

A CROSS SECTIONAL STUDY ON CARDIOVASCULAR COMORBIDITIES IN PATIENTS OF CHRONIC KIDNEY DISEASE ATTENDING TRIPURA MEDICAL COLLEGE & DR. B. R. AMBEDKAR MEMORIAL TEACHING HOSPITAL

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ABSTRACT

BACKGROUND

Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiological processes associated with abnormal kidney function and a progressive decline in glomerular filtration rate (GFR). CKD is defined as kidney damage for more than 3 months, as defined by structural or functional abnormalities of kidney, with or without decreased glomerular filtration rate (GFR), which manifests either as pathological abnormalities or markers of kidney damage, including abnormalities in composition of the blood or urine, or abnormalities in imaging tests, with or without kidney damage.

METHODS

A hospital based cross sectional study was done from February 2017 to October 2018 (1.5 years) at Department of General Medicine, Tripura Medical College & Dr BRAM Teaching Hospital, Hapania, Agartala, West Tripura, among 100 CKD patients who attended Tripura Medical College and Dr. BRAM Teaching Hospital, Hapania, Agartala.

RESULTS

In this study, the mean age was 62.4 ± 9.37 years. Males (58%) were predominant. The mean Hb% of the participants was 9.13 ± 1.55 , mean urea was 108.74 ± 61.29 , mean creatinine was 4.96 ± 6.20 . The mean TG was 175.4 ± 66 , mean cholesterol of the participants was 169.53 ± 52.49 , mean LDL of the participants was 119.26 ± 28.20 and the mean HDL of the participants was 41.06 ± 13.24 . Among the male participants, 50% of the males were in CKD stage- 3, 22.4% were in stage- 4, 15.5% in CKD- 2, 8.6% in CKD- 5 and 3.4% in CKD- 1. Among the female participants, 42.9% were in CKD- 3, 28.6% in CKD- 4, 19% in CKD- 2, 7.1% in CKD- 1 and 2.4% CKD- 5.

CONCLUSIONS

Cardiovascular Disease (CVD) is emerging as the most common cause of death in patients with End Stage Renal Disease (ESRD). Left ventricular hypertrophy (LVH) is an independent predictor of mortality in chronic kidney disease patients. Hypertension is highly prevalent in CKD patients. Anaemia is an anticipated consequence as renal function declines, and can develop at any stage of CKD. CAD, hypertension, and QTc dispersion appeared as independent factors predictive of CVA development.

KEYWORDS

Chronic Kidney Disease, Cardiovascular Risk Factor, Hapania, Tripura

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BACKGROUND

Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiologic processes associated with abnormal kidney function and a progressive decline in glomerular filtration rate (GFR).¹ CKD is defined as kidney damage for more than 3 months, as defined by structural or

functional abnormalities of kidney, with or without decreased glomerular filtration rate (GFR), manifest by either: pathological abnormalities or markers of kidney damage, including abnormalities in composition of the blood or urine, or abnormalities in imaging tests, with or without kidney damage.²

Kidney Diseases Improving Global Outcome (KDIGO) classification of chronic kidney diseases (CKD) is as follows³:

1. GFR categories (ml/min/1.73m²) description and range.
 - G1-Normal or high GFR, (GFR ≥ 90 ml/min/1.73-m²).
 - G2-Mildly decreased GFR, (GFR = 60-89 ml/min/1.73m²).
 - G3a- Mild to moderately decreased GFR, (GFR = 45-59 ml/min/1.73m²).

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- G3b- Moderately to severely decreased GFR, (GFR= 30-44 ml/min/1.73m²).
 - G4- Severely decreased GFR, (GFR= 15-29 ml/min/1.73m²).
 - G5- Kidney failure (GFR < 15 ml/min/1.73m²).
2. Persistent albuminuria categories description and ranges are as below:-
- A1- Normal to mildly increased, (<30 mg/g, or <3 mg/mmol).
 - A2- Moderately increased, (30-300 mg/g or 3-30 mg/mmol).
 - A3- Severely increased, (> 300 mg/g or > 30 mg/mmol).

