinical syndrome in SSA and other LMICs and many of the identified risk factors for PH are hyperendemic in those regions. These include LHD, lung disease, HIV and schistosomiasis. The intersection of communicable and non-communicable diseases in SSA with late presenting patients of the two entities contributing to a broad range of PH in the region (15).

According to the Pan African Pulmonary Hypertension Cohort (PAPUCO) Registry, multinational cohort registry of 209 consecutive patients (97% of African descent) from 9 specialist centres in 4 African countries, adults comprised 16% pulmonary arterial hypertension, 69% PH due to left heart disease, 11% PH due to lung disease and/or hypoxia, 2% chronic thromboembolic pulmonary hypertension, and 2% PH with unclear multifactorial mechanism. Most adults had advanced disease, 66% WHO functional Class III-IV and overall 6 month mortality was 21% (13).

A study done in a rural area, Shisong Cardiac Centre (SCC) in Cameroon showed a crude prevalence of 15.6%. Co-morbidities included long smoke (80.7%), hypertension (52%), family history of cardiovascular disease (50.0%), diabetes (31.3%), alcohol abuse (21.3%) and HIV infection (8.7%). They included 7.3% mild, 29.3% moderate and 63.4% severe PH cases. The peak prevalence of PH was noticed between 60 and 69 years. Overall, 70% presented in WHO functional class III/IV. PH due to left heart disease (PHLHD) was the commonest (64.7%), and rheumatic valvular disease accounted for 36.1%. The six-month mortality rate was 28% (30).

Another study from specialized centers in Douala, Cameroon revealed a pulmonary hypertension prevalence of 7.0% (130 out of 1855 patients). All were of black African descent, and 71 (54.6%) were women. The peak age was between 55-64yrs of age. Of these 23.1% had mild, 45.4% had moderate and 31.5% had severe PH. Of these 78.5% had PH caused by left heart disease, 8.4% had PAH, 6.9% had multifactorial causes, 5.4% had lung disease, and 0.8% had chronic thromboembolic PH. The majority (76.9%) of patients had moderate or severe PH. The most frequent risk factors/comorbidities were hypertension, diabetes, alcohol abuse and smoking. The overall mortality rate was 20.3% (31).

A study done in patients attending echocardiology clinic of Benghazi Medical Center, in eastern part of Libya showed pulmonary hypertension prevalence of 8% (50 out of 645 patient). Majority (64%) of them were female. Of these, 14% of patients had ischemic heart disease, 6% of patients had chronic lung disease, 6% had rheumatic heart disease, 2% had SLE, 2% had sickle cell anemia and 1% had thalassemia(33).

According to study done on echocardiographic abnormalities among adult cardiac patients at Ayder Hospital, Mekelle University showed that pulmonary hypertension of any etiology was diagnosed in 32.6% of cases from a total of 1028 echocardiograms reviewed (34).

