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To Study the Serial Echocardiographic Changes and their Clinical Correlation with Anaemia and Hypertension in end Stage Renal Disease (ESRD) Patients on Maintenance Haemodialysis

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Abstract
Background and Purpose: *Left ventricular systolic and diastolic dysfunction is found in patients of end stage renal disease (ESRD) on maintenance haemodialysis. Main motive of this research is to identify the major determinant of left ventricular dysfunction and shed on some light to imply proper measures to prevent it.*
Objectives: *To study the serial Echocardiographic changes and their clinical correlation with anaemia and hypertension in end stage renal disease (ESRD) patients on maintenance haemodialysis.*
Methods: *The patients of end stage renal disease were taken into detailed history, examination and investigations at presentation (0^{th} month) and at the end of 6th month. Echocardiography machine PHILIPS USA Mode – HD11XE was used with 24-2 transducer probe. Two dimensional echocardiography was performed. The LVEF was taken as measure of left ventricular systolic function. E/A ratio was taken as measure of left ventricular diastolic function. Echocardiographic findings were compared with anaemia and hypertension by serially monitoring the patients over a period of 6 months.*
Results: *Prevalence of ESRD was higher among males in anaemic, normotensive anaemic, anaemic and hypertensive groups. Prevalence of ESRD was higher among females in hypertensives, hypertensive patients without anaemia and in anaemic and hypertensive patients.*
There was overall increasing trend in prevalence of systolic dysfunction as the duration of the disease progresses in patients of ESRD on maintenance haemodialysis. However, there was improvement in systolic dysfunction in anaemic patients, anaemic patients without hypertension and it remained static in hypertensive patients. There was deterioration of systolic dysfunction in the groups of, hypertensive patients without anaemia, hypertensive and anaemic patients. There was deterioration of diastolic function in the patients of ESRD on maintenance haemodialysis in all the groups. However, overall diastolic dysfunction prevalence increased to a greater extent in hypertensive patients without anaemia when compared to other two groups. But grade III diastolic dysfunction prevalence was increased to a greater extent in patients of hypertensive and anaemic patients.
Conclusion: *The left ventricular systolic and diastolic dysfunction can occur in patients of ESRD on maintenance haemodialysis. Hypertension was the major determinant of systolic and diastolic dysfunction in patients of ESRD on maintenance haemodialysis.*
Keyword: *ESRD, Echocardiography, Left ventricular systolic function, Left ventricular diastolic function.*

Introduction

End stage renal disease (ESRD) is the irreversible deterioration of renal function which results into impairment of excretory, metabolic and endocrine functions leading to development of the clinical syndrome of ureamia. Chronic Kidney Disease (CKD) is a major public health problem worldwide with increase in incidence and prevalence. Diabetes (DM) and hypertension are the leading cause of CKD worldwide, whereas hypertension is a cause as well as effects of CKD. The known common cardiac abnormalities in ESRD are increase in LV cavity size, thickened LV posterior wall, thickened interventricular septum, region wall motion abnormality, decrease in LV compliance, pericardial effusion and calcific/sclerotic valves.(1) Cardiovascular disease is the most common cause of mortality in patients with end-stage renal disease. Determining the spectrum of echocardiographic abnormalities in these patients can help the prevention of mortality in this group of chronically ill patients.

4 main structural abnormalities of the heart have been described in patients with CKD: LV hypertrophy, expansion of the nonvascular cardiac interstitium leading to inter-myocardiocytic fibrosis, changes in vascular architecture, and myocardial calcification. All these abnormalities promote systolic dysfunction measured by LVEF measurement in haemodialysis patients(2)

The association of anemia with both acute and chronic renal failure has been recognized for over 100 years. It is a hypoproliferative anemia with generally normocytic red cells and is seen invariably when patients with ESRD become symptomatic of uremia and require hemodialysis or peritoneal dialysis. The association of anemia with the kidney is important because this organ is responsible both for sensing oxygen availability to tissues and for releasing erythropoietin (Ep) into the circulation. [3, 4] Hypertension is a frequent complication ESRD. Numerous studies have established that chronic parenchymal renal disease is the most common cause of secondary hypertension, accounting for approximately 5% of all patients with hypertension. [5]. Hypertension is an independent risk factor for ESRD, particularly in African-Americans, [6] but in many ESRD patients hypertension develops as a result of the intrinsic renal malady.

