

Prevalence of Pulmonary Hypertension among Non-Dialysis and Dialysis Dependent Chronic Kidney Disease Patients in a Tertiary Care Hospital

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Abstract: Chronic kidney disease leads to many co morbidities that affects patients at all stages of the disease. Complications are due to disease itself as well as the mode of renal replacement therapy. Cardiovascular morbidity and mortality is highest in the dialysis population. Recently there has been found an association between Renal replacement therapy and development of pulmonary hypertension. The main objective is to study the prevalence of pulmonary hypertension among non-dialysis and dialysis dependent chronic kidney disease patients. A total of 100 CKD patients, with 50 each in the non-dialysis and dialysis groups were included. The parameters like, etiology for CKD, hemoglobin levels, duration of dialysis, 2D Echocardiogram for the presence and severity of pulmonary hypertension among the patients in non-dialysis and dialysis dependent groups was studied. Among the 100 CKD patients, 44(44%) had pulmonary hypertension (PH) and in these 44 patients, 40(90.9%) patients were on dialysis which is significant with linear relation between duration of dialysis and severity of PH. The mechanisms underlying development of pulmonary hypertension in CKD patients are more complex. This unrecognized complication of maintenance hemodialysis therapy is associated with reduced survival. Detection of Pulmonary Hypertension in CKD patients may also help in prognosis in the post-transplantation period.

Keywords: Chronic kidney disease; hemodialysis; peritoneal dialysis; pulmonary hypertension.

INTRODUCTION

Chronic kidney disease (CKD) includes a spectrum of pathophysiologic processes associated with abnormal kidney function and progressive decline in glomerular filtration rate (GFR). There are different stages of CKD which are stratified by both estimated GFR and the degree of albuminuria [1]. The prevalence and incidence of CKD are increasing worldwide [2,3].

Since CKD increases the mortality and morbidity risks, they have become a major public health problem [4]. The population of India is more than one billion which is projected to become the major reservoir of chronic diseases like diabetes mellitus and hypertension⁵. About 25–40% of them are likely to develop CKD, thereby ESRD burden will rise [4].

It has been estimated that less than 10% of all Indian ESRD patients receive any meaningful renal replacement therapy (RRT) [5-8] and if not dealt at the appropriate time period it increases the cardiovascular

mortality, which is 10 – 20 times higher in patients with end stage renal disease.

Hemodialysis is a form of renal replacement therapy that relies on the principles of solute diffusion across a semi-permeable membrane. It has also been found that patient on Hemo-Dialysis are at highest risk for cardiovascular morbidity and mortality [7].

There is an association found between hemodialysis and the development of pulmonary hypertension (PH) which is estimated to be around 17-56% [7,9,10,23].

Normal pulmonary artery pressure at sea level has a peak systolic value of 18-25 mmHg. Definite pulmonary hypertension is present when pulmonary artery systolic and mean pressures exceed 30 and 20mmHg, respectively [7].

Pathogenesis of renal failure associated with Pulmonary Hypertension is complex, and it may

include metabolic and hormonal derangements, high cardiac output due to arterio-venous fistula (AVF), impaired endothelial function, anemia, fluid overload, and other factors [11-13]

It is therefore important to detect the presence of pulmonary hypertension among patients undergoing hemodialysis, this is because CKD perse has increased cardiovascular morbidity and mortality ; but the genesis of pulmonary hypertension as a consequence of hemodialysis(a mode of Renal replacement therapy] will have summation effect on the cardiovascular complications ,thus reducing the life span of these patients.

Further, detecting the presence of PAH among patients secondary to RRT who are due for transplantation will guide us about the overall prognosis in the post-transplant period.

MATERIALS AND METHODS

This prospective study was conducted among non-dialysis and dialysis dependent chronic kidney disease. Dialysis patients included both hemodialysis and peritoneal dialysis respectively. A total of 100 patients (50 non-dialysis and 50 dialysis dependent) aged more than 18 yrs, who came to SDM College of Medical Sciences, Dharwad from November 2015 to November 2016 were included in the study.

Chronic kidney disease staging was done based on the GFR values that are obtained by CKD-EPI formula. The etiology of CKD was studied. The

mode of dialysis and duration of dialysis was documented. All the patients had complete hemogram, renal function tests, ultrasound abdomen, chest radiograph and 2D Echocardiogram. Two dimensional (2D) guided M-mode echocardiogram was performed with digital cardiac ultrasound machine.