3. Conceptual Framework

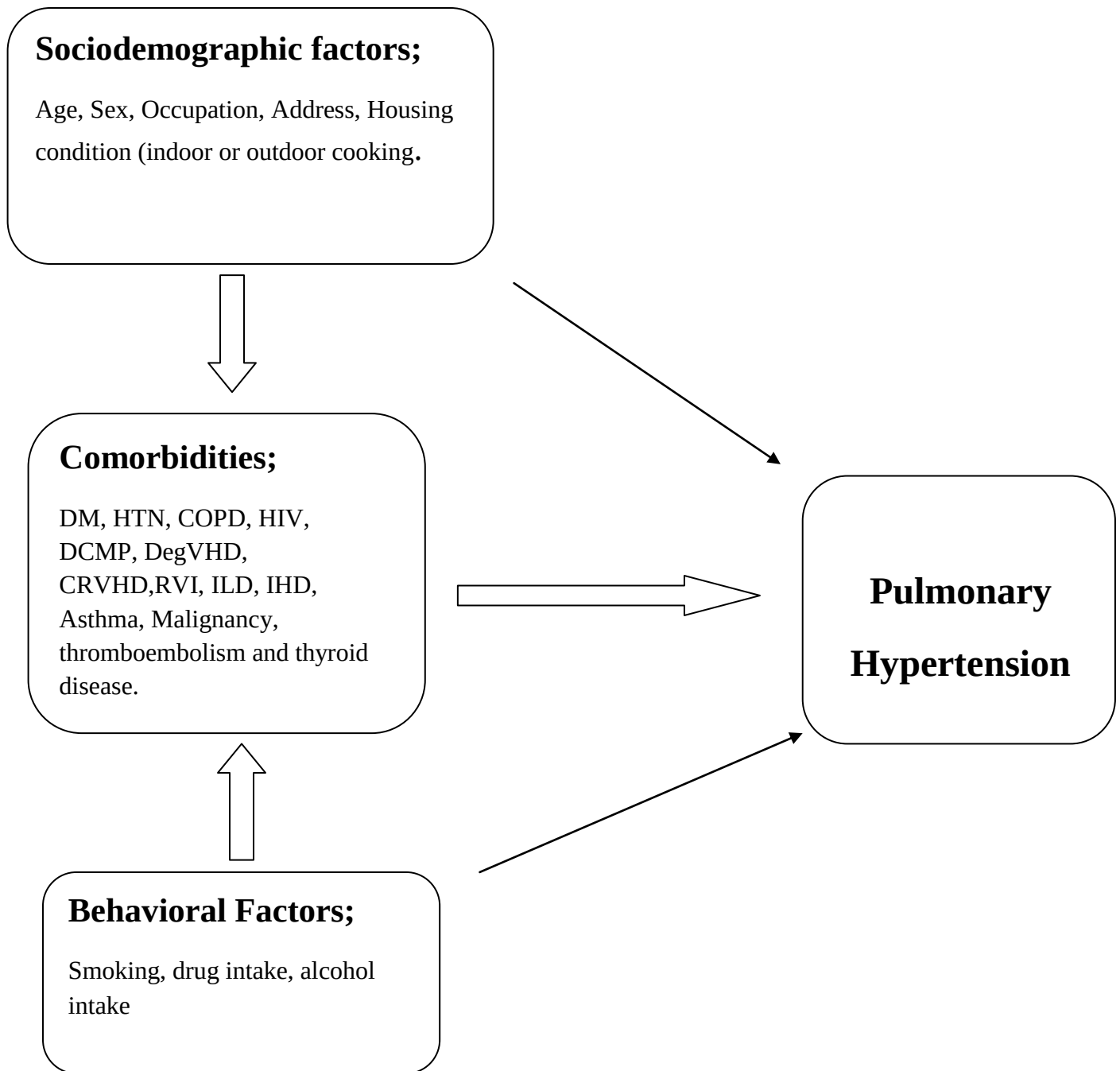


Figure 1 : Conceptual Framework showing the relationship of sociodemographic characteristics and associated factors of pulmonary hypertension.

4. General and Specific Objective

4.1 General objective

- To assess the prevalence and associated factors of pulmonary hypertension at SPHMMC in Addis Ababa, Ethiopia, 2021.

4.2. Specific objectives

- To determine the prevalence of pulmonary hypertension among patients visiting cardiac and chest clinics of SPHMMC from April 1, 2021 to May 30, 2021.

- To identify factors associated with pulmonary hypertension in patients visiting cardiac and chest clinics of SPHMMC from April 1, 2021 to May 30, 2021.

- To describe the pattern of pulmonary hypertension based on age and sex in patients visiting cardiac and chest clinics of SPHMMC from April 1, 2021 to May 30, 2021.

- To assess the functional classification of patients with pulmonary hypertension in patients visiting cardiac and chest clinics of SPHMMC from April 1, 2021 to May 30, 2021.

- To assess severity of Pulmonary HTN based on echocardiography in patients visiting cardiac and chest clinics of SPHMMC from April 1, 2021 to May 30, 2021.

- To assess distribution of causes of pulmonary hypertension in patients visiting cardiac and chest clinics of SPHMMC from April 1, 2021 to May 30, 2021.

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5. Methods & Materials

5.1 Study area

The study was conducted at St. Paul's Hospital Millennium Medical College. SPHMMC is a public hospital and medical teaching hospital, located in Addis Ababa, the capital city of Ethiopia. It was established in 1968 and is the second largest hospital in the country. It provides specialized referral services throughout Ethiopia. It has an established cardiac and chest units run by internal medicine residents, cardiac fellows and subspecialists in cardiology and pulmonology. The cardiac clinic and chest clinics see an average of 1158 and 672 patients respectively, 1830 patients totally.

5.2 Study period

The study was conducted from April 1, 2021 to June 30, 2021.

5.3. Study design

Institution based, cross sectional study was done on the prevalence of pulmonary HTN and associated factors at SPHMMC.

5.4. Source Population

The source population was all patients who have follow up at chest and cardiac clinics of SPHMMC during the study period.

5.5. Study population

The study population was all patients with a diagnosis of pulmonary HTN fulfilling the inclusion criteria's at chest and cardiac clinics of SPHMMC during the study period.

5.6. Study Variables.

Dependent Variable : Pulmonary HTN

Independent Variable : Age, Sex, Occupation, Address, Housing Condition, Behavior(smoking or alcohol or drug intake), Comorbidity (HTN, DM, CRVHD, Deg VHD, IHD, RVI, DCMP, COPD, Bronchial Asthma, ILD, PTB, CLD, Malignancy), Thromboembolism, Thyroid disease.

5.8. Inclusion and Exclusion Criterias

5.8.1 Inclusion Criteria.

- Age greater than 18yrs
- All patients with echocardiographic or CT scan diagnosis of pulmonary HTN who visit chest & cardiac clinics of SPHMMC during the study period.

5.8.2. Exclusion Criteria

- Those patients with critical illness during the time of data collection.
- Those patients with different or inconsistent echocardiographic results.
- Those patients who refuse to give consent.

5.9. Sample size determination.

- Sample size for the study was determined by using single population proportion formula by considering 50% prevalence of Pulmonary HTN, with the assumption of 95% confidence interval (CI), 5% margin of error & 10% non-response rate.

$$n = \frac{(Z^{\alpha}/2)^2 P(1-P)}{d^2}$$

n : estimated sample size.

Z : desired 95% confidence, Z= 1.96(from normal distribution table)

P : prevalence of pulmonary HTN

d : margin of error(0.05).

$$n = \frac{(1.96)^2 \times 0.5 \times (1-0.5)}{(0.05)^2} = 384$$

- Adding a 10% ($38.4 \approx 38$)for non-response rate, the total sample estimated will be $384+38=422$
- In addition, since the total number of patients at chest and cardiac clinic of SPHMMC is less than 10,000, correction formula will be used: $n_f = \frac{n_0}{1+\frac{n_0}{N}}$, where n_f is final size, n_0 is initial sample size, N is Total population($1158+672=1830$).

$$n_f = \frac{n_0}{1+\frac{n_0}{N}} = \frac{422}{1+422/1830} = 343$$

5.10. Sampling Procedure

Systematic random sampling method was used for assessing the prevalence of pulmonary hypertension and associated factors keeping inclusion and exclusion criterias. To get the sampling interval ($K=N/n$), we divided the total population (N) by our sample size (n) ($1830/343=5.33$). So, we took every fifth patient into our study to get our sample size of 343.

