

Pulmonary Hypertension: An Emerging Problem in Patients Undergoing Regular Hemodialysis

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ABSTRACT

Objective: To find out the frequency of pulmonary hypertension (PH) and its association with various contributing factors in patients undergoing regular hemodialysis (HD) due to end-stage renal disease (ESRD).

Study Design: Cross-sectional analytical study.

Place and Duration of Study: Nephrology Department, Lahore General Hospital, Pakistan, from July to December 2016.

Methodology: Fifty patients with end-stage renal disease. Various parameters, including the pulmonary arterial systolic pressure (PASP), were recorded. Pulmonary arterial pressure greater than 25 mmHg at rest was defined as pulmonary hypertension. It was further divided into three sub categories as mild (25-40 mmHg), moderate (40-55 mmHg), and severe (greater than 55 mmHg). Data were correlated with age, gender, body mass index, systemic hypertension, diabetes, duration of dialysis, and Hb (hemoglobin) concentration. Data was analysed using SPSS version 23.0.

Results: The median (IQR) duration of dialysis was 12 (11.25) months. Eighteen (36%) patients were found to have PH. It is greater in patients who had been on dialysis for more than 5 months. A positive association was seen between the duration of dialysis and the prevalence of PH ($p=0.024$).

Conclusion: A considerable number of patients on hemodialysis have pulmonary hypertension which is associated with the longer duration of maintenance hemodialysis.

Key Words: Pulmonary hypertension (PH). Hemodialysis (HD). Pulmonary arterial systolic pressure (PASP). End-stage renal disease (ESRD). Hemoglobin (Hb). Chronic kidney disease (CKD).

INTRODUCTION

Pulmonary hypertension (PH) is an elevation of pulmonary arterial systolic pressure (PASP), which can be the result of heart, lung or systemic disorders. PH is defined as a sustained elevation of PASP of ≥ 25 mm Hg at rest as determined by using a Doppler echocardiograph.^{1,2} There is significant epidemiological overlap with kidney disease and the underlying causes of World Health Organization group 1-4 pulmonary hypertension (pulmonary arteriopathy, left heart disease, chronic pulmonary disease, and chronic thrombo-embolic disease, respectively). In addition, an entity of unexplained pulmonary hypertension, group 5, has emerged in patients with chronic kidney disease and end-stage renal disease, with prevalence estimates of 30-50%.^{2,3}

Chronic kidney disease (CKD) is now becoming a major health burden day by day and cardiovascular complications are well recognised source of morbidity and mortality in patients suffering from CKD.^{4,5} Cardiovascular complications account for about 50% deaths in patients of ESRD.⁶ There is high incidence of

PH among patients with ESRD receiving long-term hemodialysis with surgical arteriovenous access. Both ESRD and long-term hemodialysis *via* arteriovenous access may be involved in the pathogenesis of PH by affecting pulmonary vascular resistance and cardiac output.⁷

In a multivariable Cox proportional hazard model, the development of pulmonary hypertension both before and after initiation of hemodialysis had significantly increased odds ratios and remained an independent predictor of mortality. The incidence of pulmonary hypertension, after initiation of hemodialysis therapy, is a strong independent predictor of mortality, nearly equal to that associated with long-standing severe cardiac abnormalities.⁸ Doppler echocardiography has made it possible to accurately estimate the pulmonary arterial hypertension non-invasively.⁹ Patients on maintenance hemodialysis are at an increased risk of developing pulmonary hypertension which has a strong correlation with the duration of maintenance hemodialysis and the arteriovenous access utilised.^{10,11}

In patients suffering from ESRD, pulmonary hypertension has multifactorial etiology.^{12,13} Factors such as metabolic derangements, chronic volume overload, metastatic pulmonary artery calcification (caused by calcium and phosphate metabolic derangements), increased blood flow caused due to the arteriovenous fistula or grafts, may be the causes of pulmonary hypertension, which may ultimately cause heart failure and death.

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It is needed to know the burden of PH in a developing country and its relationship with associated factors to generate some current data. Those found to have pulmonary hypertension, can be offered alternative method of dialysis, reversal of AV fistula or may be suggested to have early renal transplant so that they may avoid this fatal complication.

The objective of this study was to find out the frequency of pulmonary hypertension (PH) and its association with various contributing factors in patients undergoing regular hemodialysis (HD) due to end-stage renal disease (ESRD).

METHODOLOGY

A cross-sectional study was conducted in the Department of Nephrology, Lahore General Hospital, Pakistan, from July to December 2016. The study population was selected after taking appropriate informed consent, by applying proper inclusion and exclusion criteria and taking detailed history of every patient. Sample size of 50 was calculated by 95% confidence level with 10% absolute precision, taking 85% anticipated population proportion.

The study population consisted of patients aged 15 to 65 years, with end-stage renal disease, who underwent regular dialysis on maintenance basis via permanent arteriovenous access two times a week, with each session of about 4 hours duration. Patients with chronic obstructive lung disease, chest wall or parenchymal lung disease, previous pulmonary embolism, collagen vascular disease, moderate or severe mitral or aortic valve disease and having obstructive sleep apnea were excluded. Trans thoracic echocardiography was performed on those patients by a cardiologist post-dialysis when patients were at optimal dry weight. Systolic pulmonary artery pressure was measured. A pulmonary arterial pressure greater than 25 mmHg at rest was defined as pulmonary hypertension, further divided into three sub categories as mild (between 25-40 mmHg), moderate (between 41-55 mmHg), and severe (greater than 55 mmHg).

