Original paper

Burden of Cardiac Disease among Patients Undergoing Chronic Haemodialysis at Moi Teaching and Referral Hospital, Eldoret, Kenya

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Abstract

Background: Cardiovascular Disease (CVD) is the leading cause of mortality in patients with End Stage Renal Disease (ESRD) globally. Renal replacement therapy improves the quality of life of these patients but CVD remains a threat to their survival. Whereas atherosclerotic coronary artery disease is the leading culprit in high income countries, this has not been characterized in Kenya.
Objective: To determine the prevalence and spectrum of cardiac disease in patients with ESRD undergoing haemodialysis at Moi Teaching and Referral Hospital (MTRH), a tertiary medical centre in Western Kenya.
Methods: This was a cross sectional study conducted at MTRH renal unit. Consenting consecutive adults with ESRD undergoing chronic heamodialysis were enrolled into the study after obtaining ethical approval from the institution's review board. Data on socio demographics, medical and drug history was collected using a structured questionnaire followed by a focused cardiovascular examination. A standard trans-thoracic echocardiogram was done by a study dedicated sonographer and interpreted by a cardiologist using American Society of Echocardiography guidelines. A standard 12 lead resting ECG was also done and read by the same cardiologist. Outcomes of interest included Left Ventricular Hypertrophy (LVH), Left Ventricular Ejection Fraction (LVEF), pathological valve disease, pathological Q waves and arrhythmias. The prevalence estimates were reported with the corresponding 95% confidence intervals.
Results: Seventy two participants were included in the final analysis. Their median age was 41 (29.8, 60) years and 51.3% were male. Majority (93%) were on two sessions of dialysis per week, with 97.2% being known hypertensives. Almost three quarters of them (72.2%) had some form of cardiac disease as follows; left ventricular hypertrophy 58%, left ventricular systolic dysfunction 49%, pathological valvular disease 15.3%, arrhythmias 9.7% and pathological Q waves 6.9%.
Conclusion: There is a high burden of cardiac disease in patients with ESRD on heamodialysis at MTRH with the predominant lesions being LVH and left ventricular systolic dysfunction.

Key words: End stage renal disease, Haemodialysis, Cardiac disease, Sub-Saharan Africa

Introduction

Patients with End-Stage Renal Disease (ESRD) are exposed to haemodynamic stress and metabolic perturbations, which could predispose them to myocardial dysfunction, valve disease, arrhythmias and atherosclerosis (1). It is known that Cardiovascular Disease (CVD) is the leading cause of morbidity and mortality in patients with Chronic Kidney Disease (CKD). Nearly half of these deaths are secondary to myocardial infarction, cardiac arrest, malignant arrhythmias and other cardiac causes. The high prevalence of diabetes, anaemia, hyperparathyroidism and hypertension among these patients fosters structural heart diseases. Moreover, fluid overload and metabolic abnormalities such as metabolic acidosis, dyskalemia and dysmagnesemia lead to an increased risk of clinically significant arrhythmias and sudden cardiac death. ESRD is often characterized by the presence of sympathetic hyperactivity and activation of the Renin-Angiotensin-Aldosterone System (RAAS) that further compound the picture (2,3).

The prevalence of ESRD is increasing globally with great societal economic impact (3). In sub-Saharan Africa (SSA), the prevalence of CKD is also increasing especially among young adults in their economically productive years and the majority of these patients are referred to nephrologists late due to poor referral systems and inadequate skilled personnel. Poverty and lack of access to modern specialized care make them not undergo renal replacement therapy at all or only manage inadequate dialysis. Besides, management

of other modifiable cardiovascular risks is usually not optimized and this explains the increase in CVD and cardiovascular risk factors in patients on maintenance dialysis (4).

