International Journal of Research in Health and Allied Sciences
Journal home page: www.ijrhas.com
Official Publication of "Society for Scientific Research and Studies" [Regd.]
ISSN: 2455-7803

ORIGINAL RESEARCH

Prevalence of pulmonary arterial hypertension in chronic kidney disease patients

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ABSTRACT:
Background: Pulmonary arterial hypertension (PH) is a recently recognized complication of chronic kidney disease (CKD), especially in end-stage renal disease. It is an independent predictor of increased mortality in CKD patients. The aim of this study is to analyze the prevalence of PH in patients in various CKD stages, its severity in different stages of CKD, various related biochemical parameters, and their relation to PH in CKD patients were analyzed. **Materials & Methods:** Present study was conducted on 50 CKD patients. Every subject was subjected to transthoracic two dimensional echocardiography and pulmonary artery systolic pressure were obtained. **Results:** The prevalence of PH in CKD patients was 36%. The prevalence of PH increased as CKD stage advanced .Prevalence of PH is also increased in patients on dialysis and AVF group. There was a positive correlation between PH and Hemoglobin and no significant association of calcium and phosphorus in PH group compared to non-PH group. Severity of PH correlate with stages, as stage progress severity of PH increases. **Conclusion:** The prevalence of PH in CKD patients is 36%. Prevalence of PH had positive correlation with stage of CKD, those on hemodialysis, and those with AVF. The severity of PH was also directly proportional to stages of CKD, as stage progress severity of PH increases.
Key words: Pulmonary arterial hypertension, Chronic kidney disease, End-stage renal disease.

Received: 20 February, 2020 Accepted: 26 March, 2020

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This article may be cited as: Singh H, S Sivakumar, Singh G, Kumar S. Prevalence of pulmonary arterial hypertension in chronic kidney disease patients. Int J Res Health Allied Sci 2020; 6(2):8-12.

INTRODUCTION

Chronic kidney disease (CKD) is a common health problem worldwide. Cardiovascular disease is the most common cause of morbidity and mortality in CKD. [1] Though PH is a common finding in patients with ESRD but only few studies are available in the association between PH and ESRD.

Prevalence of PH in patients with CKD is difficult to estimate precisely because epidemiologic data for this disorder in patients with CKD are scarce. Bolignano D et al[2], studied PH in CKD patients and concluded that PH ranges from 9-39% in individuals with stage 5 CKD, 18.8%-68.8% in hemodialysis patients and 0-42% in patients on peritoneal dialysis therapy.

PH in CKD patients is important to recognize for 3 major reasons. The first in that several studies have indicated that PH is an independent predictor of mortality in CKD patients especially those receiving renal replacement therapy [3]. Second, many CKD patents are evaluated for renal transplantation. In general, significant PH is felt to be a relative contraindication to renal transplantation in patients with CKD [4]. In retrospective studies PH has been associated with increased early renal allograft dysfunction with reduced patient survival after renal transplantation. Perhaps third and most importantly from a clinical perspective many patients PH with CKD present with dyspnea.

Hormonal and metabolic derangement associated with ESRD might lead to pulmonary arterial vasoconstriction and an increase of the pulmonary vascular resistance. Proposed mechanisms for PH in CKD include dysregulation of endothelial growth and imbalance between vasodilators such as nitric oxide and vasoconstrictors such as thromboxane[5],arteriovenous fistulas (AVF)[6],anemia, uremic lung, volume overload with interstitial pulmonary edema and a high cardiac output state all of which can lead to pulmonary arterial vasoconstriction and an increase of the pulmonary vascular resistance.

There have been very few studies in this field and PH in CKD is undoubtedly one of the most enigmatic complications. In this background, we will try to establish the definite prevalence of PH in CKD patients and the relation of PH with the subsequent stages of CKD.

MATERIALS & METHODS

The study was conducted on fifty patients (n=50) who are diagnosed CKD (as per KDIGO criteria). The patients were picked from wards and OPDs of Guru Nanak Dev Hospital, Amritsar. This study undertook after approval of the Institutional Ethics Committee, Government Medical College, Amritsar. Written informed consent of the patients were obtained in vernacular language for their inclusion. Information regarding their age, sex and clinical diagnosis was collected. The data was statistically analyzed.

INCLUSION CRITERIA :

Patients fulfilling the following criteria :

1. Elevated blood urea, creatinine or decreased creatinine clearance or estimated glomerular filtration rate (e GFR) for more than 3 months.
2. USG changes-bilateral kidney size <8 cm in both males and female, and altered cortico-medullary differentiation.

