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PULMONARY HYPERTENSION IN CHRONIC KIDNEY DISEASE: PREVALENCE AND ASSOCIATION WITH DISEASE STAGE

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ABSTRACT

Background: Pulmonary hypertension (PH) is an emerging cardiovascular complication in patients with chronic kidney disease (CKD), especially in advanced stages and end-stage renal disease. It is associated with increased morbidity and mortality[1]. This cross-sectional study assessed the prevalence of PH among non-dialysis and dialysis CKD patients and examined the correlation between PH severity and CKD stage in a tertiary care center. **Methods:** A total of 171 adult CKD patients (Stage III–V) at a tertiary hospital in central India were evaluated. Clinical data, CKD stage (by estimated glomerular filtration rate), and relevant laboratory parameters were recorded. PH was assessed via 2-dimensional echocardiography, defined as pulmonary artery systolic pressure ≥35 mmHg at rest, and categorized as mild, moderate, or severe. Data were analyzed with appropriate statistical tests to identify associations between PH (presence and severity) and CKD stage and other clinical variables. **Results:** The overall prevalence of PH in the CKD cohort was 39.2% (67 of 171 patients). PH prevalence rose significantly with advancing CKD stage: 14.7% in Stage III, 41.3% in Stage IV, and 47.3% in Stage V ($p=0.01$)[2][3]. All PH cases were mild-to-moderate; no patient had severe PH. Patients on maintenance hemodialysis had a higher rate of PH than non-dialysis patients ($p<0.01$). Longer duration of CKD (>5 years) and the presence of an arteriovenous (AV) fistula were associated with higher PH prevalence ($p<0.05$). There was no significant difference in age or sex distribution between PH and non-PH groups. Among laboratory parameters, only hemoglobin levels were significantly different: PH patients had more severe anemia (mean Hb 7.3±1.2 g/dL) compared to those without PH (9.8±2.1 g/dL, $p=0.003$)[4][5]. Serum calcium, phosphate, calcium-phosphate product, and creatinine did not differ significantly between PH and non-PH groups in this cohort ($p>0.3$). **Conclusions:** PH is a common complication in CKD patients, observed in roughly two out of five patients in this study, and its prevalence increases with CKD progression. Advanced CKD (Stage V), coexisting diabetes and hypertension, longer dialysis vintage, and presence of an AV fistula are associated with higher risk of PH. These findings underscore the importance of screening for PH in CKD, particularly in advanced stages, and managing contributory factors like anemia and volume overload to potentially mitigate PH risk.

KEYWORDS

chronic kidney disease; pulmonary hypertension; prevalence; hemodialysis; anemia

INTRODUCTION

Chronic kidney disease is a prevalent global health problem, affecting approximately 10–15% of the population[1]. Cardiovascular disease is the leading cause of death in CKD, and pulmonary hypertension (PH) has been recognized as an important but underappreciated cardiovascular complication in this population[1]. Prior studies have reported a wide range in PH prevalence among CKD patients: from about 8–39% in non-dialysis CKD and 27–58% in end-stage renal disease (ESRD) patients on dialysis[1]. The presence of PH in CKD is clinically significant, as it has been associated with higher risks of hospitalization and mortality[1].

PH in CKD is classified under Group 5 PH (PH with multifactorial mechanisms), reflecting its complex and multifactorial pathophysiology[6]. Contributing factors include left ventricular diastolic dysfunction leading to pulmonary venous hypertension, increased cardiac output and blood flow from anemia and arteriovenous fistulae, volume overload, endothelial dysfunction, and vascular calcification, among others. Despite the high prevalence and poor prognosis associated with PH in CKD, this condition often goes undiagnosed in nephrology practice because patients' cardiopulmonary symptoms may be attributed to other causes.

There is a need for further evidence on the burden of PH in CKD patients in different populations and settings, as well as on risk factors that could be modified to improve outcomes. This study was undertaken to determine the prevalence of PH among CKD patients in a tertiary care center in central India and to evaluate the relationship between PH (and its severity) and CKD stage. We also assessed clinical and biochemical correlates of PH in this cohort. We hypothesized that PH would be common in advanced CKD and that its severity would correlate with the progression of kidney disease.

