Graduate Study Program

Department of Internal Medicine

Prevalence of pulmonary hypertension and its associated factors among chronic kidney disease patients in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia

Investigator: Yemisrach Begashaw (M.D.R3 Internal Medicine Resident)

A Thesis submitted to Tikur Anbessa Specialized Hospital (TASH) Department of Internal Medicine in Partial Fulfillment of the Requirements for the Degree of specialty in Internal Medicine

April,2025
Addis Ababa,Ethiopa

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Investigator: Yemisrach Begashaw (M.D. R3 Internal Medicine Resident)

Advisers

Dr. Hanan Yusuf (Ass. Professor of Internal Medicine, PCCM)

Dr.Lissane seyfu (Ass.professor of Internal Medicine, Nephrologist)

Declaration

I,Yemisrach Begashaw, do hereby declare that this research thesis is a result of the works of my own making except where due is made in a review of previous literature in the content and by my knowledge, has never been submitted for any prior academic award or qualification in this Institution.

Yemisrach Begashaw : Signed :_____ Date: _____
Email:yemishaw13@gmail.com

Phone: +251913398783

Approval of thesis submission

I hereby certify that I have read this thesis prepared under my direction and recommend that it can be accepted as fulfilling the thesis requirement.

Name of Thesis Advisor _____ Signature_____ Date _____

Name of Head of Department _____ Signature_____Date_____

Acknowledgments

I acknowledge Tikur Anbessa Specialized Hospital (TASH), Internal Medicine department, for providing me with the educational opportunity to conduct this research. I would also like to thank my respected advisers, Dr. Hanan Yusuf and Dr Lissane seyfu, for their unreserved professional support, and technical guidance in developing this study.

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Abbreviations

- CKD: Chronic Kidney Disease
- DM: Diabetes mellitus
- ePASP: estimated pulmonary artery systolic pressure
- ESRD: End-Stage Renal Disease
- GFR: Glomerular filtration rate
- KRT: kidney replacement therapy
- PAH: Pulmonary Arterial Hypertension
- PH: Pulmonary Hypertension
- PTE: Pulmonary thromboembolism
- TRV: Tricuspid regurgitation velocity
- HIV: Human immunodeficiency virus

Abstract

Background: Pulmonary Hypertension (PH) is associated with high morbidity and mortality in chronic kidney disease (CKD) including patients on dialysis, but its magnitude remains unknown in Ethiopia.

Objective: To determine the prevalence of PH and its associated factors among CKD patients in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

Methods: A four-year retrospective study was conducted among patients with CKD who have follow-ups from (sept.2020 to sept.2024) at renal and diabetic clinics in Tikur Anbessa Specialized Hospital, Ethiopia. The data was extracted using the Kobo collected from the patient's medical record chart and the electronic medical records software. We used SPSS version 27.1 for data cleaning and analysis. A logistic regression analysis was used to identify the variables associated with the pulmonary hypertension risk. All variables with a p-value <0.20 in the univariate analysis was selected for the multivariate analysis model. A p-value of <0.05 will be considered statistically significant.

Results: A total of 243 chronic kidney disease patients were included, with a mean age of 60.95 ± 12.53 years, and 61.7% were male. The prevalence of pulmonary hypertension (PH) was 16.04% (95% CI: 11.8–21.7%), with 6.2% classified as severe. Advanced CKD (stages 3–5) (AOR: 3.32, 95% CI: 1.95–11.58, p=0.048), type 2 diabetes mellitus (AOR: 3.18, 95% CI: 1.28–7.89, p=0.01), and hypertension (AOR: 3.11, 95% CI: 1.35–7.19, p=0.008) were identified as independent risk factors for PH.

Conclusion and recommendations: Pulmonary hypertension (PH) is a significant comorbidity among Ethiopian CKD patients, with modifiable risk factors contributing to its development. These findings highlight the need for routine PH screening in high-risk CKD populations and context-specific management strategies in resource-limited setups.

Keywords: Pulmonary hypertension, Chronic kidney disease, Prevalence, Risk factors, Ethiopia.

1. Introduction

1.1 Background

Cardiovascular disease is the most common cause of morbidity and mortality in chronic kidney disease (CKD) worldwide [1]. Heart failure (HF), coronary heart disease (CHD), and cardiac arrhythmias are common in people with chronic kidney disease (CKD). Pulmonary hypertension (PH) is now being recognized as a potentially significant and highly prevalent disease in CKD patients [2]. It is a pathological condition characterized by persistently elevated pulmonary arterial pressure (PAH), defined as a mean PAP ≥ 20 mmHg at rest [8]. According to the latest ERS/ESC classification in 2022, CKD-induced PH is classified as type V (PH due to unknown mechanisms) [3]

The prevalence of PH ranges from 21–27% for patients with CKD, and up to 47% for patients with end-stage kidney disease (ESKD) [4]. The mechanisms of PH in patients with CKD remain unclear, which might be related to the imbalance of vasoconstrictors and vasodilators, left ventricular dysfunction, arteriovenous fistulas, mineral-and-bone disorders, anemia, and recurrent pulmonary embolism [5]. The most current meta-analysis (2024) of over fifty studies revealed that black people, those with chronic obstructive pulmonary disease, those with a history of cardiovascular disease, CKD patients on prolonged dialysis, diastolic and systolic dysfunction, and the stage of CKD had significantly greater PH among CKD patients [6].