On dialysis patients echo was done in the post-dialysis day as it allowed controlling volume state of the patient since it is associated with least intravascular volume. Pulmonary artery systolic pressure was recorded by tricuspid regurgitation jet method. Based on the pulmonary artery pressure, they were classified into three groups of mild degree (25-35mmhg), moderate (35-50mmhg) severe degree (>50 mmhg).

STATISTICAL ANALYSIS

Results were analyzed and presented as frequency, percentage, mean and standard deviation. Chi square was used to find an association between variables. p value < 0.05 was taken as statistically significant.

Data entry was done using Microsoft Excel and analysis was carried out with the help of Statistical Package for Social Sciences (SPSS Statistics 21).

RESULTS

100 Chronic Kidney Disease patients, 50 were dialysis dependent and remaining 50 of them were non-dialysis dependent (conservative management).

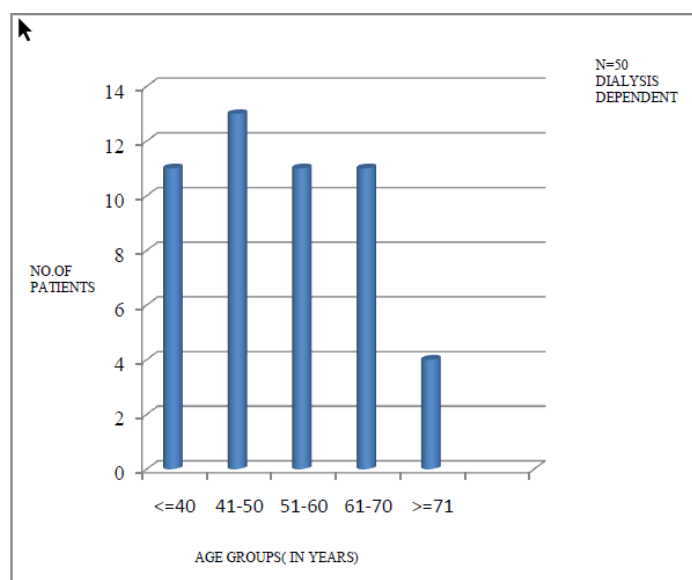


Fig-1: Age wise distribution of patients among Dialysis dependent group

Age wise distribution of patients among dialysis dependent group

Among the 50 dialysis-dependent CKD patients, 11(22%) of them were below 40 years of age; 13(26%) of were in the age groups of 41-50 years; 11(22%) were in the range of 51-60 years; 11(22%) in

the age group of 61-70 years and more than 71 years , there were 4(8%)patients.

Hence the mean age of the patients among the dialysis group is 53.04 years.

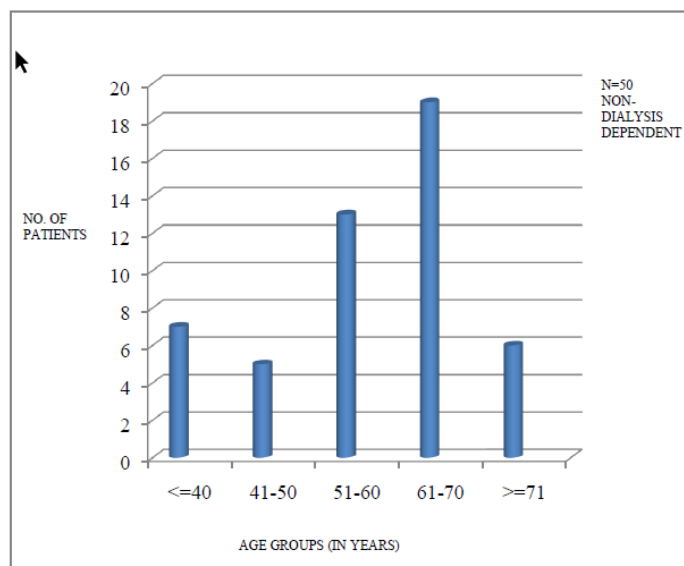


Fig-2: Age wise distribution of patients among Non –Dialysis dependent group

Age wise distribution of patients among non-dialysis dependent group

Of the 50 Non-Dialysis dependent CKD patients, 7(14%) of them were below 40 years of age, 5(10%) in the age group ranging from 41 to 50 years.

