ORIGINAL ARTICLES

Cardiac Complications in Haemodialysis Patients with Special Reference to Diabetic (NIDDM) Subset

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Summary

This cross-sectional study was done to see the prevalence of cardiac complications in maintenance haemodialysis with special attention to diabetic subset along with a yearly follow-up upto two years. Thirty patients were selected, 76.6% (n=23) were non-diabetic and 23.3% (n=7) were diabetic; mean age was 44.36 (±12.62) years; duration of MHD was 19.53 (±18.9) months; systolic BP 162.83 (± 19.32) mmHg: diastolic BP 90.10 (±9.77) mmHg; number of IHD 36.6% (n=11); Hb 6.25 (±1.33) gm/dl. On echocardiogram, 80%(n=24) lead concentric hypertrophy and 20% (n=6) eccentric hypertrophy; LV mass index (LVMI) was 246.32g/m^2 in male (n=17) and 209.11 (±53.98) g/m^2 in female (n=13). When compared between diabetic and non-diabetic subset, significant difference was seen between age of 58.42 (±12.48) years vs 40.08(±9.24) years (p<0.05); presence of IHD 71.45% vs 26.08% (p<0.05); mean duration of HD 35(±8.42) months vs 51.09 (±21.44) months (p<0.05) in the surviving patients, on second year. Fifteen patients died at the end of two years followup and in 60% most likely cause was cardiac disease. When living and deaths were compared a significant difference was seen in interventricular septal thickness (IVST) 13.7(±1.6)mm vs 16:521(±3.3) mm (p<0.05); LVMI 170.81 (±30.07)g/m^2 vs 230.6(+-2l.9) g/m^2 (p<0.05); duration of 49.27(±19.66) months vs 32.26(±19.73) months (p<0.05) and mortality 57% vs 47%. We may conclude that cardiovascular complications are highly prevalent in MHD patients; diabetic patients are of older age group with increased incidence of IHD probably had caused decreased dialysis survival with increased mortality subsequently: LVMI is an independent predictor of mortality in both diabetic and non diabetic groups.

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Introduction

Haemodialysis (HD) is the main mode of renal replacement therapy (RRT) in end stage renal disease (ESRD) patients worldwide. United States Renal Data System (USRDS) shows the distribution of dialysis modalities where 80% are on HD[1]. In Bangladesh, HD also plays the major role in RRT[2]. Heart diseases are remarkably prevalent in dialysis patients at the start of therapy for ESRD. In a study of a cohort of 433 ESRD patients in whom dialysis therapy has been started, only 21% patients were found to be normal on echocardiograrn[3]. There is also increased incidence of atrial and ventricular dysrhythmias and complex ventricular ectopics in dialysis population[3]. European Dialysis and Transplant Association (EDTA) reports that the patients receiving RRT have a 16-19 fold increased risk of myocardial ischaemia and infarction when compared with age-sex matched population without renal failure[4]. Cardiac complications are major cause of death in dialysis patients consisting of about 40%[5].

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Canadian Organ Replacement Registry (CORR) in 1990 annual report mentioned that 44.7% dialysis patients died of cardiovascular diseases[6]. USRDS confirmed that 50% of total death in dialysls patients is due to cardiovascular diseases[7].

Diabetes mellitus is a common cause of ESRD and in turn is also a risk factor for cardiovascular diseases. In some countries, diabetes mellitus is the leading cause of ESRD.

United States Renal Data System (USRDS) 1 9 9 3 report shows that 34.3% of the total ESRD patients are diabetic. As for Bangladesh, a study shows 24% of MHD patients are diabetic[8]. Diabetic patients have a higher mortality rate, three times more than that of other ESRD patients[5]. Cardiovascular disease is the most common cause of death[5]. Blindness, coronary artery disease cerebrovascular and peripheral vascular diseases, are the common causes of morbidity and mortality. For these reasons diabetics were excluded from RRT in sixties and early seventies. But due to increased number of diabetic population and improvement in RRT more and more patients with diabetes are included in replacement therapy.