Left Ventricular Hypertrophy (LVH) is the most common cardiac lesion in patients with CKD in High Income Countries (HIC) and is present in more than 75% of patients on chronic heamodialysis (5,6). The occurrence of LVH and its progression to (uremic) cardiomyopathy and later cardiac failure are influenced by high prevalence of traditional and uremia-related cardiovascular risk factors in haemodialysis patients (1,6). In CKD, there is also an increased risk for atherosclerosis, which is the main cause of ischemic heart disease in such patients. This may be due to accelerated progression of coronary plaque; greater thickening and vascular calcification preceded by dyslipidemia and mineral bone disease (1,6). In the mix of all these events, arteriosclerosis occurs due to large vessel remodeling and loss of elasticity and compliance that causes increased pulse pressure and hypertension (6).

LVH attended by secondary hypertension, LV systolic dysfunction, metabolic derangements and the uremic milieu constitute a fertile ground for arrhythmias. Further, during dialysis patients show a non-homogeneous repolarization through an increase in Q-T duration and Q-T dispersion, a phenomenon that can be highly arrythromogenic. The dialysis-related sudden variation in extra-cellular potassium, calcium and pH levels may further enhance the genesis of an electrical disequilibrium in myocardial cells thus predisposing to more arrythromogenesis (7). Various rhythm abnormalities have been described in this population ranging from benign to malignant with atrial fibrillation being the commonest (8).

Valvular heart disease is common in patients undergoing chronic dialysis. Abnormalities include valvular and annular thickening and calcification of any of the heart valves but commonly the aortic and mitral valves, with the subsequent development of valvular regurgitation and/or stenosis (9). The single most risk factor for development of valve disease is presence of secondary hyperparathyroidism with attended adynamic bone disease (9,10). Additional factors that may further enhance this pathology include the presence of hypertension, diabetes mellitus, hyperlipidemia, LVH, mitral valve prolapse, high cardiac output states, anaemia, infective endocarditis and Arteriovenous Fistulae (AV) (10 -12).

Chronic dialysis services are increasingly becoming available in Kenya with the support of the national public insurer – National Health Insurance Fund (NHIF). In middle income economies like India, approximately 9-13% of patients on haemodialysis die within the first one year, mainly attributed to CVD (13). sub-Saharan Africa and Kenya in particular is grossly under-represented in this data and we therefore sought to fill this gap by describing the spectrum of structural cardiac disease and arrhythmias in this patient population. The study was approved by Moi Teaching and Referral Hospital (MTRH)/Moi University ethics committee.

Materials and methods

This was a descriptive cross sectional study that was conducted on patients with ESRD undergoing chronic haemodialysis at the renal unit of MTRH, a tertiary medical centre in Western Kenya with a catchment population of over 16 million. A structured questionnaire was used to collect data on socio-demographics and medical history from consenting adult participants who were attending the renal unit for their routine scheduled haemodialysis. A physical exam with a bias towards cardiovascular system exam was conducted by one of the authors (MH). A standard 12 lead electrocardiogram (ECG) was then done using Philips equipment (Page writer TC20 (Andover MA, USA) by a qualified technician followed by a standard trans-thoracic echocardiogram (SE) by a qualified sonographer using a Siemens equipment (Siemens ACUSON X700TM Erlangen, Germany). These two were interpreted by a cardiologist with the latter being based on American Society of Echocardiography guidelines.

Outcome measures: From the SE we sought to obtain LVH, Left Ventricular Ejection Fraction (LVEF) as a measure of LV function, and pathological valve disease. From the ECG, we sought for presence of pathological Q waves as a marker of ischemia, arrhythmias and LVH.

Statistics: The sample size was calculated using a formula by Cohen *et al* for calculation of a sample size for a small population with 80% power based on a prevalence study by Kaze *et al* (Francois Folefack) in Yaounde Cameroon. Prevalence estimates were reported with the corresponding 95% confidence intervals. Analysis was done using software for statistical computing known as R (R core Team, 2016). Continuous variables were summarized using mean and standard deviation. Categorical variables were summarized as frequencies and the corresponding percentages. Continuous variables that did not follow the Gaussian distribution were summarized using median and interquartile range.

