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ORIGINAL RESEARCH

Study of Pulmonary Hypertension in Patients with Chronic Kidney Disease

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ABSTRACT

Background:To study the prevalence of Pulmonary Hypertension (PH) in patients with Chronic Kidney Disease (CKD).

Materials and Methods: The present study assessed the prevalence of PH in 50 patients with CKD, at DR.PSIMS & RF, Chinnavutpalli, Gannavaram.

Results: The commonly affected age group in study population was 31-50 years. The mean age of patients was 48.98±12.53years. Diabetes Mellitus was present in 15 (30%) and Hypertension in 48 (96%). Majority of the patients were in CKD stage 5, i.e.,46 (92%), CKD stage 4 -3 (6%), CKD stage 3- 1(2%). The prevalence of PH in CKD is 22 (44%). PH was not found in the patient with CKD stage 3. PH was found in 2 of the 3(66.6%) patients with CKD stage 4. Out of the 46 CKD stage 5 patients, 20 (43.4%) had PH. With reference to the severity of PH with CKD, the two patients of PH CKD stage 4 had moderate PH . Out of the 20 patients of PH with CKD stage 5, 10 patients had mild PH, 9 with moderate PH and 1 with severe PHOn Chest X ray, descending right pulmonary artery dilatation and cardiomegaly were seen in more number of patients with PH, compared to those without PH. (p<0.001). In this study, LV systolic dysfunction was present in 18 out of 50 patients (36%). Among 22 patients with PH, it was present in 13 (59.09%). Among 28 patients without PH, it was present in 5 (17.85%). LV systolic dysfunction was significantly higher among the patients with PH compared to those without PH. The mean EF of all patients with CKD is 55.62± 9.54. The mean EF of patients with PH and without PH in the study was 50.50±9.78% and 59.64±7.26% respectively. (p<0.02). LV diastolic dysfunction was present in 41 out of 50 patients (82%). Among 22 patients with PH, it was present in 20 (90.9%). Among 28 patients without PH, it was present in 21 (75%). Prevalence of LV diastolic dysfunction was significantly higher among the patients with PH, compared to those without PH. RV dysfunction was present in 1(3.6%) and in 10 (45.5%) in patients without PH and in patients with PH respectively. Significant difference was found with RV dysfunction more prominent in patients with PH than in patients without PH (p<0.001). 64%of the patients studied had CKD of less than 6 months including 24%of new cases. 16%of the patients had CKD between 6 months and 1year. 20% had CKD of more than 1yr. In relation to PH, out of the 12 new cases of CKD,7 (31.8%) had PH and 5(17.9%)were without PH. Of the 20 patients having history of CKD less than 6 months (excluding new cases), 7 (31.8%) had PH and 13 (46.4%) were without PH. Out of the 8 patients of CKD between 6 months and 1 year,4(18.2%) had PH and 4(14.3%)were without PH. In

patients having CKD of more than 1 year, 4 (18.2%) had PH and 6 (21.4%) were without PH.

Conclusion: The study showed that PH is common in patients with CKD. Left Ventricular systolic and diastolic dysfunctions are strongly related to the outcome of these patients. Unexplained dyspnoea in patients with CKD must be evaluated for PH.

Keywords: Pulmonary Hypertension, CKD, Chest X-Ray, Left Ventricle, Mortality, ECG, 2D-Echo.

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INTRODUCTION

Pulmonary arterial Hypertension (PH) and Chronic Kidney Disease (CKD) both profoundly impact patient outcomes, whether as primary disease states or as co-morbid conditions. PH is a common co-morbidity in CKD and vice versa. A growing body of literature describes the epidemiology of PH secondary to Chronic Kidney Disease (CKD) and End-Stage Renal Disease (ESRD).

Pulmonary arterial hypertension is defined as a sustained elevation of pulmonaryarterial pressure to more than 25 mm Hg at rest or to more than 30 mm Hg with exercise, with a mean pulmonary-capillary wedge pressure and left ventricular end-diastolic pressure of less than 15 mm Hg.[1]

Chronic Kidney Disease (CKD) is a worldwide public health problem, with adverse outcomes of kidney failure, Cardio Vascular Disease (CVD), and premature death. CKD is defined as kidney damage or Glomerular Filtration Rate (GFR) <60 mL/min/1.73 m2 for 3 months or more, irrespective of cause.[2]

PH with CKD usually remains asymptomatic and misdiagnosed for a variable period of time until right ventricular dysfunction begins to manifest by worsening fatigue, dyspnea, and syncope. Recent studies suggest a higher prevalence of this entity in stage 5 CKD non dialysis dependent patients and hemodialysis (HD) patients.[3-5]

Based on an echocardiographic diagnosis of PH, the reported prevalence of PH ranges from 9%–39% in individuals with Stage 5 Chronic Kidney Disease (CKD) from 18.8%–68.8% in haemodialysis patients.[2] The exact mechanisms of PH in this population remain poorly understood. Myocardial dysfunction leading on to elevated left heart filling pressure and pulmonary venous hypertension is the predominant cause of PH in CKD.[3,4] The other factors implicated are increased cardiac output (CO),[3] increased pulmonary blood flow due to shunting across arteriovenous fistula(AVF),[3] volume overload,[4] anaemia, exposure to dialysis membranes,[4] alteration in endothelial function because of hormonal and metabolic disorders in CKD, leading to pulmonary vasoconstriction and decreased compliance of pulmonary vasculature,[4] vascular calcification and stiffening,[4] increased thromboxane B2 and pro-BNP.[5] ESRD-related PH, for the first time, was grouped into the 5thsubtype (PH with unclear multifactorial mechanisms) of PH by the World Symposium of PH (WSPH) in Dana Point (2008) and then updated in Nice (2013).[6]

It is unclear how and in which stage PH originates. Early diagnosis and early intervention of PH might improve the long-term outcomes. Therefore, it is crucial to investigate for PH before CKD patients progress to ESRD.