Echocardiogram has been proved to be a sensitive/ non-invasive tool for assessing left ventricular performance at an early stage. Left Ventricular Hypertrophy (LVH) in normal population is shown to be an adverse prognostic indicator[9-10]. Left Ventricular Hypertrophy (LVS) is also shown to be an independent prognostic factor in survival of ESRD patients[11] Echocardiography provides information about left ventricular geometry, contractility, and systolic-diastolic dysfunction. The type of hypertrophy (concentric/eccentric) can also be determined. So, emphasis of echocardiogram is given in this study.

This cross-sectional study was undertaken to assess the prevalence of cardiovascular complications in HD patients with special reference to diabetic subset and to find out the prognostic impact of echocardiographic determinants in both diabetic and non-diabetic patients.

Materials and Method :

Institute of Post Graduate Medicine & Research (IPGM&R). Dhaka is a tertiary referral Institute. All modalities of RRT are provided in this center. The study was done by the Department of Nephrology and the Department of Cardiology. More than 100 patients are treated annually in Nephrology department of which 24% are diabetic[8]. Out of 60 undergoing HD at the time of this study (for a variable period of time), 30 were selected. The study was done in the year 1996 and a follow-up was made at the end of '96 and '97 to evaluate the mortality. In second year there was 4 dropouts two transplanted: two discontinued). Of the 30 selected, seven were diabetic and 23 non-diabetic. Diabetic subset represented the similar percentage of the total patients currently treated. All were noninsulin-dependent diabetic (NIDDM) and did not need any hypoglycaemlc agent for controlling diabetes. Their medical records indicate that most likely cause of renal failure was diabetic nephropathy.

Patients were on haemodialysis for at least three months to avoid immediate complications of haernodialysis like - disequilibriuim syndrome and also patients were to be adjusted on this modality of treatment.

Exclusion criteria were acute renal failure, bed ridden patient, abnormal higher psychic function, taking drugs like steroids, sympathomimeties, suffering from chronic infection (TB. kala-azar. malaria etc.), decompensated liver disease, malignancies and patients with-dysrhythmias, old myocardial infection coronary angioplasty or bypass graft.

All the patients were hypertensive except one and was on multiple antihypertensives. None was getting erythropoietin for correction of anaemia.

All patients were dialysed through forearm arterio-venous fistula (AV fistula) 4 - 5 hours session about 2-3 times a week. Dialysis was done by using hollow fibre dialyser with a surface area of 1.1 sq. meter. Acetate dialysate was used at a rate of 500 ml/minute. Blood flow was 180-200 ml/ minute. Water was used after reverse osmosis.

Patients BP (supine) was recorded after evaluating the recordings of pre-dialysis BP over a period of one month. Cardiovascular status was evaluated by taking detailed clinical history and examination. Echocardiogram was performed after a mid-week haemodialysis whenever possible.

Echocardiogram was done by using M - mode and 2D echocardiography. Data were measured as criteria set by ASE[12]. Basic measurements included left ventricular internal diameter in diastole (LVIDd) and in systole (LVIDs), posterior wall thickness of left ventricle (LVPWT), interventricular septal thickness (IVST) and fractional shortening (FS). Left ventricular mass index (LVMI) was calculated by using following formula[13].

LVMI (g/m^2) =1.04 [$(LVIDd + IVST + LVPWT)^3$ - $(LVIDd)^3$)] - 13.6/ body surface area.

Left ventricillar end-diastolic volume index (LVEDVI) was calculated by the formula[14] : LVEDVI

$$ml/m^2 = \frac{7.0}{2.4 + LVIDd} (LVIDd)^3 \text{ body surface area}$$

In case of death, cause of death was concluded from medical records.

Definitions of terms:

Left ventricular, hypertrophy : LV mass index > $131 gm/m^2$ in males and >I00 gm/m^2 in females[15].

Concentric hypertrophy: in response to pressure overload, hypertrophy with normal cavity volume[16].

Eccentric hypertrophy : in response to volume overload. hypertrophy with LV dilatation (cavity volume > 90ml/m^2)[16].

Systolic dysfunction : Fractional shortening 25% or less.

Cardiac mortality: Death recorded as due to myocardial infarction. or from other cardiac causes[17].

