

## Study Of Prevalence Of Pulmonary Hypertension In Chronic Kidney Disease And Its Co-Relation With Clinical & Biochemical Parameters.

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**ABSTRACT:-OBJECTIVES:** The objectives of this prospective observational study were to study (i) the prevalence of pulmonary hypertension (PH) in patients who are on conservative management, haemodialysis or continuous ambulatory peritoneal dialysis, (ii) the co-relation of PH with variables such as A-V fistula, hypertension, diabetes Mellitus & duration for dialysis, and (iii) the co-relation of PH with biochemical parameters.**MATERIALS AND METHODS:** The study was conducted in a tertiary care centre in Mumbai over a period 12 months after obtaining approval from the Institutional Ethics Committee. 245 CKD patients, on conservative management, haemodialysis and continuous ambulatory peritoneal dialysis were enrolled in this study, taking into consideration the inclusion & exclusion criteria and appropriate informed consent after taking detailed history of every patient. All patients underwent routine investigations and 2D ECHO for pulmonary hypertension. **RESULTS:** Our study enrolled 245 patients in the age group of 20 to 85 years where 68.6% patients were male and 31.4% were females. 28.2% patients had CKD with PH while 71.8% had CKD without PH. The proportion of patients with PH having AV fistula was significantly more than those without AV fistula. Of the 28.2% patients with PH, 33.6% had hypertension and 22% were diabetic. Our study revealed a positive association between the duration of dialysis and the prevalence of PH along-with low levels of haemoglobin and serum bicarbonate, and high levels of uric acid, BUN and creatinine. **CONCLUSION:** The prevalence of PH was found to be 28.2%. PH is positively correlated with chemical as well as biochemical parameters.

**Keywords:** A-V fistula ,CKD with PH, hemodialysis, Prevalence study, pulmonary arterial pressure.

### I. INTRODUCTION

Cardiovascular disease is a well-known and significant source of mortality in patients with chronic kidney disease (CKD),<sup>(1,2,3)</sup> inspite of the latest advances in the care of patients undergoing renal replacement treatment.<sup>(4)</sup>

Pulmonary hypertension (PH) is an overlooked cardiovascular morbidity in patients of chronic kidney disease who are on conservative management and haemodialysis. As pulmonary hypertension is a hemodynamic state defined by a resting mean pulmonary artery pressure at or above 25 mm Hg,<sup>(5)</sup> it can be the result of a variety of diseases of different causes.

Pulmonary hypertension is an elevation of pulmonary arterial pressure (PAP) that can be the result of heart, lung or systemic disorders.<sup>(6,7)</sup> PH is an increase in blood pressure in the lung vasculature, resulting in symptoms like shortness of breath, dizziness, fainting etc. that are exacerbated by exertion and can be a severe disease with a markedly decreased exercise tolerance and lead to heart failure. The evolution of PH in CKD frequently originates with the interaction of a predisposing state and one or more inciting stimuli, a concept referred to as the "multiple-hit hypothesis."<sup>(8,9)</sup>

PH has been commonly found in patients undergoing renal replacement with haemodialysis via an arterio-venous graft or fistula,<sup>(6,7)</sup> and is characterized by elevations in the pulmonary arterial pressure and pulmonary vascular resistance (PVR) that eventually result in right ventricular failure and even premature death. Chronic renal failure (CRF) is most often seen with patients with PH.<sup>(10)</sup> Chronic haemodialysis patients are continuously exposed to multifactorial pulmonary insults. Recent studies have demonstrated a 40% incidence of PH on detection by Doppler echocardiography (ECG) in patients with end-stage renal disease (ESRD) on chronic haemodialysis (HD) therapy via arterial-venous (A-V) access.<sup>(11)</sup> A study done by C. J. Rhodes et al has proved the role of iron in the natural history of pulmonary hypertension. High hepcidin levels underlie the anaemia of chronic disease, like CKD.<sup>(12)</sup>

Uric acid levels are elevated in patients with PH and correlate with haemodynamics, which was also shown by a study done by Norotoshi Nagaya et al in which serum UA increased in proportion to the clinical severity of

Primary Pulmonary Hypertension (PPH) and found to have an independent association with long-term mortality of patients with PPH.<sup>(13)</sup> This study was conducted to study to see the profile of patients of PH in CKD that are only on medical management and on renal replacement therapy.