As there is no data available in this geographical area regarding the relation between PH and CKD, this study was taken up to bring out the incidence, severity and morbidity in such cases.

The number of patients coming with CKD was on the rise to the Department of Medicine and Nephrology at Dr PSIMS & RF, Chinnaoutpalli and had given me the opportunity to explore the relation of PH with CKD.

Aims and Objectives

1. To study the prevalence of Pulmonary Hypertension (PH) in patients with Chronic Kidney Disease (CKD).
2. To assess severity of PH in different stages of CKD.
3. To identify the risk factors for PH in CKD.
4. To compare the present study done on 50 patients with the existing literature.

MATERIALS & METHODS

Type of Study: Cross sectional study conducted in patients with chronic kidney disease admitted in Dr. PSIMS and RF during the period of October 2015 to November 2017.
Sample Size: 50 patients with CKD fulfilling the inclusion and exclusion criteria.

Inclusion Criteria:

1. Patients who were known chronic kidney disease on HD.
2. Newly diagnosed cases of CKD
   a) Patients with serum creatinine more than 3 mg% and Creatinine clearance <60 ml/min.
   b) Patients with bilateral contracted kidneys on abdominal ultrasonogram with poor corticomedullary differentiation and type 2 or type 3 parenchymal changes. Patients with Autosomal Dominant Polycystic Kidney Disease and Obstructive Nephropathy were also included in the study though they did not have contracted kidney due to the underlying disorder.
3. Age ≥18 years.

Exclusion Criteria:

1. Those not willing for participating in the study
2. Age <18 years
3. Valvular heart diseases
4. Congenital heart diseases
5. Pulmonary obstructive and restrictive diseases
6. HIV infected patients
7. Chronic liver disease
8. Connective tissue diseases
9. Hypothyroidism / Hyperthyroidism

Investigations:

Consent was taken from all patients and confidentiality was maintained.
In all patients a detailed history was taken, with special interest to the duration of symptoms. Cardiovascular symptoms, like dyspnoea, chest pain, pedal Oedema, pallor were noted. Blood pressure was measured thrice and the average was taken. Cardiovascular examination was done.

Signs supporting PH were focused like,

- Prominent second heart sound- loud and palpable P2
- Left parasternal heave
- Right ventricular S3, S4

– Pansystolic murmur of TR

Following investigations were done in all patients:

1. Complete haemogram
2. serum Creatinine
3. Creatinine clearance had been calculated in all patients using the MDRD equation.
4. Blood urea
5. Random blood glucose
6. Serum electrolytes- Sodium, Potassium, Calcium, Phosphate.
7. Liver function tests HIV, HBsAg, Anti- HCV
8. T3, T4 TSH
9. Urine routine- glucose, protein, microscopy
10. Ultra Scan abdomen: focus was on size of the kidneys, corticomedullary differentiation and parenchymal changes.
11. Chest X-ray P.A view to view cardiac size, pulmonary conus, and pulmonary vasculature and parenchymal changes if any.