Material and Methods

Patients attending out-patient and in-patient from 1/1/2016 to 31/12/2016 at PG department of Medicine who are diagnosed with CKD (irrespective of etiology) having ESRD (stage 5 CKD) were included in the study. The subjects were taken into detailed history, examination and investigations at 2 times. These include at presentation (0^{th} month) and at the end of 6 month. The patients included in the study are those giving consent, illness was of more than 3 months duration, abnormal USG findings suggestive of medical renal disease, GFR was below 15 ml/min per $1.73m^2$ as per Cockcroft Gault equation, patients on haemodialysis, a known case of ESRD, a patient with clinical sign/ symptoms suggestive of ESRD. The patients excluded from the study are those with pre-existing cardiac disease like rheumatic heart disease, congenital heart disease, pre-existing cardiovascular disease like myocarditis due to infective aetiology, primary heart muscle diseases like cardiomyopathies, pre-existing coronary artery disease, acute coronary syndrome, not giving consent, who were expired or opted out of the study during the study period, acute renal failure. All patients were subjected to a detailed history and thorough clinical examination. All these patients were clinically evaluated for cardiac involvement. The findings were recorded on the proforma. Haemoglobin was measured in all the cases at 0^{th} and 6^{th} month. Creatinine clearance was calculated using the formula

$$\text{Cock Croft gault equation CrCl} = \frac{140 - \text{age} \times (\text{Wt in kg})}{\text{S. creatinine} \times 72}$$

for male[15]

$$\text{Cock Croft gault equation CrCl} = \frac{140 - \text{age} \times (\text{Wt in kg}) \times 0.85}{\text{S. creatinine} \times 72}$$

for female[15]

Those patients with Creatinine Clearance < 15 ml/min were included in the study. Plain X-ray chest (P-A view) and X-ray Abdomen (KUB) were taken and the standard 12 lead electrocardiograms recorded. Echocardiography was done at the end of 0^{th} and 6^{th} month. Echocardiography machine PHILIPS USA Mode – HD11XE was used with 24-2 transducer probe. Two dimensional echocardiography was performed. The LVEF was taken as measure of left ventricular systolic function. E/A ratio was taken as measure of left ventricular diastolic function. Following parameters of echocardiography were studied and analysed in detail - Left ventricular end-diastolic volume in systole(ml), Left ventricular end-diastolic volume in diastole(ml), LVEF(Left ventricular Ejection Fraction) (%) and E/A ratio. Ejection fraction was calculated as

LV EF (%) = (LVEDd-LVEDs)/ (LVEDd) × 100

Normal = 59.2 ± 6%

- LVEDd: Left ventricle volume at end-diastole
- LVEDs: Left ventricle volume at end-systole

E/A ratio was taken for assessment of diastolic dysfunction where E is the early diastolic mitral inflow velocity and A is late diastolic mitral inflow velocity.

Descriptive data were examined for all variables. For continuous variables results were presented as Mean±SD, statistical difference in variables were compared using one way analysis of variance ANOVA. Categorical variables were recorded as frequency counts and intergroup comparisions were analysed by Chi-square test. Statistical significance was accepted if p value <0.05.