## II. OBJECTIVES

The primary objective of this prospective observational study was to study the prevalence of PH in patients who are on conservative management, haemodialysis or continuous ambulatory peritoneal dialysis.

The secondary objective was to study the co-relation of PH with variables such as A-V fistula, hypertension, diabetes mellitus & duration for dialysis, and its co-relation with biochemical parameters.

## III. MATERIALS AND METHODS

This study was conducted in a tertiary care centre in Mumbai over 12 months after obtaining approval from the Institutional Ethics Committee. 245 CKD patients that are on conservative management, haemodialysis and continuous ambulatory peritoneal dialysis were enrolled in this study based on the inclusion & exclusion criteria.

Once all the criteria were satisfied, a written informed consent was taken and the patient was included in the study. A detailed history of every patient including age, sex, duration of illness, etiology of chronic kidney disease, type of treatment received: either conservative, haemodialysis or continuous ambulatory peritoneal dialysis (CAPD) and its duration were noted. Each patient underwent routine investigations like complete haemogram, serum electrolytes (Na, K, Ca, PO<sub>4</sub>, UA), renal function tests (BUN, serum creatinine), liver function tests (Total /direct bilirubin, AST, ALT, ALP), urine routine & microscopy and some specific investigations like arterial blood gas (ABG), Chest X-Ray, ECG, USG abdomen, autoimmune work up like ANA (as and when indicated).

Each patient underwent 2D echocardiography for PH.

### 3.1 Inclusion criteria

All patients >12 years of age with chronic renal failure either on conservative management, haemodialysis or continuous ambulatory peritoneal dialysis were included.

### 3.2 Exclusion criteria

Patients under the age of 12 years, those with a history of smoking, primary PH & PH secondary to either causes and pregnant & postpartum females were excluded from the study.

The results were statistically analysed, compared with previous studies and conclusions derived appropriately.

## IV. RESULTS

Our study enrolled patients in the age group of 20 to 85 years where 68.6% patients were male and 31.4% were females. 245 patients underwent 2D echocardiography performed by cardiologist of the tertiary institute. Pulmonary hypertension as defined previously<sup>14</sup> was found in 69 cases.

28.2% patients were found to have CKD with PH while the rest 71.8% had CKD without PH. 30.0% patients had PH and were under maintenance treatment as compared to 24.7% cases who were on conservative treatment. Our study identified 15.9% patients with mild PH followed by 9.8% patients with moderate PH and 2.5% patients with severe PH, as depicted in the below "Figure 1".

Figure 1:

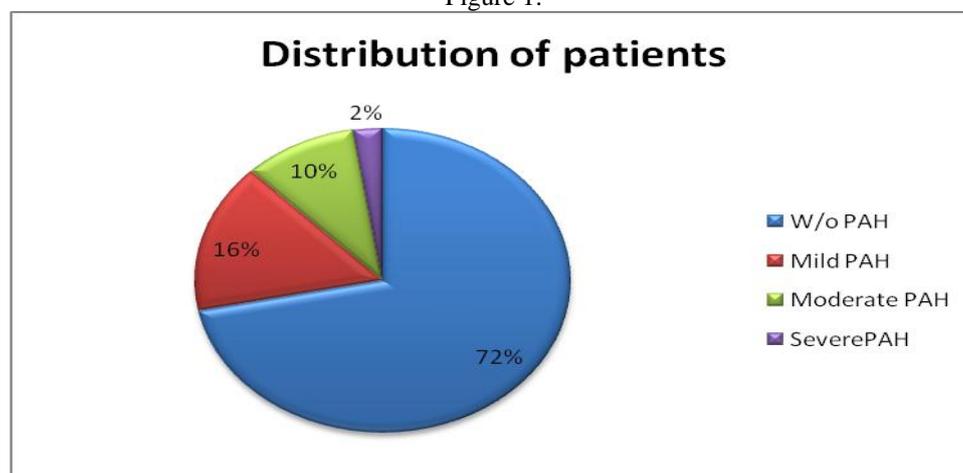


Table 1: Prevalence of PH in Chronic Kidney Disease in study group

| Treatment modality            | No. of CKD patients | No. of CKD with PH | Prevalence (%) |
|-------------------------------|---------------------|--------------------|----------------|
| <b>Group 1 Maintenance HD</b> | 160                 | 48                 | 30             |
| <b>Group 2 Conservative</b>   | 85                  | 21                 | 24.7           |