METHODS

Study Design And Patients: This was a cross-sectional observational study conducted at a tertiary care hospital in central India. We enrolled 171 patients aged 18 years or older with a confirmed diagnosis of CKD (defined by Kidney Disease Improving Global Outcomes criteria) who were either hospitalized or seen in nephrology clinics. Only patients in CKD Stage III, IV, or V were included, as these represent moderate to advanced CKD. Patients in CKD Stages I–II were not included in the study. Exclusion criteria were any co-existing conditions known to independently cause PH or confound its assessment: e.g. chronic lung diseases, valvular or congenital heart disease, ischemic heart disease, connective tissue disorders, HIV infection, and pregnancy. All patients provided informed consent, and the study received approval from the institutional ethics committee.

Data Collection: For each patient, we recorded demographic information, relevant medical history (especially etiologies of CKD such as diabetes mellitus or hypertension, duration of CKD, dialysis status and duration, presence of AV fistula), and a review of systems for CKD-related symptoms. Blood pressure and a focused physical examination were performed, noting signs such as anemia (pallor) or fluid overload (edema, raised jugular venous pressure). Laboratory investigations included complete blood count, renal function tests (blood urea, serum creatinine), electrolytes, serum calcium and phosphate, and other relevant parameters. Estimated glomerular filtration rate (eGFR) was calculated using the MDRD formula, and CKD was staged (I–V) according to eGFR.

Echocardiographic Assessment: Transthoracic 2D echocardiography with Doppler was carried out for all patients to screen for PH and evaluate cardiac function. Pulmonary artery systolic pressure (PASP) was estimated from the tricuspid regurgitation jet velocity using the modified Bernoulli equation. PH was defined as a PASP ≥35 mmHg at rest. The severity of PH was categorized based on PASP: mild PH 35–49 mmHg, moderate PH 50–69 mmHg, and severe PH ≥70 mmHg. Left ventricular ejection fraction and the presence of any left heart abnormalities were also noted to rule out significant left-sided heart disease. In patients on hemodialysis, echocardiography was performed on a non-dialysis day in an optimized volume state.

Statistical Analysis: Data were tabulated and analyzed using SPSS (v22). Continuous variables are presented as mean ± standard deviation, and categorical variables as frequencies or percentages. Group comparisons (e.g. patients with PH vs. without PH) were made using Student's t-test for continuous data and Chi-square test for categorical data. One-way ANOVA was used to compare continuous variables across CKD stages. A p-value <0.05 was considered statistically significant. A multivariate logistic regression analysis (enter method) was performed to identify independent predictors of PH, including variables that were significant in univariate analysis (such as CKD stage, CKD duration, dialysis status, AV fistula, and comorbid conditions).

RESULTS

Patient Characteristics: A total of 171 CKD patients were analyzed, of which 69.6% were male and 30.4% female. The mean age was 53.9 ± 13.1 years, with the largest proportion of patients in the 41–60 year age range. The most common identified causes of CKD were a combination of diabetes and hypertension (in 39.8% of patients) and hypertension alone (25.1%), followed by chronic glomerulonephritis (5.3%). In 26.3% of cases, no specific etiology was identified (idiopathic CKD). By design, the cohort consisted of Stage III (19.9%), Stage IV (26.9%), and Stage V (53.2%) CKD patients, reflecting a heavy representation of advanced CKD.

Prevalence Of Pulmonary Hypertension: Overall, 67 out of 171 CKD patients were found to have PH on echocardiography, yielding a prevalence of 39.2%. The majority of PH cases were mild in severity (35–49 mmHg PASP), with a smaller number of moderate cases, and none meeting criteria for severe PH in this cohort. Notably, PH was considerably more common in patients with more advanced CKD. Only 5 of 34 Stage III patients (14.7%) had PH, compared to 19 of 46 Stage IV patients (41.3%) and 43 of 91 Stage V patients (47.3%). This trend of increasing PH prevalence with higher CKD stage was statistically significant (χ^2 test, $p = 0.01$).