EXCLUSION CRITERIA:

1. Chronic Obstructive Pulmonary Disease (COPD).
2. Parenchymal Lung Disease.
3. Chest Wall Disease.
4. Previous History of PH.
5. Smoker (>5 pack years).
6. Collagen Vascular Disease.
7. LVEF <50%.
8. Significant Mitral/Aortic Valve Disease.

Following investigations were carried after detailed clinical evaluation in patients with feature suggestive of Chronic Kidney Disease:

1.Urine

- pH, Specific gravity, Protein, Sugar, Microscopy

2.Blood

- Hemoglobin
- Total Leucocyte Count
- Differential Leucocyte Count
- PBF
- FBS/PPBS
- Blood Urea,
- Serum Creatinine,
- Total Serum Protein
- Serum Albumin
- Serum Electrolytes (sodium, potassium)
- Calcium
- Phosphorus
- Lipid profile.

2.Ultrasound Abdomen.

3.Twelve lead resting Electrocardiogram.

4.X-ray chest PA view (in full inspiration for heart size).

5.Transthoracic echocardiography was done in each individual using available Colour Doppler - Echocardiography- PHILIPS IE33 machine, in the department of Medicine of Govt. Medical College, Amritsar.

Parameters assessed in Echocardiography :

Presence of valvular heart disease

LVEF

Tricuspid jet

PASP

Patients were diagnosed to have Pulmonary arterial hypertension by measurement of the systolic regurgitant tricuspid flow velocity (v) and an estimate of right atrial pressure (RAP) applied in the formula .Pulmonary arterial hypertension: $=4v^2+RAP$

RESULTS

Out of the total 50 patients included in the study, 18 (36%) patients had PH. The mean PASP of patients with PH was 49.27+_8.10. Highest prevalence (55%) were seen in 51-60 years age group. Out of the total 18 patients with PH, 12 patients were males. PH was more common in males than females but it's not statistically significant (p = 0.88). There was a statistically significant association between CKD stages and PH (p =0.037). Among 18 patients had PH, none of the patients in CKD stage III revealed PH, while 4 (22.2%), and 14 (77.8%) patients of CKD stage IV, and V respectively had PH. In Stage 4 out of four patients had PH 3 had mild PH,1 patient had moderate PH and In stage 5 Out of 14 patients had PH 3 patients had mild PH,11 patients had moderate PH. This shows severity of PH correlate with stages, as CKD stage progress severity of PH increases. There was no statistically significant correlation noted between hypertension and diabetes with PH. 14 out of 30 diabetics (46.7%) had

PH whereas 13(37.1%) out of 35 hypertensives (57.69%) had PH. There was statistically significant presence of PH in patients treated on HD than treated conservatively (p =0.022).Among 18 patients had PH,11 (61%) patients were in dialysis group. Out of 12 patients with AVF 8 had PH, this shows there was a strong association between AVF and PH. (p = 0.012). The mean Hb was significantly lower among PH group compared to non-PH group, thus implicating the role of anemia in PH. There was no significant association of calcium and phosphorus with PH group compared to non PH group .

Table 1.PREVALENCE OF PULMONARY HYPERTENSION AMONG PATIENTS STUDIED

Pulmonary Arterial Hypertension	No of patients	Percentage
Yes	18	36
No	32	64
Total	50	50

Table 2.PREVALENCE OF PH AMONG VARIOUS STAGES OF CKD

Stage	Pulmonary Arterial Hypertension		
	Yes	No	Total
Stages 3	0 0.0%	6 100.0%	6 100.0%
Stages 4	4 25.0%	12 75.0%	16 100.0%
Stages 5	14 50.0%	14 50.0%	28 100.0%
Total	18 36.0%	32 64.0%	50 100.0%

Table 3.PREVALENCE OF PH AMONG PATIENTS UNDERGOING DIALYSIS

Dialysis	Pulmonary Arterial Hypertension		
	Yes	No	Total
Yes	11 55%	9 45%	20 100.0%
No	7 23.3%	23 76.7%	30 100.0%
Total	18 36%	32 64%	50 100%

Table 4.SEVERITY OF PH AMONG CKD STAGES

Severity	STAGE			
	Stage 3	Stage 4	Stage 5	Total
Mild	0	3	3	6
Moderate	0	1	11	12
Severe	0	0	0	0
Normal	6	12	14	32
Total	6	16	28	50

Chi square test= 10.01 p value=0.0403

DISCUSSION

The prevalence of PH in CKD patients in the present study was 18 (36%) patients of 50 patients studied with mean PASP of 49.27+_8.10 mm Hg. Tarras et al,[7] found PH prevalence to be as low as 26.74% and Moniruzzaman *et* al,[8] found it to be as high as 68.6%.