Currently, the gold standard for PH diagnosis is the right heart catheterization using floating catheters. Due to the invasive nature of this diagnostic investigation, noninvasive echocardiography is often used to calculate estimated pulmonary artery systolic pressure (ePASP) to diagnose PH [7] Hence, transthoracic echocardiography is now considered an excellent noninvasive screening test for patients with symptoms or risk factors of PH despite it cannot replace the RHC and might underestimate the magnitude of the PH [8].

In the last few years, various studies have been conducted to estimate the prevalence [6, 9] predictors [6], mortality [10], and prognostic [11] of PH among CKD patients. However, the

majority of them were in developed countries and only a few reported from African countries [12, 13] and none from Ethiopia.

In Ethiopia, the emerging burden of non-communicable disease has become a serious public health concern which had a great impact on the incidence and magnitude of chronic diseases [14].According to a recent meta-analysis encompassing Twelve publications, the combined estimate of chronic kidney disease (CKD) among individuals with chronic illnesses (diabetes mellitus, Hypertension, cardiovascular disease, HIV) in Ethiopia is 21.71%, with significant regional heterogeneity [15]. Chronic kidney disease (CKD) is also a major public health problem in Ethiopia with prevalence ranges from (9.3% to 25.9%) in diabetes mellitus (DM) patients. With extensive research using popular databases like PubMed, Google Scholar, and others, no published paper has reported the prevalence or risk factors of PH among CKD patients in Ethiopia. In this study, therefore, we will examine the prevalence and predictors of PH of chronic kidney disease among patients who have follow-ups in Tikur Anbessa Specialized Hospital in Ethiopia.

1.2 Statement of the problem

Cardiovascular disease continues to be the leading cause of morbidity and mortality in patients with CKD regardless of whether kidney replacement therapy (KRT) is required [16]. Overall, CVD contributes to 40–45% of patients with advanced CKD (CKD stage 3b-4) dying from CVD [16].

PH is highly prevalent and is often associated with poor outcomes in CKD patients, especially in end-stage renal disease (ESRD), but it remains a neglected risk condition in renal patients [17]. The complex pathophysiologic interplay of the kidney and the cardiovascular system, dynamic volume status, and highly comorbid patient population make understanding, diagnosing, and managing PH in CKD challenging [18].

TB is a substantial cause of morbidity among patients with CKD in Ethiopia, detected in 12.9% of predialysis CKD populations [29] and 27% in patients with ESRD receiving maintenance hemodialysis [30].Both active and previously treated pulmonary TB are associated with the development of PH [28]. TB disproportionately affects low and middle income countries where more than 90% of incident TB cases occur and the majority of global survivors of TB reside

[31]. In these resource-constrained countries, the diagnosis of PH presents unique challenges, resulting in the under-detection and under-reporting of PH, due to infrequently available RHC.

Several systematic reviews and meta-analyses have evaluated PH in patients at various stages of CKD, whether the predictors, prevalence, and prognostic role of PH in patients with CKD differ according to individuals' characteristics are not well understood [9, 11]. Even though CKD is a major clinical and public health issue in Ethiopia [15], there is a lack of data on the prevalence of PH and its predictors among CKD patients in the country. Therefore, we will examine the prevalence of pulmonary hypertension and its associated factors among chronic kidney disease (CKD) patients who have follow-ups in our hospital. Considering the likelihood of late presentations for CKD care and the fact that patients might not receive continuous hemodialysis for a variety of reasons, such as access issues financial constraints, or other reasons, we hypothesized that PH is very prevalent in our patients.

1.3 Significance of the study

Pulmonary hypertension is robustly associated with adverse outcomes in patients with CKD and ESRD which implies that improved diagnosis and management of pulmonary hypertension may lead to improved outcomes among such patients. Our study will produce essential evidence for guideline development for early identification and early targeted intervention that is important to prevent further progression of these diseases and their complications. It will be used as baseline data to conduct a multicenter, large-scale and prospective study to understand the problem at the national level.

2. Literature review

2.1.1 Prevalence of pulmonary hypertension in CKD patients

Several meta-analyses were carried out, including different studies to determine the prevalence of PH in patients receiving hemodialysis, transplant patients, and patients at different stages of CKD. The first meta-analysis was conducted using 50 (involving 17,558 CKD patients) observational studies revealed that the prevalence of PH in CKD patients was 38% and the prevalence according to CKD status was 31% for CKD (I-V), 39% for ESKD (predialysis), 42% for ESKD (hemodialysis), and 26% for renal transplant, in this studies PH was diagnosed by Echocardiography with ePASP value ≥ 35 mmHg at rest [6]. The second, meta-analysis including twenty-one observational studies (n = 8012 participants) showed that the pooled prevalence PH was 32% based on Echocardiography ePASP ≥ 35 mmHg with significant heterogeneity between these studies [19]. The last meta-analysis including 18 studies, (with 10740 patients) among CKD patients showed that the overall prevalence of PH was 33% [20].

A retrospectively analyzed 705 CKD patients in China shows the overall prevalence of PH was 47.38%, in which mild, moderate, and severe PH accounted for 22.13%, 15.04%, and 10.21%, respectively and PH was defined as ePASP > 35 mmHg. The prevalence of PH in CKD stage (I-V) was 14.29%, 33.33%, 38.89%, 40.91% and 64.47%. The prevalence of total PH was 57.63% in PD patients and 58.82% in HD patients. Compared with non-dialysis patients, the prevalence of PH was much higher in patients receiving dialysis [21]. In Iraq, as the stage of chronic kidney disease increases the incidence of PH increases which in stage V reaches 15% compared to stage IV 3.75%, and lower in the other stages, Various PASP cutoffs have been applied, ranging from 25 to ≥45 mm Hg by using both RHC and Echocardiography [22].

