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Original Research Article

Frequency of pulmonary hypertension in chronic kidney disease patients (stages 3, 4, 5) at a tertiary care hospital

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ABSTRACT

Background: Chronic kidney disease (CKD) is a challenging issue for health care providers and major burden for health care. Cardiovascular disease is a well-recognized and important source of mortality in a patient with chronic kidney disease. The aim of this study was to observe the frequency of pulmonary hypertension in chronic kidney disease patients at tertiary care hospital.
Methods: This cross sectional observational study was conducted in the Department of Medicine, Combined Military Hospital, Dhaka Cantonment, Bangladesh over a period of six months from 17th November 2019 to 16th May 2020.
Results: It was observed that majority, e.g., 28.0% patients belonged to age 41-50 years, mean age was found 41.4±9.7 years in Group-A and 42.1±8.5 years in Group-B. On evaluation of eGER, maximum patients (e.g., 61%) had <15 ml/min/1.73 m^2, followed by 24.0% of patients had 15-29 ml/min/1.73 m^2 and 15.0% case detected 30-59 ml/min/1.73 m^2. Standard 2D, M mode echocardiographic was conducted in all patients. In this study, mPAP<25.0 mmHg was detected in 31 (62.0%) and 45 (90.0%) in group A and group B respectively. Overall prevalence of pulmonary hypertension was 24.0%. On comparison between groups, it is evident that frequency of pulmonary hypertension was predominant in patients with chronic kidney disease on maintenance haemodialysis than patients with chronic kidney disease without maintenance haemodialysis (38.0% vs. 10.0% respectively).
Conclusions: Pulmonary hypertension (PH) is common in patients with chronic kidney disease and is an independent predictor of mortality.

Keywords: Cardiovascular disease, Chronic kidney disease, Haemodialysis, Kidney damage, Pulmonary hypertension

INTRODUCTION

Pulmonary hypertension (PH) is common in chronic kidney disease patients and has been associated with increased morbidity and mortality.[1] Dialysed patients carry increasing risk for having pulmonary hypertension compare to predialysis. As the stage of chronic kidney disease increase the incidence of PH increase in which in stage V it reach 15% compare to stage IV 3.75% and lower in the other stages.[1] The reason why PH is frequently associated with CKD or end-stage renal disease is still unclear and presumed to be multifactorial. In the results from the previous study, the likelihood of prevalent PH was increased with older age, presence of anemia, left ventricular hypertrophy, lower levels of left ventricular ejection fraction, alterations in calcium and phosphate metabolism causing metastatic pulmonary artery calcification, chronically increased blood flow from arteriovenous fistula or arteriovenous graft, all these may predispose to elevated pulmonary pressures.[2,3]

Recently, the interest is increasing in studying the association between pulmonary hypertension (PH) and chronic kidney disease (CKD). PH is rare in general but

may be present in 30-40% (on the basis of echocardiographic studies) of the patients with end-stage renal disease, being associated with high morbidity and mortality.[1-3] CKD is defined as abnormal kidney structure or function persisting greater than 3 months. This can be established either through evidence of kidney damage (usually identified by the presence of persistent azotemia) or by a reduction in glomerular filtration rate (GFR). Other markers may include evidence of pathologic abnormality (e.g., detected by renal biopsy), structural abnormalities (e.g., abnormalities on imaging studies), or serum electrolyte abnormalities (e.g., renal tubular syndromes).[4] The causes of chronic kidney disease (CKD) include diabetic kidney disease, hypertension, vascular disease, glomerular disease (both primary and secondary), cystic kidney diseases, tubulointerstitial disease, urinary tract obstruction or dysfunction, recurrent kidney stone disease, and congenital defects of the kidney or bladder.[5] In 2002, the Kidney Disease Outcomes Quality Improvement Initiative (KDIGO) Work Group on CKD provided a comprehensive definition and staging system of CKD in an effort to provide a common language among providers, patients and researchers, and hopefully improve communication and care for this diagnosis.[5]