There is positive correlation between age and PH observed in our study. Highest prevalence (55%) were seen in 51-60 years age group. Most of the studies did not find correlation between age and PH. Study by Mazdeh et al,[9] (p = 0.58) and Tarras *et* al,[7] (p = 0.37), Patel *et al*, also did not find correlation between age and PH (p = 0.402).

In our study PH was more common in males (67%) than females (33.4%) .Male to female ratio of 2:1. However there was no statistically significant difference noted between gender.(p value=0.880).Tarras et al,[7] (p = 0.69) could not find a significant association between sex and PH among CKD patients. Moniruzzaman et al,[8] found a male predominance (male to female ratio of 2:1) in their study

Hypertension and diabetes mellitus, which are two dominant causes of CKD, trigger LV diastolic dysfunction, an alteration bound to increase pulmonary venous and arterial pressure There was no significant difference in prevalence of PH in hypertension (p value=0.797) and diabetes mellitus(p value=0.054) groups. Agarwal et al,[10] observed there was a statistical association of diabetes (p = 0.04) with PH but not of systemic hypertension (p =0.2). However, the study by Fabian et al,[11]showed statistically strong association of both diabetes (p = 0.021) and hypertension (p = 0.0074) with PH.

The exact mechanisms of PH in higher stages of CKD remain poorly understood. In the present study, statistically significant association between CKD stages and PH (p =0.037) was noted. Yang et al,[12] found PH prevalence of 23.76% (24/101) in stage 1-3 and 48.15% (13/27) in GFR <60 mL/min/1.73 m^2 group ($p < 0.05$).

Factors specific to HD like exposure to dialysis membrane, AV fistula contributes to pulmonary hypertension. Our study showed statistically significant presence of PH in patients treated on HD than treated conservatively (p =0.022). The prevalence of PH among patients on HD was studied by Magdy M Emra et al,[13] and Abdelwhab and Elshinnawy .[14] was found to be 42% and 44%, respectively. Patel et al,[15] demonstrated that 41 patients had PH, of whom 33% were on HD. There was a strong association between AVF and PH (p = 0.012). Havlucu et al,[16] showed similar association (p<0.05);however, Agarwal et al,[10] (p=0.1) did not find a similar association.

Low hemoglobin levels can contribute to PH by aggravating hypoxia. The mean Hb was significantly lower among PH group compared to non-PH group, thus implicating the role of anemia in PH. Study by Etemadi et al,[17] also showed similar association.

CKD patients having raised calcium and phosphorus may be attributed to increased stiffness of pulmonary vasculature caused by vascular calcification. Our study showed no significant association of calcium and phosphorus in PH group compared to non-PH group. A number of studies have compared calcium, phosphate and parathyroid hormone (PTH) levels in patients with and without PH, but the majority have failed to demonstrate. Only one study Kumbar L et al,[18] showed a positive correlation between echocardiographically estimated SPAP and calcium, phosphate and PTH in PD patients.

Severity of PH correlate with CKD stages, as stage progress severity of PH increases. Zhilian Li et al,[19] showed Mild, Moderate and Severe PH was diagnosed in 12.1%, 4.9% and 1.1% of the patients.

CONCLUSION

The prevalence of PH in CKD patients is 36%. Prevalence of PH had positive correlation with stage of CKD, and those on hemodialysis, and those with AVF. The severity of PH was also directly proportional to the stages of CKD. From this study it was found that there is indeed increase in prevalence of pulmonary arterial hypertension in chronic kidney disease patients, especially ESRD patients. Pulmonary arterial hypertension can be due to the effect of the CKD, which is in itself an inflammatory state or it may be due to the left ventricular functional compromise occurring in CKD patients. Long-standing PH is associated with increased morbidity and mortality. So it is essential to evaluate every patient of CKD especially ESRD patients for pulmonary arterial hypertension, at first by echocardiography and then by right heart catheterization, if deemed necessary.