Results

Between January and July 2016, 95 patients were screened for inclusion into the study of which 72 were recruited. Majority of them (42, 58%) were male and

their mean age was 41 years. Hypertension (97.2%) and diabetes (18%) were major co-morbidities. Almost all (90%) of the hypertensive patients were on medication with most of them being uncontrolled. Majority were on twice weekly haemodialysis sessions funded by NHIF and their mean duration of dialysis was 8 weeks. Human Immunodeficiency Virus (HIV) infection was low reflecting the national prevalence in the general population (Table 1).

Table 1: Socio-demographic and clinical characteristics

	No.	(%)
Gender		
Male	42	58.3%
Female	30	41.7%
Occupation		
Farmer	36	52.0%
Business	9	12.5%
Housewife	9	12.5%
Student	12	16.7%
Retired	6	10.3%
Known hypertensive	70	97.2%
On anti hypertensive drugs	63	90.0%
Diuretics	23	36.5%
Calcium Channel Blockers	51	81%
Angiotensin Receptor Blockers	11	7.5%
Beta blockers	17	27%
Hydralazine	7	11.1%
Known diabetics	13	18.1%
On insulin	10	76.9%
On oral hypoglycemic agents	2	16.7%
HIV positive	4	5.7%
Systolic blood pressure	72	148.0 (139.8,158.0)
Range (Min.-Max.)		90.0-201.0
Diastolic blood pressure	72	93.0 (84.0,100.0)
Range (Min.-Max.)		50.0-132.0
SBP>140mmhg/DBP>90mmhg	72	59(81.8%)
BMI (Kg/m2)	72	21.2 (18.3,23.0)
Range (Min-Max)		(14.0-31.2)
<18.5		21 (29.6%)
18.5-25.0		38 (53.5%)
25.0-30.0		10 (14.1%)
>30		2 (2.8%)
Variable	N	Mean (SD) or Median (IQR) or n (%)

The prevalence of cardiac disease in this population was high at 72% with LVH being the predominant lesion. Valvular heart disease (15%) was of low prevalence despite the region being rheumatic heart disease bedrock. Equally, ischemic heart disease/ pathological Q waves burden was surprisingly low unlike the picture in HICs (Figure 1). Of the valve pathologies, mitral regurgitation was the predominant lesion followed by tricuspid regurgitation and aortic regurgitation (Table 2). About a half of the participants had depressed LV systolic function though in the vast majority, this tended to be in the mild to moderate ranges (LVEF 30-54%). Rhythm abnormalities were uncommon and were mostly benign (Table 2).

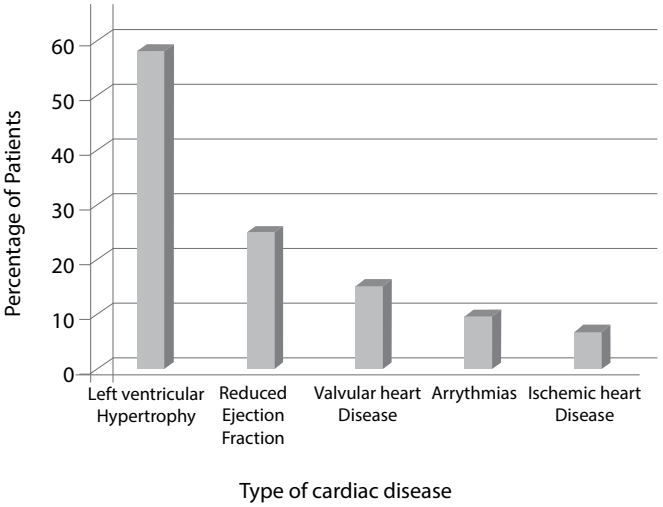

Figure 1: Spectrum of cardiac disease in patients with ESRD on haemodialysis

Table 2: Stratification of type of cardiac disease and severity in patients with ESRD

