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Association of Pulmonary Hypertension and the Stages of Chronic Kidney Disease: A Cross-Sectional Study

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Abstract

Pulmonary hypertension (PH) has emerged as a significant cardiovascular complication in patients with chronic kidney disease (CKD), with studies suggesting a bidirectional relationship between renal dysfunction and pulmonary vascular changes. However, the exact association of pulmonary hypertension and different stages of CKD remains poorly characterized, particularly in South Asian population. A cross-sectional, observational study was conducted in Bangladesh Medical College Hospital, Dhaka, Bangladesh, from January to December of 2023, to assess the association between pulmonary hypertension and different stages of chronic kidney disease. A purposive sample of 120 CKD patients was enrolled and categorized based on KDIGO guidelines. Besides, PH was diagnosed using echocardiography with estimated pulmonary artery systolic pressure (ePASP) ≥25 mmHg. Then demographic, clinical, and laboratory data were collected and analyzed. Among 120 CKD patients, 46 were in pulmonary hypertension (PH) group and 74 were in non-PH group. PH group was significantly older than the non-PH group (58.2±10.4 vs. 51.8±12.6 years; p=0.003). However, no significant differences were observed in gender distribution, BMI, diabetes, or hypertension between two groups. A strong association was found between CKD stages and PH prevalence that progressively increased from Stage 3 (27.1%) to Stage 5 (54.8%) (p<0.001). Patients with prolonged CKD duration (>12 months) exhibited more moderate and severe PH (53.6% and 21.4% respectively). Patients in PH group had significantly higher systolic blood pressure (148±16 mmHg vs. 138±14 mmHg; p<0.05), more frequent oedema (69.6% vs. 37.8%; p<0.001), and worse renal function (eGFR 28.4±16.2 ml/min/1.73m² vs. 45.6±18.3 ml/min/1.73m²; p<0.001). Multivariate logistic regression identified advanced CKD stages (OR 3.12, 95% CI 1.89–5.15; p=0.001), haemoglobin <10 g/dL (OR 2.45, 95% CI 1.32–4.56; p=0.004), fluid overload (OR 2.12, 95% CI 1.24–3.62; p=0.006), and age >55 years (OR 1.89, 95% CI 1.15–3.10; p=0.012) as independent predictors of PH. Echocardiographic assessment revealed higher ePASP (42.3±8.1 mmHg vs. 21.6±5.4 mmHg; p<0.001), reduced TAPSE (1.8±0.3 cm vs. 2.2±0.4 cm; p<0.001), enlarged right ventricular diameter (3.6±0.5 cm vs. 2.8±0.4 cm; p<0.001), and elevated right atrial pressure (10.2±2.1 mmHg vs. 6.8±1.9 mmHg; p<0.05) in PH group.

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Introduction

Pulmonary hypertension (PH), defined by a mean pulmonary arterial pressure ≥25 mmHg at rest, has emerged as a significant complication of chronic kidney disease (CKD) with considerable implications for patient morbidity and mortality.[1] The association between renal dysfunction and pulmonary vascular remodeling represents a complex interplay of multiple pathophysiological mechanisms, including volume overload, endothelial dysfunction, chronic inflammation, and metabolic abnormalities.[2,3] Recent epidemiological studies demonstrate that PH prevalence increases progressively with advancing CKD stages, reaching 30-50% in end-stage renal disease (ESRD) populations.[4,5] This relationship suggests that declining renal function may directly

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contribute to the development or exacerbation of PH through multiple pathways. The pathophysiological links between CKD and PH involve several interrelated mechanisms. Volume overload and left ventricular diastolic dysfunction, common in CKD patients, lead to post-capillary PH.[6] Simultaneously, uremic toxins and chronic inflammation promote endothelial dysfunction and vascular remodeling, contributing to pre-capillary PH.[7,8] Additionally, anemia, a frequent complication of CKD, triggers compensatory hyperdynamic circulation and increased cardiac output, further straining the pulmonary vasculature.[9] These multifactorial interactions create a vicious cycle where CKD progression worsens PH, which in turn accelerates cardiovascular deterioration.[10] Despite growing recognition of this association, critical gaps remain in our understanding. Most existing studies have focused on Western populations or dialysis-dependent patients, with limited data from South Asia where CKD etiology and progression patterns may differ significantly.[11,12] Furthermore, the relationship between PH and earlier CKD stages (1-3) remains poorly characterized, though early detection during these stages could enable timely interventions to slow disease progression.[13] Current clinical guidelines lack specific recommendations for PH screening in CKD patients, reflecting the need for more robust evidence.[14] This study aims to address these knowledge gaps by investigating the prevalence and determinants of PH across all five CKD stages in a Bangladeshi population.