Observations

Table 1 Sex Wise Distribution

	Male		Female		Total	
	No.	%	No.	%	No.	%
Anaemia	26	81.25	6	18.75	32	100
Hypertension	12	36.36	21	63.64	33	100
Anaemia+ Hypertension	15	42.86	20	57.14	35	100

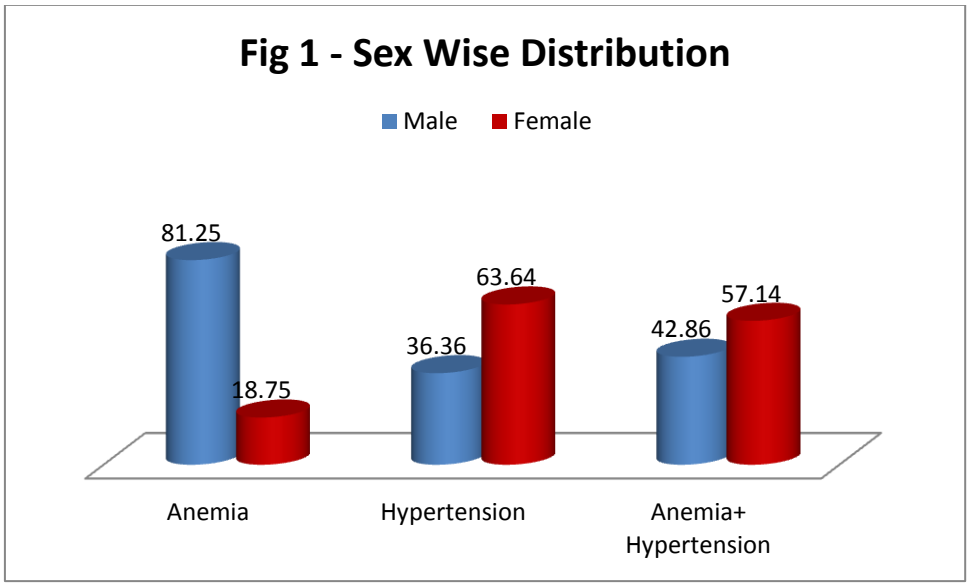


Table 2 Systolic Dysfunction [LVEF (%)] In ESRD on Maintenance Haemodialysis

	N	0th month				6th month			
		Normal		Abnormal		Normal		Abnormal	
		No.	%	No.	%	No.	%	No.	%
Anaemia	32	30	93.75	2	6.25	29	90.625	3	9.375
Hypertension	33	32	96.97	1	3.03	30	90.91	3	9.09
Anaemia with Hypertension	35	29	82.86	6	17.14	31	88.57	4	11.43
Total	100	91	91	9	9	90	90	10	10