5.11. Operational definitions

Pulmonary hypertension is defined by a systolic pulmonary artery pressure at rest of 35 mm Hg or more, measured by echocardiography or increased PA diameter (≥ 29 mm) and pulmonary artery to ascending aorta diameter ratio (≥ 1.0) or segmental artery to bronchus ratio >1 in three or four lobes on chest CT scan or cardiologist's documentation of pulmonary hypertension on echocardiographic report.

Systemic hypertension is defined as blood pressure 140/90 mmHg or use of anti-hypertensive medication

Diabetes mellitus is defined as either fasting glucose level ≥ 126 mg/dl, or HgA1c $\geq 6.5\%$ or use of anti-diabetic medication

COPD is defined as an irreversible obstructive spirometry (proportion of the forced vital capacity exhaled in the first second [FEV1/FVC] $< 70\%$).

Asthma is defined as reversible obstructive spirometry or documented history of bronchial asthma.

Smokers include former and current smokers. Former smoker is an ex-smoker (if the patient had smoked for at least 3 years in the past, but had stopped at time of presentation) or a current smoker (patients who smoked at least one cigarette per day at the time of presentation)

Alcohol abuse is intake of either more than three (two for women) standard glasses of wine per day or more than ten (five for women) local beers (one local beer contains 28 g of alcohol) per week.

5.12. Data Collection procedures & quality assurance.

The data was collected using an interviewer administered, structured questionnaire prepared in English. Four Health professionals (Physicians) were recruited as supervisors and data collectors. They were given training on data collection and the subject matter for two days. The questionnaire was pretested to ensure the understandability of questions by data collectors and study participants. Data was collected on sociodemographic variables, pulmonary hypertension and associated factors, severity of pulmonary hypertension and functional classification.

The collected data was checked for completeness, accuracy and consistency by principal investigator and communication to the data collectors on the next days. Data was collected anonymously to ensure confidentiality. Data was cleaned for valid answer and further analyzed with using SPSS version 25.

5.13. Data analysis

After the data consistency and completeness is checked throughout the data collection, data entry and analysis was conducted. Those incomplete questionnaires were omitted from the analysis. Missing value and outliers was checked by running frequencies and cross tabulation data. Erroneous data was crosschecked with the hard copies of completed questionnaire. A code was given for each questionnaire using a unique identifier for each questionnaire and was entered and analyzed by SPSS version 20. Descriptive statistics (mean with SD and range) were used for scale variables and frequency distribution for categorical parameters. The prevalence of Pulmonary Hypertension was calculated by dividing the number of patients with pulmonary hypertension by total number of patients studied and multiplied by hundred. Bi-variable and multivariable binary logistic regression analysis was used to see association between associated factors and pulmonary hypertension. Those variables with 95% confidence interval and P-value < 0.25 on bi-variable analysis were included in the multivariate logistic regression analysis to see the relative the effect of confounding variables and interaction of variables. Adjusted odds ratio with 95% confidence intervals and P-value < 0.05 was considered as statistically significant association. The data were displayed by pie chart, histogram, tables and statements.

5.14. Ethical considerations

Ethical approval and clearance was obtained from Institutional Review Board (IRB) of SPHMMC. The support letter was written to chest and cardiac clinics of SPHMMC. The study was based on verbal consent from the patients. Privacy and confidentiality was maintained respectively by not transferring data to the third body and using it for research purpose only.

5.15. Dissemination of results

The detailed result of this study which consists of the main findings will be disseminated to St. Paul Hospital Millennium Medical College, department of Internal Medicine and department of Public Health, and Ministry of health.

6) Results

Sociodemographic characteristics

Data was obtained for a total of 315 patients with 92% response rate. Pulmonary Hypertension was found in 98(31.1%) of the patients with a mean age of $49.41 \pm \text{SD of } 18.167$. Majority of the patients are in the age range between 31-60yrs (57.1%), the peak age is 31-40yrs (27.6%) and 68 (69.4%) are female. Majority of patients are from Addis Ababa 50 (51.1%) followed by Oromia 42(40.4%), Amhara 4(3.8%) and SNN 4(3.8%). Age and gender distribution is shown in table 1

Table 1 : Age and sex distribution of patients with pulmonary hypertension visiting SPHMMC, 2021. (n=315).

Age	Gender		Total (Percentage)
	Female	Male	
≤20yrs	2(2%)	1(1%)	3(3.1%)
21-30yrs	10(10.2%)	3(3%)	13(13.3%)
31-40yrs	19(19.4%)	8(8.2%)	27(27.6%)
41-50yrs	10(10.2%)	5(5.1%)	15(15.3%)
51-60yrs	10(10.2%)	4(4.1%)	14(14.3%)
61-70yrs	9(9.2%)	3(3.1%)	12(12.2%)
71-80yrs	8(8.2%)	3(3.1%)	11(11.2%)
81-90yrs	0(0%)	2(2%)	2(2%)
91 -100yrs	0(0%)	1(1%)	1(1%)
Total	68(69.4%)	30(30.6%)	98(100%)

Functional Classification

Majority of patients are NYHA Class III patients 56(57.1%), followed by Class II 29(29.6%), Class IV 9 (9.2%) and Class I 4 (4.1%).