In India, PH was present in 47 of 108 (43.5%) cases at the beginning, 41 of 83 (491.4%) at 3 months, and 32 of 64 (50%) at 6 months. The prevalence and severity of PH increased with the

progression of the CKD stage. The majority of them had moderate PH at the beginning of the study which remained the same, despite being on hemodialysis. PH is a common complication in CKD patients with a prevalence of 43.5%–50%,ePASP value of ≥35 mmHg at rest was taken to be suggestive of PH by Echocardiography [2]. Another, study in America showed that 21% (n=625) had PH,it was defined as the presence (PASP) >35 mmHg and/or tricuspid regurgitant velocity (TRV) >2.5 m/s., with higher rates among those with lower levels of kidney function [23].

In African countries, few studies also assess the magnitude of PH among CKD patients. In Egypt PH was diagnosed in 28 CKD patients confirmed by right (RT) side cardiac catheterization (mPAP) of 20 mmHg at rest, among 120 CKD patients representing 23.5%. The frequent diagnosis of PH was Group 1 pulmonary arterial hypertension (36.7%) followed by Group 2 cardiac causes (30%) followed by Group 4 chronic thromboembolic PH (26.7%) and (6.7%) experienced normal pulmonary hemodynamics by RHC [27]. In another study in Somalia, the number of patients with PH was 73 (51%) and the majority of patients were 65 years of age or older, the diagnosis of PH was done by transthoracic echocardiography (TEE) with a systolic pulmonary artery pressure ePASP value ≥ 35 mmHg at rest [12,13] .

2.2 Risk factors associated with PH in CKD patients

The different risk factors were also assessed using the metanalysis or the individual studies conducted in different countries both developed and developing countries. In a meta-analysis of about fifty studies, they found that Black individuals who have chronic obstructive pulmonary disease, cardiovascular disease history, longer dialysis, diastolic dysfunction, systolic dysfunction, and grade 5 CKD were significantly associated with PH [6] In another meta-analysis of 18 studies, PH was associated with an increased risk for cardiovascular events in patients with CKD and ESRD receiving dialysis [20].

In China, Body mass index (BMI), hemoglobin, triglyceride (TG), proteinuria, parathyroid hormone (PTH), and estimated glomerular filtration rate (eGFR) were independent risk factors of PH in CKD patients [21]. Left‐sided heart failure, anemia, fluid retention, and increased calcium phosphate product are the risk factors for developing PH based on the study conducted among CKD patients in India [2]. In an American study, older age, anemia, lower left ventricular

ejection fraction, and presence of left ventricular hypertrophy were associated with greater odds of having PH however the mechanisms that underlie these findings were not investigated [23].

In African settings, unsecured healthcare funding, arrhythmia, vascular access change, and diastolic dysfunction were independently associated with PH among CKD patients according to the study findings in Congo and [12]. In addition, in the study conducted in Somalia, LVEF, right atrium diameter, and the presence of pericardial effusion (PE) were found to be independent predictors of PH among CKD patients [13].

