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**Original Research Article**

# Outcome of pulmonary hypertension in patient on dialysis following kidney transplantation: an observational study

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## ABSTRACT

**Background:** Pulmonary hypertension (PH) is common among patients with end stage renal disease (ESRD) who are on dialysis and PH is associated with higher mortality rates among these patients. The impact of kidney transplantation on pulmonary hypertension is unknown. The purpose of this study is to evaluate the impact of successful kidney transplantation on pulmonary arterial hypertension in these patients on dialysis.
**Methods:** The study was conducted on patients who underwent kidney transplantation in Department of Nephrology PSGIMSR. Patients with pulmonary hypertension pre transplant were taken up for the study after the application of inclusion and exclusion criteria and after obtaining consent. Demographic, clinical information and laboratory results were collected. The assessment of PH was done by Doppler echocardiography pre transplant and 3 and 6 months after transplant during follow up.
**Results:** The prevalence of PH was 40%. The mean age of study population was 42 ± 8.7 years. The mean dialysis duration of study population was 32±8 months. 54.5% were male. 45.5% were female. Out of the 55 transplant recipients, 22 patients had elevated PASP on preoperative echocardiography examination. Compared to pre-transplant values, a significant decrease was observed in mean SPAP values and the severity of pulmonary hypertension 3 and6 months postoperative follow up ($p<0.003$).
**Conclusions:** The prevalence of pre-operative PH among dialysis patient was high. Kidney transplantation leads to considerable improvement in pulmonary arterial hypertension in patients on dialysis.

**Keywords:** Dialysis, Pulmonary hypertension, Transplant

## INTRODUCTION

There are many medical complications that can occur in patients with end stage renal disease (ESRD). Pulmonary hypertension (PH) is a newly recognized entity in ESRD patient on hemodialysis. PH is seen in a significant proportion of patients on dialysis.[1-3] The prevalence of PH has been reported to be high. There are various mechanisms that can contribute to the development of PH in dialysis patients. Among the various mechanisms, duration of renal replacement therapy, pulmonary calcification, high cardiac output due to arterio-venous fistula, anemia, volume overload and metabolic abnormality associated with chronic kidney disease are important predictors for elevation of pulmonary arterial pressure.[4,5] PH involves vasoconstriction and obliteration of the lumen of small vessels in the lungs by plexiform lesions resulting in increased resistance to flow. Proposed mechanisms for the formation of the plexiform lesion include dysregulation of endothelial growth and angiogenic response to local triggers. Local vascular tone and function are regulated by balance between

vasodilators such as prostacyclin and nitric oxide, and vasoconstrictors such as thromboxane A2 and endothelin-1.[6] Impaired nitric oxide production and reduced sensitivity to nitric oxide have been described in patients with ESRD.[7] Unless diagnosed early and treated appropriately, the course of PH is usually fatal due to development of right ventricular failure. In addition, it stands as an independent predictor of survival in patients with renal failure.[8] I

t is possible that pulmonary hypertension in renal transplant candidates may be a marker of patients with altered levels of vasoactive substances which may potentiate post-transplant vasoconstriction and ischaemia-reperfusion injury resulting in early graft dysfunction.[9] However, data about the impact of renal transplant on PH in patients with ESRD is limited. Therefore, in this study we aimed to evaluate the prevalence of pulmonary hypertension in patients on hemodialysis and the effect of subsequent kidney transplantation on pulmonary hypertension after three and six months post transplantation.

## METHODS

### *Study method*

The study was conducted on patients who underwent kidney transplantation in Department of Nephrology PSGIMSR. After obtaining informed consent patients with pulmonary hypertension during pre transplant evaluation were taken up for the study. Demographic, clinical information and laboratory results were collected. The assessment of PH was done by Doppler echocardiography pre transplant and 3 and 6 months after transplant during follow up. PH was defined as pulmonary artery systolic pressure (PASP) >35mmHg. Patients were categorized according to the following categories: non-measurable, normal PASP (PAPS ≤35mmHg), mild (PASP 36-45mmHg), moderate (PASP: 46-60mmHg) and severe PH (PASP >60mmHg).[10]

### *Study place*

Study was conducted with IP/OP clinic of department of Nephrology in PSG IMS and R, Coimbatore. The study was conducted during the time period of July 2016 June 2018.

### *Inclusion criteria*

- CKD due to all etiologies and patient of all age group were selected,
- CKD on MHD, who have undergone renal transplantation,
- Mild and moderate pulmonary hypertension.

### *Exclusion criteria*

- Not fit for renal transplantation.
- Severe pulmonary hypertension
- COPD
- Parenchymal lung disease
- Chest wall disease
- Previous h/o PH
- Pulmonary embolism
- Smoker >10 yr duration
- Collagen vascular Disease
- Valvular heart disease.

### *Study design*

This was a cross sectional/convenience sampling study.

### *Data collection*

Duration of illness, duration of dialysis, clinical history, chart review for lab values and echocardiography. PH was defined as PASP >35mmHg. Patients were categorized according to the following categories: non-measurable, normal PASP (PAPS ≤35mmHg), mild (PASP 36-45mmHg), moderate (PASP: 46-60mmHg) and severe PH (PASP >60mmHg).[10]

### *Statistical analysis*

Descriptive statistic for prevalence of PH. Inferential statistics using non parametric tests for qualitative and ‘t’ Test for Quantitative variables were carried out.