In the age group 51-60 years there were 13(26%) patient and in 61-70 years there were 19(38%) patients. There were 6(12%) patients above 70 years of age. The mean age in this group is 56.98 years.

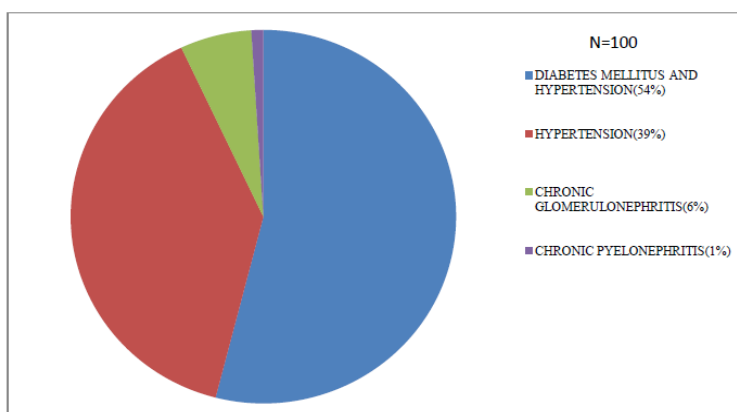


Fig-3: Etiology of chronic kidney disease among patients in the study

Etiology of chronic kidney disease among patients

Among the 100 CKD patients, 54(54%) had diabetes mellitus and hypertension as an etiology for their disease, whereas only hypertension as an etiology

was found in 39(39%) of the patients. 6(6%) patients had chronic glomerulonephritis as an cause of CKD and chronic pyelonephritis as an etiology is present in only 1(1%) patient that were included in the study.

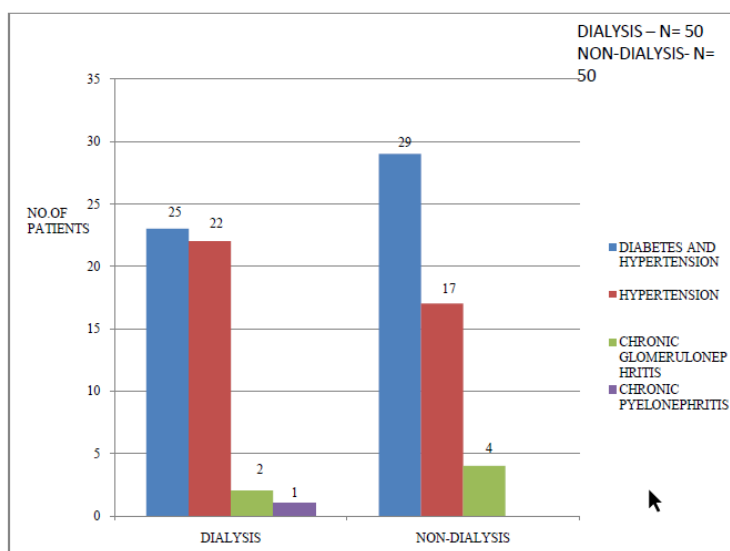


Fig-4: Etiology of chronic kidney disease among patients
Chi-square= 3.4764 P = 0.3243

Etiologies of chronic kidney disease among non-dialysis and dialysis dependent patients

In both the groups, it was found that diabetes mellitus and hypertension in combination is the most

common etiology for Chronic Kidney Disease among the patients in the study, followed by which is hypertension solely, chronic glomerulonephritis and chronic pyelonephritis.

Table-1: Duration of dialysis

Summary	Duration of dialysis (in months)
Minimum	4.00
Maximum	72.00
Mean	19.32
SD	15.52

Of the 50 dialysis dependent patients included in the study, minimum duration of dialysis is 4 months

and maximum being 72 months with mean duration being 19.32 months.

Table-2: Summary of hemoglobin levels among the patients

Groups	N	Minimum	Maximum	Mean	SD
Dialysis	50	6.20	12.70	8.67	1.44
Non-dialysis	50	7.10	11.20	9.33	1.08
Total	100	6.20	12.70	9.00	1.31

It is evident from the study that there is low level of haemoglobin among the CKD patients. The mean haemoglobin level among the 100 CKD patients is 9.00 with standard deviation of 1.31. Also it is noted

that in the dialysis group, the mean haemoglobin levels is 8.67 and in non-dialysis patients it was found to be 9.33

