ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 06 | June - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

# A COMPARATIVE STUDY OF PULMONARY HYPERTENSION AMONG CHRONIC KIDNEY DISEASE (CKD) PATIENTS ON DIALYSIS AND CONSERVATIVE LINE OF TREATMENT

General Medicine

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## ABSTRACT

**Introduction** Patients with chronic kidney disease and end-stage renal disease (CKD) are prone to pulmonary hypertension as one of the comorbid conditions. The prevalence of pulmonary hypertension (PHT) is associated with an increased risk of hospitalization and high mortality. The current study aims to compare the line of treatment in patients with CKD diagnosed with PHT. **Methods** A cross-sectional analytical study was conducted in the Department of General Medicine, R.L. Jalappa Hospital, Kolar, from January 2021 to December 2022 among patients diagnosed with pulmonary hypertension and suffering from CKD. In contrast, patients with other comorbid conditions were excluded. After the ethical approval, patients were categorized into two groups; Group A – patients with CKD and PHT receiving hemodialysis, and Group B; patients with CKD and PHT receiving conservative line treatment. Tests such as CBC and eGFR using the MDRD equation, renal function test, and ECG were conducted. **Results** Seventy-eight patients were enrolled with male predominance (56.4%), most diagnosed with diabetes mellitus and systemic hypertension. A significant difference was reported between the two groups concerning urea levels, alkaline phosphate, and serum creatinine (p-value <0.0001). The study finds that patients undergoing hemodialysis were prevalent with PHT (p-value 0.044) compared to conservative management. **Conclusion** Patients with CKD receiving hemodialysis are more prone to PHT when compared with conservative management; however, laboratory markers and tests can predict the severity of the disease.

## KEYWORDS

CKD, pulmonary hypertension, PHT, end-stage renal disease, hemodialysis, comparative study

## INTRODUCTION:

Increased pulmonary arterial pressure (PAP) and resistance are two symptoms of the rare condition known as pulmonary hypertension (PHT). The illness is caused by several different mechanisms, the most prevalent of which are systemic, cardiac, and pulmonary disorders. PHT is mainly related to cardiac problems in the group of end-stage renal disease (ESRD) patients undergoing hemodialysis (HD) therapy through surgical arterio-venous (A-V) access. [1] It is more common in patients with end-stage renal disease or chronic kidney disease (PHT), which raises the risk of death and hospitalization. Despite this, the lack of data makes it unclear if PHT and CKD are related. With a 40% incidence in CKD patients who require dialysis, PHT is more common in these individuals and is an independent predictor of death. [2]

PHT is a significant indicator of morbidity and death in CKD patients because of a lack of invasive hemodynamic data. Most studies cannot discriminate between precapillary and postcapillary PHT in randomly selected patients with and without indications. [1] Left ventricular dysfunction and CKD-related risk factors, such as volume overload, an arteriovenous fistula, sleep apnea, contact with dialysis membranes, endothelial dysfunction, vascular calcification and stiffening, and severe anemia, can cause or exacerbate pulmonary hypertension in CKD patients. [3] Echocardiography (ECG) is reportedly used to diagnose pulmonary hypertension in CKD patients, with most patients obtaining this diagnosis even though there is typically no known underlying reason. [4] The hormonal or metabolic imbalance brought on by CKD, which results in constriction of the pulmonary arteries and an increase in pulmonary vascular resistance, may be the main reason for the onset of pulmonary hypertension. The few proposed routes that might lead to the development of PHT in CKD include increased oxidative stress or endothelial dysfunction from uremic toxins and vascular calcification. [5]

Plexiform lesions, which cause the lumen of the microvessels in the lungs to be destroyed and to constrict, cause PHT by raising flow resistance. The angiogenesis response to regional stimuli and the dysregulation of endothelial maturation are two hypothesized ideas for forming the lesion. Changes in hormones and metabolism brought on by CKD may cause pulmonary artery vasoconstriction and an increase in pulmonary vascular resistance. Pneumatic artery pressure might develop due to excessive cardiac output from the arteriovenous pathway and often occurring anemia and fluid overload (PAP). [6] In all patients suspected of having PAH, evaluation for additional possible aetiologies, such as thromboembolic illness, is necessary. Confirmation of the PAH diagnosis needs a complete right heart catheterization (RHC). [2] The gold standard for diagnosis is still the suitable cardiac catheter. An approach for early PAH identification with routine pulmonary function testing. [6]

