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# Frequency of Left Ventricular Hypertrophy (LVH) in Patients on Regular Maintenance Haemodialysis and Its Risk Factors

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## ABSTRACT

**Introduction:** Cardiovascular complications are the leading cause of mortality and morbidity in hemodialysis (HD) patients accounting for 43% of all cause mortality, and the frequency of sudden cardiac death is almost 50% higher after long dialysis intervals. Left ventricular hypertrophy (LVH), a strong independent predictor of cardiovascular mortality, is potentially preventable and reversible. Hypertension is the main cause for the development of LVH, but other potentially reversible factors such as anemia may have an important role in its pathogenesis. **Objective:** The objective of the study was (i) determine the frequency of Left Ventricular Hypertrophy(LVH) in patients on regular maintenance haemodialysis (ii) to determine the frequency of hypertension, diabetes mellitus and anemia as factors leading to LVH in patients on regular maintenance haemodialysis. **Study design:** Cross-sectional survey. **Settings:** The Departments of Cardiology and Nephrology, Sheikh Zayed Hospital, Lahore. **Duration of study:** Six months after approval of the synopsis. From: August 14th, 2013 to February 14th, 2014. **Results:** In our study of 135 cases of ESRD patients on MHD who developed LVH were recorded as follows: 92.86%(n=104) had hypertension, 52.68%(n=59) had diabetes mellitus and 95.54%(n=107) had anemia. Out of 112 cases who developed LVH 2.68%(n=3) were between 18-30 years, 8.93%(n=10) were between 31-40 years, 30.36%(n=34) were between 41-50 years, 33.03% (n=37) were between 51-60 years and 25%(n=28) had age >60 years. **Conclusion:** The frequency of Left Ventricular Hypertrophy is high among patients with end stage renal disease on maintenance haemodialysis. So, it is recommended that every patient who is on maintenance haemodialysis, should be screened for LVH. However, every setup should have their own surveillance in order to know the frequency of the problem.

**Key Words:** End stage renal disease, maintenance haemodialysis, frequency, Left Ventricular Hypertrophy

## INTRODUCTION

Cardiovascular disease is the leading cause of death in patients with End-Stage Renal Disease (ESRD), being responsible for 43–52% of the overall mortality.[1] Cardiac death is up to 10-20 times more frequent in uremic patients than in the general population. Left Ventricular Hypertrophy (LVH) has been shown to be an independent risk factor related to overall mortality in such patients. Left ventricular hypertrophy is present in 75% of the patients who start haemodialysis.[2]

Both concentric hypertrophy, a result of LV pressure overload, and ec-centric hypertrophy, a result of LV volume overload, may occur.[3] Progressive LVH is characteristic of the dialysis state and has been associated with the development of de novo heart failure and QT prolongation which may predispose to sudden death. A reduction in LV hypertrophy (LVH) has been linked with an improvement in all-cause and cardiovascular survival.[4, 5]

Hypertension and anemia have been identified as risk factors for LVH in CKD patients.[6] Ifeoma I and workers[7] revealed in their study that 95.5% of their patients with CKD developed LVH and among them 85.2% had HTN, 14.8% had DM, and 66.2% patients had anemia. They determined anemia as a significant factor in development of LVH.

On the other hand Moncef EI and colleagues revealed in their study that 46.42 of ESRD patients developed LVH and out of them 42.31% patients were taking anti-hypertensive therapy[8], 46.15% had diabetes mellitus and 100% patient had anemia.

They also revealed that patients who developed LVH and those who did not develop LVH in ESRD had the same degree of anemia, identifying that anemia may not be a contributing factor to LVH in ESRD. These significant differences in the percentage of both studies have led to the need for further study.

Nonetheless, incident Haemodialysis (HD) patients without symptomatic cardiac disease exhibited progressive LVH regardless of whether anemia was treated.[9,10]

Other potential risk factors for progressive LVH in HD patients include age, gender, race, diabetes, primary renal disease, body mass index (BMI), dialysis vintage, hypertension, inter-dialytic weight gain, LV volume overload, type of vascular access,[11] and perhaps inflammation markers, some of which predict sudden death in incident HD patients.[12,13]

A study by Tian JP and colleagues recorded 68.8% developed LVH in patients on maintenance HD[14] while another study by Kadiri ME[15] demonstrated this in 46% patients .Ifeoma l determined 95.5% and Moncef El determined 46.42% developed LVH in ESRD. This wide range of variation in the frequency of LVH also creates the need of further study.