Figure 2 shows functional classification of patients.

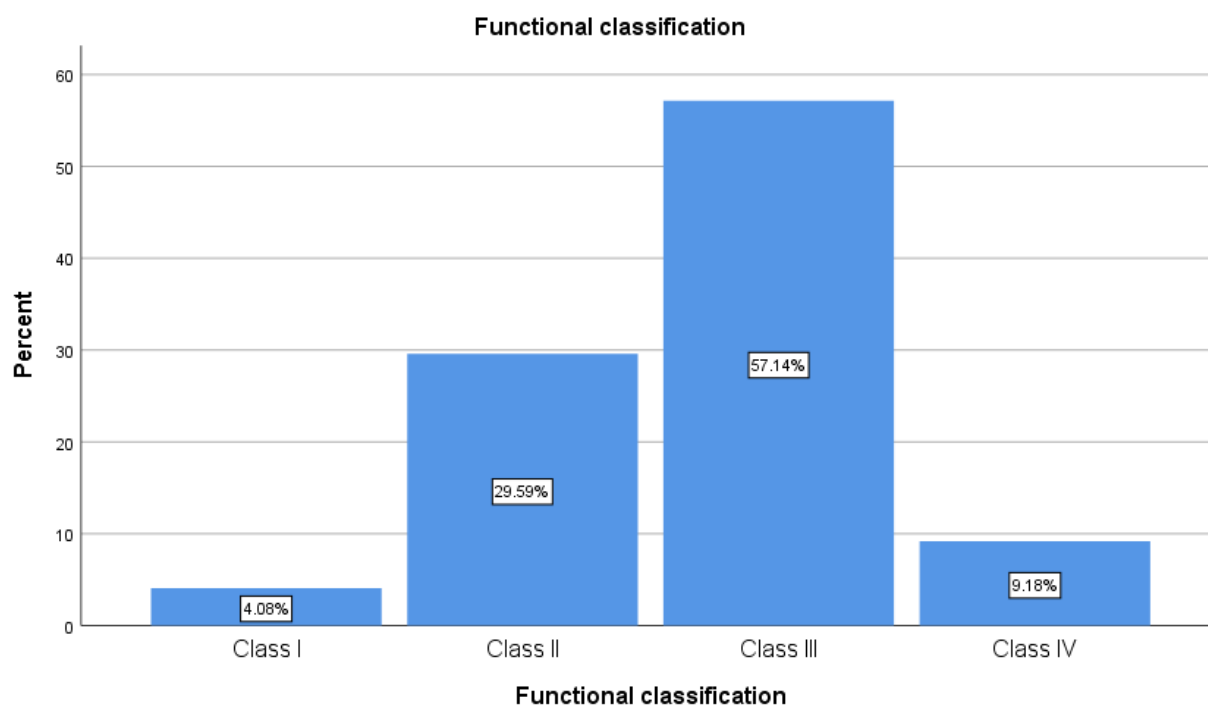


Figure 2: NYHA classification of patients with pulmonary hypertension visiting SPHMMC, 2021(n=315).

Severity of Pulmonary Hypertension

Majority of patients have Severe Pulmonary Hypertension 48(49%), followed by moderate 28(28.6%) and mild 22(22.4%). Of these 23(23.5%) patients have reduced right ventricular systolic function while 75(76.5%) patients have preserved right ventricular function.

Figure 3 shows severity of pulmonary hypertension based on echocardiography.