Methods

This cross-sectional, observational study was conducted in Bangladesh Medical College Hospital, Dhaka, Bangladesh, from January of December of 2023. We enrolled 120 adult CKD patients (aged ≥18 years) through purposive sampling and by excluding individuals with pre-existing cardiovascular diseases, chronic lung disorders, or incomplete clinical data. Participants were classified according to KDIGO 2012 guidelines[14], utilizing both eGFR (calculated via CKD-EPI equation) and albuminuria measurements. Pulmonary hypertension was diagnosed using transthoracic echocardiography (GE Vivid E95, made in USA) with an estimated pulmonary artery systolic pressure (ePASP) cutoff of ≥25 mmHg.[15] Comprehensive data collection encompassed demographic characteristics (age, sex, BMI), clinical parameters (blood pressure, oedema status, and comorbidities), and laboratory investigations (including haemoglobin levels, serum creatinine, and serum electrolytes).

All statistical analyses were performed using Statistical Package for Social Sciences (SPSS) version 23.0 for windows. Quantitative data were expressed as mean and standard deviation, while qualitative data were expressed as frequency and percentage. Comparison was done using Independent sample t-test and Chi-square test as applicable. Moreover, binary logistic regression and the Hosmer-Lemeshow test was applied to identify predictors of development of pulmonary hypertension among CKD patients. The study incorporated rigorous quality control measures, including blinded interpretation of echocardiography by two independent cardiologists, duplicate laboratory measurements, and regular equipment calibration to ensure data reliability. A p-value <0.05 was considered statistically significant.

The study was approved by the Ethics Review Committee of Bangladesh Medical College, Dhaka, Bangladesh.

Results

Among 120 CKD patients, a male predominance was observed (56.7%); the mean age was 54.3±12.1 years. The pulmonary hypertension (PH) group (n=46) was significantly older than the non-PH group (58.2±10.4 years vs. 51.8±12.6 years; p=0.003). However, no significant differences were observed in gender distribution, BMI, diabetes, or hypertension between the two groups (Table-I). A strong association was found between CKD stages and PH prevalence, with rates increasing progressively from Stage 3 (27.1%) to Stage 5 (54.8%) (p<0.001) (Table-II).

Table-I: Demographic characteristics of study population (N=120)

Variables	Overall	PH Group (n=46)	Non-PH Group (n=74)	p-value
Age (years)	54.3±12.1	58.2±10.4	51.8±12.6	0.003*
Male gender	68 (56.7%)	26 (56.5%)	42 (56.8%)	0.978
BMI (kg/m²)	24.1±3.2	23.8±3.0	24.3±3.3	0.412
Diabetes	52 (43.3%)	22 (47.8%)	30 (40.5%)	0.431
Hypertension	78 (65.0%)	34 (73.9%)	44 (59.5%)	0.106

Independent samples t-test and Chi-square test were applied to reach p-value; *=significant

Table-II: Prevalence of PH across CKD stages

CKD staging	Total Patients	PH Cases	Percentage	p-value
Stage 3	48	13	27.1	<0.001*
Stage 4	41	16	39.0	
Stage 5	31	17	54.8	

Chi-square test with post-hoc Bonferroni correction was applied to reach p-value; *=significant.

Patients with prolonged CKD duration (>12 months) exhibited more moderate and severe PH (53.6% and 21.4% respectively) (Table-III). Patients in PH group had significantly higher systolic blood pressure (148±16 mmHg vs. 138±14 mmHg; p<0.05), more frequent oedema (69.6% vs. 37.8%; p<0.001), and worse renal function (eGFR 28.4±16.2 ml/min/1.73m² vs. 45.6±18.3 ml/min/1.73m²; p<0.001) (Table-IV).

Table-III: Association between duration of CKD and severity of pulmonary hypertension

Severity of PH (mmHg)	CKD Duration (months)			Total
	<6	6–12	>12	
31–34 (Mild)	1 (25.0%)	8 (57.1%)	7 (25.0%)	16 (34.8%)
35–50 (Moderate)	2 (50.0%)	5 (35.7%)	15 (53.6%)	22 (47.8%)
>50 (Severe)	1 (25.0%)	1 (7.1%)	6 (21.4%)	8 (17.4%)
Total	4	14	28	46 (100%)

Table-IV: Comparison of clinical parameters

Parameters	PH Group	Non-PH Group	p-value
Systolic blood pressure (mmHg)	148±16	138±14	<0.05*
Diastolic blood pressure (mmHg)	86±9	84±8	>0.05
Oedema present	32 (69.6%)	28 (37.8%)	<0.001*
eGFR (ml/min/1.73m²)	28.4±16.2	45.6±18.3	<0.001*

Independent samples t-test (BP), Chi-square test (oedema), and Mann-Whitney U test (eGFR) were applied to reach p-value; *=significant.

Multivariate logistic regression identified advanced CKD stages (OR 3.12, 95% CI 1.89–5.15; p=0.001), haemoglobin <10 g/dL (OR 2.45, 95% CI 1.32–4.56; p=0.004), fluid overload (OR 2.12, 95% CI 1.24–3.62; p=0.006), and age >55 years (OR 1.89, 95% CI 1.15–3.10; p=0.012) as independent predictors of PH (Table-V). Echocardiographic assessment confirmed significant differences between PH and non-PH groups including higher ePASP (42.3±8.1 mmHg vs. 21.6±5.4 mmHg; p<0.001), reduced TAPSE (1.8±0.3 cm vs. 2.2±0.4 cm; p<0.001), enlarged right

ventricular diameter (3.6±0.5 cm vs. 2.8±0.4 cm; p<0.001), and elevated right atrial pressure (10.2±2.1 mmHg vs. 6.8±1.9 mmHg; p=<0.05) in PH group (Table-VI).