Rhythm anomalies		
Ventricular arrythmias	Premature ventricular complexes	3 (33%)
Brady-arrhythmias	1°Atrio-ventricular block	2 (22%)
	Sinus Bradycardia	1 (11%)
Bundle branch blocks	Left bundle branch block	1 (11%)
	Right bundle branch block	2 (22%)
Systolic dysfunction		
Mild	45-54%	23
Moderate	30-44%	5
Severe	<30%	7
Valvular disease		
Pathological mitral regurgitation	9	42.9%
Mitral stenosis	1	4.8%
Pathological aortic regurgitation	3	14.3%
Aortic stenosis	1	4.8%
Pathological tricuspid regurgitation	7	33.3%

Discussion

This cross sectional prospective study reveals a very high prevalence of cardiac disease among patients with ESRD on chronic haemodialysis in Western Kenya. LVH, perhaps a component of poorly controlled hypertension or uremic cardiomyopathy, was the predominant lesion. LV systolic dysfunction is also

common, affecting almost half of the participants, perhaps as part of the disease progression (from LVH) towards end stage process. An additional contributory factor is the presence of fluid overload due to inadequate dialysis amongst the participants, as it was noted that 66 (93%) of them were on two sessions of dialysis per week. This is inadequate as the Kidney Disease In Improving Global Outcomes (KDIQO) guidelines, recommend a minimum of 3 sessions per week (14). This inadequate dialysis is likely to be as a result of the NHIF policy to cover the cost of only two dialysis sessions per week. A majority of the patients depend on NHIF to meet the costs of dialysis. Valvular heart disease was surprisingly uncommon in this population, even with rheumatic heart disease being highly prevalent in the region. Given that this was relatively a young population with a mean age of 41 years, the implications of this twin co-morbidities (renal and cardiac) to the economy and family structures are disastrous.

Very few contemporary studies on a similar topic have been conducted in sub-Sahara Africa. A small old (1997) prospective study in Dakar, Senegal looking at 14 patients and a more recent one in Yaunde, Cameroon in 2014 that studied 45 patients (5,15). Despite the small numbers, the Senegal study had almost similar findings with all of the patients being hypertensive and 13 (of the 14) having cardiac abnormalities: all with LVH and a quarter with LV systolic dysfunction. The Cameroonian study on the other hand was a cross sectional study that looked at 45 ESRD patients undergoing chronic haemodialysis at one of the four government funded dialysis centers. Cardiac disease was also highly prevalent at 84%; a rate slightly higher than what we observed (72%) in our study. The longer mean dialysis duration (36.5 months) as compared to 2 months in our study as well as the relatively older mean age (52.7 years as compared to 41 years) of the study participants could possibly explain the higher cardiac disease prevalence that was observed in Cameroon.

The prevalence of LVH in our study population at 58.3% is comparable to the Cameroonian study that revealed a slightly higher prevalence at 60%. The similarity can be attributed to similar methodology and patient characteristics. The slightly higher prevalence can be attributed to a longer duration on dialysis (36.5 months) that results in a longer duration of exposure of the myocardium to both preload and uremia hence development of LVH as a compensatory mechanism. The higher mean age in the Cameroonian study (52.2 years as compared to 41 years), could also explain the higher prevalence of LVH as this increases with age (16). On the other hand, the higher prevalence of LVH in the Senegalese study could be explained by the small sample size and the fact that modern guidelines are more stringent on quantification of echocardiographic parameters unlike the past.

About a half of the participants were noted to have left ventricular systolic dysfunction. Of these, 23 (31.94%) had mild, 5 (5.94%) moderate and 7 (9.7%) severe systolic dysfunction. This is a crucial finding as LVEF is a powerful predictor of CVD outcomes in heart failure patients across a broad spectrum of ventricular function with hazard ratio for all cause mortality increasing by 39% for every 10% reduction in systolic function (16). This implies that about 10% of the participants were at a high risk of mortality based on the systolic dysfunction alone. In the Cameroonian study, prevalence of LV systolic function was not well characterized as the authors dealt more with the clinical syndrome of heart failure and diastolic filling (5). In Senegalese study, the prevalence of LV systolic function was lower at 28.5% (4 patients) and this could be due to the small sample size and use of older echocardiographic technology that was less sensitive (15).

