

Pulmonary Hypertension in Hemodialysis Patients

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Abstract:

Key words:

Chronic kidney disease,
Pulmonary Hypertension,
Haemodialysis.

Background: Pulmonary hypertension (PH) has been reported to be high among maintenance dialysis patients. There is a paucity of data on the incidence and prevalence of pulmonary hypertension in chronic kidney disease (CKD) in Bangladeshi patients.

Materials and Methods: A total 70 CKD patients (male 47, female 23), who were on conservative management and maintenance hemodialysis were studied for the presence of pulmonary hypertension. The variables studied were hypertension, diabetes, duration of dialysis and the hemoglobin, serum creatinine and serum bicarbonate levels.

Results: 68.6% of the patients on maintenance hemodialysis had pulmonary hypertension compared to 8.6% of the predialysis CKD patients. 97.1% of maintenance dialysis patients had anaemia (Hb <10gm/dl) and 42.9% of patients had metabolic acidosis.

Conclusion: The incidence of pulmonary hypertension was highest in the hemodialysis group. Significant Pearson's correlation was found between pulmonary arterial systolic pressure with the duration of hemodialysis, hemoglobin level, serum creatinine, blood sugar and serum bicarbonate level in maintenance hemodialysis patients

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Introduction:

Chronic kidney disease (CKD) leads to many comorbidities that affect patients of all stages of the disease. The complications of CKD are due to the disease itself as well as the mode of renal replacement therapy (RRT). Kidney function can only be partly replaced by maintenance dialysis, which provides only 5-10% of excretory renal function.¹ At present out of three modalities of treatment –conservative management, hemodialysis (HD) and peritoneal dialysis, maximum patients are on HD.² Cardiovascular morbidity and mortality is highest in the dialysis population. Recently an association has been found between RRT and the development of pulmonary hypertension.

The presence of PH may reflect serious pulmonary vascular disease, which can be progressive and fatal. Consequently, an accurate diagnosis of the cause of PH is essential in order to establish an effective

treatment program. Pulmonary hypertension can occur from diverse etiologies. The most common causes of PH are left heart failure and chronic hypoxic lung diseases. Less commonly, PH occurs in distinct clinical conditions such as collagen vascular disease, chronic recurrent thromboembolism, portal hypertension, human immunodeficiency virus (HIV) infection, hematological conditions, following exposure to drugs and toxins, etc. Regardless of etiology, PH increases morbidity and mortality. Moreover, the presence of PH in systemic disorders increases mortality rates beyond the expected and sometimes is the leading cause of mortality.

In 1996 Mordechai Yigla first noted unexplained PH in some long-term hemodialysis (HD) patients during an epidemiological study of this disorder. It was assumed that their PH was related to end stage renal disease (ESRD) or to long term HD therapy via an arteriovenous (AV) access.

Despite almost five decades of HD therapy via a surgically created, often large, hemodynamically significant AV access, the long-term impact of this intervention on pulmonary circulation has received little attention. The development of pulmonary hypertension in ESRD patients is associated with increased morbidity and mortality. There is non-invasive technique like Doppler echocardiography to detect pulmonary hypertension; so early diagnosis by Doppler echocardiography enables timely intervention, currently limited to changing dialysis modality or referring for kidney transplantation. Even then there is paucity of data on the incidence and prevalence of PH in chronic kidney disease in Bangladeshi patients.

Materials and Methods

This cross-sectional study was carried out in the Department of Nephrology, Dhaka Medical College Hospital from January 2010 to December 2010. A total 70 patients were included in the study out of which 35 patients on maintenance hemodialysis & predialysis CKD patients was 35.

All the participants history was taken, physical examination was done and necessary investigation was carried out. Blood pressure was recorded at least after 5 minutes rest being relaxed on a chair with a support on the back keeping bared arm on a table at heart level. A conventional sphygmomanometer was used covering more than 80% of arm by bladder. Patients estimated glomerular filtration rate (eGFR) was calculated by using Cockcroft-Gault (CG) formula-

$$eGFR = \frac{[140 - \text{age}(\text{yrs}) \times \text{body wt}(\text{kg})]}{\text{Serum creatinine}(\text{mg/dl}) \times 72}$$

Multiply by 0.85 in female to correct for reduced creatinine production.

Then all patients have a Doppler echocardiogram done by an experienced cardiologist. In the maintenance hemodialysis group the Doppler echocardiography done on the day after hemodialysis to overcome the volume overload. Pulmonary arterial systolic pressure can be measured non-invasively by tricuspid regurgitation jet method by Doppler echocardiogram. The aim is to measure PASP (Pulmonary arterial systolic pressure) assuming no pulmonary valvular

stenosis, and then this is equal to right ventricular systolic pressure (RVSP).

RVSP can be easily estimated from the maximum velocity of the tricuspid regurgitation jet (V_{TR}). The pressure gradient between the right atrium and the right ventricle across the tricuspid valve (RVSP-RAP) can be estimated by the Bernoulli equation using the maximum V_{TR} .

$$RVSP-RAP = 4V_{TR}^2$$

The value of RAP (right atrial pressure) is known. It is equal to the jugular venous pressure (JVP) which can be assessed clinically (in healthy individuals and is usually 0-5 cm of blood, measured from the sternal angle, and 1 cm of blood is almost equal to 1 mmHg.)