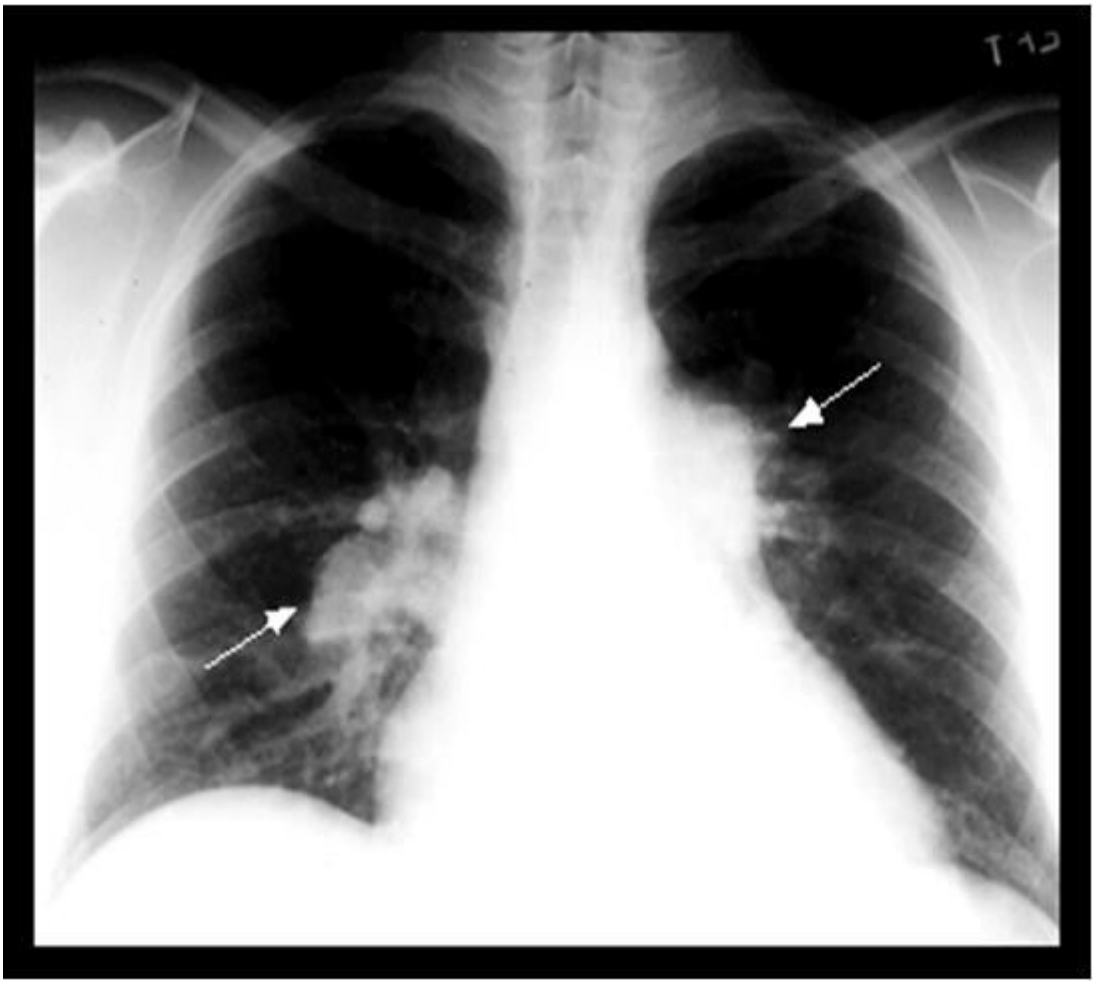

Figure 1: Chest X ray PA view

In PH, in CXR PA view, enlarged main and hilar pulmonary artery shadows, pruning or attenuation of the peripheral vasculature were noted. In lateral view RV enlargement was appreciated.
Descending right pulmonary artery was considered to be dilated if its diameter was 16 mm or more.

Other findings on CXR pointed to an associated condition such as hyperinflation with flat diaphragms in COPD or pulmonary venous congestion in left heart disease.[7]

14. ECG to record changes of PH

Tall R in V1, Right Ventricular strain, P Pulmonale, Right Axis Deviation, Deep S wave in V5 –V6.[8,7]

Echocardiographic examination with trans-thoracic two dimensional (2D) scanning was done from four standard transducer positions: the parasternal, apical, subxiphoid and suprasternal windows. Quantitative measurements of cardiac dimensions, area and volume derived from 2D images or 2D derived M- mode. In addition, 2D Echocardiography provided the framework for Doppler and color-flow imaging.

Doppler Echocardiography measured blood-flow velocities in the heart and great vessels. Tissue Doppler provided means for measuring and displaying cardiac wall motion velocities. Tissue Doppler was used to evaluate regional and global diastolic function.

PASP= 4 (TR jet velocity)^2 +10 mm Hg (estimated right atrial pressure).[9]

Pulmonary hypertension is diagnosed using various modalities including non-invasive 2D echocardiography.

RESULTS

The study was done to know the prevalence of Pulmonary Hypertension (PH) in 50 patients with Chronic Kidney Disease (CKD) admitted in the departments of Medicine and Nephrology at Dr.PSIMS & RF, Chinnavutapalli, Gannavaram from October 2015 to November 2017.

Age Distribution:

Table 1: Age distribution in this study

Age (in years)	Frequency	Percent (%)
< 20	1	2
21-30	2	4
31-40	8	16
41-50	17	34
51-60	14	28
61-70	5	10
>70	3	6
Total	50	100

In this study, 31 (62%) were in the age group of 41-60 years, 11 (22%) were between 20-40 years, 8 (16%) were between 61-70 years.

Gender Distribution:

Table 2: Sex distribution

Sex	Frequency	Percent (%)
Female	16	32
Male	34	68
Total	50	100

In this study males were more 34 (68%) and females were 16 (32%). M:F=2.1:1.

Stages of CKD in the Patients Studied:

Table 3: Stages of CKD enrolled in this study

Stage of CKD	Frequency	Percent
3	1	2
4	3	6
5	46	92
Total	50	100

Stages 1 and 2 CKD were not present in this study. 46 (92%) of stage 5 of CKD were part of this study

Categorisation of Patients Based on Duration of Diagnosis of CKD:

Table 4: Duration of CKD of the patients enrolled in this study

Duration of CKD	Frequency	Percent (%)
<6 months	20	40
6 months to 1 year	8	16
>1 year	10	20
New cases	12	24
Total	50	100

Most of the patients diagnosed with CKD were within last six months 20 (40%) and at the time of the study 12 (24%)

Categorisation of Patients Based on Duration of Dialysis:

Table 5: Categorisation of Patients Based on Duration of Dialysis

Duration of dialysis	Frequency	Percent (%)
<6 months	20	40
6 months to 1 year	3	6
>1 year	8	16
Newly initiated	15	30
No dialysis	4	8
Total	50	100

Patients on dialysis less than six months were significantly high 20 (40%). Recently initiated dialysis patients were 15 (30%). Dialysis was not required in 4 (8%) of patients.

