e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(11); 01-06

Original Research Article

# A Study to Assess the Proportion of Pulmonary Artery Hypertension in Chronic Kidney Disease Patient

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**Received: 25-08-2023 / Revised: 28-09-2023 / Accepted: 30-10-2023**
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**Conflict of interest: Nil**

**Abstract:**

**Objectives:** To measure the Pulmonary artery systolic pressure of patients diagnosed with chronic kidney disease using Echocardiogram.

**Methodology:** In this cross-sectional study, Patients seeking medical attention at Sri Aurobindo Medical College and Post Graduate Institute, who have been diagnosed with chronic kidney disease from April 2021 to September 2022 were included. Patients who attend the Emergency/OPD were asked to participate in the study. Informed written consent was taken from all the patients. A pre-structured proforma was used to record the patient data. Detailed clinical examination, Echocardiogram, Chest X ray and biochemical tests was done in all participants.

**Results:** In present study incidence of pulmonary artery hypertension (PAH) in patients with CKD was 53%. Mean SBP was higher in patients with PAH (149.06±14.042) than patients without PAH (147.66±13.386). However, no significant difference was obtained in terms of mean SBP among the patients with PAH as compared to those without PAH. P value of this association was 0.613. Mean DBP was significantly higher in patients with PAH (93.58±4.568) than patients without PAH (88.72±8.107). There was a significant difference obtained in terms of mean DBP among the patients with PAH as compared to those without PAH.

**Conclusion:** It was shown that there is a substantial association between pulmonary arterial hypertension (PAH) and chronic kidney disease (CKD) patients, with a prevalence rate of 53%. Furthermore, it was observed that the severity of PAH tends to rise as renal function deteriorates in individuals with CKD. Anemia, hypertension and left ventricular failure have been identified as risk factors associated with the development of pulmonary arterial hypertension (PAH). The mitigation of these risk factors has the potential to attenuate the progression and severity of pulmonary arterial hypertension (PAH), thereby leading to a reduction in the morbidity and mortality rates associated with chronic kidney disease (CKD).

**Keywords:** PAH; SBP; DBP; CKD.



## Introduction

The term "pulmonary hypertension" (PHT) is used to describe a range of clinical and pathophysiological entities that share similar characteristics but have different causes. [1] Multiple factors contribute to PHT's development. There are a variety of causes of pulmonary hypertension, including problems with the heart, lungs, or the body as a whole. Long-term PHT causes greater morbidity and mortality than would be predicted by the underlying cause. [2] Patient hypertension (PHT) was common in those with chronic renal failure (CRF). [3,4] Forty percent of patients with ESRD undergoing chronic hemodialysis treatment by arteriovenous access were found to have PHT, according to a review of the relevant literature. [5-7] PHT is a significant risk factor for death among those with ESRD. Increased resistance to flow is caused by plexiform lesions in the lungs, which cause vasoconstriction and blockage of tiny arteries in the lungs, leading to PHT. Dysregulation of endothelial growth and an angiogenic response to local triggers have been proposed as explanations for the development of the plexiform lesion.[3] An increase in pulmonary vascular resistance and constriction of the pulmonary arteries may result from the hormonal and metabolic disturbances seen in ESRD. [4] High cardiac output from the heart can add to already elevated pulmonary arterial pressure (PAP), as can the common conditions of anaemia and fluid

overload. [8] The abnormal myocardial diastolic dysfunction seen in ESRD patients is subclinical, not the systolic dysfunction seen in the general population. [9] Vasodilators like nitric oxide and vasoconstrictors like thromboxane work together to control the local vascular tone and function of pulmonary arteries. [10] A deficiency in nitric oxide activity is linked to the endothelial dysfunction seen in patients with CRF, and this dysfunction is not improved by hemodialysis (HD). [11] In addition to age and left ventricular hypertrophy, renal failure and PHT have also been linked to elevated levels of brain natriuretic hormone. The BNP byproduct N-terminal pro-brain natriuretic peptide (NT-pro BNP) has been shown to have prognostic value in PHT. [12] The aim of the present study was to assess the proportion of pulmonary artery hypertension in chronic kidney disease patients.

**Objectives**

To measure the Pulmonary artery systolic pressure of patients diagnosed with chronic kidney disease using Echocardiogram.