Data was correlated with variables like age, gender, body mass index, systemic hypertension, diabetes, duration of dialysis, and Hb concentration. Median (IQR) was calculated for time duration of dialysis as continuous variable, and frequencies with percentages for categorical variables. Shapiro-Wilk test was used to check the normality of the data. Chi-square test was utilised to analyse the categorical variables. Regression analysis was used to assess the predictors of pulmonary hypertension, a p-value of less than 0.05 was considered to be significant. Data was analysed using SPSS version 23.0.

RESULTS

Out of the total 50 patients enrolled in the study, 28 patients (56%) were males and 22 patients (44%) were

females. Minimum duration of hemodialysis was two months and maximum was 48 months, and the median (IQR) time duration of dialysis was 12 (11.25) months. Eighteen (36%) patients were found to have pulmonary hypertension and 32 (64%) did not have pulmonary hypertension. Out of 18 patients who developed PH, 9 (50%) had mild PH, 6 (33%) had moderate pulmonary hypertension, and 3 (17%) had severe PH.

Out of 18 (36%) patients with pulmonary hypertension, 5 (27.8%) had system hypertension ($p=0.364$). Out of 18 (36%) patients with PH, 4 (22.0%) had diabetes ($p=0.368$). There was no significant difference in different age group as p-value was 0.398 (Table I). While applying regression analysis, it was found that, a value of $R=0.552$ indicated a good level of prediction. The results also showed that the regression model was a good fit of the data. Independent variables significantly predicted the dependent variable ($F=2.63$, $p=0.024$). High body mass index ($p=0.071$), old age group ($p=0.258$), diabetes ($p=0.161$), hypertension ($p=0.112$), and low Hb concentration ($p=0.762$) were not significant predictors of pulmonary hypertension.

Table I: Comparison between pulmonary hypertension and age groups.

Age groups	Yes	No	Total	p-value
16-30	5 33.3%	10 66.7%	15 100.0%	0.398
31-45	3 23.1%	10 76.9%	13 100.0%	
46-65	10 45.5%	12 54.5%	22 100.0%	
Total	18 36.0%	32 64.0%	50 100.0%	

Table II: Regression model results for studied factors associated with pulmonary hypertension in patients on maintenance hemodialysis.

	B	P-value
Constant	3.217	0.001
Gender	0.054	0.670
Age groups	-0.087	0.258
Duration of dialysis (months)	-0.020	0.003
Body mass index (BMI)	-0.022	0.071
Hypertension	-0.213	0.112
Diabetes mellitus	-0.198	0.161
Low Hb concentration	-0.042	0.258

DISCUSSION

Chronic diseases like hypertension and diabetes are becoming the leading cause of ESRD. According to international studies, cardiovascular diseases are leading causes of mortality in ESRD, even after stratification by age, gender, race, and the presence or absence of diabetes. Cardiovascular mortality in dialysis patients is 10 to 20 times higher than in the general population and is an independent predictor of death in chronic renal disease.^{18,19} The prevalence of cardiac failure is approximately 40% among hemodialysis and peritoneal dialysis patients. Both coronary artery disease

and left ventricular hypertrophy are risk factors for the development of cardiac failure.¹⁴

A patient with ESRD needs regular hemodialysis or renal transplantation for survival. Hemodialysis has many of its own complications, one of which is pulmonary hypertension. Its prevalence has been reported to be between 25% and 51%.^{15,16} Fabio Fabbian reported the highest prevalence of 58.6%.¹⁶

In patients undergoing regular maintenance hemodialysis due to end-stage renal disease, 36% developed PH with the mean duration of dialysis being 20.17 ±12.99 months in the present study. Among the factors that contribute to the development of PH, arteriovenous access may be the one cause of development of unexplained PH.^{13,17} Patients with PH have higher arteriovenous fistula flow.²⁰ PH is more common in patients with ESRD receiving long-term hemodialysis, especially in patients with older age and longer duration of dialysis treatment.²¹

This study has shown that out of 18 patients who developed PH, 9 patients (52.9%) had mild PH, 6 patients (42.9%) had moderate pulmonary hypertension, and only 3 patients (15.8%) had developed severe PH. It is also showed that the pulmonary hypertension was more common in old age group people with age more than 46 years (45.5%).

This study showed that chronic diseases like diabetes and system hypertension are also prevalent in patients with PH. Out of 36% patients with PH, 27.8% had hypertension and 26.7% had diabetes.

Pulmonary hypertension was found to be greater in patients who had been on dialysis for more than five months. It was also noticed that longer the duration of hemodialysis, greater the prevalence of PH. This study further shows higher frequency of PH alongwith low levels of hemoglobin with mean 10.02 ±2.12 and high body mass index with mean 24.0 ±6.62.

This study has certain limitations that the baseline pulmonary artery pressure was not available so it is not known that whether the PH was present before the start of HD or developed after that. Furthermore, it is not able to estimate the exact relationship between AVF and PH, or the etiological factors of PH. So this restricts the plan to devise management plan and follow-up of PH. Further, longitudinal studies are needed in this regard.

CONCLUSION

ESRD patients on maintenance hemodialysis are at risk of development of PH. Patients who are on hemodialysis for long time have higher prevalence of PH.

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