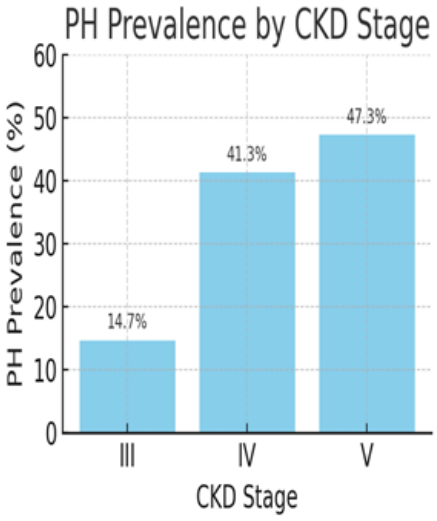

Figure 1. Prevalence of pulmonary hypertension among CKD patients by stage. The proportion of patients with PH increased markedly from Stage III to Stage V CKD (14.7% to 47.3%, $p<0.05$). Stages I–II were not represented in the study cohort.

Dialysis Status And Other Correlates Of PH: Among the 171 patients, 74 were on maintenance hemodialysis (with AV fistula in situ), while the rest were non-dialysis CKD patients. PH was significantly more prevalent in the hemodialysis group: 38 of 74 dialysis patients (51.4%) had PH, compared to 29 of 97 patients (29.9%) who were not on dialysis (Chi-square, $p<0.01$). Furthermore, longer duration of hemodialysis was associated with higher risk of PH; the mean dialysis vintage in PH patients was 4.3 ± 2.5 years versus 1.4 ± 1.1 years in those without PH ($p<0.001$). The presence of an AV fistula was also linked to PH: 50% of patients with AV fistula had PH, vs. 30.9% of those without fistula ($p=0.005$). In addition, a longer duration of CKD (regardless of dialysis) was correlated with PH prevalence – 50% of patients with CKD duration >5 years had PH, compared to only ~11% of those with CKD <1 year ($p=0.04$).

Patients with co-morbid diabetes mellitus plus hypertension (the two together) appeared more likely to have PH than those with other etiologies. Among 68 patients whose CKD was attributed to combined diabetes and hypertension, 34 (50%) had PH, whereas patients without this combination (other causes) had a lower PH rate (33/103, 32%). This association was statistically significant ($p=0.03$). Neither diabetes alone (without hypertension) nor hypertension alone was individually associated with PH in this cohort ($p>0.1$). There were no significant differences in mean age between the PH group and non-PH group (both ~54 years, $p=0.61$), and the male-to-female ratio among PH patients (1.58:1) was not significantly different from those without PH (3:1, $p=0.38$), indicating no strong influence of age or sex on PH occurrence, consistent with prior observations.

Laboratory Findings: The mean hemoglobin level of the study population was 9.3 ± 2.8 g/dL, reflective of anemia of CKD. Notably, patients with PH had significantly lower hemoglobin compared to those without PH (7.3 ± 1.2 vs. 9.8 ± 2.1 g/dL, $p = 0.003$). In fact, moderate-to-severe anemia was present in the vast majority of PH patients. Other laboratory parameters, such as serum calcium (mean ~8.4 mg/dL in the cohort), serum phosphorus (~3.8 mg/dL), and calcium-phosphate product (~31 mg^2/dL^2), showed expected trends of mineral metabolism disturbance in CKD but did not differ significantly between PH and non-PH groups ($p>0.3$ for all). Similarly, the mean serum creatinine was elevated (6.3 ± 4.0 mg/dL overall) and unsurprisingly higher in advanced CKD, but there was no statistically significant difference in creatinine levels between those with PH and those without ($p=0.31$), implying that CKD stage (rather than serum creatinine per se) was the stronger determinant of PH risk.