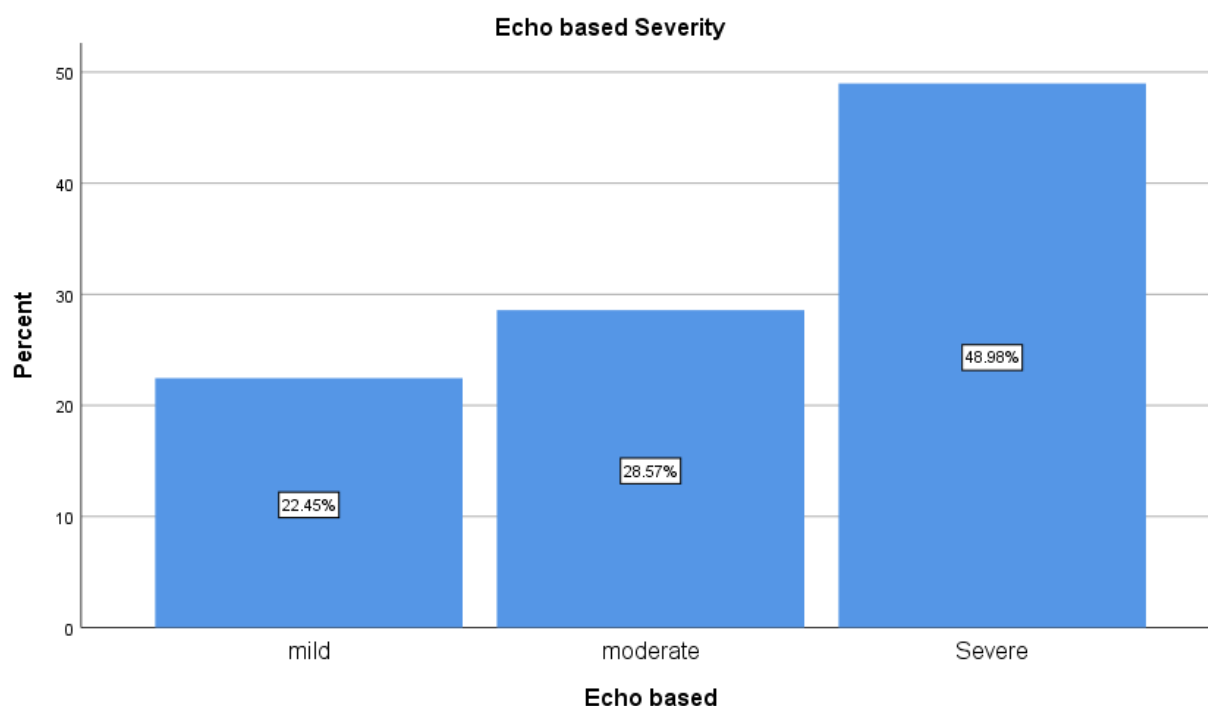


Figure 3: Severity of pulmonary hypertension based on echocardiography among patient visiting SPHMMC, 2021(n=315).

Distribution of associated factors

Overall Cardiac conditions account for the majority of the cases (65.3%), followed by lung conditions (24.5%), Chronic thromboembolism (7.1%), Pulmonary Arterial Hypertension(2%) and others(1%). The major causes of pulmonary hypertension are HHD(21.4%), CRVHD(18.4%), DCMP(14.3%), COPD(13.3%) and Thromboembolism(6.1%).

Figure 4 shows the distribution of causes of pulmonary hypertension.

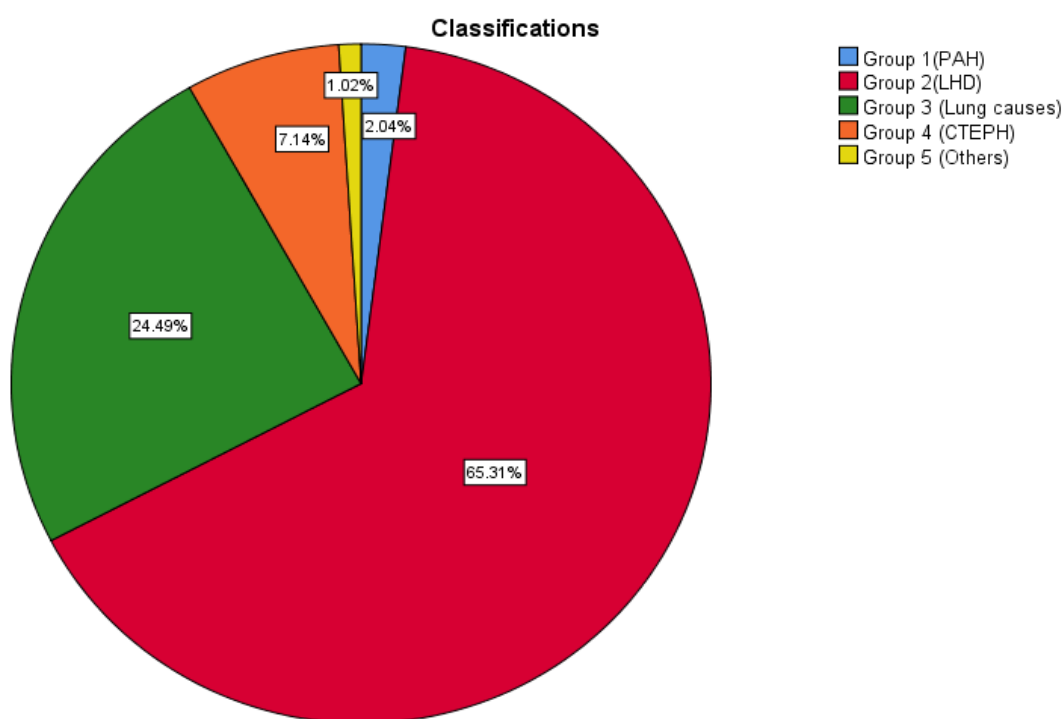


Figure 4: The distribution of associated factors based on classification for pulmonary hypertension among patients visiting SPHMMC, 2021(n=315).

Bi-variable analysis Result

Based on bi-variable analysis, age, indoor cooking, alcohol intake, smoking, diabetes, RVI, Covid-19, PTB, bronchiectasis and chest deformity didn't show significant association with pulmonary hypertension.

Age (COR[95%] = 0.995(0.972-1.018), Indoor cooking (COR[95%] = 1.35(0.476-3.825), alcohol intake (COR[95%] = 1.093(0.639-1.871), smoking (COR[95%] = 1.089(0.397-2.025), diabetes (COR[95%] = 1.289(0.522 – 3.181), RVI (COR[95%] = 1.682(0.369-7.661), Covid 19 (COR[95%] = 1.108(0.099-12.369), PTB (COR[95%] = 1.281(0.063-1.251), ILD (COR[95%] = 1.221(0.438-3.403), bronchiectasis (COR[95%] = 1.363(0.043-3.053), deg VHD (COR[95%] = 1.507(0.521- 4.358), Others(COR[95%] = 0.733(1.45 – 3.696) and chest deformity (COR[95%] = 1 (0.001-.) didn't show significant association.

Female gender, ILD, COPD, bronchial asthma, degenerative VHD, IHD, DCMP, CRVHD, HHD and thromboembolism showed significant association with pulmonary hypertension.