The balance between thromboxane, a vasoconstrictor, and nitric oxide, a vasodilator, regulates the pulmonary arteries' localized vascular tone and functionality. Because of inadequate nitric oxide activity, hemodialysis (HD) does not improve endothelial dysfunction in CRF patients. Aging, left ventricular hypertrophy, renal failure, and PHT are all associated with an elevated level of neuronal natriuretic hormone. N-terminal pro-brain natriuretic peptide (NT-proBNP), a by-product of BNP, has demonstrated predictive usefulness in PHT. [7] The study aims to quantify and evaluate the prevalence of pulmonary hypertension among chronic kidney disease patients receiving hemodialysis or conservative treatment.

## MATERIALS AND METHODS:

A cross-sectional analytical study was conducted in the Department of General Medicine, R.L. Jalappa Hospital, Kolar, from January 2021 to December 2022. After applying inclusion and exclusion criteria, patients with chronic renal disease who presented to R L JALAPPA HOSPITAL over six months were included in the research.

### Inclusion Criteria:

Patients with CKD receiving HD or conservative care were chosen, and CKD patients were selected due to all etiologies and patients of all age groups.

### Exclusion Criteria:

Patients with COPD, Parenchymal Lung Disease, Chest Wall Disease, Previous history of PHT, Previous pulmonary embolism, Collagen Vascular Disease, and Significant mitral/aortic valve disease were excluded from the study. Patients who were Smokers ( >5 pack years) and with LV EF <50% were not included in the study.

The investigation was initiated following institutional ethical approval. Patients underwent carotid Doppler and blood tests after being informed about the surgery and given the go-ahead. In a predetermined proforma, clinical (Height, Body weight, Clinical examination, BMI), laboratory, and sociodemographic (Age, gender) data were collected. A computer-generated random table was used to divide the patients into two groups.

Thirty-nine patients with end-stage renal disease and chronic kidney disease who were receiving hemodialysis and had pulmonary hypertension made up Group A, and the outcomes were examined independently. Group B Consisted of 39 patients with chronic renal disease on a conservative treatment plan who also had pulmonary hypertension, and the results were analyzed individually. The patients were investigated for the disease using an echocardiogram, CBC, and eGFR using the MDRD equation, renal function test, and ECG. MS Excel and Microsoft Word will generate various graphs, such as bar graphs, pie charts, and scatter plots. Pearson correlation or Spearman's correlation will be used to determine the correlation between quantitative and qualitative variables.

The SPSS 22 version of the software will be used to analyze the data, which will be placed into a Microsoft Excel Data Sheet. Data that is categorical will be shown as frequencies and proportions. The significance test will be conducted using chi-square. The mean and standard deviation will be used to describe continuous data. Statistical significance will be determined by the p-value < 0.05.

**RESULT:**

A total of 78 patients were included in this study. 46.2% of participants were in the 51–60 age range, followed by the above 61 age range (44.9%) in terms of prevalence. The age group less than 50 years of age, showed the least of 9.0%. The patients were divided into two main groups: the conservative and the hemodialysis groups, each with 39 patients. No significant difference was seen between the age distribution in the patients (P-value 0.415). (Table 1)

**Table 1. Demographic Data Of The Study**

| | | | Group | | Total | P-value |
|---|---|---|---|---|---|---|
| | | | Hemodialysis | Conservative | | |
| Age group | <50 | Count | 5 | 2 | 7 | 0.415 |
| | | % within Group | 12.80% | 5.10% | 9.00% | |
| | 51-60 | Count | 16 | 20 | 36 | |
| | | % within Group | 41.00% | 51.30% | 46.20% | |
| | >61 | Count | 18 | 17 | 35 | |
| | | % within Group | 46.20% | 43.60% | 44.90% | |
| Gender | Female | Count | 16 | 18 | 34 | 0.648 |
| | | % within Group | 41.00% | 46.20% | 43.60% | |
| | Male | Count | 23 | 21 | 44 | |
| | | % within Group | 59.00% | 53.80% | 56.40% | |
| Etiology | DM | Count | 7 | 12 | 19 | 0.491 |
| | | % within Group | 17.90% | 30.80% | 24.40% | |
| | DM, SHT | Count | 13 | 6 | 19 | |
| | | % within Group | 33.30% | 15.40% | 24.40% | |
| | Drug-Induced | Count | 1 | 1 | 2 | |
| | | % within Group | 2.60% | 2.60% | 2.60% | |
| | Glomerulonephritis | Count | 5 | 5 | 10 | |
| | | % within Group | 12.80% | 12.80% | 12.80% | |
| | Obstructive Uropathy | Count | 1 | 0 | 1 | |
| | | % within Group | 2.60% | 0.00% | 1.30% | |
| | SHT | Count | 5 | 5 | 10 | |
| | | % within Group | 12.80% | 12.80% | 12.80% | |
| | Unknown | Count | 7 | 10 | 17 | |
| | | % within Group | 17.90% | 25.60% | 21.80% | |