## RESULTS

We examined 75 patients on dialysis out of which 55 patient who underwent kidney transplant in our institute were taken up for the study. About 41 patients were excluded according to exclusion criteria. About 8 cases with severe PH were not included since they were started on nitrates and their dialysis were intensified. 14 patients were evaluated for further study. Doppler echocardiography was done in all 55 patients as a part of pre transplant work up and in patient with PH post operatively 3 months and 6 months echocardiography were done. Most of our cases were live related donor (76.2%) with rest of them underwent deceased donor transplant. All of them received triple immunosuppressant.

Among the 55 patients who undergone kidney transplantation 22 patients found to have pulmonary hypertension (40%). The prevalence of PH was 40%. The mean age of study population was 42±8.7 years. The mean dialysis duration of study population was 32±8 months. 54.5% were male. 45.5% were female. We analyzed systemic hypertension in all population who underwent kidney transplantation. Hypertension was present in 74% of patient. Out of 14 patients with PH, Systemic hypertension was present in 6 patient, of which 2 had mild pulmonary hypertension, 4 had moderate PH with ‘p’ value of 0.471. In association with pulmonary

hypertension and Diabetic ESRD we found only 4 patients, 2 patients with mild PH, 2 with moderate PH. calculating a 'p' value of 0.657. In our study group we found 3 patient having coronary artery disease (CAD) and ESRD. All these three had moderate pulmonary hypertension with 'p' value of 0.154 when compared to patient without CAD. This is shown in Table 1.

**Table 1: Patient with multiple risk factors (HTN, DM, CAD with PH).**

| | | Mild PH | Moderate PH | | P value |
|---|---|---|---|---|---|
| No | N | 6 | 5 | 11 | 0.154 |
| | % | 54.5% | 45.5% | 100% | |
| Yes | N | 0 | 3 | 3 | |
| | % | 0 | 100% | 100% | |
| Total | N | 6 | 8 | 14 | |
| | % | 42.9% | 57% | 100% | |

**Table 2: Post transplant at 3 and 6 months status of pulmonary hypertension.**

| | | Normal | Mild PH | | P value |
|---|---|---|---|---|---|
| No | N | 11 | 0 | 11 | 0.003 |
| | % | 100% | 0 | 100% | |
| Yes | N | 0 | 3 | 3 | |
| | % | 0 | 100% | 100% | |
| Total | N | 11 | 3 | 14 | |
| | % | 78.6% | 21.4% | 100% | |

We also analyzed the data and found 3 patients (21.4%) had multiple risk factors like SHT, DM. CAD and ESRD in the study group of 14 patients (78.4%) 'P' value of 0.154. Out of 14 patients 6 had Hypertension and ESRD of which 2 had mild PH and 4 had moderate PH, 4 patients had diabetes and ESRD of which 1 had mild PH, 3 had moderate PH, 3 patients had coronary artery disease and ESRD and all these patient had moderate PH. 3 patients had SHT, DM, CAD and ESRD. All 3 had moderate PH. Findings after 3 months of post transplantation is shown in Table 2 Mild and moderate PH improved after transplantation. About 11 patient completely cured of pulmonary hypertension and 3 patient improved from moderate PH to mild PH. These 3 patient had multiple co morbid illness before transplant.

## DISCUSSION

Pulmonary hypertension has been reported to occur in considerable number of patient with end stage kidney disease on dialysis. It is a progressive condition with prognostic significance. The prevalence of pulmonary hypertension in ESRD varies between 20- 50%.[1,2,8] In our study the prevalence of pulmonary hypertension in patient on dialysis was 40%. Duration of dialysis was not different in patient with or without pulmonary hypertension. In our study the prevalence of diabetes, hypertension or CAD were not different in patient with pulmonary hypertension on dialysis when compared to patient without PH on dialysis. Previous study reported pulmonary hypertension increases morbidity and mortality of patient on dialysis. It may affect renal allograft adversely.[8]

David et al, showed that non-invasive detection of pulmonary hypertension prior to renal transplantation is a predictor of increased risk for early graft dysfunction.[11] Pulmonary hypertension improves after successful kidney transplantation.[12] Renal transplantation is considered as the gold standard to restore renal function among end-stage renal disease patients. Simmons et al, reported that pro-inflammatory cytokines and oxidative stress markers return to a normal baseline level that is similar to that of healthy controls within two months of renal transplantation. The use of immunosuppressive medications, the restoration of renal function, or perhaps the combination of both may account for the normalization of the markers of oxidative stress and pro-inflammatory cytokines.[13] This may explain the significant reduction in PH of patients who underwent kidney transplantation.

In our study there was a significant favorable outcome in patients who underwent kidney transplant when followed up with echocardiography for first 3 and 6months of transplant. Most of our patient completely improved from pulmonary hypertension after transplantation. Even those with multiple co morbidity PH improved from moderate PH to mild PH. Kidney transplantation is an effective way of treating pulmonary hypertension in patients on dialysis.

This study has following limitation:

- Small sample size,
- Observational study,
- Echocardiography which has subjective variation, used as a parameter and right sided cardiac catheterization was not performed simultaneously.

## CONCLUSION

Till date only few studies on pulmonary hypertension in post renal transplantation have been done. Improvement in pulmonary hypertension after successful kidney transplantation suggests that patients with pulmonary hypertension on dialysis can be considered for early kidney transplantation.

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