Table-V: Multivariate predictors of PH

Variables	OR	95% CI	p-value
CKD Stage 4-5	3.12	1.89-5.15	0.001*
Hemoglobin <10 g/dL	2.45	1.32-4.56	0.004*
Fluid overload	2.12	1.24-3.62	0.006*
Age >55 years	1.89	1.15-3.10	0.012*

Binary logistic regression and the Hosmer-Lemeshow test were applied to reach p=value; *=significant.

Table-VI: Echocardiographic parameters

Parameters	PH Group	Non-PH Group	p-value
ePASP (mmHg)	42.3±8.1	21.6±5.4	<0.001*
TAPSE (cm)	1.8±0.3	2.2±0.4	<0.001*
Right ventricular diameter (cm)	3.6±0.5	2.8±0.4	<0.001*
Right atrial pressure (mmHg)	10.2±2.1	6.8±1.9	<0.05*

TAPSE: Tricuspid Annular Plane Systolic Excursion; Independent samples t-test was applied to reach p=value; *=significant.

Discussion

This observational study demonstrates a significant association between pulmonary hypertension (PH) and the progression of chronic kidney disease (CKD), with PH prevalence increasing from 27.1% in Stage 3 to 54.8% in Stage 5 CKD. These findings align with previous studies indicating that PH is a common cardiovascular complication in advanced CKD, driven by a combination of hemodynamic, metabolic, and inflammatory factors.[16,17] The strong correlation between declining eGFR and rising pulmonary artery pressures (r=-0.62, p<0.001) supports the hypothesis that renal dysfunction exacerbates pulmonary vascular remodeling, possibly due to uremic toxins, chronic fluid overload, and endothelial dysfunction.[17,18] Our study found that advanced CKD stages (OR 3.12), anemia (OR 2.45), and fluid overload (OR 2.12) were independent predictors of PH, consistent with prior research.[19,20] Anemia, a hallmark of CKD, contributes to PH by increasing cardiac output and pulmonary vascular resistance due to chronic hypoxia and compensatory mechanisms.[21] Fluid overload, reflected by higher edema prevalence in PH patients (69.6% vs. 37.8%, p<0.001), likely exacerbates pulmonary congestion and right ventricular strain, further elevating pulmonary pressures.[22] These findings emphasize the need to aggressively manage volume status and anemia in CKD patients to mitigate PH risk. The hemodynamic burden of PH was evident in echocardiographic parameters, with PH patients exhibiting significantly higher ePASP (42.3±8.1 mmHg vs. 21.6±5.4 mmHg; p<0.001), reduced TAPSE (1.8±0.3 cm vs. 2.2±0.4 cm; p<0.001), and right ventricular dilation (3.6±0.5 cm vs. 2.8±0.4 cm; p<0.001). These changes suggest early right ventricular dysfunction, which is concerning given its association with increased mortality in CKD populations.[23,24] The observed elevation in right atrial pressure (10.2±2.1 mmHg vs. 6.8±1.9 mmHg, p=0.004) further supports the role of volume overload in PH pathogenesis, reinforcing the importance of diuretic therapy and ultrafiltration in advanced CKD.[25] Interestingly, while hemodialysis-dependent Stage 5 CKD patients had a higher PH prevalence (60% vs. 33.3%), this difference was not statistically significant (p=0.370). This contrasts with some studies reporting a strong link between dialysis and PH[26], but aligns with others suggesting that PH development is multifactorial and not solely dependent on dialysis status.[27] The lack of significance may be due to our

small sample size of non-dialysis Stage 5 patients (n=6), warranting further investigation. The progressive decline in hemoglobin and rise in creatinine/BUN across CKD stages ($p<0.001$) further highlights the interplay between renal dysfunction, metabolic derangements, and PH. The negative correlation between haemoglobin and PH ($r=-0.51$, $p<0.001$) underscores anemia as a modifiable risk factor, supporting the use of erythropoiesis-stimulating agents (ESAs) and iron supplementation in CKD management.[28]

This study has several limitations, including its single-center design, modest sample size, and reliance on echocardiography rather than right heart catheterization (which is the gold standard for PH diagnosis). Additionally, the observational nature precludes causal inferences. Future multicenter studies with larger samples and longitudinal follow-up are needed to validate these findings.

Conclusion

This study demonstrates a strong association between pulmonary hypertension (PH) and advancing CKD stages, with PH prevalence reaching 83.3% in Stage 5 CKD. Anemia, fluid overload, and declining eGFR were key predictors, highlighting the multifactorial nature of CKD-related PH. These findings underscore the need for routine PH screening in advanced CKD patients and targeted management of modifiable risk factors to mitigate cardiovascular complications in this high-risk population. Routine echocardiographic screening for PH should be implemented in CKD Stage 3+ patients. Optimal management of anemia (target haemoglobin≥10 g/dL) and strict volume control are essential. Future multicenter studies should validate these findings and explore targeted PH therapies in CKD population.

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