Systolic Blood Pressure (SBP) in Patients Studied:

Table 6: Table representing the stages of SBP in the study population

Stage of SBP	Frequency	Percent (%)
Normal	2	4
Pre hypertension	9	18
Stage 1	13	26
Stage 2	26	52
Total	50	100

In this study stage 2 of SBP cases were 26 (52%). Stage 1 were 13 (26%) and pre hypertensive were 9 (18%).

Diastolic Blood Pressure (DBP) in Patients Studied:

Table 7: DBP in Patients Studied

Stage of DBP	Frequency	Percent (%)
Normal	3	6

Pre hypertension	9	18
Stage 1	11	22
Stage 2	27	54
Total	50	100

Stage 2 DBP cases were 27 (54%) and stage 1 were 11 (22%).

Clinical Features:
Percentage of Clinical Symptoms on Presentation:

Table 8: Frequency of the presenting symptoms

Clinical symptoms	Frequency	Percent (%)
Fatigue	31	62
Breathlessness	41	82
Chest pain	30	60
Pedal edema	38	76

- In this study breathlessness was identified in 41 (82%) of patients as a presenting symptom
- Fatigue was observed in 31 (62%) of patients as a presenting symptom
- Among the target patients 30 (60%) had chest pain.
- 38 (76%) of the patients studied had pedal oedema.

Clinical Signs in the Patients Studied:

Table 9: Clinical Signs in the Patients Studied

Signs	Frequency	Percent (%)
Pallor	40	80
Parasternal heave	2	4
Loud P2	12	24
Tricuspid Regurgitation murmur	5	10
Crepitations in lungs	17	34
Pedal Oedema	38	76
Ascites	11	22

- Clinical examination showed pallor in majority of patients 40 (80%)
- Parasternal heave was absent in 48 (96%) of patients.
- Loud P2 was present in 12 (24%) of patients.
- TR murmur was present in 5 (10%) of the patients studied.
- Bilateral basal lung crepitations were present in 17 (34%) of patients.
- Ascites was seen in 11 (22%) of patients.
- Pedal oedema was observed in 38 (76%) of patients.

Electrocardiographic Findings in the Patients Studied:

Table 10: ECG changes

ECG changes	Frequency	Percent (%)
P pulmonale	2	4
Signs of Ischemic heart disease	1	2

Left ventricular strain	13	26
Right ventricular strain	1	2

- P pulmonale was seen in 2 (4%) of patients only.
- Left ventricular strain was identified in 13 (26%)
- Signs of Ischemic heart disease was present in 1 (2%) patient only.
- Right ventricular strain was observed in 1 (2%)

Chest radiographic Findings among the Patients Studied:

Table 11: Chest radiographic Findings

Chest Radiography	Frequency	Percent (%)
Descending right pulmonary artery dilatation	13	26
Cardiomegaly	19	38
Pleural effusion	16	32
Pulmonary oedema	15	30

- Descending right pulmonary artery dilatation was present in 13 (26%)
- Cardiomegaly was identified in 19 (38%) of study group.
- Bilateral small pleural effusions were present in 16 (32%)
- Pulmonary oedema was identified in 15 (30%) of patients.

Echocardiographic Findings in the Patients Studied:

Table 12: 2D Echocardiographic findings

Echochardiographic findings	Frequency	Percent
LV systolic dysfunction	18	36
Left Ventricular Hypertrophy	16	32
LV DD	41	82
Pericardial effusion	7	14
RV dysfunction	11	22
Chamber dilatation	9	18

- Left ventricular hypertrophy was identified in 16 (32%). A significant number of patients 34 (68%) didn't show left ventricular hypertrophy.
- LV Diastolic Dysfunction was significantly present in 41 (82%)
- Mild Pericardial effusion was seen in 7 (14%) patients.
- Left ventricular systolic dysfunction was present in 18 (36%). Mild LV systolic dysfunction was present in 13 (26), moderate dysfunction was present in 4 (8%), severe LV dysfunction was present in 1 (2%).
- RV dysfunction was present in 11 (22%).

Prevalence of Pulmonary Hypertension in Patients Studied:

Table13: Grading of PH in the study population

Pulmonary hypertension	Frequency	Percent (%)
Normal	28	56
Mild (35 – 49 mm of Hg)	10	20
Moderate (50 - 69 mm of Hg)	11	22

Severe (≥70 mm of Hg)	1	2
Total	50	100

Pulmonary hypertension was present in 22 (44%). Mild PH was seen in 10 (20%), moderate PH was seen in 11 (22%), severe PH was seen in 1 (2%).