3. Conceptual framework

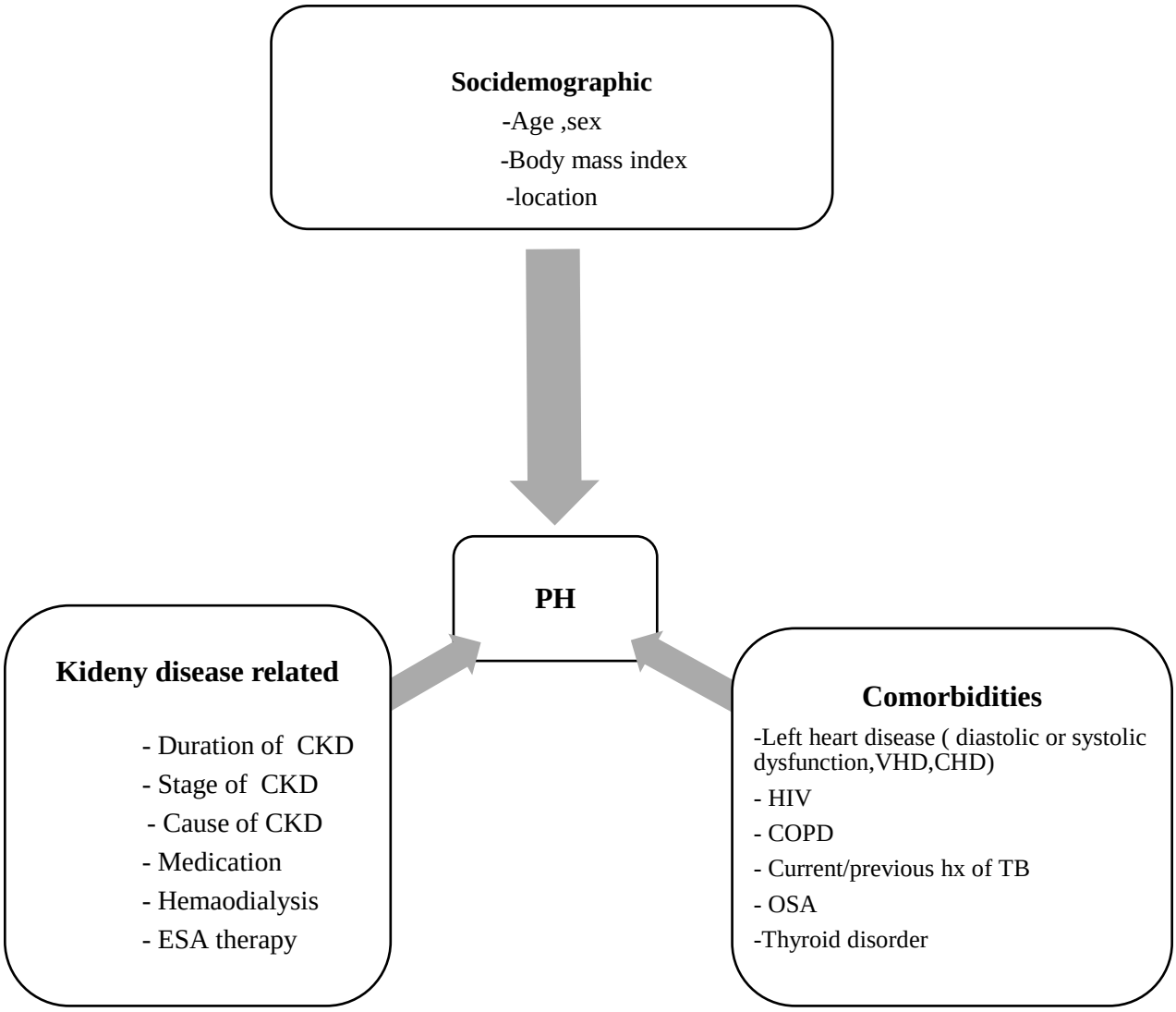


Figure1.The conceptual framework of factors affecting PH in CKD, was developed using the variables included in different studies [11, 20]

4. Objectives

General objective

- To determine the prevalence of pulmonary hypertension and its associated factors among chronic kidney disease patients in Tikur Anbessa Specialized Hospital in Addis Ababa, Ethiopia for the past four years.

Specific objectives

- To assess the prevalence of pulmonary hypertension among chronic kidney disease patients in Tikur Anbessa Specialized Hospital (TASH)
- To identify associated factors for pulmonary hypertension among chronic kidney disease patients in Tikur Anbessa Specialized Hospital (TASH)

5. Methods

5.1 Study setting and periods

This study was conducted at the renal Clinic and Diabetic clinic of Tikur Anbessa Specialized Hospital, one of the tertiary referral hospitals in Addis Ababa, Ethiopia. The study area is located at the center of the capital city of Ethiopia, Addis Ababa. TASH is the country's largest teaching and the tertiary hospital with more than 400,000 patients seen at an outpatient follow-up clinic annually. TASH is a referral center for many referral hospitals as well as a hospital under which very vast clinical service is given, including some specialty services only found in TASH. It is one of the biggest and pioneer teaching centers under the administration of Addis Ababa University. The college runs multiple postgraduate and fellowship programs, not to mention it has been the earliest center for undergraduate medicine programs for more than 50 years. In the renal department of the hospital, approximately 4000 patients have been on follow-up and it also provides dialysis and inpatient care.

5.2 Study design and period

A four-year retrospective cross-sectional study was conducted among chronic kidney diseases who had to follow-up at renal outpatient and Diabetic clinic of TASH, Addis Ababa, Ethiopia.

5.3 Population

5.3.1 Source population

All adult patients with chronic kidney disease who have follow-ups at renal and diabetic clinics in TASH in Addis Ababa, Ethiopia

5.3.2 Study population

Adult chronic kidney disease patients with complete data included in the study.

5.4 Sample size, sampling technique, and sampling procedures

5.4.1 Sample size

The sample size was calculated with the sample size determination using the single population formula at a 95% confidence interval ($Za_{1/2}$=1.96), the margin of error (d)= 5%, the proportion of PH among CKD patients is 23.5% in Egypt [27].

$$N = \frac{p(1-p)(Za/2)^2}{(d)^2} = \frac{0.235(1-0.235)(1.96)^2}{(0.05)^2} = 276$$

After adding a 10% nonresponse rate (incomplete data), the sample became 303

5.4.2. Sampling technique and procedure

First, all adult CKD patients, irrespective of the stages, from the renal clinic and diabetic clinics were listed using the medical record number. From this list, the study participants were selected through systematic random sampling techniques till the sample size was completed. The interval (K-value) calculated by dividing the number of patients by the sample size. The first patient was selected by lottery method.

5.5. Data collection tools and procedure

We used a pre-tested data retrieval (abstraction) checklist, developed after reviewing different works of literature. The checklist was prepared in English for ease of the data abstraction process; it contains socio-demographics, and disease-related variables including dialysis indicated, imaging studies, and laboratory results. The data was extracted from the electronic record and patient medical record chart. The questionnaires were prepared in the Kobo collect tool and collected in the Android tools (mobile and tablet). The trained general practitioners were collected the data.

5.6. Study variables

5.6.1. Dependent variable:

- Pulmonary hypertension

5.6.2 Independent variables:

- **Socio-demographic characteristics**: Age, sex, occupation, location/address
- **Behavioral characteristics:** Smoking, alcohol use, kchat
- **Clinical characteristics**: Duration of CKD, cause of CKD, stage of CKD, management of CKD, investigation for CKD (hgb, PTH, ca), comorbidities such as CHD, VHD,HIV Thyroid disorder, COPD, post TB lung disease,OSA, PTE

5.7. Selection criteria

4.7.1 Inclusion criteria

- Cases of CKD based on Kidney Disease Improving Global Outcome 2012 criteria, including CKD patients on hemodialysis with complete Data.
- Age ≥18 years

5.8. Data quality control

The pre-test was done on 10% (27 charts) of the same population but not on the actual data (on patients from Zewiditu Memorial Hospital). The principal investigator was instructing the data collectors on data extraction procedures, data sources, and inclusion and exclusion criteria. The investigator has conducted a daily supervision and follow-up check for the completeness and consistency of the data.

