

Clinical Profile of Echocardiographically Estimated Pulmonary Hypertension in Patients with Non Dialysis-dependent Chronic Kidney Disease Stages 3-5: A Cross-sectional Study

GUNISHETTI ADITHYA¹, RM ANITHA², BUCHIPUDI SANDEEP KUMAR REDDY³,
BHARGAV KIRAN GADDAM⁴, HEMACHANDAR RADHAKRISHNAN⁵



ABSTRACT

Introduction: Pulmonary Hypertension (PHTN) is increasingly recognised as a clinically significant complication of Chronic Kidney Disease (CKD), even before initiation of dialysis. However, the clinical profile, echocardiographic pulmonary pressure estimates, and biochemical correlates of PHTN in Non Dialysis-Dependent CKD (NDD-CKD) stages 3-5 remain incompletely characterised.

Aim: To describe the clinical profile of elevated pulmonary pressures in NDD-CKD stage 3-5, estimate Pulmonary Artery Systolic Pressure (PASP) by echocardiography and to determine PHTN prevalence and severity, and explore correlations between biochemical parameters and PHTN severity.

Materials and Methods: The present hospital-based cross-sectional study enrolled 84 NDD-CKD stage 3-5 patients at a tertiary care centre, Mahatma Gandhi Medical College and Research Institute, Sri Balaji Vidyapeeth (Deemed to be University), Puducherry, India. PASP was estimated by transthoracic echocardiography and mean Pulmonary Artery Pressure (mPAP) was derived using the Chemla formula ($mPAP = 0.61 \times PASP + 2$). Elevated pulmonary pressure was defined as $mPAP \geq 20$ mmHg and categorised as mild (≥ 20 -40 mmHg), moderate (>40 -55 mmHg), or severe (>55 mmHg); values <20 mmHg were considered normal. Demographic data, co-morbidities, CKD stage, and laboratory investigations were measured. Non parametric stage-wise comparisons with

Bonferroni correction, Spearman correlations, ordered-stage trend analyses, and binary logistic regression were performed using Statistical Package for the Social Sciences (SPSS) version 24.0. p-value of <0.05 was considered statistically significant.

Results: Mean age was 48.18 ± 14.07 ; 49 (58.3%) were male. Hypertension (HTN) was present in 70 (83.3%) participants, Diabetes Mellitus (DM) in 37 (44.0%), and smoking in 45 (53.6%). Mean mPAP was 36.29 ± 16.68 mmHg; Elevated pulmonary pressure was present in 59 (70.2%) participants, comprising mild elevation in 20 (23.8%), moderate elevation in 24 (28.6%), and severe elevation in 15 (17.9%). mPAP increased significantly across CKD stages ($p=0.006$), with an increasing ordered-stage trend ($p=0.0006$) and rising PHTN severity ($r_s=0.288$; $p=0.007$). mPAP correlated positively with serum urea ($r_s=0.335$; $p=0.001$) and creatinine ($r_s=0.332$; $p=0.002$), and negatively with estimated Glomerular Filtration Rate (eGFR) ($r_s=-0.339$; $p=0.001$)-all surviving Bonferroni correction. HTN was an independent predictor of PHTN on both univariate (OR 4.157; 95% CI 1.263-13.680; $p=0.019$) and multivariable analysis (adjusted Odds Ratio (aOR)=5.425; 95% CI=1.416-20.783; $p=0.014$).

Conclusion: PHTN burden is high in NDD-CKD stage 3-5 and increases with declining renal function. HTN independently predicts PHTN, highlighting the importance of left-heart-mediated mechanisms. Structured cardiopulmonary evaluation is warranted in advanced pre-dialysis CKD.

Keywords: Echocardiography, Glomerular filtration rate, Pulmonary circulation

INTRODUCTION

The CKD is a major and growing global health problem, affecting approximately 10-14% of adults and contributing substantially to premature cardiovascular mortality and healthcare utilisation [1,2]. Contemporary guidelines emphasise early identification and risk stratification because progression to advanced CKD markedly amplifies cardiopulmonary morbidity, with systemic vascular and myocardial changes accumulating across each disease stage [3,4]. Recent global burden analyses continue to demonstrate rising CKD prevalence and deaths, reinforcing the need to characterise high-risk comorbid states within CKD populations [5].

NDD-CKD stages 3-5 represents a clinically important subgroup in which kidney dysfunction is advanced, yet Kidney Replacement Therapy (KRT) has not commenced, permitting evaluation of cardiopulmonary complications before dialysis-related haemo-

dynamic shifts confound interpretation [6-8]. Per Kidney Disease: Improving Global Outcomes (KDIGO) criteria, these stages correspond to eGFR categories G3a (45-59), G3b (30-44), G4 (15-29), and G5 (<15 mL/min/1.73 m²), each sustained for ≥ 3 months [4,6].

The PHTN is a haemodynamic condition defined by $mPAP >20$ mmHg at rest on Right Heart Catheterisation (RHC), as adopted by the 2022 ESC/ERS guidelines [9,10]. Pulmonary Arterial Hypertension (PAH), a pre-capillary PHTN subset, additionally requires Pulmonary Vascular Resistance (PVR) >2 Wood units and Pulmonary Arterial Wedge Pressure (PAWP) ≤ 15 mmHg [10,11]. In CKD, multiple mechanisms may elevate pulmonary pressures, including chronic inflammation, endothelial dysfunction, volume overload, Left Heart Disease (LHD), disordered mineral metabolism, anaemia-related high-output states, sleep-disordered breathing, and

thromboembolic disease-making CKD-associated PHTN typically multifactorial, spanning WHO Groups 2, 3, 4, and 5 [12,13]. Systematic review evidence indicates that PHTN in CKD is associated with adverse prognosis, including increased cardiovascular events and all-cause mortality, and that identifiable clinical and biochemical correlates may stratify risk [14]. Despite increasing recognition, data remain heterogeneous, particularly for NDD-CKD stages 3-5, where PHTN may precede KRT but is often confounded by comorbid cardiovascular disease and challenges in definitive haemodynamic classification [12,15]. Transthoracic Doppler Echocardiography (TTE) is the recommended first-line non invasive screening tool, with mPAP approximated from systolic PAP (PASP) using validated empirical relationships when invasive measurement is not feasible [10,16,17].