Chronic kidney disease (CKD) is emerging to be an important chronic disease globally. One reason is the rapidly increasing worldwide incidence of diabetes and hypertension. In India, given its population >1 billion, the rising incidence of CKD is likely to pose major problems for both healthcare and the economy in future years. Indeed, it has been recently estimated that the age-adjusted incidence rate of ESRD in India to be 229 per million population (pmp), and >100,000 new patients enter renal replacement programs annually in India.⁴ Kidney diseases rank 3rd amongst life threatening diseases (after cancer and cardiac ailments). 100 / million population succumb to kidney diseases. Around 90,000 kidney transplants per year required in India.⁵ CKD is prevalent worldwide in both developed & developing countries. India alone contributes about 55,000 patients on dialysis with annual hike of 10-20%.⁶ Among the various causes, infections & cardiovascular causes contribute towards the large proportion of increased morbidity & mortality.⁷ CKD affects almost every system of the body & results in various functional & structural abnormalities. Complications of CKD includes anaemia, metabolic acidosis, high calcium-phosphate product, hyperparathyroidism, chronic inflammation & hyperhomocysteinaemia, can cause endothelial dysfunction & cardiovascular disorder.⁸ Cardiac diseases are the major cause of death in dialysis population accounting for 40% of deaths in international registries.⁹ Cardiovascular complication is the main cause of death in patients with chronic kidney disease (CKD) undergoing haemodialysis therapy in India.¹⁰

METHODS

Study Design

Cross sectional study.

Study Period

February 2017-October 2018 (1.5 years)

Place of Study

The study was carried out in TMC & Dr. B. R. Ambedkar Memorial Teaching Hospital. TMC and Dr. B. R. Ambedkar Memorial Teaching hospital is a multispecialty teaching hospital with extensive referral from all over the eight districts of the state and also among the various departments of the institution.

Sample Size

The sample size calculated to 100 by using 4 pq/L2, where p= 6% 16, q= (100-p) and L (absolute precision)= 5% and adding 10% non-response, with rounded off.

Inclusion Criteria

All adult subjects attending TMC & DR. B. R Ambedkar Memorial hospital with diagnosis of CKD.

Exclusion Criteria

Congenital heart disease, patients with documented cardiovascular disease and patients not willing to give consent.

Methods of Data Collection

All adult subjects attending medicine OPD/IPD with history suggestive of CKD were first screened by Serum urea/creatinine and urine ACR measurement for diagnosis of CKD as per KDIGO criteria of CKD. Detailed history of risk factors of development of CKD were taken along with the detailed history of risk factors of development of cardiovascular comorbidities. Demographic profile of each patient were recorded, anthropometric measurement, BMI were calculated. Detailed examination with special emphasis on Renal and cardiovascular system were done. Patients fulfilling the inclusion and exclusion criteria were taken up into account for the study. Routine biochemical parameters of blood such as CBC, LFT, KFT, Lipid Profile, urine ACR, USG KUB were done. All patients were undergone CXR-PA view, ECG measurement and 2D-echocardiography.

Statistical Analysis

All relevant data so collected have been entered in Excel 2007 and analysed using SPSS version 15. Chi square test, student t test has been applied to find out any statistically significant. p Value <0.05 is taken as a significant.

RESULTS

Gender	Frequency
Male	58
Female	42

Table 1. Distribution of the Participants according to Gender

ECG Finding	Frequency
Arrhythmia	4
Con. Dis	8
ISCH	17
LAD	8
LVH	30
P. Mitrale	6
WNL	27

Table 2. Distribution of the Participants according to ECG

ECHO Finding	Frequency
ISCH	12
LA/LV Dilatation	9
LVDD-1	5
LVH	35
PE	6
WNL	33

Table 3. Distribution of the Participants according to ECHO Finding

USG Finding	Frequency
CKD-1	5
CKD-2	17
CKD-3	47
CKD-4	25
CKD-5	6

Table 4. Distribution of the Participants according to USG Finding

Chest X-Ray Finding	Frequency
B. PL. E	1
B. Pneumonia C.	1
Meg	24
P. edema	4
Pl. Effusion	10
Pneumonia	1
Rt. Pneumo	1
WNL	58

