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FREQUENCY OF PULMONARY HYPERTENSION IN HEMODIALYSIS PATIENTS

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Abstract

Background: *Pulmonary hypertension (PH) frequently coexists with end-stage renal disease (ESRD) in patients undergoing dialysis. It serves as an independent predictor of heightened morbidity and mortality in these patients. The actual prevalence of PH in our ESRD patients remains uncertain, despite its prognostic importance.*

Methodology: *Study was carried out at Nephrology Department of PIMS Islamabad. 200 patients undergoing chronic maintenance hemodialysis for ESRD and CKD stage 5, specifically patients who have undergone hemodialysis for a minimum of 6 months having age between 18-80 years of both genders were enrolled for the study. Using the echocardiography, pulmonary arterial pressure (PAP) was measured, and those with PAP of 25 mmHg or higher at rest were classified as having pulmonary hypertension. Data was entered and analyzed using SPSS software.*

Results: *The mean age of the participants was 46.84 years ±15.24 SD. PH was observed in 28% (56 out of 200) of the study population. Among these, 58.9% were male suggesting a slightly higher prevalence in males. The analysis of age groups revealed that PH was highest (44.6%) among patients with age 36-60 years. Stratification was done for various effect modifiers and it was noticed that statistically significant association (p-value ≤ 0.05) was observed for treatment compliance, COPD and hypertension only.*

Conclusion: *Our study found a high prevalence of PH in hemodialysis patients, especially those with hypertension, COPD, and non-compliance with treatment.*

INTRODUCTION

Pulmonary Hypertension (PH) is defined as the elevated pulmonary arterial pressure (PAP), specifically a mean PAP over 20 mmHg. [i] Recent study indicates that around 1% of the population is affected by pulmonary hypertension, with an estimated 80% of cases occurring in the poor world.[ii] PH occurs in 9% to 39% of patients with chronic kidney disease (CKD) and incidence varies with kidney disease stages: 21% in stage 3.24% in stage 4 and 32% in stage 5.[iii] PH increases the mortality rate in dialysis patients making kidney transplantation a viable option lor those with this condition. [iv] Risk factors for PH in

ESRD patients encompass age, cardiac dysfunction, history of dialysis, and arteriovenous fistulas. Dialyzer membranes, chronic fluid overload, and persistent anemia, osteoporosis, uremic toxins, and vasculopathy are also among the common risk factors. [v] Vascular calcification, endothelial & diastolic dysfunction, left ventricular hypertrophy, AVF flow obstructive sleep apnea syndrome, pulmonary embolism and dialysis membrane exposures may contribute to PH.[vi] It is hypothesized that endothelial dysfunction of pulmonary arteries cannot offset the higher cardiac output brought on by AVF since it aggravates PH. Histological analysis PH reveals proliferation and hyperplasia in small arteries. Idiopathic PH is linked to BMPR2 genetic variations. [vii, viii] Patients with CKD may experience multifactorial PH. ln secondary PH, the underlying cause can mask symptoms, with right ventricular failure sometimes being the first sign before diagnosis is made. PH can now be accurately and non-invasively estimated through echocardiography. [ix, x] Given the severe impact and healthcare burden, studying the prevalence of PH in chronic maintenance hemodialysis patients is crucial. Understanding its frequency and patterns will highlight its effect on morbidity and mortality in these patients.