The current study indicates a male majority, with 23 and 21 males included in the hemodialysis and conservative methods. Males comprised 56.4% of the study participants, and gender distribution showed no significant difference (P-value 0.648).

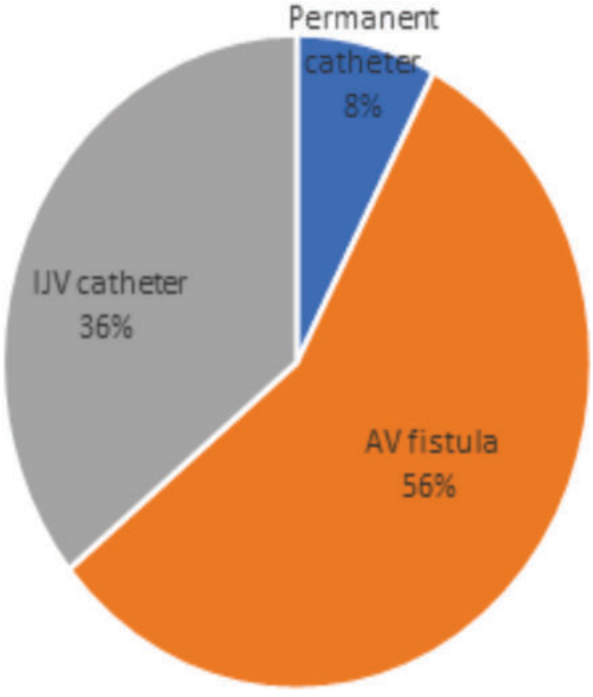


**Figure 1.** % Distribution of dialysis method

In our study, patients with diabetes mellitus comprised the largest percentage of participants—24.4%—followed by patients with diabetes and systemic hypertension. Seventeen patients (21.8%) had chronic kidney disease with no known cause, followed by ten patients (12.8%) with systemic hypertension and ten patients (12.8%) with glomerulonephritis. Two patients (2.6%) were found to have drug-induced chronic kidney disease or renal failure, while one patient (1.3%) had obstructive uropathy. (Table 2) There was a reported mean dialysis duration of 6 months ± 2.3 SD.

A total of 22 patients (56.4%) underwent AV fistula surgery, followed by 14 patients (34.9%) who underwent IJV surgery and three patients (7.7%) who underwent permanent catheterization. (Figure 1) Positive ECG alterations were seen in 4 patients in the conservative group and 8 in the hemodialysis group. When assessed for ECG changes, no significant difference was seen in both group (P-value 0.209). (Table 2) (Figure 2)

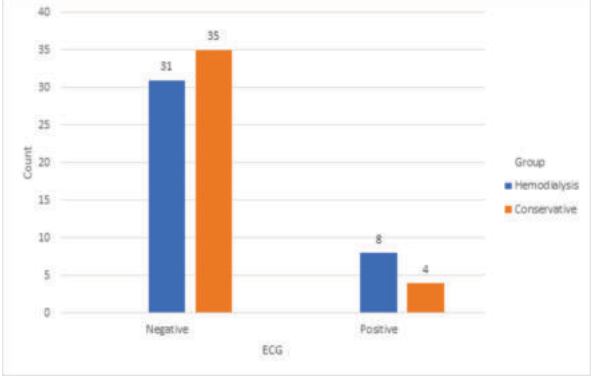


**Figure 2.** ECG changes the comparison of both the groups

**Table 2. ECG changes in patients**

| | | | Group | | Total | P value |
|---|---|---|---|---|---|---|
| | | | Hemodialysis | Conservative | | |
| ECG | Negative | Count | 31 | 35 | 66 | 0.209 |
| | | % within Group | 79.5% | 89.7% | 84.6% | |
| | Positive | Count | 8 | 4 | 12 | |
| | | % within Group | 20.5% | 10.3% | 15.4% | |
| Total | | Count | 39 | 39 | 78 | |
| | | % within Group | 100.0% | 100.0% | 100.0% | |