**Material and Methods**

This study was done among patients who have been diagnosed with chronic kidney disease, seeking medical attention at Sri Aurobindo Medical College and Post Graduate Institute, Hospital for the duration of 18 months (April 2021 to September 2022).

**Inclusion Criteria**

1. Inpatients and Outpatients patients above the age of 18 years who are admitted in Sri Aurobindo Medical College and PG institute,
2. Diagnosed with Chronic Kidney disease.
3. Are on maintenance hemodialysis at the Centre.

**Exclusion Criteria**

1. Pregnancy
2. Patients already on pulmonary artery hypertension medication
3. Patients not giving written consent

**Sample Size**

Data of 100 patients fitting in the inclusion criteria were included in the study with voluntary consent. SAIMS OPD has a yearly input of 100+ newly diagnosed and old patients with chronic kidney disease thereby making our sample size of 100 patients with chronic kidney disease as feasible.

**Methodology**

The study sought the participation of individuals who sought medical attention in the Emergency/Outpatient Department. All patients provided informed written permission. A standardized form was utilized to document the patient data and conduct a comprehensive clinical examination, including an echocardiogram, chest X-ray, and metabolic testing, which were performed on all participants.

Definition of pulmonary artery hypertension: All participants with Pulmonary artery systolic pressure greater than 30mm Hg were considered to have Pulmonary artery hypertension.

**Statistical Analysis**

The data was recorded using the Microsoft Excel software, and statistical analysis was conducted using the SPSS programme for Windows, specifically version 25 (SPSS, Chicago, Illinois). The study's findings were reported in terms of continuous variables, which were expressed as the mean value plus or minus the standard deviation. Categorical variables, on the other hand, were provided as absolute values accompanied by their respective percentages. Prior to doing the statistical analysis, the data underwent a normality check. A descriptive analysis was conducted in order to acquire a comprehensive understanding of the demographic and other relevant characteristics of the research population. The analysis of categorical variables was conducted using either the chi-square test or Fisher's exact test. The assessment of continuous variables was conducted using analysis of variance (ANOVA) or independent samples t-test. A significance level of $P<0.05$ was deemed to be statistically significant.

**Observation and Results**

In present study incidence of pulmonary artery hypertension (PAH) in patients with CKD was 53%. Mean age of patients with PAH in CKD was 47.19±14.821 years as compared to those without PAH (49.83±13.049 years). However no significant difference was seen.

**Table 1: Distribution according to pulmonary artery hypertension (PAH) status**

| CKD with PAH | Frequency | Percent |
|---|---|---|
| No | 47 | 47.0 |
| Yes | 53 | 53.0 |
| Total | 100 | 100.0 |

Table 1 shows that incidence of pulmonary artery hypertension in patients with CKD was 53%. This signifies a greater proportion of PAH in patients with CKD.

**Table 2: Comparing mean blood pressure with PAH status**

| BP | PAH (Yes/No) | N | Mean | SD | Std. Error Mean | P value |
|---|---|---|---|---|---|---|
| SBP | Yes | 53 | 149.06 | 14.042 | 1.929 | 0.613 |
| | No | 47 | 147.66 | 13.386 | 1.953 | |
| DBP | Yes | 53 | 93.58 | 4.568 | 0.986 | 0.011 |
| | No | 47 | 88.72 | 8.107 | 1.037 | |

*Independent Samples Test

Above table shows the numerically mean SBP was higher in patients with PAH (149.06±14.042) than patients without PAH (147.66±13.386). However, no significant difference was obtained in terms of mean SBP among the patients with PAH as compared to those without PAH. P value of this association was 0.613. Mean DBP was significantly higher in patients with PAH (93.58±4.568) than patients without PAH (88.72±8.107).

There was a significant difference obtained in terms of mean DBP among the patients with PAH as compared to those without PAH. P value of this association was 0.011.