Age in Relation with Pulmonary Hypertension in the Patients Studied:

Table 14: Table showing different age groups with and without PH

Age (in years)	Pulmonary hypertension				Total	
	Absent		Present			
	Count	%	Count	%	Count	%
< 20	1	3.6%	0	0.0%	1	2.0%
21-30	2	7.1%	0	0.0%	2	4.0%
31-40	3	10.7%	5	22.7%	8	16.0%
41-50	11	39.3%	6	27.3%	17	34.0%
51-60	6	21.4%	8	36.4%	14	28.0%
61-70	2	7.1%	3	13.6%	5	10.0%
>70	3	10.7%	0	0.0%	3	6.0%
Total	28	100.0%	22	100.0%	50	100.0%

Prevalence of PH was most common in the age group of 41 - 60 years 17+14 = 31 (34%+28% = 62%)
Next comes 31-40 years age group 8 (16%)

Gender Distribution in Patients with Pulmonary Hypertension:

Table 15: Gender distribution with relation to PH

Sex	Pulmonary Hypertension				Total	
	Absent		Present			
	Count	%	Count	%	Count	%
Female	12	42.9%	4	18.2%	16	32%
Male	16	57.1%	18	81.8%	34	68%
Total	28	100.0%	22	100.0%	50	100%
Chi-square value = 3.45; df = 1; P = 0.06						

Pulmonary hypertension was more prevalent in males 18 (81.8%) when compared to females 4 (18.2%) in the study group.

Pulmonary Hypertension in relation with Stage of CKD

Table 16: PH in relation with stage of CKD

Stage of CKD	Pulmonary hypertension				Total	
	Absent		Present			
	Count	%	Count	%	Count	%
3	1	3.6%	0	0.0%	1	2.0%

4	1	3.6%	2	9.1%	3	6.0%
5	26	92.9%	20	90.9%	46	92.0%
Total	28	100.0%	22	100.0%	50	100.0%
Chi-square value = 1.42; df = 2; P = 0.49						

In this study out of the 46 (92%) of patients with CKD stage 5, 20 (43.4%) have PH while 26 (56.6%) do not have PH. Out of 3 of stage 4 CKD patients 2 (9.1%) had PH. Stage 3 CKD patient studied in this group did not have PH.

Duration of CKD in relation with PH:

Table 17: Duration of CKD in relation with PH

Duration of CKD	**Pulmonary hypertension**				**Total**	
	Absent		**Present**			
	Count	**%**	**Count**	**%**	**Count**	**%**
<6 months	13	46.4%	7	31.8%	20	40.0%
6 months to 1 year	4	14.3%	4	18.2%	8	16.0%
>1 year	6	21.4%	4	18.2%	10	20.0%
New	5	17.9%	7	31.8%	12	24.0%
Total	28	100.0%	22	100.0%	50	100.0%
Chi-square value = 1.84; df = 3; P = 0.61						

64%of the patients studied had CKD of less than 6 months including 24%of new cases. 16%of the patients had CKD between 6 months and 1year. 20% had CKD of more than 1yr.

Duration of Dialysis in relation with PH:

Table 18: Duration of Dialysis in relation with PH

Duration of dialysis	**Pulmonary hypertension**				**Total**	
	Absent		**Present**			
	Count	**%**	**Count**	**%**	**Count**	**%**
<6 months	12	42.9%	8	36.4%	20	40.0%
6 months to 1 year	1	3.6%	2	9.1%	3	6.0%
>1 year	6	21.4%	2	9.1%	8	16.0%
Newly initiated	7	25.0%	8	36.4%	15	30.0%
No dialysis	2	7.1%	2	9.1%	4	8.0%
Total	28	100.0%	22	100.0%	50	100.0%
Chi-square value = 2.52; df = 4; P = 0.64						

- In the study of 50 patients, 4 (8%)patients did not undergo HD. The rest 46 patients had undergone HD.
- Newly initiated CKD patients on dialysis were 15 (30%) and patients with less than 6 months CKD were 20 (40%).
- 3 (6%) patients had HD between 6 months and 1 year and 8 (16%) patients were of more than 1-year duration of HD.

Prevalence of Type 2 Diabetes Mellitus in the Study Group:

Table 19: Prevalence of Type 2 Diabetes Mellitus in the Study Group

Type 2 diabetes mellitus	Frequency	Percent (%)
Absent	35	70
Present	15	30
Total	50	100

- In this study group of 50, 15 (30%) diabetics are present

Prevalence of Hypertension in the Study Group:

Table 20: Prevalence of Hypertension in the Study Group

HTN	Frequency	Percent (%)
Normal	2	4
Prehypertensive	9	18
Stage-1	12	24
Stage-2	27	54
Total	50	100

- In this study of 50 patients, 2(4%) are normotensives, 9 (18%) are prehypertensives, 12 (24%) have stage 1 hypertension while 27 (54%) have stage 2 hypertension.