MATERIAL AND METHODS

This study was conducted from 21st June 2024 to 30th December 2024 at Nephrology Department of Pakistan Institute of Medical Sciences Islamabad. Sample size was calculated as 200 patients using WHO sample size calculator. Confidence level was taking as 95%, absolute precision was taken as 5% and population proportion as 24.2%.[6] Consecutive non-random technique was used for sampling. Patients undergoing chronic maintenance hemodialysis for end-stage renal disease (ESRD) and CKD stage 5, specifically patients who have undergone hemodialysis for a minimum of 6 months having age between 18-80 years of both genders were enrolled for the study. Patients with a history of congenital heart disease or primary pulmonary hypertension were excluded. Patients with acute respiratory distress syndrome or active pulmonary infections were also excluded from the study. After obtaining approval from the ethical committee of PIMS Hospital, eligible patients were approached during their dialysis sessions and informed consent were obtained. Patients were screened based on the inclusion and exclusion criteria specified. A structured questionnaire was used to collect baseline demographic and clinical information. To confirm the diagnosis of PH, selected patients underwent transthoracic echocardiography. The pulmonary arterial pressure (PAP) was measured, and those with PAP of 25 mmHg or higher at rest were classified as having pulmonary hypertension. Echocardiography was used to identify the right ventricle size and function. Collected data was entered in SPSS software. Means and standard deviations were computed for continuous variables, whilst frequencies and percentages were assessed for categorical variables. Stratification was conducted for effect modifiers. The Chi-square test was utilized, with a p-value of ≤0.05 deemed significant.

RESULTS

A total of 200 hemodialysis patients participated in the study. The mean age of the participants was 46.84 years ±15.24 SD, with a range from 20 to 77 years. Study was male dominant; while, majority of patients were aged between 36 to 60 years (49.5%). Hypertension was highly prevalent in the cohort, with 91.5% of patients having a history of hypertension, while 28.5% were smokers, and 68% were compliant with their prescribed treatment regimens. Demographic and clinical profile including quantitative and qualitative variables are presented in table 2.

Pulmonary hypertension (PH) was observed in 28% (56 out of 200) of the study population (figure 1). Among these, 58.9% were male suggesting a slightly higher prevalence in males. The analysis of age groups revealed that PH was highest (44.6%) among patients with age 36-60 years. Furthermore, pulmonary hypertension was more frequently observed in patients who were married, belonged to middle income group, taking Nifedipine, having weight <70kg and duration of dialysis >12 months. Stratification was done for all the clinical and demographic variables including comorbid and it was noticed that statistically significant association (*p*-value ≤ 0.05) was observed for treatment compliance, COPD and hypertension. Detailed analysis is illustrated in table 3 and 4.

Table 1: Demographic and clinical details of the quantitative variables of the study participants (n=140)

Quantitative Variables	Minimum	Maximum	Mean	± SD
Age (Years)	20.00	77.00	46.84	15.24
Systolic Blood Pressure (mmHg)	115.00	164.00	139.51	14.60
Diastolic Blood Pressure (mmHg)	70.00	110.00	91.69	11.21
Weight (kg)	41.00	99.00	69.99	16.29
Duration of Dialysis (months)	6.00	24.00	14.05	4.95
Frequency of Dialysis	1.00	4.00	2.55	0.70
Serum Creatinine (mg/dL)	0.60	2.30	1.31	0.31
eGFR (ml/min)	4.90	19.90	12.76	2.97
Blood Urea Nitrogen (mg/dL)	17.00	55.00	36.94	7.53
Parathyroid Hormone (pg/ml)	23.50	813.20	350.89	185.50
Pulmonary Arterial Pressure (mmHg)	9.00	50.00	22.92	9.96

Table 2: Clinical, demographic and comorbid details of study subjects (n=140)

Variables		Frequency	Percentage (%)
Gender	Male	106	53.0
	Female	94	47.0
Marital Status	Married	151	75.5
	Unmarried	49	24.5
Income Group (PKR/Month)	Upto 50,000	35	17.5
	50-100,000	121	60.5
	>100,000	44	22.0
Diabetes Mellitus	Yes	52	26.0
	No	148	74.0
Ischemic Heart Disease	Yes	40	20.0
	No	160	80.0
Chronic Obstructive Pulmonary Disease	Yes	30	15.0
	No	170	85.0
Interstitial Lung Disease	Yes	27	13.5
	No	173	86.5
Hypertension	Yes	183	91.5
	No	17	8.5
Thyroid Disorders	Yes	49	24.5
	No	151	75.5
Smoking	Yes	57	28.5
	No	143	71.5
Compliance	Yes	136	68.0
	No	64	32.0
Medication	Nifedipine	82	41.0
	Hydralazine	81	40.5
	Doxazocin	37	18.5