The rationale of my study is to determine the frequency of LVH in ESRD, due to the significant discrepancy in the percentage of LVH in ESRD as determined by Tian, Kadiri, Ifeoma and Moncef EI in previous studies and because no such study has been conducted in our targeted population.

Secondly, I want to determine if anemia is a significant contributing factor to LVH in ESRD patients due to the different results of Ifeoma and Moncef El.

Thirdly, I want to identify the factor which is most significantly contributing to LVH in ESRD and compare its frequency with previous international studies to determine if any significant difference exists. This will help direct treatment for ESRD patients to correct the most significant contributing factor causing LVH in ESRD. This will give the maximum benefit to poor patients with their limited finances as these patients often cannot afford full treatment. This will help decrease LVH in our patients and will set guidelines in our population.

**The Objective of the study**

- To determine the frequency of Left Ventricular Hypertrophy(LVH) in patients on regular maintenance haemodialysis
- To determine the frequency of hypertension, diabetes mellitus and anemia as factors leading to LVH in patients on regular maintenance haemodialysis.

## OPERATIONAL DEFINITIONS

**End Stage Renal Disease**

Patients who had a GFR of less than 15ml/min. i.e. patients needing renal replacement therapy which include renal transplant or maintenance hemodialysis (GFR was calculated using the "MDRD equation “which includes four variables: serum creatinine, age, ethnicity, and gender)[16]

**Regular maintenance haemodialysis**

Patients undergoing haemodialysis two times per week

**Left ventricular hypertrophy (LVH)**

It was defined as >12mm thickening of the myocardium (muscle) of the left ventricle of the heart (assessed on Echocardiography according to the recommendations of the American Society of Echocardiography).[17]

**Anemia**

Hemoglobin < 12 g/dL for female subjects and <13 g/dL for male subjects was considered as

anemia, and these findings were confirmed through hospital laboratory examination.)[7]

**Diabetes mellitus**

It was considered according to the new diagnostic criteria based on two fasting plasma glucose levels of more than 126 milligram per deciliter (mg/dL) or subjects on anti-diabetic therapy. for ≥5years

**Hypertension**

It was those patients having hypertension or taking anti-hypertensive drugs for ≥5years (confirmed on history and medical record).

## MATERIAL AND METHODS

**Study Design**

Cross-sectional survey

**Settings**

The Departments of Cardiology and Nephrology, Sheikh Zayed Hospital, Lahore.

**Duration of Study**

Six months after approval of the synopsis from: August 14th, 2013 to February 14th, 2014

**Sample size**

The calculated sample size is 135, with 6% margin of error, 95% confidence level taking expected percentage of DM as 14.8% (least among all contributing factors leading to LVH in patients on maintenance haemodialysis).

**Sampling Technique**

- Non probability purposive sampling

**Inclusion Criteria**

- Age >18 years
- Both genders
- Diagnosed cases of end stage renal disease on maintenance haemodialysis for more than six months (confirmed on history and medical record)

**Exclusion Criteria**

- Segmental wall abnormality (confirmed by echocardiography)
- Structural valvular heart disease (confirmed by echocardiography)
- Hypertrophic cardiomyopathies (confirmed by echocardiography)

**Data Collection Procedure**

A total of 135 cases fulfilling the inclusion/exclusion criteria were enrolled from amongst patients coming to Sheikh Zayed Hospital, Lahore, for haemodialysis. Exclusion criteria were strictly followed to avoid any potential effect modifiers. Echocardiography was performed by a well-trained echocardiographer, using Toshiba Applio 50 echocardiography system using 2.5MHz transducer within 24 hours after the haemodialysis session. Two dimensionally (2D) guided M Mode echocardiographic measurements were taken according to the recommendations of the American Society of Echocardiography and the presence/absence of LVH was recorded. Blood sample was sent to the lab for hemoglobin estimation. All information including demographics i.e. age, gender and presence/absence of LVH and its risk factors (HTN, DM and anemia) was recorded on a pre-designed proforma (Annexure).

**Statistical Analysis**

The collected data was entered and analyzed in computer software SPSS software (version 14.0). The quantitative data (age) was presented as mean ± SD. Frequency and percentages of LVH in patients with end stage renal disease on maintenance haemodialysis and factors leading to of LVH (HTN, DM and anemia), and gender was calculated for qualitative data. Stratification for age (18-30, 31-40, 41-50, 51-60,>60) and gender was also done to control the effect modifiers.