**Table 3: Comparing mean urea and creatinine with PAH status**

| RFT | PAH | N | Mean | SD | Std. Error Mean | P-value |
|---|---|---|---|---|---|---|
| Urea | Yes | 53 | 96.53 | 41.529 | 5.704 | 0.340 |
| | No | 47 | 88.11 | 46.284 | 6.751 | |
| Creatinine | Yes | 53 | 6.91 | 3.620 | 0.49728 | 0.091 |
| | No | 47 | 5.77 | 2.962 | 0.43214 | |

Above table shows that numerically mean level of urea was higher in patients with PAH (96.53±41.529) than patients without PAH (88.11±46.284). However, no significant difference was obtained in terms of mean level of urea among the patients with PAH as compared to those without PAH. P value of this association was 0.340. Similarly, numerically mean creatinine level was higher in patients with PAH (6.91±3.620) than patients without PAH (5.77±2.962). However, no significant difference was obtained in terms of mean creatinine level among the patients with PAH as compared to those without PAH. P value of this association was 0.091.

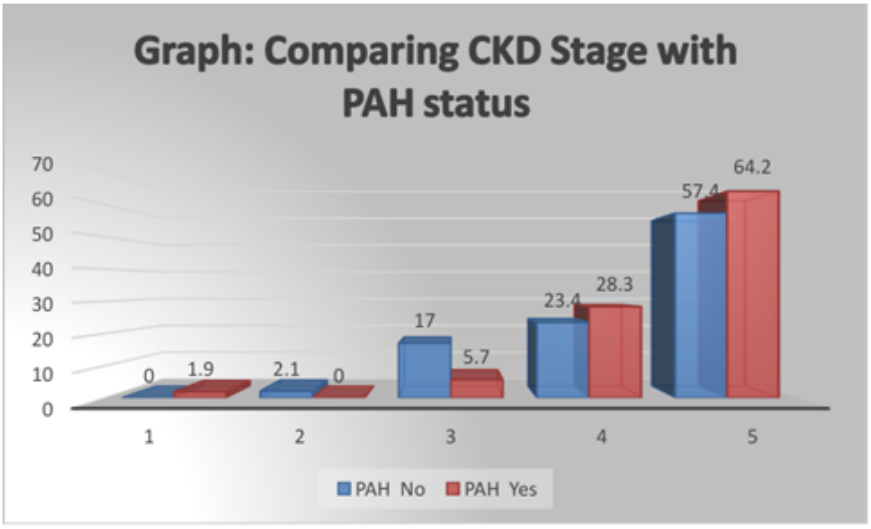


**Figure 1: Comparing CKD Stage with PAH status**

Above graph shows the majority of the patients with PAH were reported to have CKD Stage 5 (64.2%) followed by CKD Stage 4 (28.3%) and 3 (5.7%).

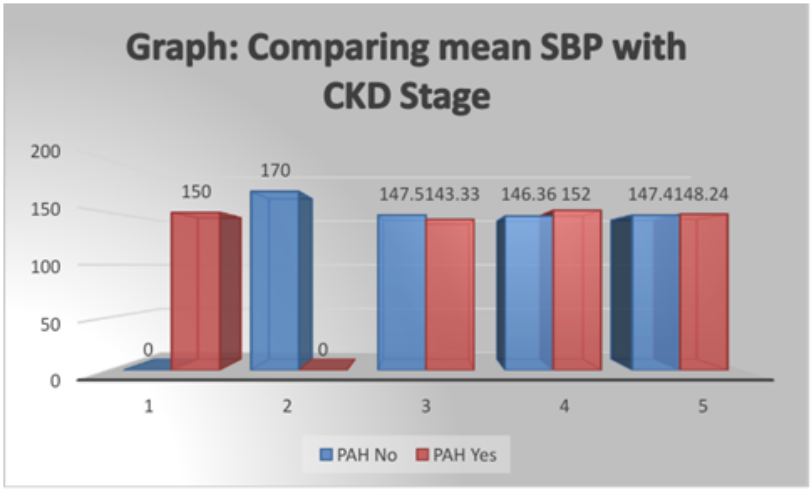


**Figure 2: Comparing mean SBP with CKD Stage in patients with/ without PAH**

Above graph shows that no significant difference was obtained in terms of mean SBP with respect to different CKD Stages among the patients with PAH. Majority of the patients with PAH were reported to have CKD Stage 5 (64.2%) followed by CKD Stage 4 (28.3%) and 3 (5.7%).

