The Frequency of Pulmonary Hypertension among End Stage Renal Disease Patients on Hemodialysis

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ABSTRACT

Background: Chronic kidney disease is one of the global public health problem. It is a major cause of mortality and morbidity. End stage renal disease patients will have either option of renal transplant or dialysis. Although dialysis is an effective form of renal replacement therapy but it also have long term side effects. Pulmonary hypertension is one of them.
Objective: To find frequency of pulmonary hypertension among end stage renal disease patients on hemodialysis in our population
Material and Methods: In this study a total of 163 patients were included, using 18.8% prevalence of pulmonary hypertension in end stage renal disease patients on hemodialysis, with 95% confidence interval and 6% margin of error, using WHO software. More over non-probability consecutive sampling technique was used for sample collection.
Results: Our study shows that mean age was 52 years with SD ± 8.21. Fifty five percent patients were male and 73(45%) patients were female. Forty eight percent patients had pulmonary hypertension.
Conclusion: Our study concludes that the incidence of pulmonary hypertension was found to be one of the major contributing factor among end stage renal disease patients on hemodialysis in our population.
Key Words: *pulmonary hypertension, end stage renal disease, hemodialysis.*

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INTRODUCTION

Chronic kidney disease (CKD) is one of the global public health problem[1]. It is estimated that more than 200 million people are affected worldwide with chronic kidney disease[2]. It is classified into five stages[3]. It is a major cause of mortality and morbidity. The rate of mortality increases as the patient approaches towards higher stage of chronic kidney disease[4]. At the end stage renal disease, patients will have either option of renal transplant or dialysis. Although dialysis is an effective form of renal replacement therapy but it also have long term side effects[5]. In Pakistan, the prevalence of chronic kidney disease is higher than expected. In one of population based study by Kazmi et al, the combine prevalence of stage 3 and 4 chronic kidney disease D is 14% with 19% in Punjab, 12% in KPK and Baluchistan and 7% in Sindh province[6].

Chronic kidney disease has complications as well. Common complications are anemia, cardiovascular complications, mineral bone disease and metabolic acidosis[7]. .Among the cardiovascular complications, pulmonary hypertension is also one of them and major cause of mortality and morbidity in end stage renal disease patients and in those who are on hemodialysis [5, 8]. Pulmonary hypertension is the increased pressure in the pulmonary arteries.it can be measure by invasive procedure like right heart catheterization and by non-invasive test, Doppler echocardiography. In chronic kidney disease patients, the mechanism of pulmonary hypertension is not clear but a few factors which may be included in the list are left ventricular disorders and other factors like fluid overload, anemia, arteriovenous fistula, vascular calcification[9]. Data regarding reducing pulmonary hypertension is lacking. Correction of the factors mentioned previously may reduce pulmonary hypertension and the results achieved by correcting such factors cannot even be matched or achieved with renal transplant. Literature review in finding the prevalence of pulmonary hypertension in early stages of chronic kidney disease i.e. stage 1-3 is lacking and unclear[10].

Studies conducted in different parts of the world show different frequencies of pulmonary hypertension among end stage renal disease patients on hemodialysis. Nationally, available data is little and at our setup, is negligible. so the aim/objective of this study is to find out the frequency of pulmonary hypertension among end stage renal disease patients on hemodialysis in Khyber Pukhtoonkhuwa (KPK) province of Pakistan and to correlate it with available data with the objective to early detect and treat the problem, identify the reversible factors and prevent complications and if found significant.

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MATERIAL AND METHODS

This study was a descriptive cross-sectional study utilizing nonprobability convenient sampling technique conducted in Nephrology Department Khyber Teaching Hospital, Peshawar over 6 months. Sample size was 163 using 18.8% prevalence of pulmonary hypertension in end stage renal disease patients on hemodialysis[9], 95% confidence interval and 6% margin of error with help of WHO software for sample size determination. Inclusion criteria included patients with chronic kidney disease on hemodialysis, age above 20 years and below 70 years, both genders. Exclusion criteria included patients with comorbid respiratory disorder, patients with cardiac disorders and all those patients who were critically ill. We defined end stage renal disease patients as those whose glomerular filtration rate was less than 15 ml/min and were on hemodialysis[3] whereas pulmonary hypertension was defined as, pulmonary artery pressure greater than 25 mm Hg at rest or 30 mmHg at exercise measured by echocardiography.[5] After getting approval from the hospital ethical and research committee, all patients meeting the inclusion criteria were included in the study and data was collected. An informed written consent was taken from the patients for inclusion in the study. All patients were worked up with detailed history, clinical examination, and underwent transthoracic echocardiography. The exclusion criterion was strictly followed to control confounders and exclude bias in the study result. Information and other demographic data were recorded in a proforma. Data was analyzed using Statistical Package for Social Sciences (SPSS) version 17 or higher version. Mean ± standard deviation was calculated for continuous variables like age, frequency of dialysis, duration of dialysis. Frequency and percentages were calculated for categorical variables like gender, route of dialysis and pulmonary hypertension. Pulmonary hypertension was stratified among age, gender, route and frequency of dialysis. Post stratification chi-square test was applied keeping p-value = 0.05 as significant. All these results were presented in the form of tables and charts.