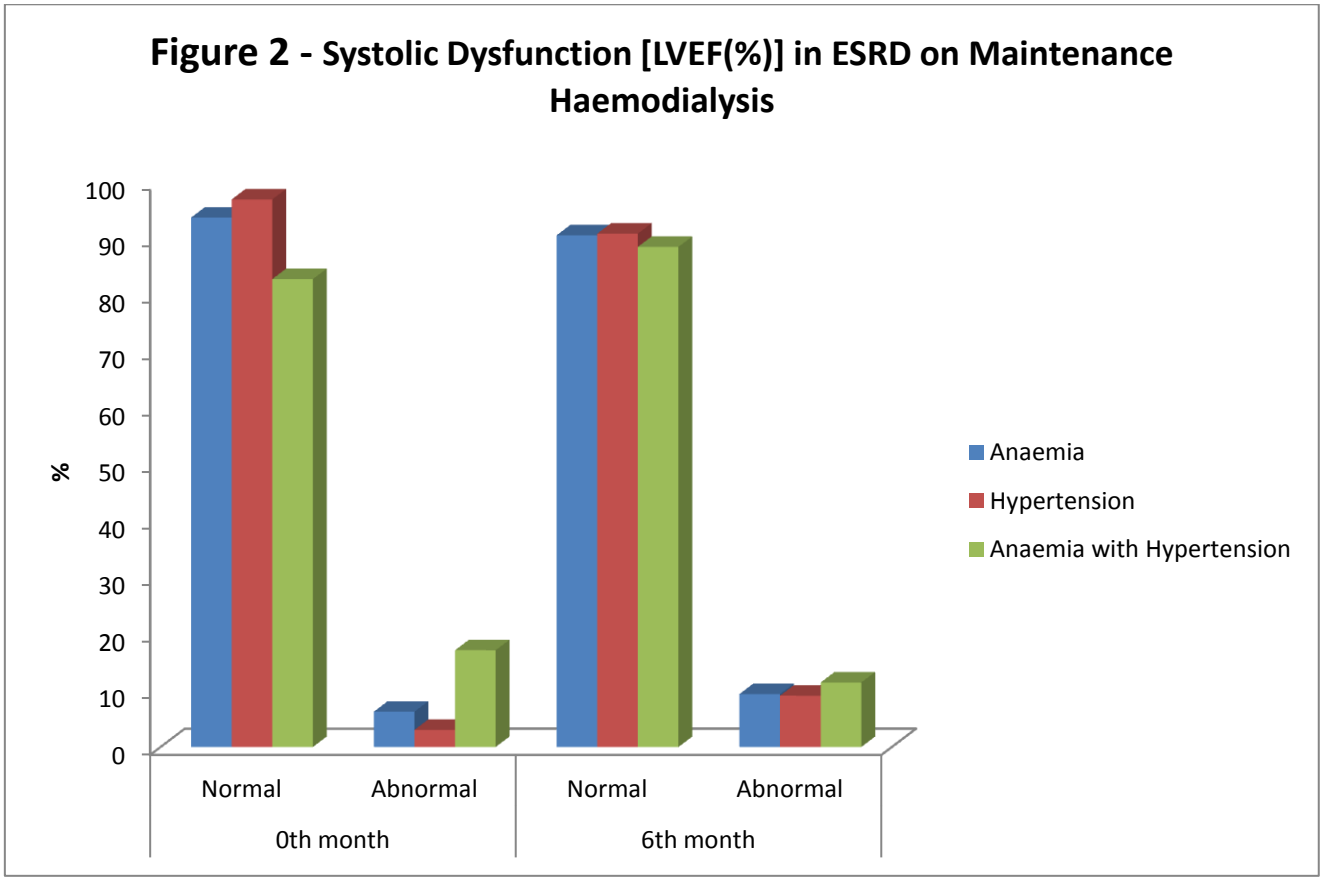
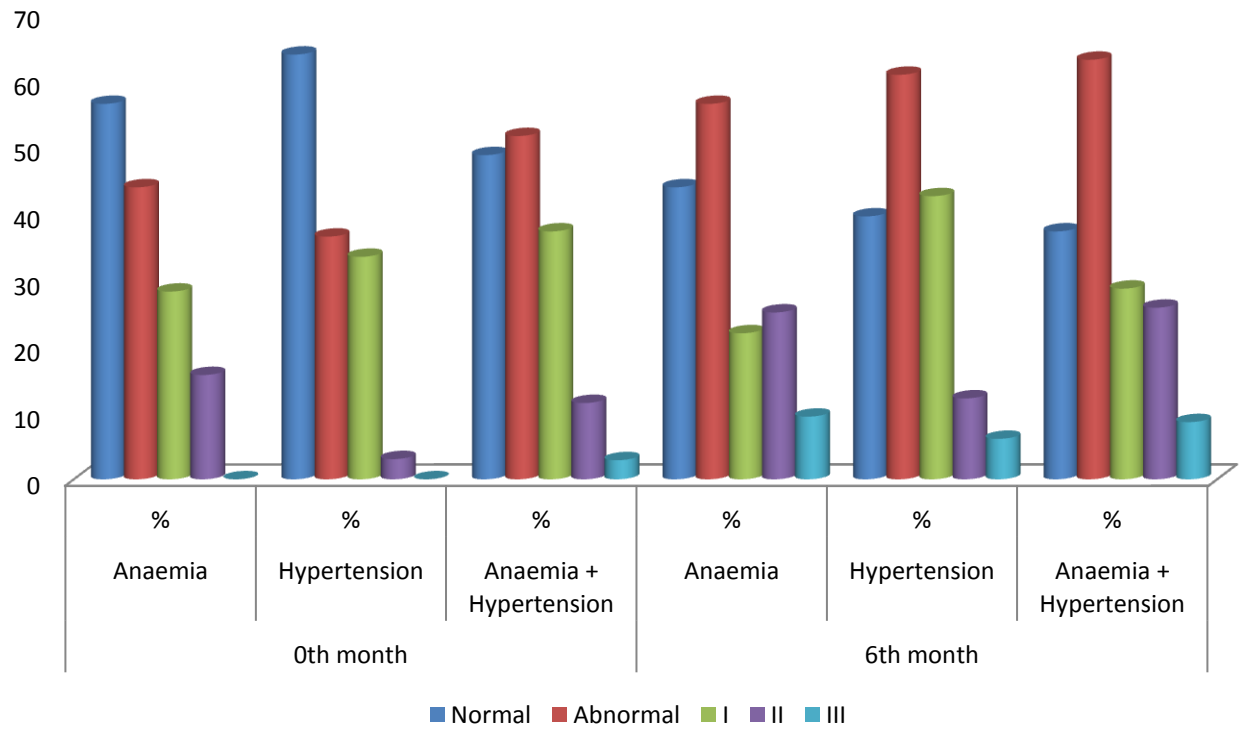