Statistical analysis

Results are expressed as mean ± SD. Students unpaired 't' test was used to see the level of significance between groups. Chi square (x^2) and "Z" tests were also used. P value <0.05 was considered significant.

Results :

Number of patients were thirty. 17 were male, 13 female and ratio was 56.7:43.3 (Table-I). Mean age was 44.36 (±12.62) years. Cause of renal failure was chronic glomerulonephritis 70% (n=21). diabetic nephropathy 23.3% (n=4) and 6.6% (n=2) were due to hypertension and obstructive uropathy. Mean duration of haemodialysis was 19.53 (±18.90) montbs at the beginning of the study with a range of 3-68 months. Systolic BP was 162.83 (±19.32), diastolic BP 91.10(±9.77) mmHg and mean pressure was 116.51 (±15.11) mmHg. Ninety seven percent (n=29) were hypertensive and were on multiple antithypertensive medications. 36% (n=11) were indentisied clinically as having angina (IHD) and they were on different nitrate preparations continuously or on demand. Congestive cardiac failure (CCF) was noted (both left and/or right) In 26.6% (n=8). Mean Hb was 6.25gm/dl.

Echocardiographic measuremeanis showed that all the patients had LVH (Table-II).

Table-I

Baseline choractertstics of the patient population

Total number of patients	-	30
Age (years)	-	44.36 (±12.62)
Male	-	17
Female	-	13
M/F Ratio	-	56.7 : 43.3
Renal Disorder		
Glomerulonephritis	-	70%
Diabetic nephropathy	-	23.30%
Hypertensive nephrosclerosis	-	3.30%
Obstructive uropathy	-	3.30%
Duration of Haemodialysis (months)	-	19.53 (±18.90)
Blood pressure (mm of Hg)		
Systolic	-	162.83 (±19.32)
Diastolic	-	91.10 (±9.77)
Mean pressure	-	116.4 (±15.11)
Hypertensive	-	97%
Antihypertensive medication	-	97%
Angina (IHD)	-	36.6%
Congestive cardiac failure (CCF)	-	26.6%
Haemoglobin (gm/dl)	-	6.25 (±1.33)

Table-II

Echocardiographic abnormalities in the patient position

LVIDd (mm)	50.56 (±7.50)
LVIDs (mm)	34.83 (±6.70)
LVPWT (mm)	14.F0 (±3.00)
IVST (mm)	F5.10 (±-2.90)
LVEDVI (ml/m^2)	74.32. (±23.90)
LVMI (g/m^2)	
Male	246.32 (±71.61)
Female	209.1 (±-53.98)
FS %	31-46 (±6.78)%
Left ventricular hypertrophy	100%
Concentric	80%
Eccentric	20%
Systolic dysfunction	20%
Pericardial effusion	10%

Concentric hypertrophy was seen in 80% (n=24) and eccentric hypertrophy in 20% (n=6).. Systolic dysfunction was seen in 20% (n=6). Of these patients, five had concentric hypertrophy one had eccentric hypertrophy. None of the patients having CCF had systolic failure. Some of the patients having CCF or systolic dysfunction also belonged to IHD group. Calculated LVMI in male was 246.32 ±71.61) g/m^2 and in female 209.11 (±53.98) g/m^2 and all were well above the normal range defined for sex and body surface area.

Diabetic subset had a mean duration of DM for 14.28 (±3.94) years and hypertension for 10.10 (±6.25) years. But in non-diabetic group, as most were diagnosed at the stage of severe renal failure, no definite history of duration could be noted. When the diabetics and non-diabetics were compared (Table- III) significant difference in age and IHD was seen. Out of 30 patients, 20 patients survived in second year. Sixty continued dialysis and 4 discontinued. Of the16 patients, 5 were diabetic and 11 non- diabetic. At the end of second year significant difference in duration of dialysis was seen between these two groups.

Of the 30 patients, 15 died at the end of two years follow up, Four of them were diabetic. The overall mortality was 57% vs 47% between diabetics and non-diabetics. Patients surviving and dead were compared at the end of second year of the study (Table –IV). In dead females, there was higher value of IVST and LVMI in dead males, there was tendency of increased LVMI. All the eight patients with CCF died. Follow up at the end of second year showed difference in duration of dialysis in both of these groups: 49.27 (±19.66) years vs 32.26 (±19.72) years.