In this context, the present study was designed to describe the clinical profile of elevated pulmonary pressures in NDD-CKD stage 3-5, estimate PASP by echocardiography, determine PHTN prevalence and severity, and explore correlations between biochemical parameters and PHTN severity, thereby addressing an important evidence gap in routine nephrology practice.

MATERIALS AND METHODS

The present study was a hospital-based cross-sectional study conducted in the Departments of General Medicine and Nephrology, a tertiary care teaching hospital, Mahatma Gandhi Medical College and Research Institute, Sri Balaji Vidyapeeth (Deemed to be University), Puducherry, India. The study was conducted over 18 months (September 2024 to February 2026) following approval from the Institutional Human Ethical Committee (IHEC) (MGMCRI/Res/01/2023/93/IHEC/94) and the Institutional Research Committee (IRC).

Inclusion and exclusion criteria: Patients between 18-75 years with confirmed NDD-CKD stages 3 to 5 with CKD established for ≥3 months and staged according to the KDIGO 2024 criteria [3,6] attending or admitted to the general medicine/nephrology services were enrolled consecutively. Exclusion criteria were pregnancy/lactation; chronic obstructive/restrictive lung disease or COPD; severe valvular or congenital heart disease; haematological disease, bleeding diathesis, or malignancy; decompensated liver disease or cirrhosis; thyroid disorders; HIV infection; use of corticosteroids, cytotoxic drugs, GPIIb/IIIa inhibitors, oral contraceptives, or thrombolytics; or refusal of consent.

Written informed consent was obtained from all participants; confidentiality was maintained throughout.

Sample size calculation: The minimum sample was calculated using the single-proportion formula (WHO manual) based on an expected PHTN prevalence of 68% (O’Leary JM et al.,) with α=0.05, Z=1.96, and absolute precision d=0.10, yielding n=84 [18].

Study Procedure

Demographic data (age, sex) and co-morbidities (DM, HTN, smoking status) were recorded by structured proforma. CKD stage was assigned per KDIGO 2024 criteria [6]. Laboratory investigations included serum urea, creatinine, eGFR (CKD-EPI equation), haemoglobin (Hb), serum calcium (Ca²⁺), phosphorus (P), potassium (K⁺), albumin, and total cholesterol. Blood was collected under aseptic conditions from the antecubital vein.

Echocardiographic Assessment and PHTN Classification: TTE was performed by a trained technician under the supervision of the principal investigator. PASP was estimated from the peak Tricuspid Regurgitation Velocity (TRV) using the simplified Bernoulli equation: $PASP = 4(TRV)^2 + \text{estimated Right Atrial Pressure (RAP)}$ [19], in the absence of right ventricular outflow tract obstruction. RAP was estimated at the time of ECHO examination based on Inferior Vena Cava (IVC) diameter and its respiratory collapsibility. The final

PASP value reported in the ECHO record was used for the present study; individual RAP and IVC measurements were not separately recorded in the study dataset. mPAP was subsequently estimated from PASP using the Chemla formula: $mPAP=0.61\times PASP + 2$ [16]. Because RHC was not performed, echocardiographic estimates were not considered a definitive haemodynamic diagnosis of PHTN or PAH. For study analyses, elevated estimated pulmonary pressure was operationally defined as echocardiography-derived mPAP ≥20 mmHg, while mPAP <20 mmHg was considered normal. Elevated mPAP was further stratified as mild (≥20-40 mmHg), moderate (>40-55 mmHg), or severe (>55 mmHg), using published echocardiographic mPAP strata [20]. These categories were used as descriptive study strata and should not be interpreted as guideline-defined RHC severity categories.

STATISTICAL ANALYSIS

Data were entered in Microsoft Excel and analysed using SPSS version 24.0. Continuous variables are presented as mean±SD; categorical variables as frequency (%). Normality was assessed by the Shapiro-Wilk test. Non parametric tests were applied throughout: Mann-Whitney U for two-group comparisons, Kruskal-Wallis for three-group, Pearson’s Chi-square (or Fisher’s exact when expected cell counts<5) for categorical variables.

Bonferroni-adjusted pairwise post-hoc testing (Mann-Whitney U) was performed for significant three-group results. Spearman rank correlations (r_s) assessed associations between mPAP and biochemical parameters, with Bonferroni correction applied for nine simultaneous correlations {adjusted threshold p<0.0056; adjusted p=min (p×9, 1.0)}. Ordered-stage trend analyses used the Jonckheere-Terpstra test (continuous variables), Cochran-Armitage test (binary PHTN presence), and Spearman correlation (ordinal PHTN severity score). Predictors of PHTN presence were explored by binary logistic regression (univariate and multivariable); the multivariable model included age, sex, DM, HTN, eGFR, and serum potassium, with multicollinearity assessed by Variance Inflation Factor (VIF). All tests were two-tailed; p<0.05 was considered statistically significant.