Table 5. Distribution of the Participants According to Chest X-Ray Finding

Blood Pressure	Frequency
Hypertensive	78
Normotensive	22

Table 6. Distribution of the Participants according to Blood Pressure

Parameters	Mean± SD
Age	62.4 ± 9.37
Hb%	9.13 ± 1.55
Urea	108.74 ± 61.29
Creatinine	4.96 ± 6.20
TG	175.4 ± 66.00
Chol	169.53 ± 52.49
LDL	119.26 ± 28.20
HDL	41.06 ± 13.24

Table 7. Descriptive Statistics of Different Variables of Study Participants

It was observed that maximum of the female (42.9%) and male (50%) participants were in stage 3 CKD group followed by stage 4 (female-28.6% and male- 22.4%) and stage 2 (female 19% and male 15.5%) and next is stage 5 among male (8.6%) and stage 1 among females (7.1%). Least number of participants among male were in CKD stage 1 (3.4%) and among the females were in CKD stage 5 (2.4%). (Table 8 and Figure 7).

USG Finding	Female	Male	Grand Total
CKD-1	3 (7.1%)	2 (3.4%)	5
CKD-2	8 (19%)	9 (15.5%)	17
CKD-3	18 (42.9%)	29 (50%)	47
CKD-4	12 (28.6%)	13 (22.4%)	25
CKD-5	1 (2.4%)	5 (8.6%)	6
Grand Total	42 (100%)	58 (100%)	100

Table 8. Cross Tabulation of USG Finding and Gender

In the present study it was observed that, majority (50%) of the participants with Conduction Disturbances having CKD stage- 3. Majority (58.8%) of the participants with ischemia having CKD stage- 3. Majority (50%) of the participants with left axis deviation having CKD-2. Majority (40%) of the participants with LVH having CKD-3. Majority (66.7%) of the participants with P. Mitrale having CKD-3. (table 9)

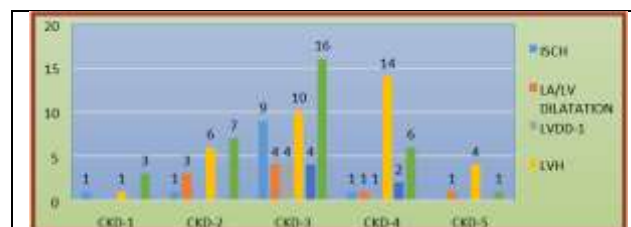


Figure 1. Composite Bar Chart Showing Echo Finding According to CKD Stage

It was observed that maximum(75%) participants having ischaemia were in stage 3 CKD, followed by stage 2 (8.3%) and stage 1(8.3%) and stage 4(8.3%). Majority of the participants with LA/LV dilation were in CKD stage 3, followed by stage 2 (33.3%), stage 4(11.1%) and stage 5 (11.1%). Most of the participants with left ventricular diastolic dysfunction were in CKD stage 3 (80%), followed by CK D stage 4 (20%). And maximum of the participants with left ventricular hypertrophy were having CKD stage 4 (40%), followed by CKD stage 3 (28.6%), CKD stage 2 (17.1%), CKD stage 5 (11.4%) and least number of participants with LVH were in CKD stage 1(2.9%).Most of the patients with pericardial effusion were in CKD stage 3(66.7%) and CKD stage 4(33.3%). It was observed that most of the participants with CKD stage 3 and stage 4 were having LVH, followed by LA/LV dilation (Figure 8).

Reve Labels	ARRHYTHMIA	CONDU	ISCH	LAD	LVH	PERICARDIAL E	WNL	Grand Total
CKD-1	-	-	1 (5.9%)	-	-	-	4 (14.3%)	5
CKD-2	-	3 (37.5%)	1 (5.9%)	4 (50%)	4 (13.3%)	-	5 (18.5%)	17
CKD-3	2 (50%)	4 (50%)	10 (58.8%)	1 (12.5%)	12 (40%)	4 (66.7%)	14 (51.9%)	47
CKD-4	2 (50%)	1 (12.5%)	5 (29.4%)	2 (25%)	9 (30%)	2 (33.3%)	4 (14.8%)	25
CKD-5	-	-	-	1 (12.5%)	5 (16.7%)	-	-	6
Grand Total	4	8	17	8	30	6	27	100