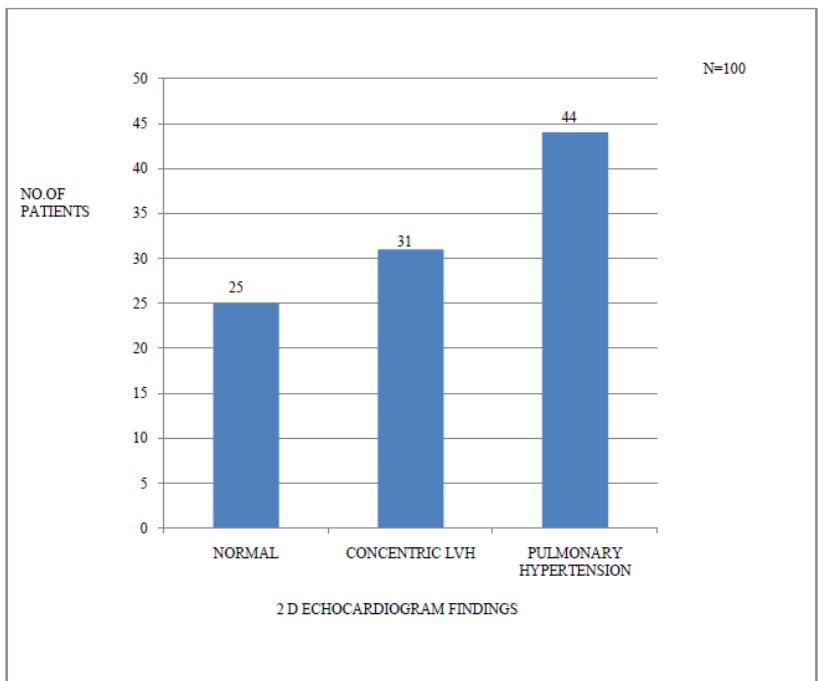


Fig-5: 2 D Echocardiogram findings

2 D echocardiogram was done in all the CKD patients those were included in the study, of them 44(44%) had pulmonary artery hypertension of varying

degrees, followed by that is 31(31%) patients had concentric left ventricular hypertrophy. 25(25%) of them had normal 2D echocardiogram study.

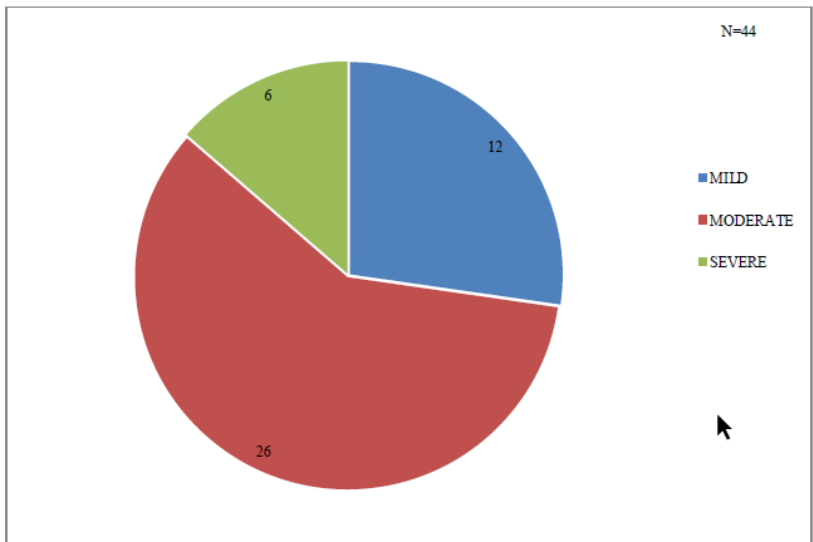


Fig-6: Severity of pulmonary hypertension

Various degrees of pulmonary hypertension are classified as mild, moderate and severe based on the pulmonary artery pressures. So, of 44 CKD patients those had pulmonary hypertension in the study,

12(27.27%) had mild pulmonary hypertension, 26(59.09%) had moderate and 6(13.63%) were having severe pulmonary hypertension.