RESULTS

Out of 163 patients 31(19%) patients were in age range 31-40 years, 37(23%) patients were in age range 41-50 years, 46(28%) patients were in age range 51-60 years, 49(30%) patients were in age range 61-70 years, Mean age was 52 years with SD ± 8.21.

Ninety (55%) patients were male and 73(45%) patients were female. Hundred and one (62%) patients had dialysis range = 2 times, while 62(38%) patients had dialysis range >2 times. Mean no of dialysis was 2 times per week with SD ± 1.63. Hundred and six (65%) patients had dialysis =1 years, 37(23%) patients had dialysis from 1-2 years, and 20 (12%) patients had dialysis from 2-3 years. Mean duration dialysis was 48 months with SD ± 11.34.

Twenty nine (18%) patients had Jugular, 33(20%) patients had subclavian, 36(22%) patients had femoral and 65(40%) patients had arteriovenous fistula as an access for hemodialysis.

Seventy eight (48%) patients had pulmonary hypertension and 85(52%) patients didn't have pulmonary hypertension. (Figure 1). Among 90 males, 35(45%) have pulmonary hypertension and out of 73 women 43(55%) have pulmonary hypertension. Chi square test was applied in which P value was 0.0109.

Stratification of pulmonary hypertension with age, route and frequency of dialysis is given in Table/ Figures below.

Figure No 1. Frequency of Pulmonary Hypertension

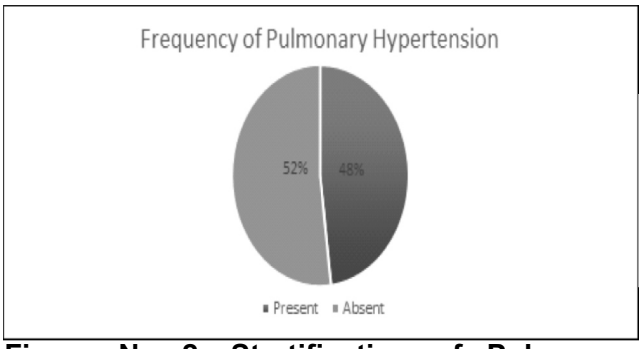
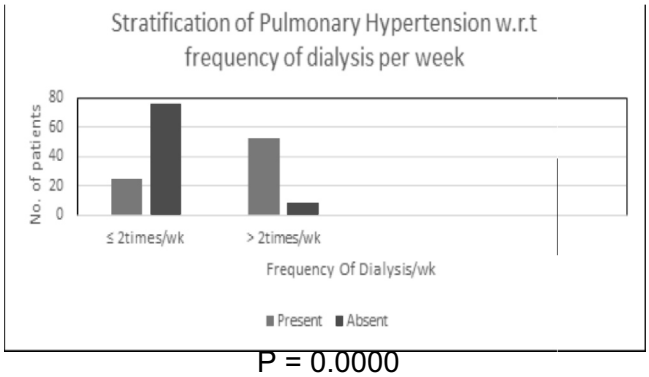


Figure No 2. Stratification of Pulmonary Hypertension w.r.t Frequency of Dialysis



P = 0.0000

Table No 1. Stratification of Pulmonary Hypertension w.r.t. age (n=163)

PULMONARY HYPERTENSION	30-40 years	41-50 years	51-60 years	61-70 years	Total
Present	4	20	24	30	78
Absent	27	17	22	19	85
Total	31	37	46	49	163

P=0.0002

Table No 2. Stratification of Pulmonary Hypertension w.r.t. route of dialysis (n=163)

PULMONARY HYPERTENSION	Jugular	Subclavian	Femoral	Arteriovenous fistula	Total
Present	0	10 (13%)	18 (23%)	50 (64%)	78
Absent	29 (34%)	23 (27%)	18 (21%)	15 (18%	85
Total	29	33	36	65	163

