

Prevalence of Pulmonary Hypertension in Patients Undergoing Regular Maintenance Hemodialysis due to End Stage Renal Disease

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ABSTRACT

Objectives: The aim of our study is to determine the prevalence of pulmonary hypertension in patients who undergo dialysis on a regular basis, as it has been associated with increased morbidity and mortality in the patient population. **Methodology:** The type of study is a cross sectional study conducted for a period of one year duration from April 2014 to March 2015, at a tertiary care hospital in Karachi, Pakistan. The study population consisted of n=90 patients with end stage renal disease, who undergo regular dialysis on maintenance basis, and had trans thoracic echocardiography performed, various parameters including the systolic pulmonary arterial pressure were recorded. A pulmonary arterial pressure greater than 30mm of Hg at rest was defined as pulmonary hypertension, and it was further divided into three sub categories mild (btw 30-40mm of Hg), moderate (btw 45-65mm of Hg), severe (greater than 65 mm of Hg). Variables such as age, gender, duration on maintenance dialysis, vascular access utilized were recorded. Data was analyzed using SPSS version 20. **Results:** Out of the total n=90 patients, n= 40 were males, and n= 50 were females, the mean duration of time duration of dialysis was 16.29 +/- 12.1 months. N= 52 patients were found to have pulmonary hypertension, and the mean value for the pulmonary arterial pressure was 38.4 +/- 19.18 mm of Hg, the mean age of patients having pulmonary hypertension was 53.45 +/- 12.4 years. Pulmonary hypertension was more common in the females as compared to the males (n= 32 versus n= 19), Pulmonary hypertension was found to be greater in patients who had been on dialysis for less than 20 months duration, and it was also noticed that the longer the duration of hemodialysis the more severe the pulmonary hypertension. **Conclusion:** According to the results of our study patients on maintenance hemodialysis are at an increased risk of developing pulmonary hypertension, it is more common in the females, and has a strong correlation with the duration of maintenance hemodialysis and the arteriovenous access utilized.

Keywords: End stage renal disease, ESRD, pulmonary hypertension, hemodialysis, chronic kidney disease, pulmonary arterial pressure, systolic pulmonary arterial pressure.

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INTRODUCTION

A systolic pulmonary arterial pressure greater than 30mm of Hg as determined by using a Doppler echocardiograph is defined as pulmonary hypertension.¹ CKD is a major health burden, and cardiovascular complications are a recognized source of morbidity and mortality in patients with CKD,^{2,3,4} and accounts for about 50% deaths in patients.⁵ Besides coronary artery disease, other major problem described in hemodialysis patients is of pulmonary hypertension,^{6,7} It is progressive and increases the morbidity and mortality of the

patients.⁸ According to a study by Yigle et al there is a lower survival rate for patients who are on hemodialysis and have concomitant pulmonary hypertension.⁹ The masking of clinical features of pulmonary hypertension due to the underlying etiology is a major concern for physicians as full blown effects are only revealed after right ventricular failure. The use of echocardiography has enabled physicians to estimate the pulmonary arterial hypertension non-invasively.¹⁰ The etiology of pulmonary hypertension in ESRD patients is

multifactorial.^{11,12} Factors such as metabolic derangements, chronic volume overload, metastatic pulmonary artery calcification (caused by calcium and phosphate metabolic derangements), increased blood flow caused due to the arteriovenous fistula or grafts, may be the causes of pulmonary hypertension, which may ultimately cause heart failure and death. The aim of our study is to figure out the prevalence of pulmonary hypertension in patients who are on maintenance dialysis, by detection of the hypertension by using echocardiograph. Those who are found to have pulmonary hypertension can be provided procedures to counteract the changes, like reversal of the fistula, alternative methods of dialysis, or renal transplant.