Table 3: Stratification of pulmonary hypertension in patients with end stage kidney disease on the basis of various clinical and demographic variables

Variables		Pulmonary Hypertension		p-Value (x2-test)
		Positive	Negative	
Gender	Male	33 (58.9%)	73 (50.7%)	0.295
	Female	23 (41.1%)	71 (49.3%)	
Marital Status	Married	41 (73.2%)	110 (76.4%)	0.639
	Unmarried	15 (26.8%)	34 (23.6%)	
Income Group (PKR/Month)	Upto 50,000	15 (26.8%)	20 (13.9%)	0.092
	50-100,000	31 (55.4%)	90 (62.5%)	
	>100,000	10 (17.9%)	34 (23.6%)	
Smoking	Yes	16 (28.6%)	41 (28.5%)	0.989
	No	40 (71.4%)	103 (71.5%)	
Compliance	Yes	23 (41.1%)	113 (78.5%)	0.000
	No	33 (58.9%)	31 (21.5%)	
Medication	Nifedipine	25 (44.6%)	57 (39.6%)	0.802
	Hydralazine	21 (37.5%)	60 (41.7%)	
	Doxazocin	10 (17.9%)	27 (18.8%)	
Age Groups	Upto 35 Years	18 (32.1%)	43 (29.9%)	0.657
	36-60 Years	25 (44.6%)	74 (51.4%)	
	>60 Years	13 (23.2%)	27 (18.8%)	
Systolic Blood Pressure Groups (mmHg)	Upto 140	31 (55.4%)	78 (54.2%)	0.879
	> 140	25 (44.6%)	66 (45.8%)	
Diastolic Blood Pressure Groups (mmHg)	Upto 90	22 (39.3%)	68 (47.2%)	0.311
	> 90	34 (60.7%)	76 (52.8%)	
Weight Groups (kg)	<70 Kg	33 (58.9%)	72 (50.0%)	0.365
	70-85 kg	13 (23.2%)	33 (22.9%)	
	>85 kg	10 (17.9%)	39 (27.1%)	
Duration of Dialysis (months)	Upto 12	27 (48.2%)	60 (41.7%)	0.402
	>12	29 (51.8%)	84 (58.3%)	

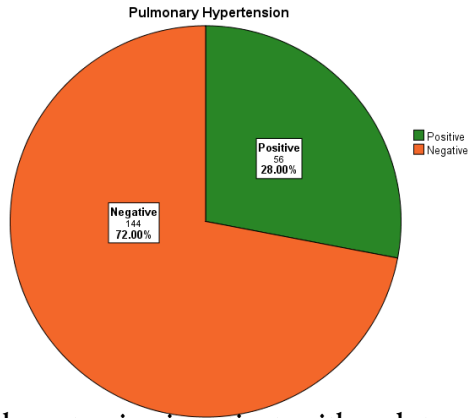

Figure 1: Frequency of pulmonary hypertension in patients with end stage kidney disease

Table 4: Stratification of pulmonary hypertension in patients with end stage kidney disease on the basis of various comorbid

Comorbid		Pulmonary Hypertension		*p*-Value (x^2-test)
		Positive	Negative	
Diabetes Mellitus	Yes	12 (21.4%)	40 (27.8%)	0.358
	No	44 (78.6%)	104 (72.2%)	
Ischemic Heart Disease	Yes	09 (16.1%)	31 (21.5%)	0.386
	No	47 (83.9%)	113 (78.5%)	
Chronic Obstructive Pulmonary Disease	Yes	23 (41.1%)	07 (4.9%)	0.000
	No	33 (58.9%)	137 (95.1%)	
Interstitial Lung Disease	Yes	09 (16.1%)	18 (12.5%)	0.507
	No	47 (83.9%)	126 (87.5%)	
Hypertension	Yes	55 (98.2%)	128 (88.9%)	0.034
	No	01 (1.8%)	16 (11.1%)	
Thyroid Disorders	Yes	14 (25%)	35 (24.3%)	0.918
	No	42 (75%)	109 (75.7%)	