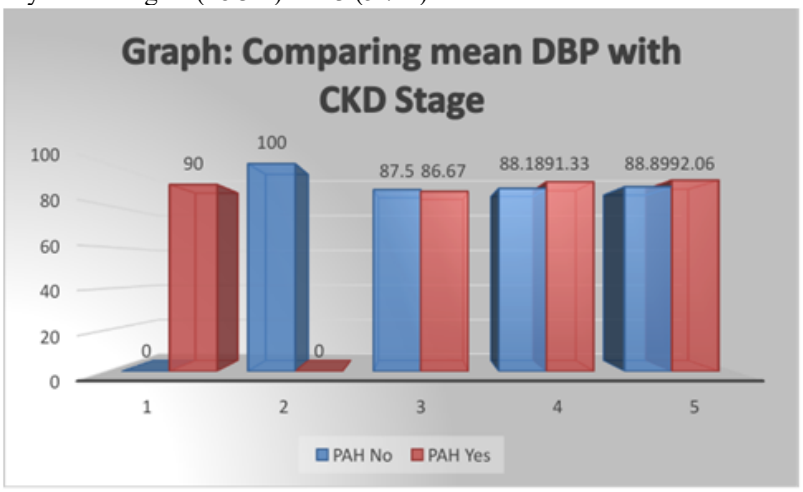


**Figure 3: Comparing mean DBP with CKD Stage in patients with/ without PAH**

Above graph shows that no significant difference was obtained in terms of mean DBP with respect to different CKD Stages among the patients with PAH.

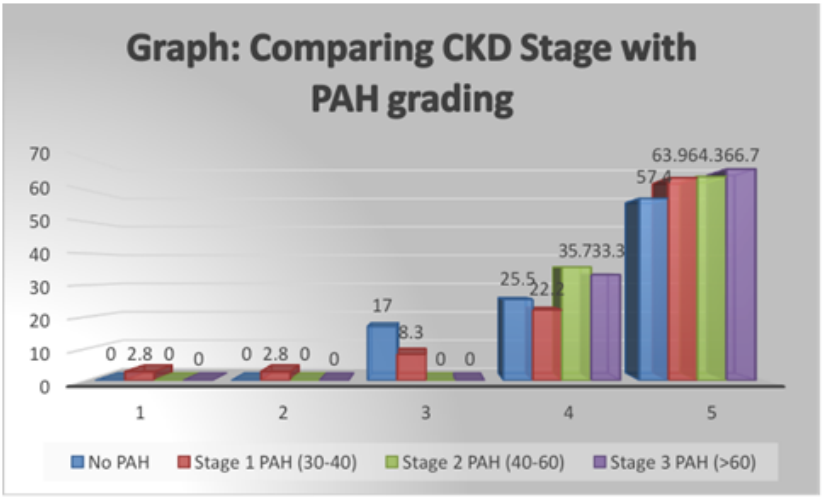


**Figure 4: Comparing CKD Stage with PAH grading**

Above graph shows that no significant difference was obtained for PAH grading across the CKD Stage as revealed by the insignificant p value of 0.772. However numerically it was observed that for CKD Stage 4 and 5 majority had stage 3 PAH.