METHODOLOGY

The type of study is a cross sectional study conducted for a period of one year duration from April 2014 to March 2015, at a tertiary care hospital in Karachi, Pakistan. The study population consisted of n=90 patients (n=50 females, n=40 males) with end stage renal disease, who undergo regular dialysis on maintenance basis (via permanent arteriovenous access) three times a week, and each session of about 4 hours duration. The exclusion criteria was all the patients who had a history of chronic obstructive pulmonary disease, previous pulmonary embolism, collagen vascular disease, mitral or aortic valve disease, or having obstructive sleep apnea. All the patients had undergone a post dialysis trans thoracic echocardiography (by a cardiologist) and various parameters including the systolic pulmonary arterial pressure, ejection fraction etc were recorded. A pulmonary arterial pressure greater than 30mm of Hg at rest was defined as pulmonary hypertension, and it was further divided into three sub categories mild (between 30-40mm of Hg), moderate (between 45-65mm of Hg), severe (greater than 65 mm of Hg). Variables such as age, gender, duration on maintenance dialysis, vascular access utilized were recorded on a pre made proforma, chi square test was utilized to analyze the categorical variables, regression analysis was used to analyze the effect of duration of hemodialysis on the pulmonary hypertension, student t test was utilized to compare the difference of mean, a p value of less than 0.05 was considered to be significant. Data was analyzed using SPSS version 20.

RESULTS

Out of the total n=90 patients, n= 40 were males, and n= 50 were females, the time the patients had been having dialysis was a minimum of 2 months and a maximum of 60 months while the mean duration of time being 16.29 +/- 12.1 months. Out of the total study population n= 77 (85.5%) had an arteriovenous fistula, while n= 12 (13.33%) had a tunneled cuff catheter, and n= 1 (1.11%) had an arteriovenous bridge graft. N= 52 patients were found to have pulmonary hypertension, and the mean value for the pulmonary arterial pressure was 38.4 +/- 19.18 mm of Hg, the mean age of patients having pulmonary hypertension was 53.45 +/- 12.4 years, while the minimum age was 18 years and the maximum age was 72 years. The mean age of patients who did not have pulmonary hypertension was 53.87 +/- 13.3 years. Among the n= 52 patients who had pulmonary hypertension, n= 13 (25%) patients were 60 years old, it was also noticed that pulmonary hypertension was more common in the females as compared to the males (n= 32 versus n= 19), out of the total n= 52 patients, n= 15 (28.84%) were found to have mild pulmonary hypertension, n= 29 (55.76%) were found to have moderate pulmonary hypertension and n= 8 (15.34%) were found to have severe pulmonary hypertension. In the patients who had arteriovenous access, pulmonary hypertension was present in = 47 (61.03%), and in those who had a tunneled cuff catheter, n= 4 (33.33%) had pulmonary hypertension. Pulmonary hypertension was found to be greater in patients who had been on dialysis for less than 20 months duration, and it was also noticed that the longer the duration of hemodialysis the more severe the pulmonary hypertension.

Table 1: Characteristics of patients in regards to pulmonary hypertension

Variables	Pulmonary Hypertension presence		P value
	Yes, n= 52	No, n= 38	
Age in years	53.45 +/- 12.4	53.87 +/- 13.3	0.22
Gender			0.048
Male	19	21	
Female	32	18	
Duration of dialysis in months	20.92 +/- 12.01	10.28 +/- 10.01	<0.001
AV access via fistula, n= 77	47 (61.03%)	30 (38.95%)	0.015