RESULTS

Eighty-four NDD-CKD patients were enrolled. Mean age was 48.18±14.07 years (median 50; IQR 39-57.25; range 21-74), with male predominance (49, 58.3%). The demographic, co-morbidities, risk factors and the stages of the CKD presented in [Table/Fig-1].

Mean serum urea was 67.40±19.46 mg/dL (median 67.5; IQR 52-83), serum creatinine 3.63±1.44 mg/dL (median 3.71; IQR 2.33-4.98), and eGFR 23.99±12.72 mL/min/1.73m²-consistent with an

Variables	Result, n (%)
Age	
Age (years) mean±SD; range	48.18±14.07; 21-74
Gender	
Males	49 (58.3%)
Females	35 (41.7%)
Co-morbidities and risk factors	
Diabetes Mellitus (DM)-Yes	37 (44.0%)
Hypertension (HTN)-Yes	70 (83.3%)
Smoking-Yes	45 (53.6%)
CKD stage distribution	
Stage 3 (eGFR 30-59 mL/min/1.73 m ²)	27 (32.1%)
Stage 4 (eGFR 15-29 mL/min/1.73 m ²)	31 (36.9%)
Stage 5 (eGFR<15 mL/min/1.73 m ²)	26 (31.0%)

[Table/Fig-1]: Demographic and clinical characteristics of study participants (N=84).

DM: Diabetes mellitus; HTN: Hypertension; CKD: Chronic kidney disease. Values present in parentheses are percentages.

advanced CKD population. Mean haemoglobin was 9.87 ± 0.99 g/dL, reflecting high prevalence of renal anaemia [Table/Fig-2].

Parameters	Mean $\pm$ SD	Range
Serum urea (mg/dL)	67.40 $\pm$ 19.46	30.0-109.0
Serum creatinine (mg/dL)	3.63 $\pm$ 1.44	1.37-6.58
eGFR (mL/min/1.73 m ²)	23.99 $\pm$ 12.72	10.0-56.0
Haemoglobin (g/dL)	9.87 $\pm$ 0.99	8.10-12.00
Serum calcium (mg/dL)	8.68 $\pm$ 0.34	8.00-9.20
Serum phosphorus (mg/dL)	5.43 $\pm$ 0.56	4.50-6.40
Serum potassium (mEq/L)	5.00 $\pm$ 0.30	4.50-5.50
Serum albumin (g/dL)	3.41 $\pm$ 0.36	2.80-4.00
Total cholesterol (mg/dL)	203.36 $\pm$ 21.80	176.20 -260.32

[Table/Fig-2]: Biochemical parameters of the study cohort.

eGFR = estimated glomerular filtration rate. Values presented as mean $\pm$ standard deviation.

Mean mPAP was 36.29 ± 16.68 mmHg (median 33.5, IQR 19-48.5, range 15-67). PH was present in 59 participants (70.2%): mild in 20 (23.8%), moderate in 24 (28.6%), and severe in 15 (17.9%). The remaining 25 (29.8%) had normal mPAP [Table/Fig-3].

Variables	Result
Mean PAP (mmHg); range	36.29 $\pm$ 16.68; 15-67
PHTN Prevalence	
PHTN present (mild + moderate + severe)	59 (70.2%)
No PHTN (normal mPAP)	25 (29.8%)
PHTN severity distribution	
Normal (mPAP <20 mmHg; PASP <40 mmHg)	25 (29.8%)
Mild (mPAP mild ($\geq$ 20-40 mmHg), PASP 40-60 mmHg)	20 (23.8%)
Moderate (moderate (>40-55 mmHg), PASP 60-90 mmHg)	24 (28.6%)
Severe (>55 mmHg, PASP >90 mmHg)	15 (17.9%)

[Table/Fig-3]: Pulmonary Hypertension (PHTN) characteristics (N=84).

mPAP: mean pulmonary artery pressure; PASP: Pulmonary artery systolic pressure; IQR: Inter-quartile range. Values presented in parentheses are percentages.

