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Research Article

A STUDY OF PREVALENCE OF PULMONARY HYPERTENSION IN PATIENTS WITH CHRONIC KIDNEY DISEASE ON MAINTENANCE HAEMODIALYSIS

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A R T I C L E I N F O

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A B S T R A C T

Context: Pulmonary arterial hypertension(PH) in patients with chronic kidney disease(CKD)(on maintenance hemodialysis) indicates poor overall prognosis with increasing day-by-day incidence owing to underdiagnosis. Detection of PH warrants comprehensive evaluation which includes noninvasive assessment with physical examination and a transthoracic echocardiogram and invasive hemodynamic assessment.
Aims: To evaluate the prevalence of primary pulmonary hypertension among CKD patients on hemodialysis and to compare clinical, hemodynamic, and metabolic variables amongst the patients with and without PH to search for possible etiologic factors.
Settings and Design: The study was conducted at a Parul Sevashram hospital over a period of 8 months, after approval from Institutional Ethics Committee. Sixty consecutive patients undergoing regular hemodialysis for at least 3 months were studied.
Materials and Methods: All patients underwent transthoracic echocardiography one hour after dialysis to avoid overestimation of pulmonary artery pressures due to fluid overload. PH was considered as a mean right ventricular systolic pressure(RVSP) greater than 25 mmHg.
Statistical Analysis Used: Clinical, hemodynamic and metabolic variables were compared between patients with and without PH with ''t'' test. Values were expressed as mean ± Standard deviation (SD) and as percentage for categorial parameters. Nominal categorical data between the groups was compared using Chisquare test.
Results: There was a statistically very significant difference in RVSP in PH group as compared to non PH group of CKD patients.
Conclusion: Among the various complications that may arise from the chronic kidney disease, development of pulmonary hypertension portends a high cardiovascular risk and thus the increased overall morbidity and mortality.

INTRODUCTION

Pulmonary hypertension (PH) is a progressive disorder complicating heart, lung, or systemic diseases, with increased morbidity and mortality regardless of its etiology [1]. The prevalence of PH in ESRD patients is reported to be around 40–50% [2]. Pulmonary hypertension, defined as systolic pulmonary artery pressure (SPAP) > 35 mmHg at rest as estimated by Doppler echocardiography, has been repeatedly reported in patients with chronic kidney disease, both predialysis and during regular renal replacement therapy, with a high but variable prevalence [3,4]. Its presence has been recently suggested to be associated with a worse outcome [5]. A number of causative factors have been related to this pathological finding: pulmonary artery calcifications secondary to hyperparathyroidism [4]; and hemodynamic modifications related to the creation of an arteriovenous fistula (AVF), caused by a reduced ability of pulmonary vessels to accommodate the AV access-mediated elevated cardiac output, possibly because of derangement of nitric oxide–endothelin metabolism [5] but its pathogenesis has not been completely elucidated. Echo-Doppler studies can provide an estimate of the pulmonary artery systolic pressure (PASP), a surrogate of mean pulmonary artery pressure, which is calculated on the basis of the tricuspid regurgitation jet velocity [6].

The aims and objectives of this study were to evaluate the prevalence of primary pulmonary hypertension amongst the CKD patients and to compare the clinical, hemodynamic and metabolic variables amongst the CKD patients to search for possible etiologic factors.

MATERIALS AND METHODS

Study Population

The study was conducted at a Parul Sevashram hospital after approval from Institutional Ethics Committee. Sixty consecutive patients undergoing regular hemodialysis for at

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least 3 months were included in the study. Data was collected over 8 months.

Inclusion Criteria

- ✓ Diagnosed Case of Chronic Kidney Disease
- ✓ On Maintenance Hemodialysis for > 3 months

Exclusion Criteria

- ✓ Smokers
- ✓ Diagnosed cases of COPD/IHD/Collagen Vascular Disease
- ✓ Patients not giving consent for the study

Investigations

The patient was investigated for Complete blood count, Blood Urea, Serum Creatinine, ECG, Serum Calcium, Serum electrolytes, Serum Phosphorus, Serum Albumin, PTH, 2D-Echocardiography.