5.9. Operational Definitions

- Pulmonary hypertension (PH): PH is suggested echocardiographically when the TRV is ≥2.8 $m.s^{-1}$,the ePASP exceeds 35 mmHg and/or when RV size wall thickness and function are abnormal [24].
- It is classified as mild (35–50mmHg), moderate (50–70mmHg), and severe (>70mmHg) based on the systolic PA pressure [25].
- Chronic kidney disease: CKD is defined as abnormalities of kidney structure or function, present for >3 months with health implications. Based on GFR estimated by (CKD-EPI without the race factor) classified as G1 (GFR ≥ 90), G2 (GFR 60- 89), G3a (GFR 45–59), G3b (GFR 30-44), G4 (GFR15-29) and G5 (GFR < 15) mL/min/1.73 m2 [26].

5.10. Data processing and analysis

The data in Excel format (downloaded from Kobo Collect) uploaded to SPSS version 27.1 for cleaning and analysis. We used proportions (percentages) to describe categorical data. For continuous variables, the normal distribution variables' mean (±standard deviation) was utilized, while the non-normal distribution variables' median (interquartile range) was employed. To compare categorical variables, the chi-square test or Fisher's exact test was employed. A logistic regression analysis used to identify the variables associated with the PH. All variables with a p-

value <0.20 in the univariate analysis were selected for the multivariate analysis model. A p-value of <0.05 and a 95% confidence interval was considered statistically significant.

5.11. Ethical consideration

Ethical clearance and approval were obtained from the TASH Research Ethical Review Committee. The data will be fully anonymized and will not be accessible by any third party other than the study team. Informed consent will not be applicable for the secondary data and was waived by the ethical review committee.

5.12. Results dissemination

The findings of the study will be submitted to the TASH Department of Internal Medicine and the college library. The result will be published in open-access and peer-reviewed journals for international readers.

6. Results

6.1. Sociodemographic and behavioral characteristics

The total estimated sample was 303, with data collected from 243 participants, resulting in a response rate of 80.2%. The mean age of participants was 60.95 ± 12.53 years. Most participants were male (61.7%) and aged 46-65 years (52.7%). 21% of patients are from diabetic clinic where as 79% of individual from Renal clinic .The majority resided in the highlands (86.0%) and in Addis Ababa (77.4%). 13.6% of has history of smoking . Additionally 30.7% of individuals has body mass index > 25.(table 1).

Table 1: Demographic and Lifestyle Characteristics of CKD Patients in a Tertiary Hospital in Addis Ababa, Ethiopia

Variables		**Count**	**Percentage**
Sex	Female	93	38.3
	Male	150	61.7
Age groups (years)	<35	8	3.3
	35-45	23	9.5
	46-65	128	52.7
	>65	84	34.6
Location	Highlands (Dega)	209	86.0
	Lowlands (Kolla)	20	8.2
	Midland (Woina Dega)	14	5.8
Living	Addis Ababa	188	77.4
	Out of Addis Ababa	57	22.6
Smoking history	Never smoke	210	86.4
	Previous smoker	31	12.7
	Current smoker	2	0.8
Alcoholic history	Never drink	210	86.4
	Occasionally	27	11.1
	Regularly	6	2.5
Chat chewing	Never Chew chat	230	94.6
	Occasionally	7	2.9
	Regularly	6	2.5
Body mass index (n=189)	<18.5	4	2.1
	18.5-25	127	67.2
	25-29.99	52	27.5
	>30	6	3.2

6.2 Cause of CKD, staging, and comorbidities

The major findings of the study highlight that Stage 3b CKD (GFR 30-44) was the most prevalent, affecting 29.6% of patients, followed by Stage 3a (GFR 45-59) at 21.0%. Type II Diabetes Mellitus was the leading cause of CKD, contributing to 53.1% of cases, followed by hypertension at 30.5%. A large majority of patients (65.0%) had CKD for less than 5 years, with a mean duration of CKD of 3.9 ± 2.5 years, indicating recent diagnoses or slow progression. Currently 7 patients are on Hemodialysis. Comorbidities such left heart disease (23.5%), valvular heart disease (10.2%) and HIV (8.6%) were common. In terms of treatment, Enalapril/losartan (57.6%), statin (55.6) and Dapagliflozin (49.4%) were frequently prescribed medication.