Female gender (COR[95%] = 1.637(0.986- 2.718), COPD (COR[95%] = 0.025(0.004-0.139), bronchial asthma (COR[95%] = 0.055(0.007- 0.412), IHD (COR[95%] = 1.443(1.147-1.340), DCMP (COR[95%] = 3.718(1.790-7.724), CRVHD (COR[95%] = 2.637(1.271-5.470), HHD (COR[95%] = 1.901(1.164-3.105) and Thromboembolism (COR[95%] = 2.765(0.823-9.290) significantly associated with pulmonary hypertension.

Table 2 and 3 show the results of bi-variable analysis with respect to pulmonary hypertension.

Table 2: Sociodemographic characteristics, associated factors and their association with pulmonary hypertension among patients visiting SPHMMC, 2021 (n=315).

Variables	Pulmonary HTN		P-value	COR	95% CI
	Yes (n=98)	No(n=217)			
Age					
≤ 30yrs	16 (16.3%)	33 (15.3%)	0.646	0.995	0.972 -1.018
31-60yrs	56 (57.2%)	129 (59.4%)			
≥ 61yrs	26 (26.5%)	55 (25.3%)			
Gender					
Female	68 (69.4%)	126 (41.9%)	0.057	1.637	0.986 – 2.718
Male	30 (30.6%)	91 (58.1%)			
Indoor Cooking					
Yes	6 (6.1%)	10 (4.6%)	0.572	1.350	0.476 – 3.825
No	92 (93.9%)	207 (95.4%)			
Smoking					
Yes	9 (9.2%)	22 (10.1%)	0.792	1.089	0.397 – 2.025
No	89 (90.8%)	195 (89.9%)			
Alcohol intake					
Yes	27 (27.6%)	56 (25.8%)	0.745	1.093	0.639 - 1.871
No	71 (72.4%)	161 (74.2%)			
Diabetes					
Yes	8 (8.2%)	14 (6.5%)	0.582	1.289	0.522 – 3.181
No	90 (91.8%)	203 (93.5%)			
CKD					
Yes	2 (2.1%)	5 (2.3%)	0.883	1.183	0.168 – 4.634
No	96 (97.9%)	212 (97.7%)			
RVI					
Yes	3 (3.1%)	4 (1.8%)	0.502	1.682	0.369 – 7.661
No	95 (96.9%)	213 (98.2%)			
Covid 19					
Yes	1 (1.1%)	2 (1.9%)	0.933	1.108	0.099 – 12.369
No	97 (98.9%)	215 (99.1%)			
PTB					
Yes	2 (2.1%)	15 (6.9%)	0.296	1.281	0.063 – 1.251
No	96 (97.9%)	202 (93.1%)			
Bronchiectasis					
Yes	1 (1.1%)	6 (2.8%)	0.351	1.363	0.043 – 3.053
No	97 (98.9%)	211 (97.2%)			

Table 3: Sociodemographic characteristics, associated factors and their association with pulmonary hypertension among patients visiting SPHMMC, 2021 (n=315).

Variables	Pulmonary HTN Yes(n=98) No(n=217)		P-value	COR	95% CI
Bronchial Asthma					
Yes	1 (1.1%)	34 (15.7%)	0.154	1.114	0.404 – 2.412
No	97 (98.9%)	183 (84.3%)			
ILD					
Yes	5 (6.1%)	11 (5.1%)	0.702	1.221	0.438 – 3.403
No	92 (93.9%)	206 (94.9%)			
COPD					
Yes	20 (10.4%)	15 (6.9%)	0.001	3.453	1.683 – 7.084
No	78 (79.6%)	202 (93.1%)			
Chest deformity					
Yes	1 (1.1%)	0 (0%)	1.000	0.000	0.000 - .
No	97 (98.9%)	217 (100%)			
HHD					
Yes	45 (56.3%)	67 (30.8%)	0.010	1.901	1.164 – 3.105
No	35 (43.7%)	150 (69.2%)			
IHD					
Yes	4 (4.1%)	19 (8.8%)	0.050	1.443	1.147 – 1.340
No	94 (95.9%)	198 (91.2%)			
DCMP					
Yes	20 (20.4%)	14 (6.5%)	0.001	3.718	1.790 – 7.724
No	78 (79.6%)	203 (93.5%)			
Deg VHD					
Yes	6 (6.2%)	9 (4.2%)	0.449	1.507	0.521 – 4.358
No	92 (93.8%)	208 (95.8%)			
CRVHD					
Yes	17 (17.3%)	16 (7.4%)	0.009	2.637	1.271 – 5.470
No	81 (82.7%)	201 (92.6%)			
Thromboembolism					
Yes	6 (6.2%)	5 (2.3%)	0.100	2.765	0.823 – 9.290
No	92 (93.8%)	212 (97.7%)			
Others					
Yes	1 (2.1%)	6 (2.8%)	0.706	0.733	1.450 – 3.696
No	96 (97.9%)	211 (97.2%)			
PAH	2(4.2%)		0.999	0.000	0.000 - .

Multivariate Analysis Result

To avoid excessive number of variables that reached P-value less than 0.25 during the bivariate analysis were included in multivariate analysis to see the relative effect of confounding variables. The multivariate logistic analysis identified female gender (AOR[95%] = 2.193(1.211-3.972), COPD (AOR[95%] = 7.227(2.883-18.120), Thromboembolism(AOR[95%] = 6.821(1.635-28.463), DCMP (AOR[95%] = 9.752(3.858-24.650), CRVHD (AOR[95%] = 8.254(3.230-21.093) and HHD (AOR[95%] = 4.361(2.157-8.819) showed significant association with pulmonary hypertension. But bronchial asthma (AOR[95%] = 0.123(0.010-1.564), and IHD (AOR[95%] = 1.640(0.470-5.722) didn't show significant association with pulmonary hypertension.