METHOD

All patients were explained in detail about the purpose of the study and an informed consent was taken. Patient's details were incorporated into a proforma. Biochemical parameters were assessed via blood samples drawn after hemodialysis session. All patients then underwent 2D Doppler echocardiography one hour after the dialysis to avoid overestimation of pulmonary artery pressures due to fluid overload. Pulmonary hypertension was considered as a mean right ventricular systolic pressure (RVSP) greater than 25 mmHg. Mean RVSP was preferred as it has been found to correlate with invasively measured pulmonary artery pressures greater than peak RVSP. Echocardiographic assessment was done. 2D M mode CW/PW/Tissue doppler techniques were used in assessment of cardiac structure and hemodynamics by an experienced echocardiologist, as per guideline of American Society of Echocardiography. Various parameters were measured. PH was calculated by adding estimated right atrial pressure (RAP) to tricuspid regurgitant (TR) jet velocity. To get a better estimate of right atrial pressure, inferior vena cava collapsibility was used. The TR jet peak was utilized to obtain RVSP according to Bernoulli's equation: 4× (peak tricuspid regurgitant jet velocity) 2 +estimated right atrial pressure. Mean RVSP was calculated by planimetering TR jet envelop obtained by Doppler. Mean RAP was added to it to give true mean PAP.

Statistical analysis

Data was collected & tabulated. Clinical, hemodynamic and metabolic variables were compared between patients with and without PH with ''t'' test. Values were expressed as mean ± Standard deviation (SD) and as percentage for categorial parameters. Nominal categorical data between the groups was compared using Chisquare test.

RESULTS

Sixty patients were enrolled in the study. Fifty six patients were detected to have pulmonary hypertension. Most of the patients enrolled in the study were in the age group of 30-60 yrs. Of the 60 patients, 12 were females and 48 were males. Mean values of all the demographic and biochemical parameters under study did not show any significant differing factor in the two populations (PH and Non- PH group) (Table 1 and 2), except PTH levels which was statistically significant ($p<0.0001$). There was a statistically very significant difference in RVSP in PH group as compared to non PH group meaning that a maximum number of CKD patients had significant PH (Table 3). All the patients underwent dialysis via AV fistulas. Compared with the non-PH group, the patients with PH had increased incidences of diabetes and hypertension (Table 1).

DISCUSSION

Yigla *et al*. [7] first noted unexplained PH in some long-term hemodialysis (HD) patients during an epidemiologic study. Both end-stage renal disease and long-term hemodialysis via arteriovenous fistula may be involved in the pathogenesis of pulmonary hypertension by affecting pulmonary vascular resistance and cardiac output. Abdallah *et al*. [8] demonstrated that PH (systolic PAP= 35 mmHg) was observed in 25 (56.8%) patients receiving hemodialysis with a mean systolic PAP of 46.4± 13.6 mmHg. Yigla *et al*. [5] 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. Fabbian *et al*. [9] demonstrated that PD patients with PHT had lower ejection fraction (45 ±15 versus 62± 5%, P = 0.003) than those without PH. In another study, significant increases in the cardiac index, the IVC diameter, and the left atrial diameter, which are all markers of volume overload, were noted in the PH patients receiving long-term HD [10]. Collectively, these studies illustrate that chronic volume overload may play a role in the pathogenesis of PH.

PH in CKD patients is important to recognize for 3 major reasons.