Table 9. Echocardiographic Findings according to CKD Stage

USG Finding	ISCH	LA/LV Dilatation	LVDD-1	LVH	PE	WNL	Grand Total
CKD-1	1 (8.3%)	-	-	1 (2.9%)	-	3 (9.1%)	5
CKD-2	1 (8.3%)	3 (33.3%)	-	6 (17.1%)	-	7 (21.2%)	17
CKD-3	9 (75%)	4 (44.4%)	4 (80%)	10 (28.6%)	4 (66.7%)	16 (48.5%)	47
CKD-4	1 (8.3%)	1 (11.1%)	1 (20%)	14 (40%)	2 (33.3%)	6 (18.2%)	25
CKD-5	-	1 (11.1%)	-	4 (11.4%)	-	1 (33%)	6
Grand Total	12	9	5	35	6	33	100

Table 10. Cross Tabulation of USG and ECHO Findings

USG Finding	Hypertensive	Normotensive	Grand Total
CKD-1	3 (3.8%)	2 (9.1%)	5
CKD-2	11 (14.1%)	6 (27.3%)	17
CKD-3	36 (46.2%)	11 (50%)	47
CKD-4	22 (28.2%)	3 (13.6%)	25
CKD-5	6 (7.7%)	-	6
Grand Total	78	22	100

Table 11. Cross Tabulation of Blood Pressure and CKD Stage

Variables	USG Finding				F value	P value
	CKD - 1	CKD - 2	CKD - 3	CKD - 4		
Age	62.0 ± 11.81	61.8 ± 10.35	62.8 ± 9.89	62.5 ± 8	60.8 ± 8.35	0.09 0.98
Hb%	10.56 ± 2.99	9.66 ± 1.79	9.03 ± 1.33	9.00 ± 1.4	8.82 ± 1.49	0.79 0.55
Urea	72.6 ± 48.3	67.5 ± 26	110 ± 48.5	131 ± 83.9	151.5 ± 55.5	7.77 0.00
Creatinine	2.30 ± 0.255	3.70 ± 0.61	4.16 ± 2.08	8.22 ± 11.46	6.34 ± 2.11	13.5 0.00
Triglycerides	167 ± 76.9	175 ± 66.1	181 ± 69.5	169 ± 60.6	164 ± 68.7	0.19 0.936
Cholesterol	163 ± 58.1	156 ± 40.3	182 ± 48.8	159 ± 55.1	160 ± 85.1	1.38 0.28
LDL	124 ± 34.35	122 ± 31.81	119.2 ± 37.75	123.6 ± 40.01	89.8 ± 52.27	0.53 0.71
HDL	44.6 ± 4.98	42.2 ± 14.77	38.4 ± 11.62	46.1 ± 13.79	35 ± 18.50	2.02 0.13

*ANOVA, p value <0.05 taken as significant

Table 12. Descriptive Statistics of Different Parameters of the Participants

It was observed that most of the participants among hypertensive were in CKD stage 3 (46.2%) and CKD stage 4 (28.2%). x stage which is statistically significant (p value. 0.00) (Table 12).

DISCUSSION

Cardiovascular disease is a major cause of death in patients with chronic kidney disease (CKD). Mortality due to cardiovascular events is ten to twenty times greater than in general population. Left ventricular hypertrophy (LVH) is an independent predictor of mortality in chronic kidney disease patients. In our study also we found 30% of patients with CKD are having LVH.¹¹ After age, left ventricular hypertrophy (LVH) is considered to be the strongest independent predictor of cardiovascular disease and events, cardiovascular death and total mortality. In CKD patients, LVH contributes to diastolic dysfunction, congestive heart failure, arrhythmia and sudden death.¹² Left ventricular hypertrophy is the commonest abnormality observed in CKD both on ECG and Echocardiography. Echocardiography is a more sensitive diagnostic procedure to detect left ventricular hypertrophy. After LVH most common abnormality found on Echocardiography is Left ventricular diastolic dysfunction. Pericardial effusion and conduction abnormalities are more common in patients of CKD on haemodialysis.¹³ MV Krishna, Ashish Jindal, Saurav Das in a study found that LVH is the commonest abnormality observed in CKD both on ECG and echocardiography. Echocardiography is a more sensitive diagnostic procedure to detect LVH. After LVH other most common abnormalities found on Echocardiography in CKD patients on haemodialysis were pericardial effusion and conduction abnormalities.¹⁴ Behera BK et al, in a study found that Patients with CKD have LVH, which is more marked in patients with severe CKD. So, these patients should have a thorough cardiovascular evaluation even if there were no symptoms, and efforts should be made to prevent LVH, during the early course of renal insufficiency, such as strict control of hypertension, anaemia.¹⁵

In our study also maximum of the participants (30%) were having left ventricular hypertrophy according to ECG

findings and 35% of the participants were having LVH according to echocardiography findings.