## Discussion

In present study, we observed prevalence of the pulmonary artery hypertension (PAH) in patients with CKD was 53%. According to several studies, the prevalence of PH ranged from 9 to 39% in people with stage 5 CKD, 18.8 to 68.8% in people receiving hemodialysis, and 0 to 42% in people receiving peritoneal dialysis. [13] According to Wei Shi et al., the prevalence of PH was 2.2, 6.7, 7.9, 15.2, 20.0, and 37.5%, respectively, in CKD Stages 1 to 5 respectively. [14] The prevalence of PH in CKD stage 1–5 was 14.29, 33.33, 38.89, 40.91 and 64.47%. [15] Prevalence estimates are variable due to several possible reasons. First, varying definitions of PH might account for varying prevalence estimates. Second, variable degrees of volume overload might also confound the prevalence. Third, some of CKD patients' lacks echocardiography data were excluded. In present study, the mean SBP was higher in patients with PAH (149.06±14.042) than patients without PAH (147.66±13.386). However, no significant difference was obtained in terms of mean SBP among the patients with PAH as compared to those without PAH. Mean DBP was significantly higher in patients with PAH (93.58±4.568) than patients without PAH (88.72±8.107). Lowering systemic blood pressure reduces the rate of CKD progression and international consensus guidelines recommend a systemic systolic blood pressure below 140 mmHg and a diastolic blood pressure below 90 mmHg in non-diabetic patients with CKD. [16] Elevated systemic blood pressure is an increasingly recognized co- morbidity in PAH and was reported in recent PAH registries between 27% and 40%. [17] In older patients with CKD, SBP predicts ESRD and a higher SBP and lower DBP predicts all- cause mortality. Lower BP of <110/70 mmHg is a marker of higher mortality in older individuals with advanced CKD.[18] We reported the mean urea level (96.53±41.52 vs 88.11±46.28) and mean creatinine level (6.91±3.62 vs 5.77±2.96) higher in patients with PH compared to non-PH CKD patients but the difference was not statistically significance ($p>0.05$). Mehta et al. reported mean blood urea nitrogen (BUN) and serum creatinine were found to be statistically associated with PH, $p = 0.02$ and $p < 0.001$, respectively.[19] The current study observed a statistically significant correlation ($p < 0.001$) between stages of chronic kidney disease (CKD) and pulmonary hypertension (PH), suggesting that as the CKD stage progresses, there is an increased occurrence of PH. As a tertiary referral facility, the majority of our patients are often referred at a later stage, and all individuals included in our research cohort were classified as being in stage III, IV, or V. In their study, Yang et al. (20) discovered a prevalence of 23.76% (24/101) for pulmonary hypertension (PH) in stage II, and 48.15% (13/27) in the group with a glomerular filtration rate (GFR) below 60 mL/min/1.73 m2 ($p < 0.05$). These findings indicate that PH may be present and prevalent even before a decline in GFR to below 60 ml/min/1.73 m2, therefore warranting attention. The study conducted by Li et al. observed the presence of severe pulmonary hypertension (PH) in patients with stage-V and stage-VD chronic kidney disease (CKD), as well as an elevated incidence of PH and cardiovascular morbidity as the renal illness advanced. [21] The precise processes behind pulmonary hypertension (PH) in advanced stages of chronic kidney disease (CKD) are still not well comprehended. The occurrence and exacerbation of pH may be influenced by left ventricular abnormalities and common risk factors associated with chronic kidney disease (CKD), such as volume overload, arteriovenous fistula (AVF), sleep apnea, exposure to dialysis membranes, impaired endothelial function, vascular calcification and stiffness, and severe anaemia. [13,22] ESRD-related pulmonary hypertension (PH) was classified as the fifth subtype, namely PH with uncertain multifactorial causes, by the World Symposium of Pulmonary Hypertension (WSPH) for the first time. [23] This cohort comprises individuals with chronic kidney disease (CKD) who do not have substantial cardiac or pulmonary comorbidities. The process of excluding these concomitant disorders, which were observed in a majority of patients (ranging from 40% to 70%) across various cohorts, often entails the use of chest radiography, pulmonary function tests, CT scans, and ventilation/perfusion studies. [22]

## Conclusion

The study findings indicate a substantial association between pulmonary arterial hypertension (PAH) and chronic kidney disease (CKD), with a prevalence rate of 53%. Furthermore, the severity of PAH appears to escalate as renal function deteriorates in individuals with CKD. Anemia, hypertension and left ventricular failure have been identified as risk factors associated with the development of pulmonary arterial hypertension (PAH).

The mitigation of these risk factors has the potential to attenuate the progression and intensity of pulmonary arterial hypertension (PAH), thereby leading to a reduction in the morbidity and mortality rates associated with chronic kidney disease (CKD).

## Acknowledgement

Authors would like to thank the whole staff of the medicine department who helped to collect the data from the Emergency/OPD. We would like to express our gratitude to everyone who has offered support and assistance in any way during the course of our research.

**Funding:** None

**Authors' Contributions**

KT- Definition of intellectual content, literature review, prepared first draft of manuscript, implementation of study protocol, data collection, data analysis, and manuscript preparation; PSS- Concept, design, clinical protocol, manuscript preparation, editing, and manuscript revision; HR- Design of study, literature survey, statistical analysis and interpretation, manuscript preparation, review, and submission of article; AJ- editing, and manuscript preparation, manuscript submission.

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