## RESULTS

A total of 135 cases fulfilling the inclusion/exclusion criteria were enrolled to determine the frequency of Left Ventricular Hypertrophy (LVH) in patients on regular maintenance haemodialysis and to determine the frequency of anemia, hypertension and diabetes mellitus as factors leading to LVH in patients on

regular maintenance haemodialysis.

Age distribution of all the patients enrolled in the study was done which shows that 5.19%(n=7) were between 18-30 years, 11.85%(n=16) were between 31-40 years, 28.89%(n=39) were between 41-50 years, 30.37%(n=41) were between 51-60 years while 23.70%(n=32) had >60 years of age. Mean±SD was calculated as 50.61±11.25 years. (Table 1)

Gender distribution of all the patients was done which shows 60 % (n=81) were male and 40% (n=54) were females (Table 2).

**Table 1: Age distribution (n=135)**

| Age(in years) | No. of patients | % |
|---|---|---|
| 18-30 | 7 | 5.19 |
| 31-40 | 16 | 11.85 |
| 41-50 | 39 | 28.89 |
| 51-60 | 41 | 30.37 |
| >60 | 32 | 23.70 |
| **Total** | **135** | **100** |
| **Mean±SD** | **50.61±11.25** | |

**Table 2: Gender distribution (n=135).**

| Gender | No. of patients | % |
|---|---|---|
| Male | 81 | 60 |
| Female | 54 | 40 |
| **Total** | **135** | **100** |

The frequency of left ventricular hypertrophy (LVH) was 82.96% (n=112) while 17.04% (n=23) had no LVH (Table 3).

**Table 3: Frequency of LVH in patients on regular maintenance haemodialysis (n=135)**

| LVH | No. of patients | % |
|---|---|---|
| Yes | 112 | 82.96 |
| No | 23 | 17.04 |
| **Total** | **135** | **100** |

The frequency of the risk factors with LVH was that 95.54% (n=107) had anemia, 92.86% (n=104) had hypertension and 52.68% (n=59) had diabetes mellitus. The number of patients with these risk factors but with no LVH was that 39.13% (n=9) had HTN, 39.13% (n=9) had DM and 21.74% (n=5) had anemia. P-value was determined to find statistical significance of risk factors between the LVH group and those who did not have LVH and this is given in Table 4

**Table 4: Frequency of hypertension, diabetes mellitus and anemia in patients on regular maintenance haemodialysis (n=135)**

| Factors | With LVH (n=112) | | Without LVH (n=23) | | P value |
|---|---|---|---|---|---|
| | No. | % | No. | % | |
| Hypertension (113) | 104 | 92.86 | 9 | 39.13 | 0.00 |
| Diabetes mellitus (68) | 59 | 52.68 | 9 | 39.13 | 0.261 |
| Anemia (112) | 107 | 95.54 | 5 | 21.74 | 0.00 |

Stratification for age was done for patients with LVH which shows that out of 112 cases 2.68% (n=3) were between 18-30 years, 8.93% (n=10) were between 31-40 years, 30.36% (n=34) were between 41-50 years, 3303% (n=37) were between 51-60 years and 25% (n=28) had >60 years. Significantly more patients developed LVH in the age group >40 years versus those <40 years of age when compared with those who did not have LVH (p=0.0003) (Table 5a and 5b).

**Table 5a: Stratification for age (n=135)**

| Age (in year) | With LVH (n=112) | | Without LVH (n=23) | |
|---|---|---|---|---|
| | No. | % | No. | % |
| 18-30 | 3 | 2.68 | 4 | 17.39 |
| 31-40 | 10 | 8.93 | 6 | 26.09 |
| 41-50 | 34 | 30.36 | 5 | 21.74 |
| 51-60 | 37 | 33.03 | 4 | 17.39 |
| >60 | 28 | 25 | 4 | 17.39 |
| **TOTAL** | **112** | **100** | **23** | **100** |

**Table 5b: Stratification for age (n=135)**

| Age (in year) | With LVH (n=112) | | Without LVH (n=23) | |
|---|---|---|---|---|
| | No. | % | No. | % |
| 18-40 | 13 | 11.61 | 10 | 43.48 |
| >41 | 99 | 88.39 | 13 | 56.52 |
| **Total** | **112** | **100** | **23** | **100** |

P value=0.0003

Out of 81 males 66 developed LVH making 81% and out of 54 females 46 developed LVH making 85 % (Table 6).