This allows us to estimate that:

$$PASP = RVSP = 4V_{TR}^2 + JVP/\text{or}, RAP$$

For estimation of hemoglobin, serum creatinine, blood sugar and serum bicarbonate venous blood samples were collected by sterile disposable syringe with strict aseptic precaution. For estimation of blood sugar 2 cc of blood was poured to blood sugar bottle and 3 cc blood was kept in syringe for estimation of hemoglobin, serum creatinine and serum bicarbonate. All samples sent immediately to clinical pathology, DMCH. Serum creatinine was estimated using kinetic model; blood sugar was estimated by Glucose oxidase method. Echocardiography was done by colour Doppler Echocardiographic Equipment model GE system five by GE Vingmed ultrasound, Norway.

The relationship of all the variables to pulmonary hypertension in CKD was assessed by Pearson's correlation coefficient. All data was analyzed by using computer based SPSS (Statistical Program for Social Science) program.

Observation and Results

In our study 70 patients were included of whom 35 patients on maintenance hemodialysis and rest 35 patients on predialysis CKD patients which are categorized as Group I and Group II respectively. The male/female ratio was almost 2:1. Most of the patients belongs to 30 to 40 years age range in both group.

The scatter diagram shows significant relationship ($r=0.424$) between pulmonary arterial systolic

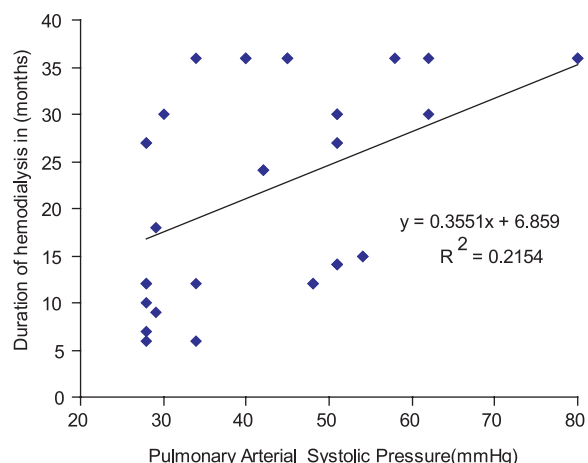


Fig 1: Correlation between pulmonary arterial systolic pressure (mmHg) with duration of hemodialysis (in months) of the study patients (n=35)

pressure (mmHg) with duration of hemodialysis (months) in group I patients (n=35).

In this study it was found that 68.6% of group I and 8.6% of group II patients had pulmonary hypertension. Mild pulmonary hypertension was

found in 22.9%, moderate and severe pulmonary hypertension was found in 40% and 5.7% respectively. However only 8.6% patients had mild pulmonary hypertension in group II patients. The mean pulmonary arterial systolic pressure (PASP) was 44.1±14.4 mmHg with range from 28 to 80 mmHg in group I. In group II the mean PASP was 28.9±4.1 mmHg with range from 24 to 38 mmHg. The mean PASP difference was statistically significant (p<0.05) in unpaired t-test.

Significant Pearson’s correlation was found between pulmonary arterial systolic pressure with the duration of hemodialysis (r=0.424; p=0.023), hemoglobin level (r=-0.539; p=0.001), serum creatinine (r=0.568; p=0.001), blood sugar (r =0.535; p=0.001) and serum bicarbonate level (r=-0.470; p=0.003) in group I patients.

In group II patients no correlation were found in Serum Creatinine, Hemoglobin, Blood sugar and Serum bicarbonate level with pulmonary arterial systolic pressure, which were r=0.195; p=0.636, r=0.199; p=0.251, r=0.161; p=0.326 and r=0.282; p=0.133 respectively.

Table I

Shows mean Pulmonary Arterial Systolic Pressure (mm Hg) distribution of the study patient (n=70).

PASP (mm Hg)	Group I(n=35)		Group II(n=35)		PValue
	n	%	n	%	
Normal (≤30 mmHg)	11	31.4	32	91.4	
High (PASP)>30 mmHg					
Mild (31-45 mmHg)	8	22.9	3	8.6	
Moderate (46-65 mmHg)	14	40.0	0	0.0	
Severe (>65 mmHg)	2	5.7	0	0.0	
Mean±SD	44.1	±14.4	28.9	±4.1	0.001 ^S
Range (min - max)	(28	-80)	(24	-38)	

S= Significant

P value reached from unpaired ‘t’ test

Table-II

Correlation of different parameters with pulmonary arterial systolic pressure of the study patients (n=70)

	Group I(n=35)		Group II(n=35)	
	Correlation coefficient	P value	Correlation coefficient	P value
Duration of hemodialysis in (months)	0.424	0.023 ^s	-	-
Hemoglobin (gm/dl)	-0.539	0.001 ^s	0.199	0.251 ^{ns}
Serum Creatinine (mg/dl)	0.568	0.001 ^s	0.195	0.636 ^{ns}
Blood sugar 2h ABF (mmol/L)	0.535	0.001 ^s	0.161	0.326 ^{ns}
Serum bicarbonate level (mmol/L)	-0.470	0.003 ^s	0.282	0.133 ^{ns}

p value reached from Pearson’s correlation

Discussion:

An echocardiography diagnosis of pulmonary hypertension (PH) is made when systolic pulmonary arterial pressure (PAP) exceeds normal values (30mmHg). In mild PH, values ranges up to 45 mmHg, in moderate PH, PAP is between 45 and 65 mmHg and in severe PH, PAP values are greater than 65 mmHg. Systolic PAP equals cardiac output times pulmonary vascular resistance (PVR), (i.e., $PAP = \text{cardiac output} \times PVR$). Increased cardiac output by itself does not cause PH because of the enormous capacity of the pulmonary circulation to accommodate the increase in blood flow. Therefore development of PH requires marked elevation of pulmonary vascular resistance.

There are several potential explanations for the development of PH in patients with ESRD. Hormonal and metabolic derangement associated with ESRD might lead to vasoconstriction of pulmonary vessels and increased pulmonary vascular resistance.³ Values of PAP may be further increased by high cardiac output resulting from the AV access itself,⁴ worsened by commonly occurring renal anemia and fluid overload. Medical conditions with shunting of blood from the left to the right side of the heart and increased cardiac output and pulmonary blood flow, such as congenital heart disease, are well recognized as possible causes of PH.^{5,6}

Excess mortality rates due to cardiovascular disease in end-stage renal disease (ESRD) patients had been described by epidemiological and clinical studies. It accounts for approximately 50 percent of deaths in dialysis patients. Although controversial, this may be due in part the presence of excess vascular calcification, particularly in the form of extensive coronary artery calcification, which can be observed even in very young dialysis patients. It was suggested that abnormalities of the right ventricular function in patients with ESRD were largely due to pulmonary hypertension, which usually develops secondary to pulmonary artery calcifications.⁷

In the present study it was observed that the mean age was 39.5 ± 10.3 years and 42.5 ± 12.8 years in group I and II respectively ($p > 0.05$). Male was predominant in both groups and male female ratio was almost 2:1 in the whole study patients.

HTN was observed in 85.7% and 71.4% in group I and group II respectively ($p = 0.145$). DM was present 20.0% in group I and 22.9% in group II ($p = 0.770$).

Majority (42.9%) of the patients had 13–24 months of hemodialysis and the mean duration of hemodialysis was 22.9 ± 10.4 months with range from 6 to 36 months.

Pulmonary hypertension was found 68.6% (24) on maintenance hemodialysis patients whereas only 8.6% (3) in predialysis CKD patients. The mean systolic pulmonary arterial pressure (PAP) was 44.1 ± 14.4 mmHg with range from 28 to 80 mmHg in group I. In group II the mean systolic PAP was 28.9 ± 4.1 mmHg with range from 24 to 38 mmHg. The mean systolic PAP was significantly ($p < 0.05$) higher in group I patients.

In this study it was observed that 97.1% and 74.3% patients had anaemia (< 10 gm/dl hemoglobin) in group I and group II respectively ($p = 0.001$). The mean hemoglobin was 8.7 ± 0.7 gm/dl in group I and 9.5 ± 0.9 gm/dl in group II ($p = 0.001$).

The mean serum creatinine was 9.4 ± 1.5 and 5.1 ± 1.3 mg/dl in group I and group II respectively. The mean blood sugar 2h ABF was 6.7 ± 1.2 mmol/L in group I and 5.6 ± 0.3 mmol/L in group II. The mean hemoglobin level was significantly ($p < 0.05$) higher in group II but the mean S. creatinine and blood sugar 2h ABF were significantly ($p < 0.05$) higher in group I.

Regarding the serum bicarbonate level 42.9% and 17.1% in group I and group II patients had metabolic acidosis, which was significant ($p < 0.05$) between the two groups.

In group I patients significant Pearson's correlation were found between pulmonary arterial pressure with duration of hemodialysis ($r = 0.424$; $p = 0.023$), hemoglobin level ($r = -0.539$; $p = 0.003$) creatinine ($r = 0.568$; $p = 0.001$) blood sugar (2h ABF) ($r = 0.535$; $p = 0.001$) and serum bicarbonate level ($r = -0.470$; $p = 0.001$).

In group II patients no significant correlation were found between pulmonary arterial pressure with hemoglobin level, creatinine, blood sugar (2h ABF) and serum bicarbonate level.

The study demonstrates that CKD patients on maintenance hemodialysis are significantly more likely to develop pulmonary hypertension.

Conclusion:

This study demonstrated that 68.6% of patients with CKD on MHD have PH which is much higher value compared to other study. The sample size of this study is relatively small, and for this reason, multicenter studies are required. PAP was non-invasively measured by Doppler echocardiography without right heart catheterization. Since follow-up of this study was not done to evaluate the effect of pulmonary hypertension on morbidity and mortality, long-term follow-up of patients with pulmonary hypertension is needed.

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