REFERENCES

1. Locatelli F, Marcelli D, Conte F, D Amico M, Del Vecchio L, Limido A, et al. Cardiovascular disease in chronic renal failure: the challenge continues. Nephrology Dialysis Transplantation. 2000 Oct 2;15(90005):69-80.
2. Bolignano D, Rastelli S, Agarwal R, Fliser D, Massy Z, Ortiz A, et al. Pulmonary hypertension in CKD. Am J Kidney Dis 2013;61:612-22.
3. Adekunle L, Schmidt F, Quist J, Enriquez D, Nasser N, Ali A, et al. Pulmonary hypertension in 78 patients with ESRD. Chest Meet Abstr 2006;130: 253S.
4. Zlotnick DM, Axelrod DA, Chobanian MC, Friedman S, Brown J, Catherwood E, et al. Non-invasive detection of pulmonary hypertension prior to renal transplantation is a predictor of increased risk for early graft dysfunction. Nephrology Dialysis Transplantation. 2010 Mar 17;25(9):3090-6.
5. Jeffery TK, Morrell NW. Molecular and cellular basis of pulmonary vascular remodeling in pulmonary

hypertension. Progress in cardiovascular diseases. 2002 Nov 1;45(3):173-202.
6. Havlucu Y, Kursat S, Ekmekci C, Celik P, Serter S, Bayturan O, et al. Pulmonary hypertension in patients with chronic renal failure. Respiration. 2007;74(5):503-10.
7. Tarrass F, Benjelloun M, Medkouri G, Hachim K, Benghanem MG, Ramdani B. Doppler echocardiograph evaluation of pulmonary hypertension in patients undergoing hemodialysis. Hemodialysis International. 2006 Oct;10(4):356-9.
8. Moniruzzaman M, Islam MN, Alam MB, Alam AM, Khan MM, Ali Z, et al. Pulmonary Hypertension in Hemodialysis Patients. Cardiovascular Journal. 2012 Apr 22;4(2):148-52.
9. Mahdavi-Mazdeh M, Alijavad-Mousavi S, Yahyazadeh H, Azadi M, Yoosefnejad H, Ataiipoor Y. Pulmonary hypertension in hemodialysis patients. Saudi Journal of Kidney Diseases and Transplantation. 2008 Mar 1;19(2):189.
10. Agarwal R. Prevalence, determinants and prognosis of pulmonary hypertension among hemodialysis patients. Nephrology Dialysis Transplantation. 2012 Jan 30;27(10):3908-14
11. Fabbian F, Cantelli S, Molino C, Pala M, Longhini C, Portaluppi F. Pulmonary hypertension in dialysis patients: a cross-sectional Italian study. International journal of nephrology. 2011;2011.
12. Yang QM, Bao XR. Pulmonary hypertension in patients with stage 1-3 chronic kidney disease. Genet Mol Res. 2014 Jul 25;13(3):5695-703.
13. Emara MM, Habeb MA, Alnahal AA, Elshazly TA, Alatawi FO, Masoud AS. Prevalence of pulmonary hypertension in patients with chronic kidney disease on and without dialysis. Egyptian Journal of Chest Diseases and Tuberculosis. 2013;62(4):761-8.
14. Abdelwhab S, Elshinnawy S. Pulmonary hypertension in chronic renal failure patients. Am J Nephrol. 2008;28(6):990-7. doi: 10.1159/000146076. Epub 2008 Jul PubMed PMID: 18635926.
15. Patel P, Abraham G, Pratap B, Ramalakshmi R, Mathew M, Jeevan JM, et al. Clinical and biochemical parameters in chronic kidney disease with pulmonary hypertension. Indian Journal of Nephrology. 2007 Jan 1;17(1):4.
16. Havlucu Y, Kursat S, Ekmekci C, Celik P, Serter S, Bayturan O, et al. Pulmonary hypertension in patients with chronic renal failure. Respiration. 2007;74(5):503-10.
17. Etemadi J, Zolfaghari H, Firoozi R, Ardalan MR, Toufan M, Shoja MM, et al. Unexplained pulmonary hypertension in peritoneal dialysis and hemodialysis patients. Revista Portuguesa de Pneumologia (English Edition). 2012 Jan 1;18(1):10-4.
18. Kumbar L, Fein PA, Rafiq MA, Borawski C, Chattopadhyay J, Avram MM. Pulmonary hypertension in peritoneal dialysis patients. Adv Perit Dial. 2007;23:127-31.
19. Li Z, Liang X, Liu S, Ye Z, Chen Y, Wang W, et al. Pulmonary hypertension: epidemiology in different CKD stages and its association with cardiovascular morbidity. PLoS One. 2014 Dec 19;9(12):e114392.