**Table 6: Stratification for gender in patients with LVH.**

| Gender | Total | LVH | % |
|---|---|---|---|
| Male | 81 | 66 | 81 |
| Female | 54 | 46 | 85 |
| Total | **135** | **112** | |

## DISCUSSION

Cardiovascular disease is the most common cause of death in patients with end-stage renal disease (ESRD) and accounts for most of the morbidity in these population.[18-19] Dialysis patients are subject to atherosclerosis eventually leading to ischemic heart disease and myocardial dysfunction causing heart failure all which are highly prevalent. Eighty-four percent of patients at initiation of ESRD therapy have left ventricular hypertrophy (LVH), left ventricular (LV) dilatation, or low fractional shortening, and LVH has been found in 38% of patients with chronic renal failure (CRF) prior to the requirement for dialysis.[20] The presence of LVH or LV dilatation (or both) is clearly a poor prognostic factor.[21-23]

The current study was designed to determine LVH in ESRD patients on maintenance hemodialysis (MHD), due to the significant discrepancy in the percentage determined in previous studies and because no such study has been conducted in our targeted population.

Our study showed that the percentage of patients who had developed LVH in ESRD on MHD was 82.96%.This result was more in agreement with results of Ifeoma[7] and Tian[14] ,they determined it in 95.5% and 68.8% patients respectively, both which were over 50% and significantly high. The study by Kadiri[15] and Moncef El determined it in 46% and 46.42% patients respectively both which were less than 50% and considerably lower.

Our study also showed that in the patients, who developed LVH, 95.54% had anemia, 92.86% had hypertension and 52.68% had diabetes mellitus. These findings are more in agreement with Moncef EI and colleagues' study as they showed that 100% patients had anemia, 42.31% had hypertension and 46.15% had diabetes mellitus. These results signify that anemia was the most significant contributing risk factor leading to LVH in patients on MHD followed by hypertension and then diabetes mellitus.

London noted that anemia is present in most patients initiating dialysis and that it could explain the high prevalence of LVH in these patients.[24]

In a study by Ulasi et al[25], a strong relationship was found between anemia and the prevalence of LVH in patients with chronic renal failure. Anemia has been consistently associated with cardiovascular morbidity and LVH in the ESRD population and the results of this study are consistent with those in the literature.[26-27] Anemia leads to an increase in cardiac workload which subsequently leads to development of LVH.

Several studies have been done to demonstrate if the reversal of anemia, using erythropoietin therapy, results in partial regression of LVH in the dialysis population with conflicting results.[28-29]

In our study, on stratification for the risk factors for LVH and without LVH (table 4), Anemia and Hypertension were significantly higher in the LVH group than in the non LVH group (P=0.00). Diabetes was commonly seen but as it was present in almost similar percentage in both the LVH and non-LVH groups (P=0.261) it could not be identified as a significant risk factor for the development of LVH. May be a study with a larger sample size could show significance.

On stratification for age (Table 5) for LVH and without LVH, we determined that age groups >40years were significantly more prone for the prevalence of LVH as compared to the age group 18-40years.The most likely reason that can explain this variation with age is due to the longer duration of the risk factors and ESRD in the elderly age group.

Lastly on the stratification for gender for LVH and without LVH there was no significant difference.

The main limitation of our study is that it is a single center study with relatively small number of patients and the long term outcome for our patients

is not available.

We have identified anemia as the most significant contributing factor for LVH in ESRD followed by hypertension but diabetes mellitus could not be established as a significant risk factor. These results will be helpful in directing our management of ESRD patients towards correction of anemia and hypertension to prevent LVH and its associated morbidity and mortality. This will give the maximum benefit to poor patients with their limited finances as these patients often cannot afford full treatment. By controlling the contributing factors in this order we may decrease LVH in our patients and the subsequent morbidity and mortality.

## CONCLUSION

We concluded that the frequency of Left Ventricular Hypertrophy is high among ESRD patients on maintenance hemodialysis and that anemia and hypertension are the leading risk factors for the development of LVH in these patents. These factors should be controlled to prevent the development of LVH which is an independent marker for subsequent morbidity and mortality.

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