Systolic Blood Pressure (SBP) in Relation to PH:

Table 21: SBP in Relation to PH

Stage of SBP	Pulmonary hypertension				Total	
	Absent		Present			
	Count	%	Count	%	Count	%
Normal	2	7.1%	0	0.0%	2	4.0%
Prehypertension	6	21.4%	3	13.6%	9	18.0%
Stage 1	5	17.9%	8	36.4%	13	26.0%
Stage 2	15	53.6%	11	50.0%	26	52.0%
Total	28	100.0%	22	100.0%	50	100.0%
Chi-square value = 3.64; df = 3; P = 0.3						

- Out of the 22 patients with PH in this study, 3 (13.6%) were prehypertensives, 8 (36.4%) were stage 1 hypertensives and 11 (50%) were stage 2 hypertensives. Out of the 28 patients without PH 2 (7.1%) are normotensives, 6 (21.4%) were prehypertensives, 5 (17.9%) were stage 1 hypertensives and 12 (53.6%) were stage 2 hypertensives. There was small but no statistically significant variations in SBP between the PH group and non PH group.

Diastolic Blood Pressure (DBP) in Relation to PH:

Table 22: DBP in Relation to PH

Stage of DBP	Pulmonary hypertension				Total	
	Absent		Present			
	Count	%	Count	%	Count	%

Normal	2	7.1%	1	4.5%	3	6.0%
Prehypertension	6	21.4%	3	13.6%	9	18.0%
Stage 1	4	14.3%	7	31.8%	11	22.0%
Stage 2	16	57.1%	11	50.0%	27	54.0%
Total	28	100.0%	22	100.0%	50	100.0%
Chi-square value = 2.39; df = 3; P = 0.5						

- In patients with PH, 3 (13.6%) had prehypertension, 7 (31.8%) had stage 1 diastolic hypertension while 11 (50%) patients had stage 2 diastolic hypertension.
- In patients without PH, 6(21.4%) had prehypertension, 4 (14.3%) had stage 1 diastolic hypertension, 16 (57.1%) had stage 2 diastolic hypertension
- There was small but no significant variation could be found between the patients with PH and patients without PH

Relation of Type 2 Diabetes Mellitus to PH:

Table 23: Relation of Type 2 Diabetes Mellitus to PH

Type 2 Diabetes mellitus	**Pulmonary hypertension**				**Total**	
	Absent		**Present**			
	Count	**%**	**Count**	**%**	**Count**	**%**
Absent	21	75.0%	14	63.6%	35	70.0%
Present	7	25.0%	8	36.4%	15	30.0%
Total	28	100.0%	22	100.0%	50	100.0%
Chi-square value = 0.76; df = 1; P = 0.38						

- No significant relationship was found between the patients with PH and in those without PH in relation to Type 2 DM.

Ejection Fraction (EF) Relevance in PH with CKD:

Table 24: Relation between EF and PH

LV systolic dysfunction	**Pulmonary hypertension**				**Total**	
	Absent		**Present**			
	Count	**%**	**Count**	**%**	**Count**	**%**
Normal	23	82.1%	9	40.9%	32	64.0%
Mild	3	10.7%	10	45.5%	13	26.0%
Moderate	2	7.1%	2	9.1%	4	8.0%
Severe	0	0.0%	1	4.5%	1	2.0%
Total	28	100.0%	22	100.0%	50	100.0%
Chi-square value = 10.32; df = 3; P = 0.02						

Among the 50 patients in the study, 32 (64%) had a normal EF, remaining 18 (36%) had either mild, moderate or severe LV systolic dysfunction. There was significant difference (p=0.02) in EF between patients with PH and patients with no PH. In the patients with PH (22), 9 (40.9%) had normal EF, 10 (45.5%) had mild LV systolic dysfunction, 2 (9.1%) had moderate LV systolic dysfunction, 1 (4.5%) had severe LV systolic dysfunction.

In the non PH group (28), 23 (82.1%) had a normal EF. 3 (10.7%) had mild LV systolic dysfunction, 2 (7.1%) had moderate LV systolic dysfunction and no patient had severe LV systolic dysfuntion.
It was thus significant (p=0.02) that EF in patients with PH was statistically lower than in patients without PH

Clinical Symptoms in Relation with PH:

Table 25: Clinical Symptoms in Relation with PH

Clinical Symptoms	Pulmonary hypertension				Total		Chi-square value	P-value
	Absent		Present					
	Count	%	Count	%	Count	%		
Fatigue	13	46.4%	18	81.8%	31	62.0%	6.55	0.01
Breathlessness	20	71.4%	21	95.5%	41	82.0%	4.82	0.03
Chest pain	14	50.0%	16	72.7%	30	60.0%	2.65	0.1
Pedal edema	20	71.4%	18	81.8%	38	76.0%	0.73	0.39

- Fatigue is statistically higher in presentation in patients with PH 18 (81.8%) than in patients without PH 13 (46.4%). P = 0.01
- Breathlessness is statistically higher in patients with PH 21 (95.5%) than in patients without PH 20 (71.4%). P=0.03
- Chest pain is present in 16 (72.7%) of the PH group and 14 (50%) of the no PH group.
- Pedal edema is present in 18 (81.8%) of patients in PH group and in 20 (71.4%) of the no PH group.