Risk factors for CKD progression include advanced GFR decline, high albuminuria, advanced age, male gender, poorly controlled hypertension, hyperglycemia, dyslipidemia, smoking, cardiovascular disease history, and nephrotoxic exposure.[6] These factors contribute to electrolyte and acid-base imbalances, which worsen patient outcomes but can be managed with preventive measures and pharmacological therapy.[7] Pulmonary hypertension (PH) is a common comorbidity in CKD and end-stage renal disease (ESRD), significantly increasing hospitalization and mortality risks.[1] Previous studies highlight a higher prevalence of PH in ESRD patients on dialysis, linking it to LV dysfunction, AV fistulas, anemia, and imbalances in vasoconstrictor and vasodilator substances. Despite its prognostic importance, the true prevalence and pathogenesis of PH in CKD remain unclear, with most studies defining PH via echocardiography and various mechanisms potentially contributing to its development.[8,9]

The objective of this study was to observe the frequency of pulmonary hypertension in chronic kidney disease patients at tertiary care hospital.

METHODS

This cross-sectional observational study was conducted at the Department of Medicine, Combined Military Hospital, Dhaka Cantonment, Bangladesh, over six months from November 17, 2019, to May 16, 2020, to assess the frequency of pulmonary hypertension in chronic kidney disease (CKD) patients. A total of 100 patients with CKD stages 3, 4, and 5 were recruited and divided into two groups: 50 patients on maintenance hemodialysis (Group A) and 50 patients not on hemodialysis (Group B). Patients aged ≥18 years who provided consent were included, while those with significant co-morbid conditions, secondary pulmonary hypertension due to various causes (e.g., cardiac disease, COPD, previous pulmonary embolism), current malignant diseases, or pregnancy were excluded. Data collection involved detailed history taking, clinical examination, and relevant investigations. A pre-designed questionnaire was used to collect socio-demographic and clinical data, which were then processed, validated, and analyzed using SPSS software. Ethical approval was obtained from the Combined Military Hospital's Ethics Review Committee, and informed consent was secured from all participants, adhering to the principles of the Helsinki Declaration. The results were considered significant with a "P" value of <0.05.

RESULTS

Table 1 presents the socio-demographic characteristics of study patients aged 23-67 years. Most patients (28.0%) were aged 41-50 years, followed by 26.0% aged 31-40 years. The mean ages were 41.4±9.7 years in Group A and 42.1±8.5 years in Group B, with no significant difference between the groups. The male-to-female ratio was 1.9:1. A majority (73.0%) were from urban areas, and 47.0% were service holders or workers. Housewife representation was 26.0% in Group A and 22.0% in Group B, with no significant difference. Economically, 42% were poor, 38% middle class, and 20% upper class. The p values indicated no statistical significance between the groups.

Table 1: Socio demographic characteristics of the study patients (n=100).

Characteristics		Number of patients		P value
		Group A (n = 50) No. (%)	Group B (n = 50) No. (%)	
Age (years)	<30	8 (16.0)	7 (14.0)	0.213
	31-40	11 (22.0)	15 (30.0)	
	41-50	16 (32.0)	12 (24.0)	
	51-60	13 (26.0)	12 (24.0)	
	61-70	2 (4.0)	4 (8.0)	
	Mean ± S.D.	41.4±9.7	42.1±8.5	

Continued.

Characteristics		Number of patients		P value
Residence	Rural	12 (24.0)	15 (30.0)	0.083
	Urban	38 (76.0)	35 (70.0)	
Occupation	Business	14 (28.0)	15 (30.0)	0.158
	House wife	13 (26.0)	11 (22.0)	
	Service and worker	23 (46.0)	24 (48.0)	

Figure 1 shows the coexisting diseases of the study subjects. In Group A, 40% had hypertension, 28% had diabetes, 24% had CAD, and 34% had a history of smoking. In Group B, 34% had hypertension, 46% had diabetes, 14% had CAD, and 28% had a history of smoking. The differences in coexisting diseases between the two groups were not statistically significant.

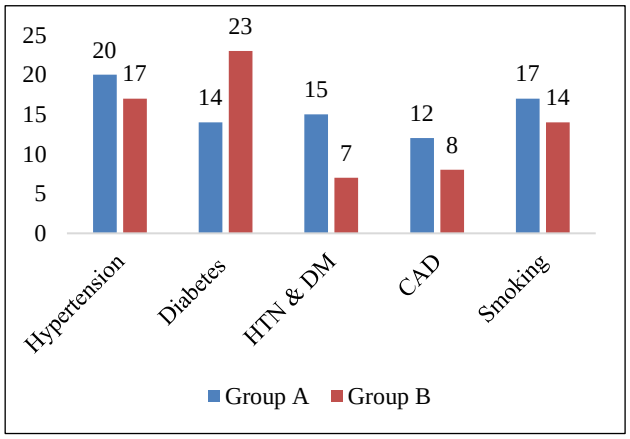

Figure 1: Distribution of the patients according to risk factors (n=100).