Variables	Stage 3 (n=27)	Stage 4 (n=31)	Stage 5 (n=26)	Overall p-value	S3 vs S4 adjusted p-value	S3 vs S5 adjusted p-value	S4 vs S5 adjusted p-value
Demographic/clinical variables							
Age (years)	49.07 $\pm$ 12.56	46.81 $\pm$ 16.43	48.88 $\pm$ 12.87	0.722 ^a	1.000	1.000	1.000
Male, n (%)	11 (40.7)	19 (61.3)	19 (73.1)	0.053 ^b	0.355	0.053	1.000
Diabetes Mellitus (DM), n (%)	15 (55.6)	12 (38.7)	10 (38.5)	0.343 ^b	0.599	0.638	1.000
Hypertension (HTN), n (%)	20 (74.1)	26 (83.9)	24 (92.3)	0.204 ^b	1.000	0.425	1.000
Smoking, n (%)	15 (55.6)	16 (51.6)	14 (53.8)	0.995 ^b	1.000	1.000	1.000
Renal function parameters							
Serum urea, mg/dL	40.07 $\pm$ 5.40	62.35 $\pm$ 11.02	91.08 $\pm$ 7.61	<0.001 ^a	<0.001	<0.001	<0.001
Serum creatinine, mg/dL	1.76 $\pm$ 0.26	3.28 $\pm$ 0.59	5.33 $\pm$ 0.46	<0.001 ^a	<0.001	<0.001	<0.001
eGFR, mL/min/1.73 m ²	45.33 $\pm$ 6.87	22.61 $\pm$ 4.09	12.46 $\pm$ 1.17	<0.001 ^a	<0.001	<0.001	<0.001
Other biochemical parameters							
Haemoglobin, g/dL	9.87 $\pm$ 1.25	10.25 $\pm$ 1.18	9.97 $\pm$ 1.25	0.441 ^a	0.662	1.000	1.000
Serum calcium, mg/dL	8.68 $\pm$ 0.35	8.73 $\pm$ 0.33	8.62 $\pm$ 0.34	0.503 ^a	1.000	1.000	0.747
Serum phosphorus, mg/dL	5.32 $\pm$ 0.57	5.48 $\pm$ 0.54	5.48 $\pm$ 0.57	0.450 ^a	0.724	0.968	1.000
Serum potassium, mEq/L	5.03 $\pm$ 0.32	4.97 $\pm$ 0.30	5.02 $\pm$ 0.28	0.679 ^a	1.000	1.000	1.000
Serum albumin, g/dL	3.41 $\pm$ 0.37	3.36 $\pm$ 0.38	3.48 $\pm$ 0.33	0.460 ^a	1.000	1.000	0.702
Total cholesterol, mg/dL	201.33 $\pm$ 19.55	203.32 $\pm$ 20.29	205.50 $\pm$ 26.01	0.578 ^a	1.000	1.000	1.000
Echocardiographic pulmonary-pressure variables							
Estimated mPAP, mmHg	28.22 $\pm$ 10.37	37.16 $\pm$ 18.45	43.62 $\pm$ 16.62	0.006 ^a	0.324	0.002	0.846
Elevated estimated mPAP, n (%)	20 (74.1)	18 (58.1)	21 (80.8)	0.152 ^b	0.602	1.000	0.199

[Table/Fig-4]: CKD stage-wise comparison of clinical, biochemical, and PHTN variables with Bonferroni post-hoc.

^a Kruskal-Wallis test (continuous variables). ^b Pearson's chi-square test. ^c Bonferroni-adjusted pairwise Mann-Whitney U. p-value <0.05 is statistically significant and indicated in boldface. Continuous questions were presented in mean $\pm$ SD, categorical variables presented in frequencies and percentages. Values presented in parentheses are percentages. DM: Diabetes mellitus; HTN: Hypertension; mPAP: Mean pulmonary artery pressure; Sr. U: Serum urea; Sr. Creat: Serum creatinine; eGFR: Estimated glomerular filtration rate; Hb: Haemoglobin; Sr. Ca²⁺: Serum calcium; Sr. P: Serum phosphorus; Sr. K: Serum potassium; Sr. Alb: Serum albumin; CHOL: Total cholesterol.

Age, sex, DM, and smoking did not differ significantly across CKD stages [Table/Fig-4]. HTN increased numerically across stages was 20/27 (74.1%) in stage 3, 26/31 (83.9%) in stage 4, and 24/26 (92.3%) in stage 5, but the overall association was not significant (p=0.204). Bonferroni-adjusted pairwise comparisons were also non-significant (stage 3 vs 4: p=1.000; stage 3 vs 5: p=0.425; stage 4 vs 5: p=1.000) [Table/Fig-4].

Stage-wise values for each biochemical parameter are tabulated in [Table/Fig-4]. Serum urea, creatinine, and eGFR differed significantly across CKD stages (all overall p<0.001), and Bonferroni-adjusted pairwise comparisons were significant for each stage pair (all adjusted p<0.001). Other biochemical parameters did not differ significantly across stages.

Estimated mPAP differed significantly across CKD stages, with the highest value in stage 5 (stage 3: 28.22 $\pm$ 10.37; stage 4: 37.16 $\pm$ 18.45; stage 5: 43.62 $\pm$ 16.62 mmHg; p=0.006). Bonferroni-adjusted pairwise analysis confirmed a significant difference between stages 3 and 5 (adjusted p=0.002), but not between stages 3 and 4 (p=0.324) or stages 4 and 5 (p=0.846). Ordered-stage analysis demonstrated an increasing trend in estimated mPAP (Jonckheere-Terpstra Z=3.450; p=0.0006) and PHTN (Spearman r_s=0.288; p=0.007). The binary presence of elevated estimated mPAP did not show a significant linear trend (Cochran-Armitage p=0.609). These trend results are included in [Table/Fig-4].

Pulmonary-pressure categories differed significantly across CKD stages (p=0.004). On Bonferroni-adjusted pairwise analysis, the distribution differed significantly between stages 3 and 4 (adjusted p=0.001) and between stages 3 and 5 (adjusted p=0.007), whereas no significant difference was observed between stages 4 and 5 (adjusted p=0.824) [Table/Fig-5].

The mPAP correlated positively with serum urea (r_s=0.335; p=0.001) and serum creatinine (r_s=0.332; p=0.002), and negatively with eGFR (r_s=-0.339; p=0.001). All three associations remained statistically significant after Bonferroni correction (adjusted p: 0.016, 0.018, and 0.014 respectively), indicating that higher pulmonary pressures

Pulmonary-pressure category	Stage 3 (n=27), n (%)	Stage 4 (n=31), n (%)	Stage 5 (n=26), n (%)	Overall p-value
Normal	7 (25.9)	13 (41.9)	5 (19.2)	0.004 ^a
Mild elevation	14 (51.9)	2 (6.5)	4 (15.4)	
Moderate elevation	6 (22.2)	9 (29.0)	9 (34.6)	
Severe elevation	0 (0.0)	7 (22.6)	8 (30.8)	

[Table/Fig-5]: Association between CKD stage and severity of echocardiographically estimated pulmonary pressure (N=84).
Fisher's test; Values are presented as n (%), with percentages calculated within each CKD stage. A p-value <0.05 was considered statistically significant. Bonferroni-adjusted pairwise comparisons were performed following the significant overall association. Stage 3 vs 4 -0.001; stage 3 vs 5-0.007; stage 4 vs 5-0.824

track with worsening renal function. Serum potassium showed a weak unadjusted correlation with mPAP ($r_s=0.219$; $p=0.045$) that did not survive Bonferroni correction (adjusted $p=0.408$). No significant correlations were observed between mPAP and haemoglobin, calcium, phosphorus, albumin, or total cholesterol [Table/Fig-6].