According to the study, there was a significant difference in the urea levels between the two groups (p-value 0.0001, showing that the hemodialysis group had a higher amount of serum urea). The serum creatinine level in the conservative group (mean 3.71 ± 1.12 SD) and in the hemodialysis group (mean 8.70 ± 1.32 SD) showed a significant difference (p-value <0.0001). No significance between the hemoglobin levels (p-value 0.259) in both groups was found in this study; however, the hemodialysis group recorded a mean of 10.20 ± 1.88 SD, and the conservative group recorded a mean of 9.73 ± 178 SD. The research shows a significant difference in the serum calcium group (p-value = 0.021). A mean calcium level of 8.56 ± 2.05 was recorded for the hemodialysis group and 9.68 ± 2.11 for the conservative group. The serum phosphorous level showed no significant difference in both groups (P-value 0.289). The current investigation found a significant difference in serum alkaline phosphatase levels, with the conservative group reporting a mean of 150.15 9.47 SD and the hemodialysis group reporting a mean of 356.33 29.03 SD (p-value 0.0001). (Table 3)

**Table 3. Various Serum Level Comparisons In Both Groups**

| Group | Mean | | Standard Deviation | | P-value |
|---|---|---|---|---|---|
| | Hemodialysis | Conservative | Hemodialysis | Conservative | |
| Urea | 166.77 | 79.52 | 29.35 | 10.10 | <0.0001 |
| Creatinine | 8.70 | 3.71 | 1.32 | 1.12 | <0.0001 |
| Hb | 10.20 | 9.73 | 1.88 | 1.78 | 0.259 |
| Calcium | 8.56 | 9.68 | 2.05 | 2.11 | 0.021 |
| Phosphorous | 5.61 | 5.13 | 1.07 | 1.74 | 0.289 |
| Alk. phosphatase | 356.33 | 150.15 | 29.03 | 9.47 | <0.0001 |

The current study shows that the groups receiving hemodialysis and those receiving conservative therapy significantly differed in PHT (p-value 0.044). In 15 patients getting hemodialysis, the prevalence of PHT was 38.5 percent, compared to 17.9 percent in 7 patients receiving conservative therapy. (Table 4) (Figure 3)

**Table 4. PHT comparison**

| | | | Group | | Total | P-value |
|---|---|---|---|---|---|---|
| | | | Hemodialysis | Conservative | | |
| PHT | No | Count | 24 | 32 | 56 | 0.044 |
| | | % within Group | 61.5% | 82.1% | 71.8% | |
| | Yes | Count | 15 | 7 | 22 | |
| | | % within Group | 38.5% | 17.9% | 28.2% | |
| Total | | Count | 39 | 39 | 78 | |
| | | % within Group | 100.0% | 100.0% | 100.0% | |