Electrocardiographic Changes in Relation with PH:

Table 26: ECG Changes in Relation with PH

ECG changes	Pulmonary hypertension				Total		Chi-square value	P-value
	Absent		Present					
	Count	%	Count	%	Count	%		
P pulmonale	0	0.0%	2	9.1%	2	4.0%	2.65	0.1
Left ventricular strain	4	14.3%	9	40.9%	13	26.0%	4.54	0.03
Ischemic heart disease	1	3.6%	0	0.0%	1	2.0%	0.8	0.37
Right ventricular strain	0	0.0%	1	4.5%	1	2.0%	1.3	0.25

- P pulmonale was absent in patients without PH while it is present in 2 (9.1%) in patients with PH.
- Left ventricular strain was statistically higher (p=0.03) in patients with PH 9 (40.9%) than in patients without PH 4 (14.3%)
- Changes of Ischemic heart disease was present in 1 patient (2%)
- Right ventricular strain was present in 1 patient (2%)

Chest radiography Findings in Relation with PH:

Table 27: Chest radiography Findings in Relation with PH

Chest Radiography	Pulmonary hypertension				Total		Chi-square value	P-value
	Absent		Present					
	Count	%	Count	%	Count	%		
Descending right pulmonary artery dilatation	1	3.6%	12	54.5%	13	26.0%	16.64	<0.001
Cardiomegaly	4	14.3%	15	68.2%	19	38.0%	15.19	<0.001
Pleural effusion	6	21.4%	10	45.5%	16	32.0%	3.27	0.07
Pulmonary edema	5	17.9%	10	45.5%	15	30.0%	4.47	0.04

- The presence of descending right pulmonary artery dilatation was statistically higher (p<0.001) in patients with PH 12 (54.5%) than in patients without PH 1 (3.6%).
- Cardiomegaly was present in 15 (68.2%) of the patients with PH and in 4(14.3%). It was statistically significant (p<0.001)
- Pulmonary edema was present in 5 (17.9%) in patients without PH and 10 (45.5%) in patients with PH. (P=0.04)
- Mild bilateral Pleural effusion was present in 6 (21.4%) in patients without PH and 10 (45.5%) in patients with PH

DISCUSSION

Pulmonary Hypertension (PH) remained an overlooked issue in Chronic Kidney Disease (CKD) patients until very recent years. This study was conducted at Dr.PSIMS & RF, Chinnavutpalli, Gannavaram to determine the prevalence of PH in CKD patients in this region, hitherto not recorded. The results of this study was compared with the studies done at various places.

The prevalence of chronic kidney disease (CKD) in the developed world is 13% and is recognized as a condition that elevates the risk of cardiovascular complications as well as kidney failure and other complications. End-stage kidney disease (ESKD) substantially increases the risk of death, cardiovascular disease, and use of specialized health care. Pulmonary hypertension (PH) has been reported to be high among end-stage renal disease (ESRD) patients.

Chronic Renal function impairment or CKD is indicated by reduced estimated glomerular filtration rate (eGFR). Mean eGFR in our study of total 50 patients is 10.95±6.10. In patients with PH the mean eGFR is 10.60±5.36 and in patients without eGFR is 11.23±6.70.

In clinical practice, shunting of blood from the left to the right side of the heart and increased cardiac output and pulmonary blood flow are common medical conditions resulting in PH. However, Yigla et al. first noted unexplained PH in some long-term hemodialysis (HD) patients during an epidemiologic study.[7] 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. Hormonal and metabolic derangement associated with end-stage renal disease might lead to pulmonary arterial vasoconstriction and an increase in pulmonary vascular resistance.

There has been increasing interest recently in studying the association between pulmonary hypertension (PH) and CKD.[4,10] PH, defined by elevated pulmonary arterial pressure, is rare in the general population but seen in 30%–40% of patients with ESRD (on the basis of echocardiographic studies).[7,8]

After it is established, PH is often progressive and associated with high morbidity and mortality.[3]

Age distribution:

The age of the patients varied from 18 to 78 years. The commonly affected age group in study population was 31- 50 years. The mean age of patients was 48.98±12.53 years. The minimum age at which PH in CKD was found is 32, while the maximum age is 65,the mean age being 49.23 ± 9.73. In a study by Yigla et al,[2]

Sex Distribution

Gender has also been implicated as an independent risk factor for PH. Males were more commonly affected by CKD in our study. Sex ratio was 2.1:1.In the study 34 males and 16 females were examined. In males 18 (52.94%) and in females 4 (25%) had PH. This study showed males had more incidence of PH in CKD than females. These results were consistent with other studies.[2,8,11]

Prevalence of PH in CKD Patients:

Prevalence of PH in CKD in this study showed 22 patients out of a sample of 50 ie 44%. This is consistent with other studies., which show prevalence ranging from 16% (Yigla,2009),[25] to 58.6%(Fabbian).[12]

This wide range in reported prevalence of PH in CKD is attributable to lack of uniformity in diagnostic criteria of PH, stage of CKD patients studied, duration of CKD, mode and duration of dialysis and various other factors.

Prevalence and Severity of PH in Different Stages of CKD:

In the present study there was only 1(2%) patient with CKD stage 3, while there were 3(6%) patients with CKD stage 4 and 46(92%) with CKD stage 5 with a total of 50 patients.