Biochemical parameters	r_s	p-value	Bonferroni-adjusted p
Serum urea (mg/dL)	0.335	0.001†	0.016†
Serum creatinine (mg/dL)	0.332	0.002†	0.018†
eGFR (mL/min/1.73m ²)	-0.339	0.001†	0.014†
Haemoglobin (g/dL)	-0.108	0.326	1.000
Serum calcium (mg/dL)	0.117	0.290	1.000
Serum phosphorus (mg/dL)	0.037	0.741	1.000
Serum potassium (mEq/L)	0.219	0.045	0.408
Serum albumin (g/dL)	0.121	0.273	1.000
Total cholesterol (mg/dL)	-0.045	0.681	1.000

[Table/Fig-6]: Spearman rank correlations between mPAP and biochemical parameters (N=84).
†Significant after Bonferroni correction. Adjusted $p=\min(p \times 9, 1.0)$; adjusted significance threshold $p<0.05$ (Bonferroni adjustment was performed using the full-precision p-values before rounding). r_s : Spearman rank correlation coefficient; eGFR: Estimated glomerular filtration rate; mPAP: Mean pulmonary artery pressure.

In univariate logistic regression, HTN was significantly associated with elevated echocardiographically estimated pulmonary pressure (OR 4.157; 95% CI 1.263-13.680; $p=0.019$). Serum potassium also showed a significant univariate association (OR 5.612; 95% CI 1.083-29.080; $p=0.040$). In the multivariable model adjusted for

age, sex, DM, HTN, eGFR, and serum potassium, HTN remained independently associated with elevated pulmonary pressure (aOR 5.425; 95% CI 1.416-20.783; $p=0.014$). Serum potassium also retained a borderline significant association (aOR 6.393; 95% CI 1.017-40.181; $p=0.048$), although the wide confidence interval indicates considerable uncertainty. Age, sex, DM, and eGFR were not independently associated with the outcome [Table/Fig-7].

DISCUSSION

The present cross-sectional study assessed echocardiographically estimated pulmonary pressures in 84 patients with NDD-CKD stages 3-5 and identified four principal findings. First, elevated estimated pulmonary pressure was observed in 59 (70.2%) participants. Second, estimated mPAP differed significantly across CKD stages, with greater pulmonary-pressure severity in the more advanced stages. Third, estimated mPAP correlated significantly with renal dysfunction markers, including serum urea, serum creatinine, and eGFR, and these associations remained significant after Bonferroni correction. Fourth, HTN remained independently associated with elevated estimated pulmonary pressure after multivariable adjustment (aOR 5.425; 95% CI 1.416-20.783; $p=0.014$). Serum potassium also demonstrated a borderline independent association (aOR 6.393; 95% CI 1.017-40.181; $p=0.048$), although the wide confidence interval indicates considerable imprecision and warrants cautious interpretation.

The observed PHTN prevalence of 70.2% substantially exceeds estimates from large community-based NDD-CKD cohorts. The Chronic Renal Insufficiency Cohort (CRIC) study (Navaneethan SD et al.,) reported echocardiographically-defined PHTN in 21.1% of NDD-CKD participants (PASP>35 mmHg or TRV>2.5 m/s), with stage-specific prevalence rising from ~21% in stage 3 to 32.8% in stage 5 [7]. The 2024 meta-analysis by Lin et al., reported pooled prevalence of 31% in CKD stages 1-5 and 39% in pre-dialysis ESKD [14]. In contrast, the present estimate aligns more closely with haemodynamic-based referral cohorts: O'Leary JM et al., reported PHTN in 67.6% of CKD stage 3-5 patients undergoing RHC [18], and Edmonston DL et al., found PHTN in 73.4% of CKD patients referred for catheterisation [21]. Differences reflect study setting (single-centre hospital-based vs community-based), diagnostic modality (echocardiography vs RHC), and case-mix enrichment toward more symptomatic patients. Clear reporting of diagnostic modality and case definition is therefore essential when comparing PHTN prevalence estimates across studies.