Table 2: Distribution of Study Participants by CKD Stage, Duration, Causes, Comorbidities, and Medication Use

Variables		Count	Percentage
	Stage of CKD		
	Stag 1(GFR>90)	14	5.8
	Stage 2(GFR 60-89)	41	16.9
	Stage 3a (GFR 45-59)	51	21.0
	Stage 3b (GFR 30-44)	72	29.6
	Stage 4(GFR 15-29)	40	16.5
	Stage 5(GFR<15ml)	25	10.3
Duration of CKD			
	Less than 5 years	158	65.0
	5 to 10 years	79	32.5
	Above 10 years	6	2.5
Cause of CKD			
	Type II diabetes Mellitus	129	53.1
	Hypertension	74	30.5
	Obstructive uropathy	16	6.6
	Glomerulonephritis	8	3.3
	Cardiorenal syndrome	7	2.9
	Others	6	2.5
	Not documented	3	1.2
Comorbidities			
	Chronic obstructive lung disease	10	4.1
	Current/Previous pulmonary TB	19	7.8
	Valvular heart disease	25	10.2
	Left heart disease	57	23.5
	Human immunodeficiency virus	21	8.6
	Thyroid dysfunction	6	2.4
CKD medication (n=152)			
	Dapagliflozin	120	49.4
	Enlapril /Losartan/	140	57.6
	Statin	135	55.6

	Others	14	5.8

6.3 Laboratory findings

The major findings show that the largest proportion of patients had creatinine levels between 1.6-2.5 mg/dL (37.0%), with 8.2% having levels above 4.5 mg/dL. In terms of hemoglobin levels, the majority of females (64.5%) and males (74.0%) had levels above normal, with males generally showing higher levels. Most patients had normal total calcium levels (8.5-10.5 mg/dL) (44.4%), while 13.2% had low levels (<8.5 mg/dL). The majority had LDL levels below 100 mg/dL (49.8%), and the mean LDL was 77.54 mg/dL. A significant portion of patients had triglyceride levels below 150 mg/dL (42.4%), with 20.2% showing elevated levels (table 3). The mean parathyroid hormone (PTH)(n=26) was 397.34 ± 279.12 pg/mL, with a range from 99.5 to 935 pg/mL. HBV was present in 1.65% of patients, and HCV was detected in 0.41% of patients.

Table 3: Laboratory findings of CKD patients in tertiary hospital in Addis Ababa Ethiopia

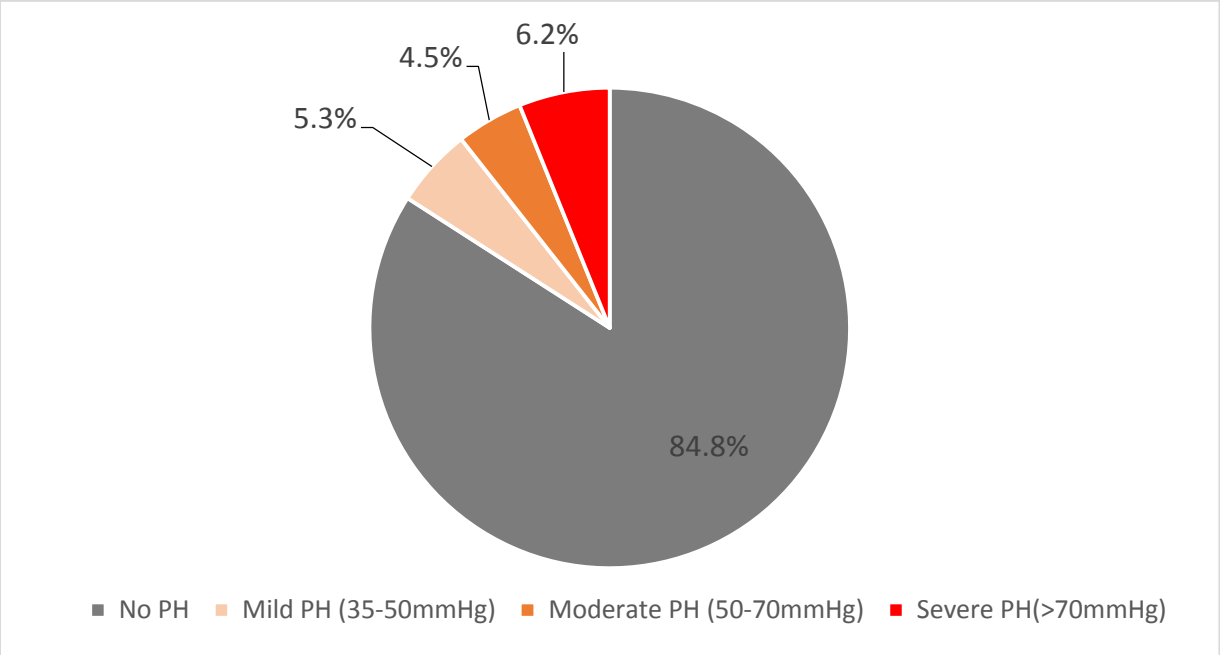
Variables	Count	Percentage
Creatinine level		
<1.2	47	19.3
1.2-1.5	53	21.8
1.6-2.5	90	37.0
2.6-4.5	33	13.6
>4.5	20	8.2
Hemoglobin level		
Female		
<8 g/dL	6	6.5
8–9.9 g/dL	9	9.7
10–11.9 g/dL	18	19.4
>12g/dl	60	64.5
Male		
<8 g/dL	6	4.0
8–10.9 g/dL	13	8.7
10–12.9 g/dL	20	13.3
>13g/dl	111	74.0
Total calcium		
Less than 8.5	32	13.2
8.5-10.5	108	44.4
>10.5	15	6.2
Mean Low-density lipoprotein (n= 155)	77.54+32.52	
<100 mg/dL	121	49.8
>100 mg/dl	34	14.0
Triglyceride level(n=152)	135.19+74.2	
<150 mg/dL	103	42.4

>150 mg/dL	49	20.2

6.4. Prevalence of PH among CKD

The overall prevalence of pulmonary hypertension (PH) is 16.04% (39/243)(95%CI,11.8-21.7%) with 6.2% of individuals exhibiting severe PH (>70 mmHg), 5.3% with mild PH (35-50 mmHg), and 4.5% with moderate PH (50-70 mmHg) (Figure 1). Additionally, right ventricular hypertrophy (RVH) was observed in 15.3% of individuals, and 64 % had documented tricuspid regurgitation (TR). Among 215 individuals with documented left ventricular ejection fraction (LVEF), 57.2% had a normal LVEF (>50%), 22.2% had a mildly reduced LVEF (40-49%), and 9.1% had a reduced LVEF (<40%).