Table-III

Comparison between diabetic and non-diabetic patients

Variable	Diabetic (7)	Non diabetic (23)	p value
Age	58.42 (±12.48)	40.08 (±9.24)	< 0.05
Duration of HD			
• Starting	13.28 (±7.46)	21.43 (±20.90)	NS
• End of First year	24.57 (±8.54)	33.22 (±21.70	NS
• End of Second year	35.00 (±8.42)	5F.09 (2F.44)	<0.05
Systolic BP	161.42 (±13.45)	16F (±20.08)	NS
Diastolic BP	90.00 (±7.63)	90.00 (±8.86)	NS
Mean pressure	112.42 (±7.00)	114(±11.95)	NS
Hb	07.13 (±1.37)	06.35 (±1.30)	NS
IHD	71.45	26.08	<0.05
LVIDd	53.14 (±9.50)	49.56 (±6.90)	NS
LVEDVI	83.92 (±32:90)	72.58 (±20.40)	NS
LVMI	269.6 (±92.30)	233.14 (±60.45)	NS
FS%	31.00 (±7.50)	31.50 (±6.50)	NS

Table-IV

Comparison between living and those who died

Variable	Living (11)	Dead (15)	P value
Age 47.45 (±12.75)	45.4 (±11.03)	NS	
Starting HD duration	25.27 (±19.66)	19.53 (±19.14)	NS
Total HD duration	49.27 (±19:66)	32.26 (±19.73)	<0.05
Mean pressure	113.27 {±13.30)	114.6 (±8.30)	NS
IHD	27.20	46.60	NS
Hb	6.63 (±90)	6.44 (±1.50)	NS
LVPWT	13.45 (±2.20	15 (±3.60)	NS
IVST	13.7 (±1.60)	16.53 (±3.30)	<0.05
LVIDd	51.9 (±7.60)	49.09(±8.10)	NS
LVEDVI	78.74 (±26.70)	70.69 (±22.60)	NS
LVMI (female)	170.81 (±30.00)	230.60 (±21.90)	<0.05
LVMI (male)	245.37 (±87.49)	265.50 (±68.90)	NS
FS%	30.9 (±6.40)	32 (±7.50)	NS

Cause of death was not confirmed by autopsy but careful evaluation of history regarding death and medical records was done-to point out the most likely cause. Of the 15 dead patients, nine died of CVS complication 60%; 2 from CVD (13%) and four from other cause (27%) like irregular dialysis, fistula failure etc.

Discussion:

The strict selection criteria of study population was aimed at minimizing the effects of other factors on cardiovascular system and to observe only cardiovascular complications in haemodialysis population of end stage renal disease patients. The variable duration of haemodialysis with a wide range (Table-I) also enabled us to observe different cardiac complications of different dialysis time period. Hypertension has been reported to be present in 75-80% ESRD patients[18]. In this study it was present in 97% of the patients and all were on anti- hypertensive therapy. Suspected causes of hypertension in general are volume overload, elevated angiotensin II, uraemic toxins, sympathetic overactivity etc. By effective dialysis, majority patients show control of pressure by removal of excess body fluid and sodium. It is recommended that the BP should be at 140/90mmHg or below[19]. Increased BP with increased mean pressure in the study patients indicated increased peripheral resistance which in turn may be due to angiotensin and sympathetic overactivity.

The haemoglobin level among the patients was quite low. Anaemia is a common finding in renal failure. It contributes to hyperdynamic circulation, left ventricular hypertrophy, left ventricular dilatation and ischaemic heart disease. In HD patients chronic blood loss during dialysis procedure is an added reason along with low erythropoitin activity. Effective therapy with recombinent erythropoictin improves haemoglobin level and reduces left ventricular rnass[20]. None of the patients was getting erythropoietin but received multiple units of blood transfusion which is usually not sufficient for restoration of normal haemoglobin level.