Variables	Total (N=84)	PHTN present (n=59)	Univariate OR (95% CI); p*	Adjusted OR (95% CI); p*
Demographic and clinical predictors				
Age (years)	48.18±14.07	46.59±13.75	0.972 (0.938-1.007); 0.116	0.976 (0.940-1.014); 0.215
Male	49 (58.3%)	33 (55.9%)	0.714 (0.272-1.874); 0.494	0.811 (0.271-2.430); 0.708
CKD stage (per 1-stage increase)	3.99±0.80	4.02±0.84	1.167 (0.646-2.107); 0.609	—
Diabetes Mellitus (DM)-Yes	37 (44.0%)	24 (40.7%)	0.633 (0.247-1.622); 0.341	0.710 (0.250-2.018); 0.520
Hypertension (HTN) -Yes	70 (83.3%)	53 (89.8%)	4.157 (1.263-13.680); 0.019	5.425 (1.416-20.783); 0.014
Smoking-Yes	45 (53.6%)	30 (50.8%)	0.690 (0.267-1.782); 0.443	—
Biochemical Predictors				
Serum urea (mg/dL)	67.40±19.46	65.46±23.04	1.010 (0.988-1.032); 0.380	—
Serum creatinine (mg/dL)	3.63±1.44	3.53±1.56	1.169 (0.848-1.612); 0.341	—
eGFR (mL/min/1.73 m ²)	23.99±12.72	26.47±14.69	0.995 (0.963-1.028); 0.767	1.000 (0.962-1.040); 0.987
Haemoglobin (g/dL)	9.87±0.99	9.91±1.21	0.728 (0.487-1.087); 0.121	—
Serum calcium (mg/dL)	8.68±0.34	8.69±0.35	1.282 (0.320-5.138); 0.726	—
Serum phosphorus (mg/dL)	5.43±0.56	5.42±0.56	0.936 (0.403-2.177); 0.878	—
Serum potassium (mEq/L)	5.00±0.30	5.05±0.29	5.612 (1.083-29.080); 0.040	6.393 (1.017-40.181); 0.048
Serum albumin (g/dL)	3.41±0.36	3.45±0.35	2.619 (0.684-10.034); 0.160	—
Total cholesterol (mg/dL)	203.36±21.80	202.95±22.86	0.997 (0.976-1.019); 0.791	—

[Table/Fig-7]: Binary logistic regression for predictors of PHTN presence (univariate and multivariable).
Values are presented as mean±standard deviation or n (%), as appropriate. * $p<0.05$ (statistically significant; bold row). OR: Odds ratio; aOR: Adjusted odds ratio; CI: Confidence interval; DM: Diabetes mellitus; HTN: Hypertension; eGFR: Estimated glomerular filtration rate; Sr. U: Serum urea; Sr. Creat: Serum creatinine; Hb: Haemoglobin; Sr. K: Serum potassium; Sr. Alb: Serum albumin; CHOT: Total cholesterol. Multivariable model adjusted for age, sex, DM, HTN, eGFR, and serum potassium.

The significant stage-wise increase in both mPAP and PHTN severity is consistent with a growing body of evidence that PHTN burden tracks with CKD stage [14,15,18]. In the CRIC cohort, PHTN prevalence increased progressively from stage 3 to 5 [7], and Zhang X et al., reported stage-specific PHTN prevalence of 38.9%, 40.9%, and 64.5% for stages 3, 4, and 5 respectively [22]. The 2024 meta-analysis by Lin C et al., demonstrated a relative risk of 5.64 for PHTN in grade 5 CKD compared to lower stages [14]. The absence of a significant binary PHTN trend (Cochran-Armitage $p=0.609$) despite a significant severity trend in the present cohort reflects the already high PHTN prevalence across all three stages (74.1%, 58.1%, 80.8%), which limits power to detect a linear binary progression.

The Bonferroni-corrected significant correlations of mPAP with serum urea, creatinine, and eGFR confirm that pulmonary pressure elevation in NDD-CKD closely tracks the degree of uraemia [12,13]. Advancing CKD amplifies volume overload through reduced nephron mass and neurohormonal activation, promotes endothelial dysfunction through reduced nitric oxide bioavailability and heightened endothelin-1 signalling, exacerbates anaemia-related high-output physiology, and drives uraemic vasculopathy through accumulation of indoxyl sulphate and p-cresyl sulphate [13]. These mechanisms collectively raise mPAP through pre-capillary, post-capillary, and mixed haemodynamic pathways. The findings are consistent with the CRIC data and with Zhang X et al., who identified kidney dysfunction as a factor associated with PHTN in a large pre-dialysis CKD cohort [7,22].

A central finding of this study is that HTN was an independent predictor of PHTN in both univariate (OR 4.157; $p=0.019$) and multivariable regression (aOR 5.425; $p=0.014$). This is biologically plausible and clinically important. HTN in CKD promotes Left Ventricular Hypertrophy (LVH), diastolic dysfunction, and elevated left ventricular end-diastolic pressure, which transmit backward through the left atrium and pulmonary veins to produce pulmonary venous HTN (Group 2 PHTN) [12]. Over time, chronically elevated pulmonary venous pressures can trigger pulmonary vascular remodelling, generating a combined pre and post-capillary phenotype, the subtype carrying the highest mortality risk across CKD stages [14]. With 83.3% of the present cohort hypertensive substantially higher than in many prior studies, the preponderance of Group-2 disease is likely. This has a direct and critical management implication: PHTN-targeted therapy should not be initiated without RHC confirmation of a pre-capillary component, as vasodilatory agents are contraindicated in isolated post-capillary disease [10,11].

Serum potassium showed a nominal univariate association (OR 5.612; 95% CI 1.083-29.080; $p=0.040$) and retained a borderline association in the multivariable model (aOR 6.393; 95% CI 1.017-40.181; $p=0.048$). The wide confidence intervals indicate considerable statistical imprecision; therefore, this finding should be interpreted cautiously. Although potassium-channel dysfunction in pulmonary artery smooth muscle is mechanistically implicated in vascular remodelling [16], direct clinical evidence linking serum potassium concentrations to PHTN risk in NDD-CKD remains limited. The absence of significant associations with haemoglobin, mineral metabolism markers, albumin, or cholesterol differs from some published cohorts [12], likely reflecting the modest sample size and narrower biochemical variability.