On multivariate logistic regression analysis, four factors emerged as independent predictors of PH in our CKD cohort: (1) CKD stage (each advance in stage significantly increased odds of PH, OR ~2.3 per stage, $p<0.001$), (2) the presence of combined diabetes and hypertension as CKD etiology (OR ~1.4, $p=0.001$) (3) longer hemodialysis duration (OR ~6.8 for PH per unit increase in years of dialysis, $p<0.001$), and (4) presence of an AV fistula (OR ~3.5, $p<0.001$). Age, sex, and diabetes alone were not significant predictors in the multivariate model. These results reinforce that advanced CKD, prolonged dialysis exposure, and associated conditions like AV fistula and co-morbid diabetes/ hypertension are key factors linked to PH in CKD patients.

DISCUSSION

In this cross-sectional study of CKD patients in a tertiary center, we found a high prevalence of pulmonary hypertension (39%) with a clear trend of increasing PH frequency in more advanced stages of CKD. This finding is consistent with a growing body of evidence that PH is a common complication of CKD. Prior studies from various regions have reported a prevalence of PH in CKD in the range of roughly one-third to one-half of patients. Our observed prevalence (39.2%) falls near the middle of this range. For instance, a large retrospective study by Zhang et al. (2018) noted an overall PH prevalence of 47% among 705 CKD patients in China, with prevalence rising from about 14% in CKD Stage 1 up to 64% in Stage 5. An Indian single-center study by Suresh et al. (2018) found PH in 43.5% of CKD patients at baseline, increasing to 50% at 6-month follow-up. Another study of Stage IV–V CKD patients in New Delhi reported PH in 61% of cases. Thus, our results corroborate that a substantial proportion of CKD patients develop PH, and the risk appears to accelerate as renal function declines to the very advanced stages.

Importantly, we demonstrated a significant association between CKD stage and PH: over half of Stage V patients had PH versus only ~15% in Stage III. This stage-PH correlation aligns with reports by other investigators. Atul et al. (2021) similarly observed that PH severity increased with CKD severity, with those on dialysis having more severe PH than predialysis CKD patients. The underlying mechanisms likely relate to the cumulative burden of risk factors in advanced CKD – prolonged exposure to fluid overload, high-flow state from AV fistulae, secondary hyperparathyroidism, and uremic vascular changes – which collectively drive pulmonary vascular remodeling and elevated pulmonary pressures. It is noteworthy that in our study no patients had "severe" PH (PASP ≥70 mmHg); most PH was mild. This may reflect earlier detection via echocardiography or perhaps the exclusion of other severe cardiopulmonary illnesses. In contrast, some other series have reported moderate to severe PH in a subset of CKD patients. For example, Mehta et al. (2019) found that among 60.5% of CKD patients with PH, nearly half had moderate PH. These differences could be due to variations in study population (ours included many newly diagnosed CKD patients and excluded significant cardiac disease) or differing thresholds for PH diagnosis.

Our analysis identified several factors associated with higher PH risk in CKD, many of which correspond to findings in the literature. Anemia was strongly linked to PH in our patients; the PH group had significantly lower hemoglobin levels. Anemia is nearly universal in advanced CKD and can contribute to high-output cardiac states and hyperdynamic circulation, potentially exacerbating pulmonary pressures. Previous studies have similarly noted an association between low hemoglobin and PH in CKD. In fact, Zhang et al. (2018) identified anemia as an independent predictor of PH in CKD. This underscores the importance of optimal anemia management in CKD,

not only to improve oxygen delivery but perhaps also to mitigate PH risk.

We also found that CKD patients with the combined comorbidity of diabetes and hypertension were more likely to have PH than those without this combination. Mehta et al. reported a comparable finding: the coexistence of diabetes and hypertension was significantly associated with PH in CKD. This likely reflects the fact that these conditions contribute to both CKD progression and cardiovascular changes (e.g. left ventricular dysfunction, arterial stiffness) that promote PH. Interestingly, in our cohort, diabetes or hypertension alone did not show a significant correlation with PH, suggesting that it is the synergistic effect of multiple comorbidities and end-organ damage that heightens PH risk.