Figure 2 evaluates eGFR level in CKD patients. On evaluation of eGER, maximum patients (e.g., 61%) had <15 ml/min/1.73 m^2, followed by 24.0% of patients had 15-29 ml/min/1.73 m^2 and 15.0% case detected 30-59 ml/min/1.73 m^2.

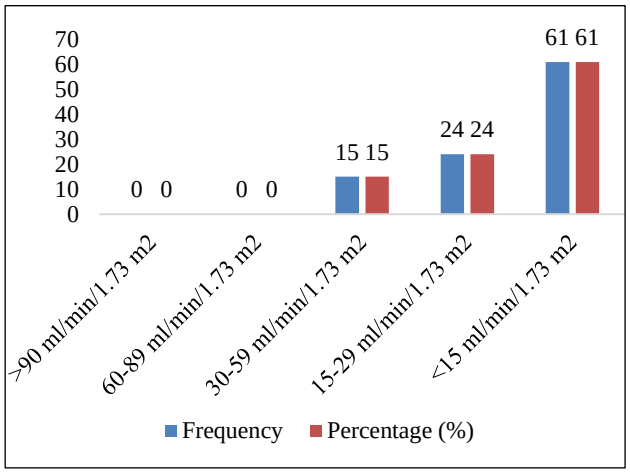

Figure 2: Evaluation of eGFR level in CKD patients (n=100).

Figure 3 shows the comparison of different stages of CKD in between groups. On evaluation of GFR, 24 patients had stage IV CKD and all cases were group-B. Stage III was detected in 15 patients, all belongs to group B. sixty one patients was diagnosed as stage IV CKD, 50 in group-A and 11 in group B.

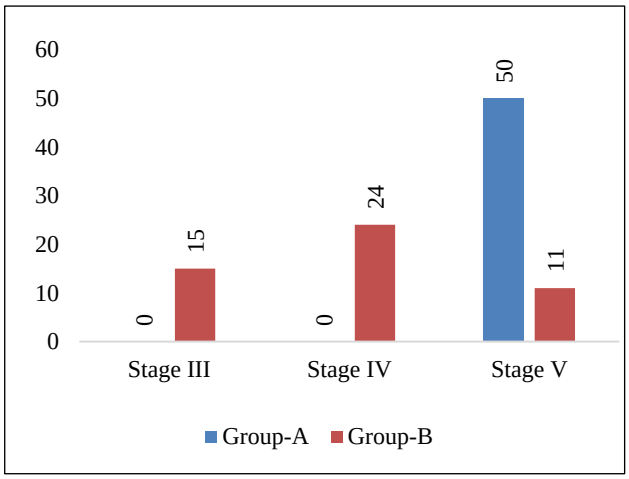

Figure 3: Comparison of stages of CKD in between groups (n=100).

Table 2 shows no significant differences in baseline hemodynamic status between groups. Group A had a mean temperature of 37.63°C, HR of 95.43 bpm, RR of 12.23 breaths/min, and MABP of 92.50 mmHg. Group B had a mean temperature of 37.72°C, HR of 92.53 bpm, RR of 16.17 breaths/min, and MABP of 91.82 mmHg.

Table 3 shows that Group A had higher mean LVIDd, LVIDs, LV end-systolic and diastolic volumes, and PAP, but lower LVEF compared to Group B. Specifically, LVIDd was 51.0 mm vs. 44.1 mm, and LVEF was 52.4% vs. 59.9%.

Table 4 shows the mean pulmonary artery pressure. In this study, mPAP <25.0 mmHg was detected in 31(62.0%) and 45(90.0%) in group A and group B respectively.

Figure 4 shows that pulmonary hypertension was more prevalent in CKD patients on maintenance hemodialysis (38%) compared to those without it (10%).