The findings support systematic echocardiographic evaluation for PHTN in NDD-CKD stage 3-5. Persistent dyspnoea, exercise intolerance, or lower-limb oedema should not be attributed reflexively to uraemia, anaemia, or fluid overload [12]. The ESC/ERS 2022 guidelines recommends progression from clinical suspicion to echocardiographic detection, with RHC for haemodynamic classification in selected patients [10]. The Chemla formula provides a validated non-invasive mPAP approximation for screening purposes [23]. Because Group-2 mechanisms likely predominates particularly in hypertensive CKD patients the initial management should prioritise

strict blood pressure control, volume optimisation (dietary sodium restriction <2 g/day, judicious diuretic use), and treatment of left heart failure, in alignment with KDIGO 2024 guidance [6]. Sodium-glucose co-transporter 2 (SGLT2) inhibitors, recommended for CKD with $eGFR \geq 20$ mL/min/1.73m², may be particularly beneficial given their cardiac-renal protective mechanisms [6]. PHTN-specific pharmacotherapy carries dose-adjustment constraints in advanced CKD (tadalafil and riociguat are not recommended when $CrCl < 30$ mL/min) and should only be initiated after careful haemodynamic phenotyping [13,18,22].

The present study characterised a specifically pre-dialysis CKD population, avoiding confounders from AV fistulae, dialysis-induced volume shifts, and dialysis vintage. Broad biochemical phenotyping across multiple CKD-relevant domains was performed, and multiple testing correction (Bonferroni) was applied throughout.

Limitation(s)

The present single-centre, hospital-based cross-sectional design may introduce selection bias toward more symptomatic or complicated patients and limits generalisability. Pulmonary pressures were echocardiography-derived rather than RHC-confirmed, precluding definitive haemodynamic phenotyping and formal diagnosis of PHTN subtype. Important potential confounders-including detailed left-ventricular diastolic echocardiographic parameters, objective volume-status assessment, sleep-disordered breathing evaluation, lung-function testing, iPTH, vitamin D, and systematic thromboembolic work-up-were not obtained. The modest sample size ($n=84$) also limits subgroup and multivariable analyses and increases the risk of imprecise estimates.

Future multicentre prospective studies with larger samples should incorporate RHC where clinically appropriate and use standardised assessment of volume status and left-heart function. Longitudinal follow-up is also required to validate the observed associations, clarify haemodynamic mechanisms, and determine prognostic significance in NDD-CKD.

CONCLUSION(S)

In this cross-sectional study of 84 patients with NDD-CKD stages 3-5, elevated echocardiographically estimated pulmonary pressure was observed in 59 (70.2%) participants, with a mean estimated mPAP of 36.29 ± 16.68 mmHg. Estimated mPAP and pulmonary-pressure severity differed significantly across CKD stages, with greater pressure elevation observed in advanced CKD. Estimated mPAP correlated positively with serum urea and creatinine and negatively with eGFR, indicating a significant relationship between worsening renal function and higher pulmonary-pressure estimates. HTN remained independently associated with elevated pulmonary pressure after multivariable adjustment (aOR 5.425; 95% CI 1.416-20.783; $p=0.014$), while serum potassium showed a borderline association with considerable statistical imprecision (aOR 6.393; 95% CI 1.017-40.181; $p=0.048$). As pulmonary pressures were estimated by echocardiography without RHC, these findings should not be interpreted as haemodynamically confirmed PHTN or as evidence of a specific PHTN subtype.

The key clinical message is that patients with advanced pre-dialysis CKD, particularly those with HTN and worsening renal function, warrant careful cardiopulmonary assessment, with echocardiography serving as a useful screening tool and RHC reserved for definitive haemodynamic diagnosis when clinically indicated.