DISCUSSION

It has been noted in the medical community that chronic diseases are on the rise like diabetes and hypertension, these chronic diseases are the leading causes of end stage renal disease. Cardiovascular disease accounts for half of the mortalities associated with ESRD.¹³ Various factors are associated with this high mortality rate such as homocysteinemia, dyslipidemia, oxidative stress caused by uremia, and hemodialysis. Roles of various other factors such as elevated calcium phosphorus products, hyperphosphatemia, arteriovenous fistula, hyperparathyroidism have been evaluated.¹⁴ After the development of ESRD the patient's needs regular dialysis or renal transplantation, dialysis has its own myriad of complications, one of which is newly being recognized and its pulmonary hypertension that is seen in patients who are on maintenance dialysis. It is under rated and shows associations with high morbidity and mortality.⁸ Its prevalence have been reported to be between 25% and 51%.^{14,15,16} Fabio Fabbian et al reported the highest prevalence of 58.6%.¹⁶ But these studies are retrospective and had pre selection bias. Our study addresses this issue in that it is a prospective study. The results of our study are consistent with international data, and we found the prevalence of pulmonary hypertension to be 57.77% in patients undergoing hemodialysis. Among the factors that could contribute to the development of pulmonary hypertension one is the arteriovenous access that is created. They have been attributed to the development of unexplained pulmonary hypertension in ESRD. According to a study by Yigla et al of the 58 patients they studied who had chronic renal failure and received long term hemodialysis via an arteriovenous access 39.7% had pulmonary hypertension.⁶ In another study by Modechai Yigla, of the 12 chronic kidney disease patients they had studied 42% of the patients which did not have pulmonary hypertension showed an increase in the pulmonary arterial pressure by more than 10mm of Hg following the formation of arteriovenous access.¹⁷ Similar results were observed in our studies. A significant relationship was established between arteriovenous fistula and pulmonary hypertension with 61% patients being dialyzed via arteriovenous fistula (p value of 0.05), we also studied other methods for hemodialysis access such as permanent catheters and AV bridge graft, we found a 27% prevalence of

pulmonary hypertension in patients who had tunneled cuff catheter but the group was small and could not be followed hence the results are not statistically significant.

It is also observed that pulmonary hypertension is more common in females, according to a study by Mona Amin et al there is prevalence of 48% pulmonary hypertension in women.¹⁸ Havlucu et al reported the male to female ratio of 40% versus 60%, which is similar to our study 36.53% versus 61.53%, the male to female ratio, which is statistically significant. The time duration of dialysis has a strong relation to the development of pulmonary hypertension,¹⁹ we also observed similar results in our study. We observed that in patients who had underwent dialysis for 30 months of more, had moderate pulmonary hypertension in 3 patients and severe pulmonary hypertension in 4 patients, hence the duration of dialysis (dialysis vintage) shows strong association with pulmonary hypertension, but further long term studies are required to validate this association. As we found out in our study that the most number of cases of pulmonary hypertension was in those who were having maintenance dialysis for a period of less than 20months duration. For patients who had pulmonary hypertension the mean duration for hemodialysis was 20.92 +/- 12.01, where as in a study by Mona Amin et al the mean duration of hemodialysis with pulmonary hypertension was 60 +/- 36 months,¹¹ and in a similar study by Fabio Fabbian et al it was 40 +/- 48 months.¹⁶ We were unable to determine the exact etiology for this discrepancy of earlier onset on pulmonary hypertension as it relates to the duration of hemodialysis, but it could be due to the late onset of starting hemodialysis, as most patients do not undergo hemodialysis, until they are late in the uremia and end stage renal disease have been developed to full blown effect, and this is due to various reasons such as economic, financial and lack of education, and all this leads to fatal complications and irreversible right sided heart failure thus increasing the morbidity and mortality. Further studies are needed to find the exact etiology and case of early onset pulmonary hypertension in the Pakistani population.

CONCLUSION

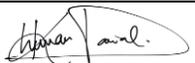
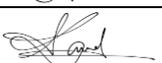
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AUTHORSHIP AND CONTRIBUTION DECLARATION

Name of Author	Contribution to the paper	Author's Signatures
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Dr. Khurram Danial	Concept, Drafting, Data collection	
Dr. Kamal Ahmed	Concept, Drafting, Layout	
Dr. Zain Ali	Write-up, Statistical analysis, Final layout	