Table 2: Clinical parameter of the study subjects (n=100).

Variables	Group A (n=50) (Mean±S.D)	Group B (n=50) (Mean±S.D)	P value
Temperature (C)	37.63±1.27	37.72±1.02	1.025
Heart rate (b/pm)	95.43±19.34	92.53±15.13	0.857
Respiratory rate (breath/min)	12.23±7.23	16.17±8.21	0.502
Mean arterial BP (mmHg)	92.50±28.43	91.82±25.70	1.008

Table 3: Evaluation of echocardiographic findings between groups (n=100).

Variables	Group A (n=50) (Mean±S.D)	Group B (n=50) (Mean±S.D)	P value
LVIDd (mm)	51.0±4.9	44.1±4.5	0.001
LVIDs (mm)	30.5±3.1	26.7±3.0	0.089
LV end systolic volume (ml)	77.3±10.8	59.2±10.5	0.001
LV end diastolic volume (ml)	162.5±18.9	147.8±16.4	0.171
LVEF (%)	52.4±6.5	59.9±4.6	0.001
mPAP (mmHg)	39.5±6.1	27.1±5.2	0.001

Table 4: Distribution of the patients according to mean pulmonary artery pressure (n=100).

mPAP (mmHg)	Group A (n=50) No. (%)		Group B (n=50) No. (%)	
	n	**%**	**n**	**%**
<25.0	31	62.0	45	90.0
25.1-40	10	20.0	4	8.0
41-55	7	14.0	1	2.0
>55.0	2	4.0	0	0

Table 5: Univariate analysis of factors influencing the pulmonary hypertension in CKD (n=100).

Variables	Total number of patients (n=100)	Number of patients with PH (n=24)	Percentage (%)	p-value
Age				
<50 year	69	14	20.2	0.035
>50 year	31	10	32.2	
Sex				
Male	66	16	24.2	0.959
Female	34	8	23.5	
HTN				
Yes	37	14	37.8	0.001
No	63	10	15.8	
DM				
Yes	37	16	43.2	<0.0001
No	63	8	12.6	
Stages				
Stage III	15	1	6.6	
Stage IV	24	4	16.7	0.016
Stage IV	61	19	31.1	

Table 5 shows that stage V CKD had the highest prevalence of pulmonary hypertension (31.1%), with progression of CKD being a significant risk factor ($p<0.0001$). Extreme age (>50 years: 32.2%) and co-existing hypertension and diabetes also increased risk ($p<0.0001$). Gender did not impact prevalence.

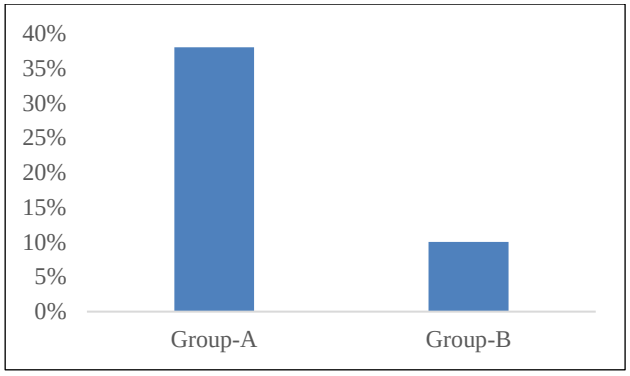

Figure 4: Prevalence of pulmonary hypertension (PHT) among CKD patients stage (n=100).

DISCUSSION

This cross-sectional observational study was conducted at the Combined Military Hospital, Dhaka, with ethical approval from the review board. Patients with CKD stages 3, 4, and 5 were included via purposive sampling. Most patients were aged 41-50 years (28.0%), followed by 31-40 years (26.0%). The mean age was 41.4±9.7 years in Group A and 42.1±8.5 years in Group B. Of the 100 cases, 66.0% were male and 34.0% female, giving a male-to-female ratio of 1.9:1. These findings align with studies like Rahman T's, where the mean age was 50.9±11.9 years.[10] In developed countries, CKD prevalence increases with age, peaking between 70-90 years, whereas our study found a sharp decline in incidence post-60 years, likely due to lower life expectancy and healthcare access in Bangladesh.[11,12] Advanced countries see peak incidence in the 7th and 8th decades.[13,14] The discrepancy may stem from genetic, socio-cultural, diagnostic, and therapeutic factors.[15]

No significant differences in risk factors were noted between groups. Group A had 40.0% with hypertension, 28.0% with diabetes, 24.0% with CAD, and 34.0% with a history of smoking. Group B had 34.0% with hypertension, 46.0% with diabetes, 14.0% with CAD, and 28.0% with smoking history. These differences were not statistically significant. In evaluating eGFR, 61% of patients had <15 ml/min/1.73 m², 24.0% had 15-29 ml/min/1.73 m², and 15.0% had 30-59 ml/min/1.73 m².