DISCUSSION

As the patients with CKD are at a heightened risk for various cardiovascular and pulmonary complications, it becomes crucial to explore and understand the prevalence, associated risk factors, and clinical implications of PH in this population.[xi] By investigating the prevalence of pulmonary hypertension in hemodialysis patients, the study highlights key clinical characteristics associated with its development, such as hypertension, COPD, and non-compliance with prescribed treatments. This information can significantly impact clinical practices by encouraging healthcare providers to screen for PH in hemodialysis patients, particularly those with pre-existing risk factors. Possible early recognition and targeted interventions could limit cardiopulmonary sequelae and enhance quality of life, thus decreasing overall morbidity and mortality in this at-risk patient-population. The results of this study are consistent with prior studies that demonstrated the high prevalence of pulmonary hypertension among hemodialysis patients; however, prevalence estimates can vary based on the study population, diagnostic criteria utilized, and geographical considerations. PH is prevalent and often underdiagnosed in dialysis patients, with rates varying from 30% to 80% in different cohorts of hemodialysis patients.

A study by Mirza et al. In agreement with our study, in which 28% of the participants were found to have PH, 48% of hemodialysis patients have been shown to have evidence of PH.[xii] Shamim et al. in near past, reported a similar trend where mean pulmonary artery systolic pressure was also over 29.47±9.16 mmHg (mean ± SD). Fifteen (18.75%) patients were found to have PH. They also noted that PH was more prevalent in patients with diabetes, hypertension, and COPD, which we observed in our study as well.[xiii] Patients with ESRD undergoing hemodialysis exhibit a pronounced propensity to develop PH. Our study indicated that PH is more prevalent in males; however, Mukhtar KN and colleagues showed a higher prevalence in females, and the length of hemodialysis is significantly associated with the development of PH. In this study, 45 out of 80 patients (56%) exhibited PH. They also determined the severity of PH. The average duration of hemodialysis in months for patients with PH was 20.93±12, compared to 10.29±10 for patients without PH ($p<0.05$). This study found no correlation between age and the development of PH.[xiv] Khemchandani M et al. in a separate study emphasized the incidence of PH in hemodialysis patients and identified the associated risk factors. Their conclusion was that comprehending these relationships can facilitate the

management of PH in ESRD patients. This study exhibits a demographic and clinical profile that closely resembles ours. The average age was 50.65 ± 14.4 years, comprising 131 (59.5%) males and 89 (40.5%) females. The mean duration of hemodialysis was 5.3 ± 2.8 years. Hypertension (89.5%) and ischemic heart disease (24.1%) were significant comorbidities. The mean pulmonary artery pressure was 35.2 ± 15.3 mmHg. Among 220 patients, 109 (49.8%) exhibited mild pulmonary hypertension (PH), nine (4.1%) presented with severe PH, and 72 (32.7%) were diagnosed with moderate PH.[xv]

Research conducted in Somalia revealed analogous results, with pulmonary hypertension present in 51% of patients. The median pulmonary arterial pressure was determined to be 35 mmHg. They also observed a positive correlation between systolic pulmonary artery pressure and right atrium (RA) diameter (r: 0.6, $p < 0.001$), and a negative correlation with left ventricular ejection percent (LVEF) (r: -0.4, $p < 0.001$). Moreover, left ventricular ejection fraction (LVEF), right atrial diameter, and the presence of pericardial effusion (PE) were identified as independent predictors of PH. The relationship between hypertension and pulmonary hypertension in the hemodialysis population is well-established.[xvi] Patients with longstanding hypertension are at a significantly higher risk of developing PH. In our study, 98.2% of PH-positive patients had hypertension, corroborating the findings of previous studies that highlight the contribution of elevated blood pressure to the development of PH in CKD patients. Previous studies have also described the relationship between COPD and PH in patients on hemodialysis, where the individual effects of dysfunction of the pulmonary and cardiovascular systems are exacerbated.[xvii,xviii] Our study reported that 41.1% of patients with PH had COPD, which supports the association and highlights the importance of regular monitoring of pulmonary function in hemodialysis patients.