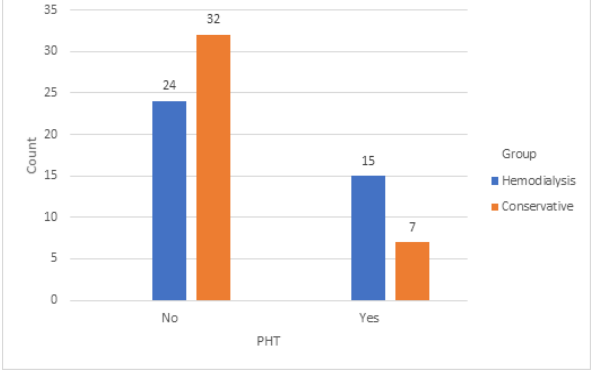


**Figure 3.** PHT comparison in hemodialysis and conservative group

**DISCUSSION:**

Pneumatic arterial pressure may be further increased by the high cardiac output brought on by arteriole-venous access, which is frequently influenced by anemia and fluid overload. As a result, the study's goals included comparing patient characteristics regarding their clinical, hemodynamic, and metabolic profiles and figuring out the prevalence of PHT in CKD patients with and without dialysis. Estimates show that 13% of persons in industrialized nations have CKD, linked to a higher risk of cardiovascular issues and a higher chance of renal failure. PHT is considered very susceptible to ESRD, significantly increasing the likelihood of the illness progressing. Studies show that people with ESRD have pulmonary hypertension much more frequently. [8] The research indicates that long-term hemodialysis and ESRD can impact cardiac output and pulmonary vascular resistance, which may help explain the etiology of pulmonary hypertension. [9]

In our investigation, pulmonary hypertension was seen in both patient groups and 22 patients (28.2%) with CKD participants. Seven (17.9%) of the total PHT patients were handled with conservative therapy, while 15 (38.5%) received hemodialysis treatment. In 41 patients reporting PHT, 33 percent receiving hemodialysis, Patel et al. identified a comparable prevalence of PHT. [10] Similar findings were observed in another study with chronic hemodialysis patients with a 30–40% PH frequency. 113; PHT was discovered in 32.3 percent of the group receiving conservative therapy and 44.4 percent of hemodialysis patients. [11] The current study also found a significant difference between the hemodialysis and conservative treatment groups, with the hemodialysis group having a higher prevalence of PHT (38.5%), with a p-value of 0.044.

The age group >61 years (44.9%) with a male predominance (56.4%) was followed by the age group between 51-60 years (46.2%) with the highest prevalence of CKD and hemodialysis or conservative therapy. No appreciable alterations were noted, though. Another study showed comparable results, with the mean patient age for the hemodialysis group being 45.72 7.83 SD and the mean patient age for the conservative treatment group being 45.45 □ 3.77 SD. [12] Diabetes mellitus (24.4%), followed by both diabetes and hypertension (24.4%), was the most common comorbid condition seen in CKD patients.

Moreover, systemic hypertension (12.8%) ranked third in prevalence, and 21.8% reported having CKD with an unclear cause. These findings were in line with those of the study by Magdy et al., which revealed that patients with CKD had high prevalences of DM (40.9% in the group receiving conservative management and 29.24% in the group receiving hemodialysis), hypertension (36.36% in the group receiving conservative management), and hyperlipidemia (40.9% in the group receiving conservative management) in both groups. [12] A study reported identical results, indicating hyperglycemia as the most common cause of CKD. [11] The length of HD was recorded as a mean year of 16.0 ± 35.76 with a permanent catheter in 3 patients, an AV fistula in 22 patients, and an IJV catheter in 14 patients.

Serum urea, serum creatinine, alkaline phosphatase, and serum calcium showed significant differences in both groups, with a p-value of <0.0001 for each (p-value 0.021). No significant differences were noted regarding AV access location, ECG alterations, Hb, and serum phosphorus. Comparing the HD group to the conservative management group, the overall laboratory parameters were considerably higher in the HD group. This study's findings were comparable to those of Madgy et al., who showed that individuals in the HD group significantly differed in similar laboratory measures. [12] Cardiac output values favourably influenced AVF flow and chronic renal failure length, as Havlucu et al. observed in 23 predialysis and 25 HD patients. However, residual urine volume was negatively impacted by arterial pressure in PHT patients. [5] Similar findings were shown in the research, which showed that patients on hemodialysis and PHT had considerably greater AVF flow and mean arterial pressure and AV flow were correlated. [13]

Due to physiological alterations, including increased AV flow, raised blood creatinine, serum calcium, serum urea, and alkaline phosphatase when compared to the conservative group, the HD group exhibited a significantly higher incidence of PHT in the current research (38.5%). In a similar study, mean fistula flow and arterial pressure were positively correlated; however, they also discovered an inverse relationship between PAP and ejection fraction. [14] Our study found, as did other research that most patients on hemodialysis have increased

laboratory values and pulmonary hypertension.

## CONCLUSION:

It was discovered that CKD patients receiving hemodialysis had a higher prevalence of pulmonary hypertension than CKD patients receiving conservative treatment and using echocardiography, alkaline phosphatase, and laboratory markers to gauge the disease's severity.

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