Pulmonary Hypertension and Leading Factors in Patients Undergoing Dialysis

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ABSTRACT

Objective: To determine the frequency and leading factors of pulmonary hypertension among chronic hemodialysis patients.

Study Design: Case series.

Place and Duration of Study: Hemodialysis Unit, Department of Nephrology, Sindh Institute of Urology and Transplantation, Karachi, from September 2011 to March 2012.

Methodology: Patients of either gender aged between 16 to 60 years of age undergoing hemodialysis for at least 3 months not having pre-existing valvular heart disease, chronic lung disease or connective tissue disorder were included. Pulmonary hypertension was prospectively estimated by Doppler echocardiogram on patients undergoing dialysis. Pulmonary artery pressure was calculated on the post-dialysis day and leading factors were compared between patients with and without pulmonary hypertension.

Results: A total of 178 patients were included in study with male to female ratio 120/58 (2.06:1). The mean age was 33.84 ± 11.9 years. The mean duration of hemodialysis was 23.85 ± 22.48 months. Pulmonary hypertension was found in 76 (42.7%) patients. Out of the studied factors, low serum albumin (< 3.4 mg/dl, p = 0.01) was found to be statistically significant in patients with pulmonary hypertension.

Conclusion: Pulmonary hypertension was frequently present in dialysis population (42.7%). This subset of patients had significantly lower albumin levels in serum. More research is needed in its pathogenesis to arrest its course.


INTRODUCTION

Pulmonary Hypertension (PH) is said to be present when mean Pulmonary Artery Pressure (PAP) exceeds 30 mmHg.1,2 Regardless of etiology, it is associated with increased morbidity and mortality.3 It is increasingly being recognized as a factor that can affect outcome in End Stage Renal Disease (ESRD). Most cases of PH are consequent to myocardial or pulmonary diseases. Chronic left ventricular failure and resulting elevation in pulmonary venous pressure is the most common cause of PH.4 Factors associated with development of pulmonary hypertension are still debated. In addition to type of dialysis, several other serum biochemical factors have been linked to its development i.e. low hemoglobin, low bicarbonate, low albumin and high calcium phosphorus product.5,6

Most studies performed in chronic renal failure patients suggest that vessel wall mineralization is more dynamic.7 Various mechanism have been postulated for the development of pulmonary hypertension in patients with ESRD, including disturbance of endothelial and vascular smooth muscles function, high output state related to graft or fistula, micro-bubble pulmonary emboli and pre-existing or acquired left sided cardiac dysfunction.8 Increasing the frequency and length of treatment have been shown to improve the fluid overload and enlargement of the heart that is commonly seen in dialysis patients.

Doppler echocardiography has enabled non-invasive and accurate estimation of pulmonary artery pressure.9,10 Identifying the condition helps in controlling complications including suitability for transplant candidacy.

The objective of this study was to determine the frequency and leading factors of pulmonary hypertension among chronic hemodialysis patients.

METHODOLOGY

This cross-sectional analytical study was conducted in Hemodialysis Unit of Nephrology Department, Sindh Institute of Urology and Transplantation, after the approval of Ethical Review Committee. It was completed over a period of 6 months from September 2011 to March 2012, with non-probability purposive sampling method. Inclusion criteria was set as those who were on maintenance hemodialysis over 3 months via arteriovenous fistula. Age group was selected from 16 to 60 years of either gender. Those who were a known case of
either valvular heart disease, chronic lung disease or connective tissue disorder were excluded from the study. Sample size was calculated by obtaining mean prevalence (35%) from a previous study.\(^{11}\)

A detailed history was taken and the site of Arterio-Venous fistula (A-V fistula) was noted on a structured proforma. A-V fistula at brachial site was taken as proximal fistula and at wrist was taken as distal fistula. A complete two dimensional Doppler echocardiography study was obtained on each patient on next day of dialysis. A tricuspid regurgitation systolic jet was recorded from parasternal or apical window with continuous wave Doppler echocardiography probe. By applying Bernoulli equation, pulmonary artery pressure was calculated as tricuspid systolic jet plus 10 to 15 mmHg (estimated right atrial pressure). If the result was more than 30 mmHg, it was considered pulmonary hypertension.

Blood tests for each patient was taken next day of dialysis. These included hemoglobin, serum calcium, serum phosphorus, serum albumin and bicarbonate. All data was entered, edited and analyzed using the Statistical Package for Social Sciences (SPSS) software version 20. Frequencies and percentages were calculated for pulmonary hypertension, anemia, increased calcium and phosphorus product, low bicarbonate, low albumin, site of A-V fistula and were compared between pulmonary hypertension and non-pulmonary hypertension groups by chi-square test. Mean and standard deviation were calculated for age and duration of hemodialysis. P-value < 0.05 was considered significant.

### RESULTS

Out of 178 patients, 120 (67.41%) were males and 58 (32.58%) were females. The mean age of study population was 33.84 ± 11.9 years. The mean duration of hemodialysis was 23.85 ± 22.48 months. All the patients studied were having arteriovenous fistula over their arms. Out of them, 108 (60.67%) had proximal (at elbow) and 70 (39.32%) had distal (at wrist) A-V fistula. Pulmonary hypertension was seen in 76 (42.7%) patients.