Figure 1: Prevalence of PH among CKD patients in a tertiary Hospital in Addis Ababa, Ethiopia



6.5. Comorbidities for PH among CKD patients

The major findings of the study highlighted that left heart disease was the most prevalent comorbidity found in 30.8% of PH patients followed by valvular heart disease 25.6%. Current/previous pulmonary TB accounted for 17.9%, HIV 7% and HIV with TB coinfection accounts for 10.3% of total PH patients with CKD.

Table 4: The proportion of PH among the comorbidities

Variables	Count	Percentage
HIV	3	7.7
Current/previous TB	7	17.9
HIV+ TB	4	10.3
Valvular heart disease	10	25.6
Left side heart disease	12	30.8
COPD	2	5.1
Thyroid disease	1	2.6

6.6. Risk factors for PH among CKD patients

In the crude analysis (COR), variables with a p-value less than 0.2 were considered for further analysis. Stage 3-5 CKD (p=0.031), presence of type 2 diabetes mellitus (p=0.043), presence of hypertension (p=0.008), creatinine level (p=0.09), and hemoglobin level (p=0.08) met the inclusion criteria for multivariable analysis.

In the multivariable analysis, patients with stage 3-5 CKD had a 3.32 times higher likelihood of developing pulmonary hypertension (PH) compared to those with stage 1-2 CKD (AOR: 3.32, 95% CI: 1.95-11.58, p=0.048). The presence of type 2 diabetes mellitus was associated with a 3.18-fold increased risk of PH compared to those without diabetes (AOR: 3.18, 95% CI: 1.28-7.89, p=0.01). Similarly, patients with hypertension had a 3.11-fold higher likelihood of developing PH compared to non-hypertensive individuals (AOR: 3.11, 95% CI: 1.35-7.19, p=0.008)(table 4).

Table 4: Binary logistic Analysis of Factors Associated with Pulmonary Hypertension in CKD Patients in tertiary hospital in Addis Ababa, Ethiopia

Variables	COR (95%CI)	P-Value	AOR (95%CI)	P- value
Stage 3-5 CKD staging	3.83(1.13,12.98)	0.031	3.32(1.95,11.58)	**0. 048**
Creatinine level	1.18(0.98,1.39)	0.09	1.08(0.87,1.33)	0.49
Hemoglobin level	0.89(0.79,1.01)	0.08	0.92(0.81,1.05)	0.22
Presences of T2DM	2.45(1.03,5.86)	0.043	3.18(1.28,7.89)	**0.01**
Presences of HTN	2.93(1.32,6.53)	0.008	3.11(1.35,7.19)	**0.008**

COR: Crude Odds Ratio, AOR: Adjusted Odds Ratio

7. Discussion

This study aimed to determine the prevalence of PH among CKD patients attending follow-up at a tertiary hospital in Ethiopia. The overall prevalence of PH was 16.04%, with 6.2% of individuals exhibiting severe PH (>70 mmHg). Stage 3-5 CKD, the presence of T2DM, and hypertension were identified as independent risk factors for PH.

The prevalence of PH in CKD patients varies significantly across studies. In our study, the overall PH prevalence was 16.04%, with 6.2% of cases classified as severe. This is notably lower than global meta-analyses, which reported rates of 30–42% in CKD populations, particularly among dialysis-dependent patients [6,19,20]. However, it aligns more closely with regional data from Iraq (15%) in stage V CKD) [22] and Egypt (23.5%) [27]. These discrepancies may stem from differences in diagnostic criteria, such as the use of echocardiography in our study versus right heart catheterization in Egypt [27], which captures milder cases. Additionally, our cohort includes 7 dialysis patients compared to meta-analyses that predominantly pool data from these high-risk subgroups. For example, China and India reported PH prevalence as high as 47–50% in dialysis populations [21,2], underscoring the impact of renal replacement therapy on PH risk. Somalia's exceptionally high prevalence (51%) [13] Highlights how regional factors, such as older age and limited healthcare access, may exacerbate the PH burden.

The 6.2% prevalence of severe PH (sPAP >70 mmHg) in our study further highlights a high-risk subgroup. Severe PH is often irreversible and linked to poor outcomes, as seen in China, where 10–25% of CKD patients on hemodialysis develop severe PH due to vascular calcification and chronic volume overload [21]. Our lower severe PH prevalence may reflect earlier detection, less advanced cardiac remodeling, or differences in diagnostic rigor (e.g., echocardiography vs. catheterization)**.**

Advanced CKD (stages 3–5) emerged as a central risk factor in our study aligns with global trends, including studies from China, where advanced (on dialysis) populations exhibit high PH prevalence (42–58%) might be related to prolonged fluid shifts and vascular stress [21]. In our patients, the development of the PH might be due to mechanisms such as fluid overload from impaired sodium excretion, uremic toxin accumulation, and secondary hyperparathyroidism, which promote endothelial dysfunction and vascular calcification [6,21]. Type 2 diabetes mellitus was independently associated with PH in our study which aligns with findings from India and the U.S.**,** where T2DM amplifies PH risk [2,23]. Lastly, HTN a well-documented PH

risk factor, was another factor identified in our findings, consistent with India [2] and U.S. [23] studies that tie HTN to left ventricular dysfunction and pulmonary venous congestion. However, dialysis-centric cohorts (e.g., China [21]) prioritize fluid overload and arteriovenous fistula hemodynamics, whereas our non-dialysis-heavy cohort underscores Hypertension metabolic contributions.