Statistical test use - Chi Square Test

P value >0.05 Not Significant

The data represented in the above “TABLE 1”, shows that 30.0% patients with PH were on maintenance HD which was more when compared to 24.7% patients that were on conservative treatment, though the difference was not found to be statistically significant.

The proportion of patients with PH having AV Fistula was significantly more (42.2%) when compared to those without AV Fistula (25%).

Of the 28.2% patients with PH, 33.6% had hypertension and 22% were diabetic.

The association between the duration of dialysis and PH, after applying the Chi-square test, is graphically represented in “Fig. 2”.

Figure 2: Association between duration of dialysis and PH

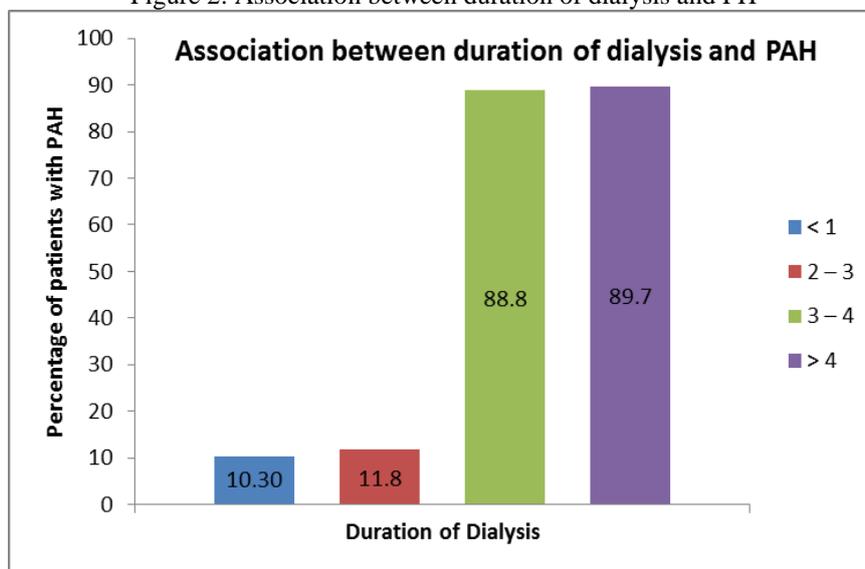


Table 2: Biochemical parameters

| Sr. No. | Biochemical parameters (units) | No. of PH (Y/N) | Mean value ( $\bar{X} \pm SD$ ) | P value |
|---------|--------------------------------|-----------------|---------------------------------|---------|
| 1       | Haemoglobin (g%)               | Yes - 69        | 7.91 ± 1.21                     | *0.034  |
|         |                                | No - 176        | 8.53 ± 1.31                     |         |
| 2       | Uric Acid (mg%)                | Yes - 69        | 6.44 ± 1.76                     | *0.012  |
|         |                                | No - 176        | 5.95 ± 1.44                     |         |
| 3       | Serum Bicarbonate (mmol/L)     | Yes - 69        | 8.68 ± 0.21                     | *0.029  |
|         |                                | No - 176        | 11.06 ± 0.94                    |         |
| 4       | BUN (mg%)                      | Yes - 69        | 75.48 ± 30.20                   | *0.042  |
|         |                                | No - 176        | 66.34 ± 32.17                   |         |
| 5       | Serum Creatinine (mg%)         | Yes - 69        | 0.83 ± 0.01                     | *0.036  |
|         |                                | No - 176        | 0.79 ± 0.40                     |         |

Statistical Test used – ANOVA

P value < 0.05 is significant

## V. DISCUSSION

The prevalence of PH in the haemodialysis group is 30% and that in the conservative management group is 24.7%, which indicates the role of renal replacement treatment in the pathogenesis of PH. The prevalence of PH in CKD in our study group was 28.2%, which is comparable to 26.74% from a previous study by F. Tarrass et al,<sup>(15)</sup> which is comparable to another previous study done by Amin M et al<sup>(16)</sup> whose study demonstrated that 29% of patients with CRF receiving regular haemodialysis have PH.