1. Several studies have indicated that PH is an independent predictor of mortality in CKD patients, especially those receiving renal replacement therapy.[11,12,13]
2. Many CKD patients are evaluated for renal transplantation. In general, significant PH is felt to be a relative contraindication to renal transplantation in patients with CKD. In retrospective studies, PH has been associated with increased early renal allograft dysfunction in these patients, [14] and is also associated with reduced patient survival after renal transplantation.[15]
3. Most importantly, from a clinical perspective, many patients with CKD present to their treating physicians with dyspnea. PH is often picked up on diagnostic echocardiograms in these patients, and not infrequently PH is invoked as a potential etiology of dyspnea and targeted with pulmonary vasodilating medications.[16]

Sleep apnoea, AV fistula, accumulation of endogenous inhibitors of nitric oxide synthase, alteration in pulmonary microcirculation attributable to exposure to dialysis membranes mostly contributes to the unique propensity of dialysis patients to PH. In different studies the prevalence of PH has been found to vary from 30-50%.[17] In our study, no significant association was detected between pulmonary hypertension and age, gender, history of comorbidities such as diabetes and hypertension. Lower hemoglobin levels have been associated with PH in studies as done by Zhilian *et al* in China [18] and Patel *et al* in Chennai. [19] This, however, was also detected in our study.

Also, there are rare cases of idiopathic PH or connective tissue disease-associated PH with associated CKD, but the physiology of these patients is typically driven primarily by PVD more so than pathophysiologic features unique to CKD. [16] Indeed, some features are common to many patients with PH associated with CKD, including impaired salt and water handling, systemic hypertension, LV diastolic dysfunction, and left heart congestion. [16] A simple echo-Doppler scoring system can help to differentiate a pulmonary vascular from a pulmonary venous etiology of PH.[20] The keys to noninvasive assessment of PH in these patients rest in the assessment of RV structure and function, to evaluate for high cardiac output syndromes, and to evaluate carefully for evidence of elevated PVR using a thorough assessment of the pulsed wave doppler signal in the right ventricular outflow tract. [20,21] Using this type of comprehensive physical examination and echo-Doppler assessment should provide the PH clinician with an overall impression of the hemodynamic basis of PH in the majority of patients presenting with dyspnea even prior to cardiac catheterization. [16]

Limitations

Small sample size of the study did not allow for a logistic regression analysis thus affecting the assessment of correlation of the significant associating factors. Right heart catheterization (RHC) is the gold standard invasive method for assessment of cardiac status but echocardiogram is feasible and best modality for non-invasive assessment of cardiac status was utilized in the present study. The study also excluded non-dialysis CKD patients, thus a comparison could not be made. Assessment of Kt/v would have added value to the study. However present study does add value to existing knowledge, as it provides data in an Indian population, which so far has not been much studied.

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Table 1 Demographic Profile of CKD Patients

Parameters	PH Group (n=56)	Non- PH Group (n=4)
AGE	49.89 yrs	45.25 yrs
H/O DM	6 (10 %)	2 (3.33 %)
H/O HTN	41 (68.33 %)	3 (5%)
H/O IHD	4 (6.66 %)	0 (0 %)

Table 2 Biochemical Profile of CKD Patients

Parameters	PH Group (n=56)	Non- PH Group (n=4)	P-Value
HEMOGLOBIN	9.58 ± 1.59	9.65 ± 1.59	0.9325
ALBUMIN	3.68 ± 0.52	3.97 ± 0.33	0.2782
CALCIUM	8.9 ± 0.89	8.9 ± 1.2	1.0000
PHOSPHORUS	4.54 ± 2.43	4.25 ± 1.36	0.8152
PTH	162.33 ± 40.35	59.1 ± 23	<0.0001
SODIUM	136.76 ± 6.6	136.5 ± 1.91	0.9381
POTASSIUM	4.8 ± 0.6	5.15 ± 0.75	0.2711
S. CREATININE	8.1 ± 1.59	9.6 ± 3.93	0.1104

Table 3 Echocardiographic Profile of CKD Patients

Parameters	PH Group (n=56)	Non- PH Group (n=4)	P-Value
RA PRESSURE	12.14 ± 1.73	13.25 ± 1.5	0.2171
RVSP	45.66 ± 5.05	31 ± 1.15	<0.0001

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