The odds of developing pulmonary hypertension in females is 2.1times higher than males. The odds of developing pulmonary hypertension in patient with COPD is 7.2 times higher than those who do not have. The odds of developing pulmonary hypertension in thromboembolism patients is 6.8 times higher than that who do not have. The odds of developing pulmonary hypertension in DCMP patients is 9.8 times higher than those who do not have. The odds of developing pulmonary hypertension in CRVHD patients is 8.3 times higher than that who do not have. The odds ratio of developing pulmonary hypertension in HHD patient is 4.4 times higher than those who do not have.

Table 4 shows the results of multivariate analysis with respect to pulmonary hypertension.

Table 4: Summary of multivariable analysis of sociodemographic and associated factors with pulmonary hypertension among patients visiting SPHMMC, 2021(n=315).

Variables	Pulmonary HTN		P-value	AOR	95% CI
	Yes(n=98)	No(n=217)			
Gender					
Female	68 (69.4%)	126 (41.9%)	0.010	2.193	1.211 – 3.972
Male	30 (30.6%)	91 (58.1%)			
HHD					
Yes	45 (56.3%)	67 (30.8%)	0.001	4.361	2.883 – 18.120
No	35 (43.7%)	150 (69.2%)			
DCMP					
Yes	20 (20.4%)	14 (6.5%)	0.001	9.752	3.858 – 24.650
NO	78 (79.6%)	203 (93.5%)			
CRVHD					
Yes	17 (17.3%)	16 (7.4%)	0.001	8.254	3.230 – 21.093
No	81 (82.7%)	201 (92.6%)			
IHD					
Yes	4 (4.1%)	19 (8.8%)	0.438	1.640	0.470 – 5.722
No	94 (95.9%)	198 (91.2%)			
COPD					
Yes	20 (10.4%)	15 (6.9%)	0.001	7.227	2.883 – 18.120
No	78 (79.6%)	202 (93.1%)			
Thromboembolism					
Yes	6 (6.2%)	5 (2.3%)	0.008	6.821	1.635 – 28.463
No	92 (93.8%)	212 (97.7%)			

7. Discussion

Pulmonary Hypertension remains one of non-communicable disease associated with increased morbidity and mortality irrespective of the underlying condition. There is general scarcity of published data related to the pulmonary hypertension in Africa. This study tried to assess the prevalence of pulmonary hypertension and associated factors. Overall, we found that pulmonary hypertension as assessed by echocardiography has a prevalence of 31% with a mean age of $49.41 \pm \text{SD of } 18.167$ of which 68(69.4%) are female. PH is a disease affecting adults of all ages. Majority of the patients are in the age range between 31-60yrs (57.1%).

The prevalence of pulmonary hypertension in our center is similar to a study done in Mekele which showed 32.6% prevalence(34) and a study in Australia which showed 32% prevalence(21) but it is high when compared to other studies done in Cameroon which is 15.6% (30) and Lybia which is 8%(33). Despite the number of scientific evidence that the prevalence of pulmonary hypertension increases in older age group, this study showed that pulmonary hypertension occurs at an earlier age than in other studies. The peak age is 31-40yrs in our study, while it is higher in previous studies. This result might be related to the underlying causes like rheumatic heart disease which occurs more in younger individuals. Female predominance was also seen in all of the literatures.

Most patients have advanced disease. Majority 56(57.1%) of patients are NYHA Class III patients, 48(49%) patients have severe pulmonary hypertension and 23 (23.5%) patients have right ventricular systolic dysfunction. This is also comparable to other studies done in Cameroon in which 70% of patient are Class III/IV, 31.5% had severe PH(31) and the PAPUCO registry in which 66% are Class III/IV patients(13).

According to classification of Pulmonary Hypertension, the leading causes are Group 2(cardiac conditions)(65.3%) and Group 3(lung conditions) (24.5%) followed by Group 4(thromboembolism)(7.1%), Group1(Pulmonary Arterial Hypertension (2%) and Group 5(others)(1%). This result is almost similar to previous literatures from Australia(21), Cameroon(31) and PAPUCO registry(13).

The associated factors are female gender, COPD, Thromboembolism, DCMP, CRVHD and HHD. Age, Indoor coking, behavioral factors, multifactorial conditions, bronchial asthma, bronchiectasis, Deg VHD, IHD, CKD, RVI, PTB and Covid 19 were not significantly associated with the development of pulmonary Hypertension. Indoor cooking is not associated with pulmonary hypertension in this study while it is associated factor in other studies. This might be explained by the majority of patients coming from Addis Ababa with access to electricity. Similarly, behavioral factors were not associated with PH, because most patients do not tell their real behavior like smoking and alcohol intake.

Generally the major causes of pulmonary hypertension in our center are HHD(21.4%), CRVHD(18.4%), DCMP(14.3%), COPD(13.3%) and Thromboembolism(6.1%). Hypertension and chronic valvular heart disease are prevalent and carry a large burden in Ethiopia, but they are one of the preventable or modifiable diseases.