Table 3 Diastolic Dysfunction in ESRD on Maintenance Haemodialysis

Grade	0th month							6th month						
	Anaemia (N=32)		Hypertension (N=33)		Anaemia + Hypertension (N=35)		Total	Anaemia (N=32)		Hypertension (N=33)		Anaemia + Hypertension (N=35)		Total
	No.	%	No.	%	No.	%		No.	%	No.	%	No.	%	
Normal	18	56.25	21	63.64	17	48.57	56	14	43.75	13	39.39	13	37.14	40
Abnormal	14	43.75	12	36.36	18	51.43	44	18	56.25	20	60.61	22	62.86	60
I	9	28.125	11	33.33	13	37.14	33	7	21.88	14	42.42	10	28.57	31
II	5	15.625	1	3.03	4	11.43	10	8	25	4	12.12	9	25.71	21
III	0	0	0	0.00	1	2.86	1	3	9.38	2	6.06	3	8.57	8

Figure 3 - Diastolic Dysfunction in ESRD on Maintenance Haemodialysis



Results

In the present study, 100 cases of ESRD patients on maintenance haemodialysis were taken. Cases were divided into 3 groups. Group-1 had normotensive anaemic patients, group-2 had hypertensive patients without anaemia patients and group-3 had hypertensive with anaemic patients. Serial echocardiography was done in these patients at presentation (0^{th} month) and at the end of 6^{th} month. Results were analysed.

The prevalence of the patients in different disease groups in our study is anaemia with normotensive patients (Blood Pressure is either drug controlled/by default) (32%), hypertension without anaemia (Anaemia is either drug controlled/ by default) (33%) and hypertension with anaemia(35%). In these groups 15 and 20 out of 35 anaemic and hypertensives; 26 and 6 out of 32 normotensive anaemics; 12 and 21 out of 33 hypertensive patients without anaemia were males & females respectively.

The prevalence of systolic dysfunction increased from 9% at 0^{th} month to 10% at 6^{th} month in our study. The prevalence of systolic dysfunction increased from 6.25% at 0^{th} month to 9.375% at 6^{th} month in anaemic patients without hypertension. The prevalence of systolic dysfunction increased from 3.03% at 0^{th} month to 9.09% at 6^{th} month in hypertensive patients without anaemia. The prevalence of systolic dysfunction reduced from 17.14% at 0^{th} month to 11.43% at 6^{th} month in hypertensive and anaemic patients.