Furthermore, non-compliance to the treatment is the area to be explored regarding PH in ESRD patients. Existing research has demonstrated that non-compliance to medication plans including antihypertensives may lead to secondary pulmonary hypertension.[xix] 58.9% of PH-positive patients in this study were non-compliant to their prescribed treatments, emphasizing the need for patient education, periodic follow-ups, and formulation of effective strategies to increase compliance in low-resource settings. Our study's finding shows no significant association between PH and diabetes mellitus, which is inconsistent with some prior studies, which reported that diabetic hemodialysis patients had a higher risk of PH. [xx] This difference could be due to the demographic features of the patients, the diagnostic techniques for PH, or other unassessed confounders. In conclusion, these results are clinically important as they represent an early diagnostic tool for PH especially in patients with underlying hypertension and COPD, and non-compliance with medications among hemodialysis patients. Detecting these risk factors allows providers to intervene early, better manage patients, and ultimately decrease the morbidity of PH. Detection of PH allows for timely therapeutic management of patients with PH, including the increase in oxygen supply, the use of vasodilators or other pharmacological therapies that can potentially reduce the right ventricular strain in patients with PH and improve hemodynamics. In low-resource settings, where advanced diagnostic tools such as echocardiography or right heart catheterization may not be available, this study's results could be used to prioritize clinical assessments and diagnostic imaging (e.g., chest X-ray, electrocardiograms) for patients at high risk of PH. Furthermore, the study encourages non-invasive monitoring of pulmonary pressure through clinical assessments, helping to detect PH in its early stages. The study's findings on non-compliance highlight the need for improved patient education and adherence strategies to ensure better health outcomes. Non-compliance in patients with chronic conditions like hemodialysis can significantly affect their prognosis and increase the risk of complications, including PH. Interventions such as mobile health applications to remind patients of their medications, community health workers, and peer support programs can be vital tools in improving adherence in low-resource settings.

This study has several strengths that contribute to its significance in understanding the prevalence and risk factors of PH in hemodialysis patients. comprising of 200 patients, an optimum sample size, this study can detect significant associations between PH and demographic and clinical characteristics. Second,

they are adjusted for a wider variety of covariates such as age, gender, income, medical comorbidities, dialysis duration and treatment compliance, providing a broader view of the correlates of PH in this patient group. Focusing on a local population provides a better recognition of the burden of pulmonary hypertension in hemodialysis patients in the particular geographical, socio-economic, and healthcare context of the population studied.

Although the study offers key insights, limitations need to be acknowledged. First, the cross-sectional nature of the study allows it to establish associations but not causations. Further longitudinal studies will need to determine whether these aforementioned risk factors are directly responsible for the development of PH over time. Secondly, in this study, important clinical variables (e.g., cardiac function, pulmonary function tests, and family history of pulmonary hypertension) were not collected, which may provide more clues regarding the etiology of PH in patients on hemodialysis. Our study population was limited to a single center and may not apply to other populations or regions. Other factors, such as healthcare access, socioeconomic resources, and cultural practices, could potentially contribute to the prevalence and management of the condition in different settings.

CONCLUSION

Our research underscored the substantial frequency of PH among hemodialysis patients, especially those with hypertension, chronic obstructive pulmonary disease, and treatment non-compliance. The results highlighted the significance of early detection and suitable care of PH in this at-risk patient population. Notwithstanding these constraints, the study offers significant insights that can be useful for clinical decision-making, enhance screening initiatives, and elevate patient outcomes. Further research is required to investigate the long-term impacts of pulmonary hypertension on hemodialysis patients and to formulate tailored therapies aimed at alleviating the burden of this condition.

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