8. Strength and limitations

This study represents the first investigation of pulmonary hypertension (PH) among chronic kidney disease (CKD) patients in Ethiopia, addressing a critical gap in regional nephrology and cardiology literature. The use of standardized diagnostic criteria for PH (echocardiographic thresholds) and CKD (KDIGO 2012 guidelines) ensures consistency with global practices, enhancing comparability with international studies by integrating sociodemographic, clinical, and laboratory variables, this holistic approach aligns with mechanistic frameworks from global studies while contextualizing findings to the Ethiopian clinical setting.

The study has several limitations. The retrospective cross-sectional design introduces potential selection bias, as incomplete medical records (20% non-response rate) may exclude high-risk patients or those lost to follow-up. Reliance on echocardiography (sPAP ≥35 mmHg) rather than right heart catheterization (the gold standard) risks underestimating PH prevalence, particularly in milder cases, and may misclassify patients due to technical limitations. The single-center setting at a tertiary hospital limits generalizability to rural or non-specialized healthcare settings, where CKD management and diagnostic resources may differ substantially.

9. Conclusion and recommendations

This study underscores PH as a significant comorbidity in Ethiopian CKD patients, with an overall prevalence of 16.04% and severe PH observed in 6.2% of cases. Advanced CKD (stages 3–5), hypertension, and type 2 diabetes mellitus (T2DM) emerged as critical independent risk factors, aligning with global mechanistic pathways.

To address the burden of pulmonary hypertension (PH) in chronic kidney disease (CKD) patients in Ethiopia, a multifaceted approach is essential. Clinically, PH screening via echocardiography should be integrated into routine care for high-risk CKD patients, particularly those with advanced stages (3–5), type 2 diabetes mellitus (T2DM), and or hypertension. Further research, including prospective multicenter studies with biomarker integration and expanded regional

collaborations, is needed to elucidate longitudinal PH trajectories and improve generalizability across diverse settings.

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Questionnaire

This extraction sheet is designed to assess Prevalence and associated factors of pulmonary hypertension among chronic kidney disease patients in Tikur Anbessa Specialized Hospital in Addis Ababa, Ethiopia.

No	**Variables**	**Response**	Skip
I.	**Sociodemographic variables**		
1.	Age (year)	_____	
2.	Sex	1. Male 2. Female	
3.	Location/ address	1. Kolla(lowlands) 2. Woina dega (midlands) 3. Dega (highlands)	
4.	Height (in cm)	_____	
5.	Weight (in kg)	_____	
6.	Body mass index		
II.	**Lifestyle and medical history**		
7.	Smoking history	1. Never smoke 2. Current smoker 3. Previous smoker	
8.	Alcohol consumption	1. Never 2. Occasionally 3. Regularly	
9.	Khat use	1. Never 2. Occasionally 3. Regularly	
III.	**Chronic kideny disease**		
10	Duration of CKD	_____	
11	Stage of CKD	1. G1 (GFR ≥ 90) 2. G2 (GFR 60- 89) 3. G3a (GFR 45–59) 4. G3b (GFR 30-44) 5. G4 (GFR15-29) 6. G5(GFR< 15 mL/min/1.73)	
12	Primary cause of CKD	1. Diabetes: specify type _____ 2. Hypertension 3. Glomerulonephritis 4. Polycystic kidney disease 5. Other (please specify):_____	
13.	Comorbidities	1. HIV 2. Left heart disease	

		a) Diastolic dysfunction or systolic dysfunction b) VHD c) CHD 3. COPD 4. Post TB lung disease 5. PTE 6. OSA 7. Thyroid disorder_____	
IV.	**Treatment and Management of CKD and it's complication**		
14.	Are you currently on dialysis?	1. Yes 2. no	
15.	Duration on dialysis		
16.	Are you taking medications for CKD?	1. Yes 2. No	
17.	If yes specify	_____	
18.	Use of erythropoiesis-stimulating agents (ESA)	1. Yes 2. No	
19.	If on ESA, duration		
V.	**Diagnosis of PH**		
20.	If PH diagnosed	1. Yes 2. No	
21.	If yes, severity of PH	1. mild (35–50mmHg) 2. moderate (50–70mmHg) 3. severe (>70mmHg)	
22.	Echocardiography findings:	1. Presence of right ventricular hypertrophy 1. Yes 2. No 2. Presence of tricuspid regurgitation (Yes/No) 1. Yes 2. No 3. Estimated pulmonary artery systolic pressure (mmHg)_____ 4. LV ejection fraction _____	
23.	New York Heart Association (NYHA) Functional Classification (I-IV),if symptoms		
VI.	**Investigation**		
24.	Updated creatinine		
25.	Hemoglobin		
26.	Calcium		
27.	PTH		
28.	eGFR		

29.	LDL cholesterol		
30.	Total Triglycerides		
31.	Hepatitis B virus surface antigen	1. Positive 2. Negative	
32.	Hepatitis C virus Ab	1. Positive 2. Negative	