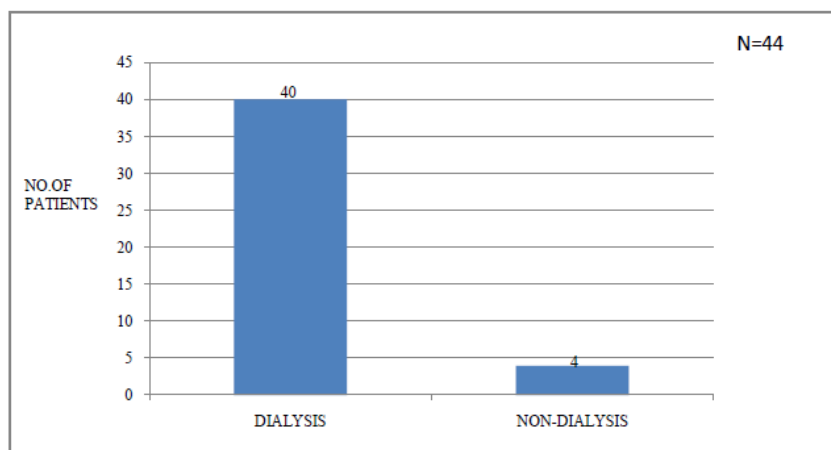


Fig-7: Comparison of pulmonary hypertension among non-dialysis and dialysis dependent patients
Chi-square= 52.6601 P = 0.0001

Among 44 CKD patients who had pulmonary artery hypertension, 40(90.9%) were on maintenance dialysis which is statistically significant with

remaining 4(9.09%) on conservative management, that is they are non-dialysis dependent patients

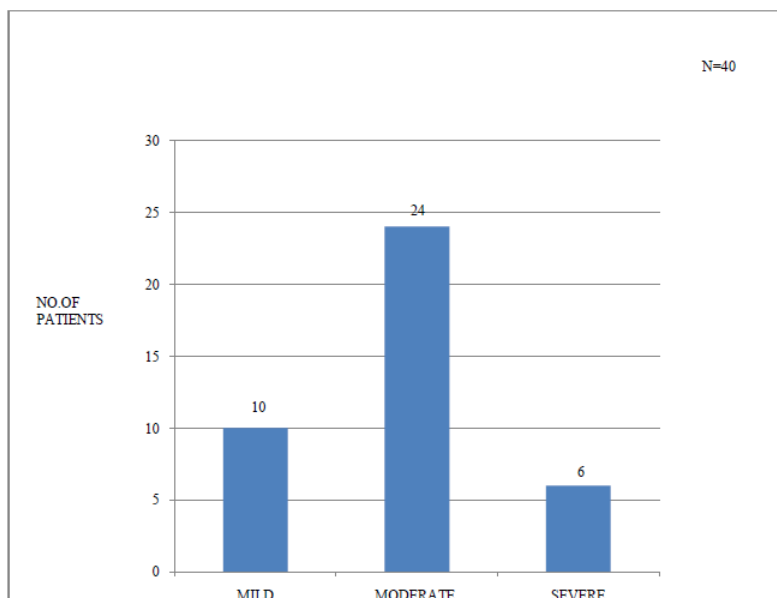


Fig-8: Degrees of pulmonary hypertension among dialysis dependent patients

Out of the 40 dialysis dependent patients those had pulmonary hypertension, 10(25%) had mild

24(60%) had moderate and 5(15%) had severe pulmonary hypertension.

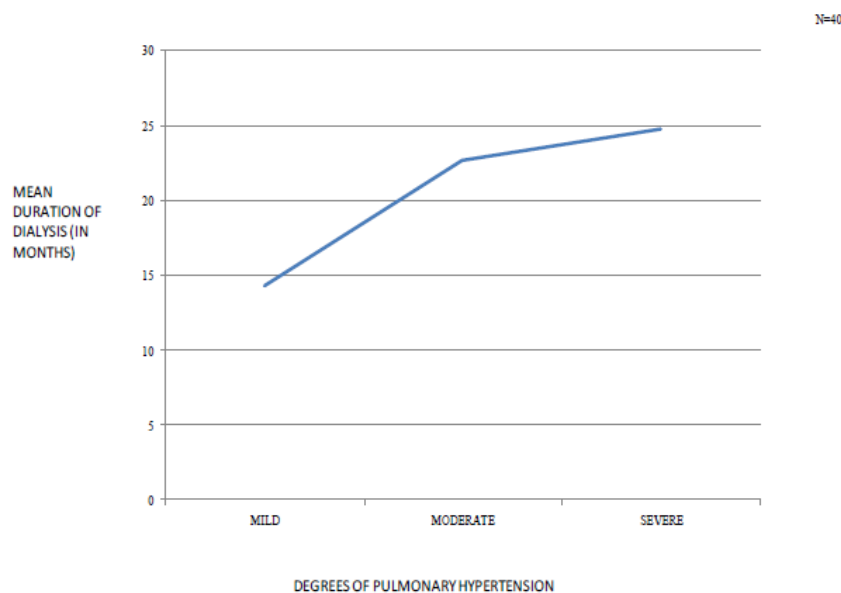


Fig-9: Relationship between mean duration of dialysis and severity of pulmonary hypertension