The prevalence of diastolic dysfunction increased from 44% at 0^{th} month to 60% at 6^{th} month among which prevalence of grade III diastolic dysfunction increased from 1% at 0^{th} month to 9% at 6^{th} month. The prevalence of diastolic dysfunction increased from 43.75% at 0^{th} month to 56.25% at 6^{th} month in anaemic patients without hypertension among which prevalence of grade III diastolic dysfunction increased from 0% at 0^{th} month to 9.38% at 6^{th} month. The prevalence of diastolic dysfunction increased from 36.36% at 0^{th} month to 60.61% at 6^{th} month in hypertensive patients without anaemia among

which prevalence of grade III diastolic dysfunction increased from 0% at 0th month to 6.06% at 6th month. The prevalence of diastolic dysfunction increased from 51.43% at 0th month to 62.86% at 6th month in hypertensive and anaemic patients among which prevalence of grade III diastolic dysfunction increased from 2.86% at 0th month to 8.57% at 6th month.

Discussion

Although it is well established that compromised systolic function predicts cardiovascular (CV) complications in symptomatic and asymptomatic patients with ESRD, it still is unknown whether repeated echocardiographic measurements of systolic and diastolic function in asymptomatic patients with ESRD is useful for monitoring the evolution of cardiomyopathy in these patients. The detection of echocardiographic abnormalities associated with subclinical cardiac disease is considered to be an important step for the characterization of individuals at risk for developing cardiac complications in the general population. [7]

In our study, both systolic and diastolic function worsened on serial monitoring over 6 months in patients of ESRD on maintenance haemodialysis. In previous studies, Sanjay Gupta. et al. reported that patients with end-stage renal disease have impaired LV diastolic function that improves with haemodialysis[8]; Robert N. et al. has reported that clinical and echocardiographic cardiovascular disease are already present in a very high proportion of patients starting ESRD therapy and are independent mortality factors[9] ; and Robert N. et al. reported that even moderate hypertension worsens the echocardiographic and clinical outcome in ESRD patients, especially in those without previous clinical cardiac disease. [10]

In our study, there was overall worsening of systolic and diastolic function in hypertensive and anaemic groups. However, systolic function improved in anaemia with hypertension patients of ESRD on maintenance haemodialysis. Previously, Levin. et al. reported association between elevated systolic blood pressure and low hemoglobin level with LVH in predialysis patients.[11]

In our study, the prevalence of systolic dysfunction increased from 9% at 0th month to 10% at 6th month in our study; and of diastolic dysfunction increased from 44% at 0th month to 60% at 6th month among which the prevalence of grade III diastolic dysfunction increased from 1% at 0th month to 9% at 6th month in patients of ESRD on maintenance haemodialysis. In previous studies, Zoccali C et al. has reported incidence of LVH and systolic dysfunction of 77% and 22% respectively in ESRD population on hemodialysis[12] ; S.Agarwal. et al. has observed diastolic dysfunction in 60% and systolic dysfunction in 15% of patients of ESRD[13]; and Laddha M et al., reported LVH in 74%, systolic dysfunction in 24.3%, diastolic dysfunction in 61.4% and pericardial effusion in 14.35% of ESRD patients on haemodialysis.[14]

There was overall increasing trend in occurrence of systolic dysfunction as the duration of the disease progresses in patients of ESRD on maintenance haemodialysis.. There was more obvious deterioration of systolic dysfunction in the groups of hypertensive patients without anaemia and in hypertension with anaemic patients. This shows hypertension was the major determinant of systolic dysfunction in patients of ESRD on maintenance haemodialysis.

There was overall increasing trend in occurrence of diastolic dysfunction as the duration of the disease progresses in patients of ESRD on maintenance haemodialysis. However, overall diastolic dysfunction occurrence increased to a greater extent in hypertensive patients without anaemia when compared to other two groups. But grade III diastolic dysfunction occurrence was increased to a greater extent in patients of hypertensive and anaemic patients. This again concludes that hypertension was the major determinant of diastolic dysfunction in patients of ESRD on maintenance haemodialysis.

ESRD was more common among males in anaemic patients whereas it was more common among females in hypertensive groups.

Conclusion

The anaemia is more common in males as compared to females; hypertension is more common in females as compared to males in patients of ESRD on maintenance haemodialysis. The left ventricular systolic and diastolic function can occur in patients of ESRD on maintenance haemodialysis. Hypertension was the major determinant of systolic and diastolic dysfunction in patients of ESRD on maintenance haemodialysis.

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