Dialysis-related factors emerged as important contributors. CKD patients on maintenance hemodialysis had significantly more PH than non-dialysis patients, and longer duration of dialysis was an independent risk factor for PH. This association has been documented in prior studies. Hemodialysis can induce PH through several mechanisms: volume shifts, microembolization or endothelial dysfunction from exposure to dialysis membranes, and the creation of high-flow AV fistulas necessary for dialysis access. Our finding that patients with AV fistulas had higher PH prevalence is in line with reports by others, including Atul et al. who observed more PH in patients with AV fistula than those without. While an AV fistula is life-saving for dialysis, its presence causes increased cardiac output and may worsen pulmonary circulation stress over time. Some researchers have debated the extent of AV fistula contribution to PH, but our data add to evidence that it is a significant factor.

Notably, neither patient age nor sex was associated with PH in our study, which mirrors findings from other cohorts. PH occurred across a broad age range of adults with CKD, and while more men had CKD in our sample (as often seen in tertiary care data), the proportion of men and women affected by PH did not significantly differ. This suggests that the pathogenesis of PH in CKD is more related to disease-specific factors than demographic characteristics.

We did not observe significant differences in serum calcium, phosphate, or calcium-phosphate product between PH and non-PH patients, although trends toward higher phosphate and Ca–P product in advanced CKD were noted. Mehta et al. had reported an association of elevated Ca–P product with PH in their study, which we could not confirm, possibly due to our modest sample size or differences in mineral metabolism management. Similarly, although mean serum creatinine was higher in advanced CKD (Stage V) patients who also had more PH, creatinine itself was not a distinguishing factor for PH presence in multivariate analysis (once CKD stage was accounted for). Essentially, CKD stage encapsulates the decline in kidney function and associated metabolic derangements better than a single lab parameter.

Limitations: The cross-sectional design of this study limits the ability to infer causality or temporal relationships. We assessed PH at a single time-point; a longitudinal follow-up would be valuable to observe how PH progresses with CKD and whether it impacts survival. Additionally, PH was diagnosed by Doppler echocardiography estimation of PASP. While echocardiography is a practical and non-invasive screening tool, it can both underestimate or overestimate pulmonary pressures[6]. Right heart catheterization is the gold standard for PH diagnosis, but was not feasible in this context – thus some misclassification is possible. We also did not include CKD stage I–II patients, so conclusions apply only to moderate and advanced CKD. Despite these limitations, the study provides clinically relevant insights into PH among Indian CKD patients. The findings likely generalize to similar resource-limited healthcare settings where late presentation of CKD is common and echocardiography is used for cardiovascular evaluations.

CONCLUSION

This study confirms that pulmonary hypertension is a frequent complication in CKD patients, particularly in those with advanced disease. Approximately 39% of CKD stage III–V patients in our cohort had PH on echocardiographic assessment. The likelihood and severity of PH rise with worsening CKD stage, indicating a direct correlation between declining kidney function and pulmonary vascular changes. Furthermore, co-morbid conditions (especially the combination of diabetes and hypertension), prolonged dialysis exposure, and presence of an AV fistula are significant contributors to PH in CKD. Clinicians caring for CKD patients should be vigilant for signs of PH, such as unexplained dyspnea or elevated pulmonary pressures on echocardiograms, since timely recognition may prompt interventions (like stricter volume control, anemia management, or cardiac evaluation) to improve patient outcomes. Future research and longitudinal studies are warranted to determine if controlling risk factors (e.g. optimizing anemia treatment, refining dialysis practices) can reduce the development or progression of PH in CKD. Ultimately, a multidisciplinary approach involving nephrologists and cardiologists is recommended for managing CKD patients at risk of PH, to mitigate cardiovascular complications and enhance survival in this vulnerable population.

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