Congestive cardiac failure was present in about one-fourth of the patients. As these patients had left ventricular hypertrophy with normal systolic function, the possible cause of cardiac failure was diastolic dysfunction resulting from ischaemic heart disease[21].

In 20% of the patients, systolic dysfunction was evident in the advance of previously described features of uraemic cardiomyopathy. It may be assumed that coronary insufficiency may be the cause of systolic dysfunction in these patients.

Left Ventricular Hypertrophy (LVH) is present in 30%-80% patients of end stage renal failure as is shown by several studies[22]. This hypertropy may be concentric, eccentric or asymmetric. Concentric hypertrophy is the commonest. It is mainly due to pressure overload and eccentric variety is due to volume overload[23]. Volume overload may result from anaemia, AV fistula and fluid retention. In these-patients, majority had concentric hypertrophy. Probably hypertension played a dominant role in them.

It has been described by different authors that in ESRD patients, hypertension is not the only factor for LVH. Hypertrophy may progress in dialysed patients even when they become normotensive. In contrast, following renal transplantation, LVH may regress even if hypertension persists: So it is postulated that other than hypertension, anaemia, fluid overload, uraemic toxins (like PTH), A-V fistula all may contribute to development of LVH in different proportions in different patients.

In the series, patients of diabetic subset were of older age group and incidence of IHD was also significantly more in this group. Usually onset of NIDDM occurs in older age and diabetic nephropathy develops over a period of 10-30 years of diabetes. These patients developed ESRD after a mean interval of 14-16 years. Patients of primary cause of renal failure may present at any age. So there is significant age difference. The diabetic patients were also hypertensive. Diabetes, hypertension and older age all contributed to increased incidence of ischaemic heart disease. Thus in the diabetic subset IHD is more common than in non-diabetic patients. There is significantly lower duration of HD in diabetics in the second year (Table-III) of our followup. This is because death of diabetic patients during different dialysis duration. Previous reports also showed reduced survival in diabetics on dialysis compared to those with other primary renal disorders. It is about 60% of the non-diabetics[24].

When living and dead are compared, significant increase in septal thickness was found in the later group; LVMI was also increased in this group. Increased LVMI in the dead in comparison to the living made this is an important prognostic marker influencing the mortaltiy as majority died of cardiac and vascular causes. Increase in LV mass as an adverse prognostic factor has been shown by several studies in both renal and non-renal patients[9,10,25]. Silberberg et al showed that LVMI >125g/m^2 had a significantly lower survival than those who had LVMI <125g/m^2[,11]. It has been reported that in patients of ESRD with diabetes, LV hypertrophy is an additional risk actor for mortality and morbidity[26]. This is in conformity with this study as there is 57% mortality in diabetics vs 47% in non-diabetics at the end of second year of this study. In this series all the patients who developed clinically overt failure succumbed to death indicating that clinically overt heart failure is also a predictor of mortality. This is supported by some previous studies[5].

The limitation of this study was that the sample size was small. Other cardiovascular risk factors (lipid profile, coagulation factors etc.) were not evaluated and diastolic function of the left ventricle could not be assessed.

It may be concluded that cardiovascular complications are highly prevalent in patients on haemodialysis. LMVI is an important prognostic marker. Heart failure is a predictor of mortality. Diabetic subset is of higher age group with increased incidence of clinically evident ischaemic heart disease which has affected their survival. It is advisable that echocardiography should be performed at an early stage and then at regular intervals.

References

1. USRDS Annual Data Report. Improvements in data quality in the USRDS data base: determining treatment modalities. Am J Kidney Dis 1992; 20 (Suppl.2): 89.
2. Rashid HU, Khan F, Ahmed S, Rahman M. Experience of haemodialysis in Bangladesh. Bangladesh Renal J 1993; 12 : 17.
3. Harnett JD, Parfrey PS. Left ventricular dysfunction in dialysis subjects. In : Henrich WL (editor) Principles and Practice of Dialysis. Baltimore, Williams and Wilkins, 1994 pp170.
4. Wheeler DC. Cardiovascular diseases in patients with chronic renal failure (Commentary). Lancet 1996; 348 : 1673.
5. Foley RN, Parfrey PS, Harnelt JD, et al. Clinical and echocardiographic disease in patients starting end stage renal disease therapy. Kidney Int 1995; 7 : 186.