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REFERENCES

- [1] Gallego D. A patient perspective on kidney disease in the public health agenda. *Nat Rev Nephrol.* 2024;20(7):426-27. Doi: 10.1038/s41581-024-00846-w.
- [2] Tangri N, Svensson MK, Bodegård J, Adamsson Eryd S, Thuresson M, Gustafsson S, et al. Mortality, Health Care Burden, and Treatment of CKD: A multinational, observational study (OPTIMISE-CKD). *Kidney360.* 2024;5(3):352-62. Doi: 10.34067/kid.0000000000000374.
- [3] Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the evaluation and management of chronic kidney disease. *Kidney Int.* 2024;105(4S):S117-S314. Doi: 10.1016/j.kint.2023.10.018.
- [4] Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Update Work Group. KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). *Kidney Int Suppl.* 2017;7-59. *Kidney Int Suppl.* 2017;7(3):e1. Doi: 10.1016/j.kisu.2017.10.001.
- [5] GBD 2023 Chronic Kidney Disease Collaborators. Global, regional, and national burden of chronic kidney disease in adults, 1990-2023, and its attributable risk factors: A systematic analysis for the Global Burden of Disease Study 2023. *Lancet.* 2025;406(10518):2461-82. Doi: 10.1016/S0140-6736(25)01853-7.
- [6] Levin A, Ahmed SB, Carrero JJ, Foster B, Francis A, Hall RK, et al. Executive summary of the KDIGO 2024 clinical practice guideline for the evaluation and management of chronic kidney disease: Known knowns and known unknowns. *Kidney Int.* 2024;105(4):684-701. Doi: 10.1016/j.kint.2023.10.016.
- [7] Navaneethan SD, Bansal N, Cavanaugh KL, Chang A, Crowley S, Delgado C, et al. KDOQI US Commentary on the KDIGO 2024 clinical practice guideline for the evaluation and management of CKD. *Am J Kidney Dis Off J Natl Kidney Found.* 2025;85(2):135-76. Doi: 10.1053/j.ajkd.2024.08.003.
- [8] Khan YH, Sarriif A, Adnan AS, Khan AH, Mallhi TH, Jummaat F. Progression and outcomes of non-dialysis dependent chronic kidney disease patients. *Value Health.* 2016;19(7):A847-A848.
- [9] Kovacs G, Bartolome S, Denton CP, Gatzoulis MA, Gu S, Khanna D, et al. Definition, classification and diagnosis of pulmonary hypertension. *Eur Respir J.* 2024;64(4):2401324. Doi: 10.1183/13993003.01324-2024.
- [10] Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger RMF, Brida M, et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heart J.* 2022;43(38):3618-731. Doi: 10.1093/eurheartj/ehac237.
- [11] Maron BA. Revised definition of pulmonary hypertension and approach to management: A clinical primer. *J Am Heart Assoc.* 2023;12(8):e029024. Doi: 10.1161/jaha.122.029024.
- [12] Walther CP, Nambi V, Hanania NA, Navaneethan SD. Diagnosis and management of pulmonary hypertension in patients with CKD. *Am J Kidney Dis.* 2020;75(6):935-45.
- [13] Yuan S, Li S, Ruan J, Liu H, Jiang T, Dai H. Chronic kidney disease and pulmonary hypertension: Progress in diagnosis and treatment. *Transl Res J Lab Clin Med.* 2024;273:16-22.
- [14] Lin C, Ge Q, Wang L, Zeng P, Huang M, Li D. Predictors, prevalence and prognostic role of pulmonary hypertension in patients with chronic kidney disease: A systematic review and meta-analysis. *Ren Fail.* 2024;46(2):2368082. Doi: 10.1080/0886022x.2024.2368082.
- [15] Helal EH, Abdella AMA, Hantera MS, Faraghy AA, Farhat AA. Assessment of pulmonary hypertension in patients diagnosed with chronic kidney disease. *Egypt J Bronchol.* 2024;18:86. Doi: 10.1186/s43168-024-00337-3.
- [16] Parasuraman S, Walker S, Loudon BL, Gollop ND, Wilson AM, Lowery C, et al. Assessment of pulmonary artery pressure by echocardiography- A comprehensive review. *Int J Cardiol Heart Vasc.* 2016;12:45-51. Doi: 10.1016/j.ijcha.2016.05.011.
- [17] Jin J, Hao W, Xie D. Meta-analysis of the correlation between pulmonary hypertension and echocardiographic parameters in patients with chronic kidney disease. *Peer J.* 2024;12:e17245.
- [18] O'Leary JM, Assad TR, Xu M, Birdwell KA, Farber-Eger E, Wells QS, et al. Pulmonary hypertension in patients with chronic kidney disease: Invasive hemodynamic etiology and outcomes. *Pulm Circ.* 2017;7(3):674-83. Doi: 10.1177/2045893217716108.
- [19] Huitema MP, Post MC, Grutters JC, Wells AU, Kouranos V, Shlobin OA, et al. Echocardiographic estimate of pulmonary artery pressure in sarcoidosis patients-real world data from a multi-national study. *Sarcoidosis Vasc Diffuse Lung Dis.* 2021;38(4):e2021032.
- [20] Tyagi R, Kant S, Pradhan A, Waklu A, Bajaj DK, Bajpai J. Estimates of prevalence of pulmonary hypertension according to different international definitions. *Can Respir J.* 2021;2021:1385322. Doi: 10.1155/2021/1385322.
- [21] Edmonston DL, Parikh KS, Rajagopal S, Shaw LK, Abraham D, Grabner A, et al. Pulmonary hypertension subtypes and mortality in CKD. *Am J Kidney Dis.* 2020;75(5):713-24. Doi: 10.1053/j.ajkd.2019.08.027.
- [22] Zhang X, Zhao W, Ma X, Li Y, Shang H, Zhang J, et al. Prognostic value of pulmonary hypertension in pre-dialysis chronic kidney disease patients. *Int Urol Nephrol.* 2020;52(12):2329-36. Doi: 10.1007/s11255-020-02589-6.
- [23] Chemla D, Castelain V, Provencher S, Humbert M, Simonneau G, Hervé P. Evaluation of various empirical formulas for estimating mean pulmonary artery pressure by using systolic pulmonary artery pressure in adults. *Chest.* 2009;135(3):760-68. Doi: 10.1378/chest.08-0904.

PARTICULARS OF CONTRIBUTORS:

1. Resident, Department of General Medicine, Mahatma Gandhi Medical College and Research Institute, Sri Balaji Vidyapeeth (Deemed to be University), Puducherry, India.
2. Assistant Professor, Department of General Medicine, Mahatma Gandhi Medical College and Research Institute, Sri Balaji Vidyapeeth (Deemed to be University), Puducherry, India.
3. Assistant Professor, Department of General Medicine, Mahatma Gandhi Medical College and Research Institute, Sri Balaji Vidyapeeth (Deemed to be University), Puducherry, India.
4. Associate Professor, Department of General Medicine, Mahatma Gandhi Medical College and Research Institute, Sri Balaji Vidyapeeth (Deemed to be University), Puducherry, India.
5. Professor, Department of Nephrology, Mahatma Gandhi Medical College and Research Institute, Sri Balaji Vidyapeeth (Deemed to be University), Puducherry, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

RM Anitha,
Assistant Professor, Department of General Medicine, Mahatma Gandhi Medical College and Research Institute, Sri Balaji Vidyapeeth (Deemed to be University), Puducherry-607402, India.
E-mail: dranitharam123@gmail.com

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