All CKD patients underwent 2D echocardiography. Based upon the tricuspid regurgitation velocity, systolic pulmonary arterial pressure can be estimated according to the following equation: Systolic PAP= 4 (TR)+ RAP. PH in CKD patients is graded by the reporting cardiologist as mild (35–45 mmHg), moderate (45–60 mmHg) or severe (>60 mmHg).<sup>(17)</sup> In this study, out of 245 patients, we found PH according to echographic criteria in 69 patients. Patients were graded according to pulmonary artery systolic pressure. We found 39 patients have mild PH, 24 have moderate PH and 6 patients have severe PH.

The presence of 42.2% patients having AV Fistula for haemodialysis in patients with CKD along-with PH are comparable with two previous studies by Yingla et al<sup>(11)</sup> and Abassi Zaid et al.<sup>(18)</sup>

There are no previous studies that show the prevalence of PH in hypertensive and diabetic patients.

Our study revealed a positive association between the duration of dialysis and the prevalence of PH. A similar study by Patel P et al<sup>(19)</sup> showed that as duration of renal failure increased so did the chance of developing PH.

PH is positively correlated with clinical parameters like RRT-haemodialysis, A-V fistula, duration of dialysis and biochemical parameters like low haemoglobin, low sr. bicarbonate, high levels of uric acid, BUN, creatinine.

Our study result demonstrated high mean Haemoglobin indicating a role of anaemia in the pathogenesis of PH in CKD. This co-relation is supported by C. J. Rhodes et al<sup>(12)</sup> showing the role of iron in the natural history of PH. Iron availability influences the pulmonary vasoconstrictor response to hypoxia and accumulating evidence indicates that iron deficiency is prevalent in idiopathic and heritable forms of PH.

The mean serum uric acid level found in our study is supported by Norotoshi Nagaya et al<sup>(13)</sup> showing that serum UA increases in proportion to the clinical severity of PH and has independent association with long-term mortality of patients with Primary PH indicating it as a predictor of morbidity & mortality in PH.

The findings of mean serum bicarbonate levels are comparable to the study done by Patel et al<sup>(19)</sup> and indicate a positive correlation between PH and low bicarbonate level, leading to metabolic acidosis. The results of BUN & serum creatinine levels in our study are comparable to that of Patel et al<sup>19</sup> indicating PH in CKD and correlates with high levels of both.

## VI. CONCLUSION

In this prospective study, prevalence of pulmonary arterial hypertension (PAH) in chronic kidney disease is 28.2%. The prevalence of pulmonary arterial Hypertension [PAH] in hemodialysis group i.e. Group 1 is 30% and in conservative management group i.e. Group 2 is 24.7%, indicating the role of renal replacement treatment in the pathogenesis of pulmonary hypertension. Pulmonary hypertension in CKD group having A-V fistula is 42.2%, indicating role of A-V fistula in the pathogenesis of PAH. Though PAH is found more in previous hypertensive patients but is insignificant statistically, same with the case of diabetes mellitus. Duration of dialysis is important factor in the pathogenesis of PAH, indicated by 88.8% of cases with PAH has 3 – 4 years of dialysis and 89.7% with PAH has > 4 years of dialysis which is significantly more as compared to 11.8% with 2 – 3 yrs of dialysis and 10.3% with < 1 year of dialysis.

Thus in summary, prevalence of pulmonary hypertension in chronic kidney disease is 28.2%. Pulmonary hypertension is positively correlated with clinical parameters like RRT-hemodialysis, A-V fistula, duration of dialysis and biochemical parameters like low haemoglobin, low sr. bicarbonate, high levels of uric acid, BUN, creatine. 6] PAH is also correlated positively with biochemical parameters like anaemia (low Hb%), low bicarbonate level, high serum uric acid, high blood urea nitrogen (BUN), high serum creatine level.

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