The proportion of participants with pathological valve disease was 11/72 (15.3%). Only three of these valve pathologies were found to be of rheumatic origin. Nine participants (45%) were found to have mitral valve regurgitation (one severe, four moderate and four mild severity). One participant (4.8%) had mild mitral stenosis. Three (14.5%) had aortic regurgitation with one having a severe and two, a mild forms. One participant had aortic stenosis (4.8%). Seven participants (33.3%) had tricuspid regurgitation with two having severe disease, three having moderate and two with mild forms. In the Cameroonian study, aortic stenosis was highly prevalent at 40% in contrast to this study where the prevalence was 4.8%. This can be explained by the higher mean age (thus older) Cameroonian population (52.7 years) compared to this study (5). Mitral regurgitation was prevalent at 43% in this study, comparable to the Cameroonian study where it was prevalent at 50%, whilst tricuspid regurgitation was prevalent at 33.3% in this study also comparable to the Cameroonian study at 20%. This similarity can be explained by the similar patient characteristics, environmental factors and similarities in the methodology. The Senegalese study did not document any valve disease perhaps due to the small sample size.

Our study revealed the proportion of participants with pathological Q waves (ischemic heart disease) to be at 6.9%. This was a significantly low rate as compared to the proportion of other cardiac lesions. Not withstanding this, our study populations were fairly high risk for Coronary Artery Disease (CAD) with 97.2% being hypertensives and 18.1% with diabetics (17). The Cameroonian study showed an even lower prevalence of IHD at 2.22%, despite the fact that more than a fifth (22.2%) of their study population were smokers (another significant risk factor for CAD), a risk that was absent in all our study population (17). The differences between the two studies can be explained

by a study by Herzog *et al* (18) who showed that very adverse long term survival of such patients after acute myocardial infarction. Thus extremely low prevalence of IHD in the Cameroonian study could be due to the longer duration of dialysis of 36.5 months (3 years 4 months), which may have resulted in mortality within the first, second and third years whilst on dialysis thus significantly reducing the overall prevalence. In HICs the prevalence of IHD is extremely high perhaps due to the advanced age of their patients attended by other traditional risk factors (19). The Senegalese study did not report on ischemic burden because they did not do ECGs (15).

Our study found a prevalence of rhythm anomalies at 9.7%. These were all benign arrhythmias and this is comparable to the Cameroonian study where predominantly mild atrioventricular blocks 10 (67%) and bundle branch blocks 5 (33%) were described. The similarities could be attributed to similar patient characteristics and study methodology. This is in sharp contrast to what is seen in the HIC countries where sudden cardiac death, mainly caused by malignant arrhythmias is responsible for more than 40% of all-cause mortality in patients with ESRD. This difference could be due to the high prevalence of CAD in the HIC which predisposes them to the malignant rythms due to chronic myocardial and conduction system ischemia (19,20).

Limitations

Firstly, we did not do invasive evaluation (coronary angiography) thus we were likely to have missed less severe forms of coronary artery disease. Secondly, we also probably missed paroxysmal variants of arrhythmias as we did not do 24-hour holter monitoring.

Finally, there could have been some degree of intra-operator variability as the echocardiograms were done by one sonographer and interpretation of the archived images were only done by one cardiologist.

Conclusion and recommendations

Patients with ESRD undergoing chronic haemodialysis have a high burden of cardiac disease. The predominant lesions are LVH and depressed LV systolic dysfunction. Based on these findings, we recommend that cardiac evaluation should be part of care for patients with ESRD on chronic haemodialysis. The economic and survival benefits of such a strategy should be further interrogated in future prospective studies.

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