P=0.0000

DISCUSSION

Chronic kidney disease is one of the major public health problems[1] worldwide including Pakistan. In Pakistan, the prevalence of chronic kidney disease is higher than expected. Recent data suggest a close relationship between end stage chronic kidney disease and hemodialysis patients with pulmonary hypertension. Also prevalence of pulmonary hypertension increases with decline of renal function[11]. .Internationally in one study the prevalence of pulmonary hypertension in stage 5 of chronic kidney disease was found to be 9-39 % and 18.8-68.8% in hemodialysis patients[9] while another study shows prevalence of 41.53% among patients with end stage renal disease on hemodialysis[12].Meta-analysis by Tang et al showed overall prevalence of 23%[13] .Nationally in a study conducted by Shoukat et al, the prevalence of pulmonary hypertension in hemodialysis patients was found to be 42.7%[14]. In another study by Mukhtar et al, the prevalence was 56%[5]. Other have reportred the prevalence of pulmonary hypertension to be between 25%-51% [15, 16]. The highest incidence of about 58.6% was reported by Fabio Fabbian et al.[17] and 60.5% by Mehta KS et al[18]. However, most of these studies were retrospective and based on patients undergoing echocardiography for clinical indications hence may had pre-selection bias. Our study, to the best of our knowledge, is the first one to address this important issue in this part of the world. The results of our study were also consistent with International data and we found 48% prevalence of pulmonary hypertension in hemodialysis patients.

We also looked at factors that could be contributing to the development of pulmonary hypertension in this population. Among these was vascular access created for dialysis has been found as an important causative factor in unexplained pulmonary hypertension in patients with end-stage disease[11, 18]. Yigla et al. in their study of 58 patients with chronic kidney disease receiving long-term hemodialysis via arteriovenous access found pulmonary hypertension in 39.7% of patients[19]. Another study by Mordechai Yigla in 12 chronic kidney disease patients found 42% of patients without pulmonary hypertension increased their systolic pulmonary artery pressure values by more than 10 mm Hg following arteriovenous access formation[20]. Although these studies were small, however they suggest that arteriovenous access formation is a risk factor for pulmonary hypertension.

Our study supported what has been found in the above studies. We found significant relationship of pulmonary hypertension and arteriovenous fistula with 60% of patients being dialyzed through arteriovenous fistula had pulmonary hypertension (p=0.05). We also studied the effect of various other hemodialysis accesses on the development of pulmonary hypertension including patients with permanent catheters and arteriovenous bridge graft. Although our tunneled cuff catheter group was small and could not be followed for progression of pulmonary hypertension for longer time however they were also noted to have a 27% prevalence of pulmonary hypertension which was not statistically significant.

Gender has also been implicated as an independent risk factor for pulmonary hypertension. various studies have demonstrated that pulmonary hypertension is detected more frequently in women than in men. Mona Amin et al.[21] reported a higher prevalence of pulmonary hypertension, 48% in women. Havlucu et al studied 25 patients; female to male ratio of patients with pulmonary hypertension was 60% vs. 40%[22]. Our study also found higher prevalence in females, 52% compared to 48% in males that was statistically significant. Similarly, we could not find a strong correlation between increasing age and development of pulmonary hypertension. Volume overload has also been implicated as a risk factor in development of pulmonary hypertension [23, 24, 25]. In our setup, because most of our patients are underdialysed due to different reasons, volume overload can be one of the factor responsible for pulmonary hypertension.

Duration on hemodialysis (dialysis vintage) has direct relationship to the development of pulmonary hypertension [26]. We also found the same relationship of pulmonary hypertension with the dialysis vintage. In addition, it was observed that patients who were on hemodialysis for 30 months or above, moderate pulmonary hypertension was present in 3 patients and severe in 4 patients, hence dialysis duration can be associated with increased severity of pulmonary hypertension, however longer studies and more number of patients are required to validate this observation. An important finding in our study was that more number of cases of pulmonary hypertension was found in our patients who were below 20 months of duration on hemodialysis. For patients with pulmonary hypertension, the mean value for duration on hemodialysis (in months) was 20.93 ± 12 This is in contrast to other studies where it was 60 ± 36 months by Mona Amin.[21] In study by Fabio Fabbian et al. it was 40 ± 48 months[17]. We do not know the exact etiology of early onset of pulmonary hypertension but in our patients it could be probably the result of late onset of hemodialysis. Most of our patients do not start hemodialysis till they are uremic and although have been staged as ESRD, they delay it due to financial, socioeconomic, cultural and low literacy rate reasons. The early onset of pulmonary hypertension is however a challenging issue, because if it progresses in the same fashion would lead to fatal consequences and irreversible right sided heart failure resulting in increased morbidity and mortality. Further studies are needed to find the exact etiology and cause of early onset of pulmonary hypertension in our population so that proper measures may be taken.

CONCLUSION

Our study concludes that the incidence of pulmonary hypertension was found to be 48% among end stage renal disease patients on hemodialysis in our population.

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