8. Strength and limitation of the study

7.1 strength of the study

- As to my knowledge, this study is the first study in our country and it will serve as a baseline information for further research and important for policy makers to design strategy for prevention and management of pulmonary hypertension.
- The standard tool which is developed by World Health Organization was used.

7.2 Limitation of the study

- The limitation of this study is that echocardiographic estimation of pulmonary hypertension was used instead of Right Heart Catheterization, which is the gold standard test.

9. Conclusion

Generally, pulmonary hypertension as measured by echocardiography is common in patients having follow up at chest and cardiac clinics of SPHMMC. Pulmonary Hypertension occurred at earlier age and female gender is one of the determining factors. Majority of patients have advanced disease. The leading causes are cardiac and lung conditions, the major ones being HHD, CRVHD, DCMP, COPD and thromboembolism. This study fills the gap related to lack of data on prevalence of pulmonary hypertension and associated factors. Further study is needed to describe the mortality and outcome of patients with pulmonary hypertension.

10. Recommendation

Healthcare workers in this setting should be made more aware of this prevalent condition. Most of the prevention and management of pulmonary hypertension is directed to the underlying diseases. Conditions leading to PH need to be identified early and managed accordingly. Early detection and management of chronic diseases is very important. Most of the treatment options are limited often to heart failure management, so optimal management of heart failure is important.

Ministry of Health

- Increasing awareness about hypertension and it's complications among the population and public education on primary prevention through life style changes, exercise and other measures.
- Increasing awareness and public education on chronic rheumatic heart disease and it's complications and primary prevention through timely treatment of tonsillopharyngitis.

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- The cardiac clinic should work on optimal management of heart failure patients.
- The cardiac clinic should work on optimal management and control of hypertension.
- The newer therapies for management of pulmonary hypertension like vasodilators and pulmonary thromboendarterectomy should be started.

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12. Appendices

Part -I: English version questionnaire

This study will be conducted on the assessment of prevalence of pulmonary HTN and associated factors among patients who visit chest and cardiac clinics of Saint Paul Hospital Millennium Medical College in 2021.

I. Information sheet

Hello, I am _____ from Saint Paul Hospital Millennium Medical College. I would like to ask few questions about factors associated with pulmonary HTN. Your genuine information that you are going to provide will help policy makers to design strategy/give priority for improvement of patient care. Your answers will remain confidential and your name will not be taken down. Participation in this study is voluntary and you are not obligated to answer any questions that you do not want to answer and it takes 20 minutes.

Title of the study: Prevalence of pulmonary HTN and associated factors at Saint Paul Hospital Millennium Medical College, Addis Ababa, Ethiopia 2021.

Objective of the study: To assess the prevalence of Pulmonary HTN and associated factors among patients at SPHMMC, Addis Ababa, Ethiopia 2021.

Rights of the participant: participating and not participating is the full right and participants can stop from participation in the study at any time. And also the participant can skip question which he/she does not want to respond. Participants can ask any questions which is not clear for understanding.

Confidentiality: - Any information forwarded will be kept private and his/her name will not be specified

Informed consent

I have read all this form or it has been read to me in the language I comprehend and understood all conditions stated above.

Therefore, would you willing to participate in this study

Yes.

No.

Name of researcher Tigist Ajema

Signature -----

Address: 0922973366 (ajematigist@gmail.com)

Name of witness _____

Signature_____

Date_____starting time _____Ending time_____

Result of administration 1.Completed 2.Respondent not available 3. Refused 4. Partially completed.

If the respondent is not voluntary, please skip to the next participant.

Part II. Socio-Demographic factors-please circle a number for your response

Characteristics	Possible response	skip
Age		
Sex	Female-----1 Male ----- 2	
Address	Addis Ababa--1 SNN-----4 Oromia-----2 Tigray-----5 Amhara-----3 Others-----6	
Occupation	Farmer-----1 Student-----5 Employee-----2 Daily Laborer---6 Merchant-----3 Jobless-----7 Housewife-----4	
Housing Condition	Indoor Cooking -----1 Outdoor Cooking-----2	

Table 1: Sociodemographic factors

Part III : Associated factors

Variables	Yes	No
Smoking		
Alcohol intake		
HTN		
Bronchial Asthma		
Bronchiectasis		
COPD		
ILD		
Previous PTB		
HIV		
CKD		
Covid 19		
CRVHD		
IHD		
DCMP		
Degenerative VHD		
Thromboembolism		
CTD, RA,SLE		
CLD/PortalHTN		
Other(drugs, altitude,malignancy)		
Schistosomiasis		
Family history of PHTN		
NO risk factor identified		

Table 2: Associated factors of Pulmonary HTN

Part IV : NYHA Functional Classification

Asymptomatic	1
Symptoms at ordinary activities	2
Symptoms at sub-ordinary activities	3
Symptoms at rest	4

Symptoms include dyspnea, fatigue, chest pain, palpitation or syncope.

Table 3: NYHA functional classification.

Part V: Severity of Pulmonary HTN on Echocardiography

Mild	1
Moderate	2
Severe	3

Table 4: Severity of Pulmonary Hypertension.

13. Declaration

I, the undersigned, declare that this is my original work and has never been presented by another person in this or another college and that all the source materials and references used for this thesis have been duly acknowledged.

Name _____ ID.No. _____
Signature _____ Date _____

14. Approval

The thesis has been submitted for examination with our approval as college advisors.

Name of advisors: Dr. Abdusamed Adem (MD, Interventional Cardiologist)

Signature _____
Date _____

Mr. Eyoel Berhan (MPH)
Signature _____
Date _____