Most patients had stage V CKD, followed by stage IV, possibly due to minor symptoms in earlier stages. Patients often remain asymptomatic until GFR drops below 30 ml/min, only seeking tertiary care after significant symptoms arise. This is why stages I and II were underrepresented in our study.

Recent evidence shows mild to moderate pulmonary hypertension (PH) is more common than previously thought, often undetected until symptoms like fatigue, dyspnea, and syncope emerge.[16,17] PH in CKD patients is not confined to those with systemic diseases; it can develop directly from declining kidney function. The prevalence of PH is reported as 9-39% in stage 5 CKD, 18.8-68.8% in hemodialysis patients, and 0-42% in peritoneal dialysis patients.[18] Factors contributing to PH in CKD include left ventricular disorders, arteriovenous fistulas, anemia, and imbalances in vasoconstrictor and vasodilator substances. Despite its significance, the prevalence and pathogenesis of PH in CKD remain poorly understood.

Echocardiographic analysis showed mean LVIDd (mm) was 51.0±4.9 in Group A and 44.1±4.5 in Group B; mean LVIDs (mm) was 30.5±3.1 in Group A and 26.7±3.0 in Group B; mean LV end-systolic volume (ml) was 77.3±10.8 in Group A and 59.2±10.5 in Group B; mean LV end-diastolic volume (ml) was 162.5±18.9 in Group A and 147.8±16.4 in Group B; and mean LVEF was 52.4±6.5 in Group A and 59.9±4.6 in Group B. Mean PAP was 39.5±6.1 in Group A and 27.1±5.2 in Group B. PASP <35.0 mmHg was found in 62.0% of Group A and 90.0% of Group B. Overall, PH prevalence was 48%, with a higher frequency in dialysis-naive CKD patients compared to those on dialysis (38.0% vs. 10.0%).

PH, common in dialysis-dependent CKD, is an independent mortality predictor. However, its hemodynamics, changes due to hemodialysis, and classification into pre- or post-capillary PH need further exploration.[19] PH, often subclinical in CKD, is linked to left ventricular disorders and CKD risk factors like volume overload, arteriovenous fistulas, sleep-disordered breathing, and anemia.[20] The prevalence of PH rises with CKD stage progression, particularly post-capillary causes.[21] The pathophysiology of PH in CKD includes hypertension and diabetes-induced LV diastolic dysfunction, leading to increased pulmonary venous and arterial pressure. Chronic volume overload, common in CKD, exacerbates pulmonary venous hypertension by increasing blood flow and affecting LV function. Myocardial stiffness, another CKD complication, also contributes to PH. The WHO classifies patients with LV disorders and volume overload under group II, and those with lung diseases under group III, with chronic hypoxia in COPD leading to pulmonary vasoconstriction.[22]

CKD is a major public health issue in Bangladesh, associated with increased mortality risk due to PH. Early detection and routine echocardiographic evaluation of PH are crucial to mitigate CKD's burden.[23]

This study has few limitations. The study, limited to a single hospital with a small sample size, may not represent the national picture. A larger-scale study is needed for broader conclusions. The findings may not reflect primary or secondary care settings.

CONCLUSION

It is concluded that pulmonary hypertension is prevalent in patients with CKD, particularly in patients with stage 5 maintained on HD. In this study frequency of pulmonary

hypertension was 48% patients of CKD. Pulmonary hypertension in CKD patients worsens mortality and morbidity. Key risk factors include LV dysfunction, hypertension, diabetes, elderly age, AVFs, and imbalances in vasoconstrictors and vasodilators. Early detection and multidisciplinary management are crucial to reduce CKD burden and improve patient outcomes.

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