Relation of Systemic Blood Pressure with PH in CKD:

Hypertension is a strong predictor for left ventricular hypertrophy, cardiac dilatation, cardiac failure, ischemic heart disease and worsening of atherosclerosis.[13] Blood pressure is an important determinant of left ventricular mass more so in CKD. There is a blunting of nocturnal dip in blood pressure in CKD. Whether the non-dipping leads to left ventricular hypertrophy or left ventricular hypertrophy is the cause of the blunted nocturnal dip, this puts the patients at higher risk for vascular disease.[14]

In the present study of 50 patients, 2(4%) were normotensives, 9 (18%) were prehypertensives, 12 (24%) had stage 1 hypertension while 27 (54%) had stage 2 hypertension.

Out of the 22 patients with PH in this study, 3 (13.6%) were prehypertensives, 8 (36.4%) were stage 1 hypertensives and 11 (50%) were stage 2 hypertensives.

The Mean SBP in the 50 patients studied is 155.24±19.09. In patients with PH, the mean SBP was 157.27±16.89. In patients without PH the mean SBP was 153.64±20.83.

The mean DBP in the 50 patients studied is 97.40±11.35. in patients with PH 97.73±9.82. in patients without PH 97.14±12.60.

Role of LV Dysfunction in Causing PH in CKD

This is the most important mechanism contributing to PH (WHO Group 2) in CKD patients and has been extensively evaluated in many studies. In the present study, LV systolic dysfunction was present in 18 out of 50 patients (36%). Among 22 patients with PH, it was present in 13 (59.09%). Among 28 patients without PH, it was present in 5 (17.85%). LV

systolic dysfunction was significantly higher among the patients with PH compared to those without PH. The mean EF of all patients with CKD is 55.62± 9.54. The mean EF of patients with PH and without PH in the study was 50.50±9.78% and 59.64±7.26% respectively. (p<0.02). Thus, the mean EF among the patients with PH was significantly lower compared to those without PH. This was in consistent with study by Fabbian et al,[11] in which mean EF among the patients with and without PH was 54±13% and 60±7% respectively. (p=0.0216).

RV dysfunction's role in patients with PH in CKD

In this study RV dysfunction was present in 1(3.6%) and in 10 (45.5%) in patients without PH and in patients with PH respectively. Significant difference was found with RV dysfunction more prominent in patients with PH than in patients without PH (p<0.001).
This is consistent with the findings of Dini, Frank L. et al.[15]

Role of Anemia in Causing PH in CKD

Anemia is a common manifestation of CKD and important risk factor for developing PH. The kidney being main source of erythropoietin, anemia is apparently an integral part of advancing renal failure. Anemia exerts an independent effect on the cardiovascular system. For every 1 g/dl drop in mean hemoglobin, the risk of cardiac failure increases by 25%, echocardiographically demonstrable left ventricular hypertrophy by 42%, and risk of death increases by 14%. Even moderate degree of anemia developing early in chronic renal disease, are associated with progressive cardiac enlargement.

Clinical Symptoms and Signs in Relation with PH:

Of the total 50 patients, breathlessness is found to be present in 41 patients (82%) followed by pedal edema which is seen in 38 (76%) patients, fatigue in 31 (62%) and chest pain in 30 (60%) patients with p values of 0.03, 0.39, 0.01, 0.1 respectively.
Out of the 22 patients with PH, 21 (95.5%) have breathlessness. In the 28 patients without PH, breathlessness is present in 20 (71.4%). This shows the statistical significance (p value = 0.03) that breathlessness is more in patients with PH in CKD than in patients without PH in CKD.
In the study by Zhilian Li et al,[16] the most common complaint in moderate to severe PH patients was fatigue, followed by peripheral edema, chest distress and dyspnea.

Chest Radiographic Findings of PH in this Study:

Descending right pulmonary artery dilatation is present in 13 (26%) patients in the whole study group. In the 22 patients with PH, 12 (54.5%) have Descending right pulmonary artery dilatation when compared with 1 (3.6%) from 28 in the non PH group. It is statistically significant with a p value<0.001.
Cardiomegaly was seen in a total of 19 (38%) patients. In patients with PH cardiomegaly was seen in 15 (68.2%). In patients without PH it was seen in 4 (14.3%). Thus cardiomegaly in patients with PH is significantly more (p<0.001) than in patients without PH.

PH and Mortality

There is substantial evidence that the presence of PH in patients with ESRD is associated with increased mortality rates. The effect of PH on mortality in patients with CKD was not assessed in this study. In an observational study by Yigla M, Nakhoul F et al,[7] out of 58 patients with ESRD on HD without concomitant cardiac or pulmonary disease, HD patients with PH had a mortality of 30.4% compared with 8.5% in HD patients without PH, with a mean follow-up of 30 months, (p<0.03).[7]

CONCLUSION

This study conducted at Dr.PSIMS & RF, Chinnavutpalli, Gannavaram to determine the prevalence of PH in CKD patients was the first of such studies done in this region. The study showed that PH is common in patients with CKD. Left Ventricular systolic and diastolic dysfunctions are strongly related to the outcome of these patients. Unexplained dyspnoea in patients with CKD must be evaluated for PH.

Treatment aimed at diastolic dysfunction and chronic volume overload should be evaluated to determine whether it could lower the rates of PH in CKD and ESRD patients. PH in CKD is associated with increased morbidly and mortality and routine echocardiographic screening must be done in all the patients with CKD to diagnose or follow up for PH as early as possible. It is hoped that this important complication of CKD be recognised, evaluated and managed appropriately.

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