Frequencies and percentage of the leading factors were studied and compared between high pulmonary pressure and normal pulmonary pressure (Table I). Among those who developed pulmonary hypertension (42.7%), proximal A-V fistula was seen in 53 (69.73%) is compared to 55 (53.9%) those with normal pulmonary pressure (p = 0.33).

### DISCUSSION

Pulmonary Hypertension (PH) is no more an uncommon problem among the patients on maintenance hemodialysis (HD) irrespective of the leading factors. Previously reported data has shown that pulmonary hypertension occurs in about 25 - 45% patients with end stage renal disease on hemodialysis.\(^{11,12}\) These observations were mainly in retrospective way which cannot be concluded without pre-selection bias. A prospective study conducted in USA found pulmonary hypertension more prevalent in dialysis patients (47%). Even high was seen by Mousavi \textit{et al.} (49.3%) in Iran.\(^5\)

This prospective study which was conducted over a period of 6 months demonstrated the frequency of pulmonary hypertension as 42.7%.

The mean age (33.78 ± 11.91 years) in this study was lower than previous studies. Among the factors which are though to be leading towards development of pulmonary hypertension, only low serum albumin (80.26%) was found to be at statistically significant level (p = 0.01) in PH sub-group while low hemoglobin (89.47%), low bicarbonate (92.1%) and high calcium phosphorus product (17.1%) were not so.

Mousavi \textit{et al.} also found similar phenomenon as Mahdavi in respect of these two factors.\(^1,5\) Contrary to this, prospective study in USA, does not see low Hb as leading factor but Pulmonary Capillary Wedge Pressure (PCWP) has been detected the major contributor to this entity.

In this study, high calcium phosphorus product was not seen in high percentage in either group. This may be due to undernutrition status consequent to low socio-economic condition of our population. This needs to be more researched.

Yigla \textit{et al.} demonstrated that patients with PH evaluated by echocardiography at the beginning of HD treatment, and with PH developing soon after HD initiation, had shorter survival than their counterparts without PH.\(^3\) The mechanisms involved in PH development are still under investigation, but it has been reported that HD patients with PH show a significantly higher cardiac output than HD patients with normal PAP (Pulmonary Artery Pressure). It has been suggested that some factors, such as the size or the location of AVF, are involved in the mechanism that increases PAP. In this study, majority of the patients who have developed PH had proximal A-V fistula, this shows some relationship in the development of PH with proximal A-V fistula (proximal to...
the heart). On the contrary, Tarrass et al. did not find any difference in cardiac output between patients with and without PH, and the effect of A-V fistula location was not statistically significant. Beigi et al. reported a positive correlation between mean fistula flow and PAP.

PH may evolve due to the inability of the pulmonary circulation to accommodate increased cardiac output (resulting from increased volume, anemia, arteriovenous fistula) or as a result of increased pulmonary vascular stiffness due to endothelial dysfunction (decreased nitric oxide). Vascular involvement is one of the most striking forms of extraosseous calcification in chronic renal failure. The aorta and the coronary arteries are mainly affected, but peripheral small vessels in the systemic and the pulmonary circulation are also affected. The ability of the pulmonary circulation to dilate and recruit unused blood vessels prevents development of pulmonary hypertension in conditions characterized by increased pulmonary blood flow.

Despite the possibility of common mediators for all the mechanisms of pulmonary hypertension, there are clear differences observed in the potential reversibility of pathophysiological responses of the three components of pulmonary artery pressure that include volume of pulmonary blood flow, resistance in the pulmonary vascular bed and pulmonary venous pressure. Bark and Katz hypothesized that micro-bubbles, which originate from the dialysis tubes or filter, may be trapped in the pulmonary circulation. Thus, hemodialysis patients may suffer lung injury due to the micro-bubble shower. Chronically, the recurrent ongoing micro-bubble-induced inflammatory response and lung injury may explain the high pulmonary morbidity, manifested as increased pulmonary artery pressure in the chronic hemodialysis patients.

This study was limited to determine the frequency and some of the leading factors, which are quite well established. Other factors like relation of Parathyroid Hormone (PTH) and recurrent air embolism need to be researched further. Pulmonary Artery Pressure (PAP) increased significantly following initiation of HD therapy via Arteriovenous access (A-V access) and decreased significantly after successful kidney transplantation, as well as after short A-V access compression, indicating that both ESRD and A-V access contribute to the pathogenesis of PH. However, only about half of the uraemic patients developed PH suggests that mechanisms other than uraemia may be involved in this disorder. These may include underlying concomitant diseases such as diabetes mellitus or systemic hypertension, although the percentages of diabetic or hypertensive patients in both sub-groups of patients with and without PH were identical.

There is a need to work about the outcome of those who developed PH in relation to those who did not develop the PH and their survival.

**REFERENCE**

There are substantial number of ESRD patients who are on maintenance HD, have functional abnormality of pulmonary circulation (42.7%). This underrecognized complication is not uncommon and is associated with reduced survival. Early detection is important in order to avoid the serious consequences of the disease. Secondly, PH should be incorporated in the decision making for renal transplantation, since it is associated with worse survival and appears to improve after renal transplantation.

**REFERENCES**


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