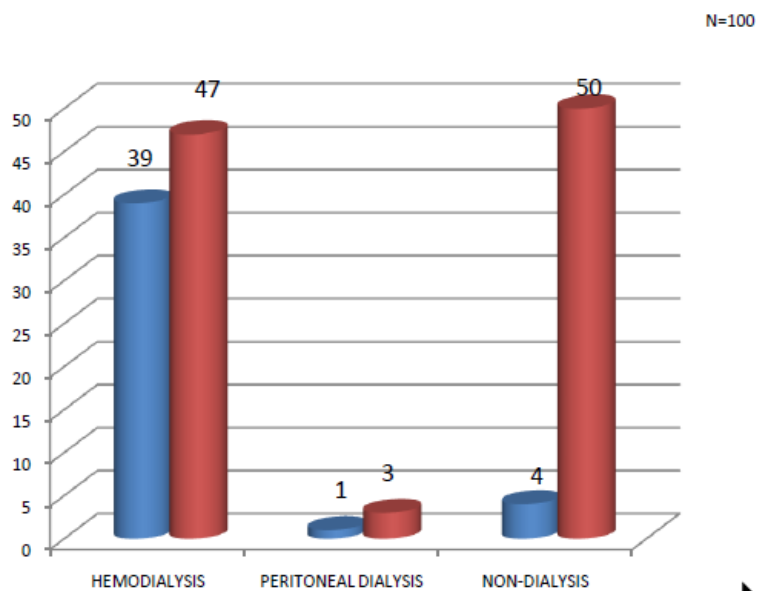


Fig-10: Comparison of pulmonary hypertension among different groups

From the above graph it is evident that, as the duration of dialysis increases the severity of pulmonary hypertension also raises that is seen in this study (Fig-9).

In the study it is also found that, among 47 patients on hemodialysis 39(82.97%) had pulmonary hypertension of varying degrees, out of 3 patients on peritoneal dialysis those met the inclusion criteria who were included in the study only 1(33.33%) had pulmonary hypertension. And out of 50 patients on conservative management, only 4(8%) had pulmonary hypertension.

DISCUSSION

Pulmonary hypertension (PH) is highly prevalent in end stage renal disease. The pathogenesis of PH in this population remains poorly understood. Reported associations include arteriovenous fistulae, cardiac dysfunction, fluid overload, bone mineral disorder and non-biocompatible dialysis membranes.

Due to small numbers and cross-sectional nature of majority of studies no consistent association with any particular risk factor has been demonstrated. Further, little is known about impact of ‘uraemicvasculopathy’ on pulmonary vasculature.

Hence there is a need for better understanding of natural history and the pathogenesis of the condition

which would help to individualize treatment of Pulmonary Hypertension in end stage renal disease.

In this study, an attempt was made to study the prevalence of pulmonary hypertension and probable etiology among CKD patients attending our hospital who were non-dialysis and dialysis (hemodialysis and peritoneal dialysis) dependent. Patients undergoing PD were on Continuous Ambulatory Peritoneal Dialysis (CAPD).

In our study, there were total of 100 CKD patients, who included 50 patients on conservative management (non-dialysis) and 50 patients were dialysis dependent. Among 50 dialysis patients, 47 were on hemodialysis and 3 were undergoing CAPD. Patients undergoing hemodialysis had access through arteriovenous fistula (AVF).

The mean age of patients in the dialysis group was found to be 53.04 years, and was 60.8 years in the study done by Farid N *et al.* [19]. In the non-dialysis group it was 56.95 years.

In our study, there were 35 males and 15 females each in non-dialysis and dialysis dependent groups. Considering the etiology of CKD in our patients, it was found that 54% of patients had diabetes mellitus plus hypertension as the cause which is comparable to the study done by Esam H *et al.* where he found that both these factors contributed to 65% as an etiology for CKD [21].