6. Canadian Organ Replacement Registry, 1990 Annual Report. Hospital Medical Records Institute, Don Mills. Ontario, April 1992.
7. USRDS Annual Data Report. The National Institute of Health. National Institute of Diabetes and Digestive and Kidney Diseases. August, 1990.
8. Rashid HU. Ahmed S, Rahman M, Noor Y, Mosaddeque M. Experience of haemodialysis in Bangladesh. Bangladesh Renal J 1996; 15 : 54.
9. Levy D. Garrison RJ, Savagel DD, et al. Prognostic implications of echocardio-graphically determined left ventricular mass in the Framingham Heart Study. N Eng J Med 1990; 322 : 1561.
10. Ghali JR, Liao Y, Simmons B, et al. The prognostic role of left ventricular hypertrophy in patients with or without coronary artery disease. Ann Intern Med 1992; 117 : 83.
11. Silberberg JS. Barre P. Prichard S, et al. Left ventricular hypertrophy: An independent determinant of survival in end stage renal failure. Kidney lnt 1989; .36 : 286.
12. Sahn DJ. De Maria A. Kisslo J, et al. Recommendation regarding quantitation in M-mode echocardiographic measurements. Circulation 1978: 58 : 1072.
13. Devereux RB, Alonso DR, Lutask EM, et al, Ecocardiographic assessment of left ventricular hypertrophy : Comparison to necropsy findings. Am J Cardiol 1986; 57 : 450.
14. Teichloz LE, Krenden T, Herman MV, et al. Problems in echocardiographic volume determinations. Echocardiographic-angiographic correlation in the presence or absence of asynergy. Am J Cardiol 1976; 37 : 7.
15. Lavy D, Savage DD, Garrison RJ, et al. Echocardiographic criteria for left ventricular hypertrophy : The Farmingham study. Am J Cardiol 1987; 59 : 956.
16. Huwez FU, Pringle SD, Mocjarlane PW. A new classification of left ventricular geometry based on M-mode echocardiography. Am J Cardiol 1992; 70 : 681.
17. Lipid research clinics program. The lipid research clinic coronary primary prevention trial results: In. Reduction in the incidence of coronary heart disease. JAMA 1984; 25 ; 351.
18. Ma WN, Greene EL Raij L. Cardiovascular risk factors in chronic renal failure and haemodialysis population. AM J Kdriey Dis 1992; 19 : 505.
19. Luke RG, Reiy MC. Hypertension, In : Massry SG, Glassock RJ (editor) Text book of Nephrology. Baltimore, Willmas and Wilkins, 1995; 11 : 1361.
20. Fellner SK, Lang RM, Neumann A et al. Cardiovascular consequences of correction of anaemia of renal failure with erythropoitin. Kidney Int. 1993; 44 : 1309.
21. Rostand SG, Kirk KA, Rulsky EA. Dialysis - associated ischemic heart disease: Insights from coronary angiography. Kidnay Int. 1984; 25 : 653.
22. Kramer W, Wizemann V, Mardelbaum AP, et al. Cardiological problems in uraemic patients. In: Cameron S, Davison AM, Grlinfeld JP, Kerr D, Ritz E. (eds) Oxford Text Book of Clinical Nephrology. London. Oxford University Press. 1992;1265.
23. Greaves SC, Sharpe DN. Cardiovascular disease in patients with end stage renal failure. Aust NZ J Med 1992; 22 : 153.
24. Brunnen PP, Selwood NH, Results of renal replacement therapy in Europe, 1980-1987. Am J Kidney Dis 1990, 15 : 38.
25. Korem MJ, Devereux RB, Lasale PN, et al. Relation of left ventricular mass and geometry to morbidity and mortality in uncomplicated hypertension. Ann Intern Med 1991; 11 : 35.
26. Grossman E, Shemesh J, Sharriss A, et al. Left ventricular mass in diabetes - hypertension. Arch Intern Med 1992; 152 : 1001.