Among the dialysis dependent patients included in our study diabetes plus hypertension contributed to 47%, as an etiology which is comparable to the study done by M. Yigla *et al.* [18] that is 42.5%.

Chronic glomerulonephritis and chronic pyelonephritis as an etiology was seen in 6% and 1% of 100 CKD patients in our study; whereas among dialysis dependent patients it is 4% and 2% respectively that is comparable to the study done Esam H *et al.* [21] and Magady M *et al.* [20]. As compared to the last two factors, diabetes mellitus and hypertension ranks the list as common cause of CKD worldwide.

Among the dialysis dependent patients those were included in the study, the minimum and maximum duration of dialysis is 4 and 72 months respectively with mean of 19.32 months and standard deviation of 15.52, and whereas in the study done by P. Patel *et al.* the minimum duration was 10 months and maximum duration was 50 months [7]

Also, among 40 dialysis dependent patients who had pulmonary hypertension, 39(97.5%) were on hemodialysis and 1(2.5%) patient was undergoing CAPD. Such a high prevalence of pulmonary hypertension among hemodialysis patients is found in

various studies, one of the studies done by P. Patel *et al.* [7]. Mitra M *et al.* [14] found that Pulmonary Hypertension among hemodialysis patients was 51.6%.

About 40% of patients on HD with A-V fistula had pulmonary hypertension as shown in the study done by Mordechai Y *et al.* [15]. 49.3% of patients receiving HD had pulmonary hypertension as evidenced in the study done by Seyed A *et al.* [16].

Pulmonary hypertension was found in 30.6% of patients on hemodialysis as shown in the study done by Hugo H *et al.* [24]. 39% of patients had pulmonary hypertension undergoing HD as seen in cross sectional study done by Fabio F *et al.* [17]. 28(48%) of 42 HD patients had pulmonary hypertension as evidenced in the study done by Farid N *et al.* [19].

A high prevalence of pulmonary hypertension was demonstrated among 41.53% patients receiving hemodialysis as shown in study done by Magdy M *et al.* [20].

Regarding peritoneal dialysis, out of 3 patients undergoing CAPD that was included in my study, 1 patient (33.33%) had pulmonary hypertension; in the study done by Lalathaksha K *et al.* [22] prevalence of PH was 42% among PD patients. Therefore, as compared with hemodialysis patients, prevalence of PH is much less in CAPD patients which is comparable with study done by P. Patel *et al.* [7].

But, the limitation is that subjects included in the PD group are less. So, when three groups (conservative management, hemodialysis and peritoneal dialysis) were compared in terms of the prevalence of PH, high prevalence was noted in hemodialysis group as compared to other two which is similar to the observations in the study done by P. Patel [7].

Severity of pulmonary hypertension among the dialysis dependent group were classified into three, that comprised of 10(25%) patients having mild pulmonary hypertension, 24(60%) moderate and 6(15%) of them had severe pulmonary hypertension.

In our study, it was also found that the mean duration of dialysis in months is directly proportional to the severity of pulmonary hypertension. LVH is the common cardiac abnormality seen in ESRD patients; this is more marked in anemic populations [8]. In our study, among 100 CKD patients who had concentric LVH on 2 D Echo, their mean hemoglobin level was 8.74gm% which is comparable to the study done by Singh S *et al.* [8].

All the patients undergoing hemodialysis those were included in our study had AVF access and low hemoglobin levels, which probably could be the

reason for high prevalence of PH among these patients; along with other factors like lower hematocrit, serum bicarbonate and higher serum creatinine levels, which is also seen in the study done by Farid N *et al.* [19].

CONCLUSION

Cardiovascular complications are more common in patients with chronic kidney disease and certain complications gets aggravated when they are subjected to long term dialysis. Among those complications, pulmonary hypertension is of more importance. So in our study, it was found that prevalence of pulmonary hypertension is more common among patients on dialysis rather than those on conservative management.

Among dialysis group, hemodialysis patients had high prevalence as compared to peritoneal dialysis (PD), owing to their AVFs and other factors. Also, the prevalence linearly increases with the duration of hemodialysis. So this complication should be anticipated early in the course of the disease and should be addressed early.

Because the long term prognosis and mortality in these patients are directly proportional to the severity of pulmonary hypertension. So do we need to switch to alternate mode of dialysis, like PD should be thought upon; but again its efficacy as compared to hemodialysis is low.

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