Anaemia is an anticipated consequence as renal function declines, and can develop at any stage of CKD. There is a strong association between anaemia and cardiovascular complications in CKD patients and many studies have proven that anaemia plays a key role in worsening CVD in CKD patients. In my study as the CKD stage increases haemoglobin concentration decreases i.e. Hb concentration is inversely proportionate to the stage of CKD. Chronic kidney disease (CKD) is now recognized as a risk factor of both end-stage renal disease (ESRD) and independently cardiovascular disease (CVD). Anaemia, a predictable complication of CKD, plays a key role for worsening both CKD and cardiac performance in a vicious circle. Thus, an increased awareness of an unmistakable association between CKD, CVD and anaemia, prompt identification of the common risk factors as well as aggressive treatment for anaemia with erythropoietin have been recommended to help slow the progression to ESRD and prevent cardiac events in CKD patients.¹⁶

Hypertension is highly prevalent in subjects with CKD with suboptimal awareness, treatment, and control rates. Appropriate health strategies should be implicated to improve prevention, early diagnosis, and treatment of hypertension, which is one of the leading causes of CKD.¹⁷ High blood pressure and kidney disease are closely related. High blood pressure is both a cause and a complication of kidney disease.¹⁸ High blood pressure increases the chance that kidney disease will get worse and that heart problems will develop. Keeping blood pressure well-controlled reduces the chance of these complications.¹⁹

In our study also 78% participants were hypertensive and 22% were normotensive. Cardiovascular Disease (CVD) is emerging as the most common cause of death in patients with End stage Renal Disease (ESRD). Risk factors for the increased prevalence Of CVD in CKD include traditional factors-Age, Sex, Diabetes, Hypertension, Smoking, Obesity and those specific to CKD-Blood pressure changes, fluid imbalance, anaemia, malnutrition, Hypo Albuminemia, Hyperhomocysteinaemia, inflammation, oxidant stress, insulin resistance, altered renin angiotensin axis and endothelial dysfunction. The high index of suspicion is necessary for early diagnosis. While there is no specific investigation to confirm its presence, Cardiac catheterization is an important tool. Intravascular Ultrasound and Electron beam computer Tomography to image coronary arteries are prospective investigations. High Sensitivity C Reactive Protein (hs- CRP) is emerging as not only an important risk marker but also a risk factor. Preventive strategies include lifestyle modifications, tight control of diabetes and blood pressure, use of statins, antioxidants, drugs to block the angiotensin system, correction of anaemia and divalent iron abnormalities.

Never Therapies are the vaso peptidase inhibitors. Revascularisation procedures are reserved for patients who are refractory to medical treatment, LV Dysfunction or extensive CAD. Early referral to the Nephrologists by the

primary physician when the serum creatinine is more than 1.4 mg/dl will enable early prevention of CVD, morbidity and mortality.²⁰

In our study, the mean age of the participants was 62.4 ± 9.37. The mean Hb% of the participants were 9.13 ± 1.55. The mean Urea of the participants were 108.74 ± 61.29. The mean creatinine of the participants was 4.96 ± 6.20. The mean TG of the participants were 175.4 ± 66. The mean Chol of the participants were 169.53 ± 52.49. The mean LDL of the participants was 119.26 ± 28.20. The mean HDL of the participants were 41.06 ± 13.24. CRF patients with and without haemodialysis are at high risk of development of dyslipidaemias. Haemodialysis can effectively reduce the accumulation of nitrogenous waste products but fails to clear dyslipidaemias generated during the course of CRF. But still the patients on haemodialysis are still exposed to several of the metabolic consequences of renal failure. A strict monitoring of lipid profile and lipoproteins can reduce the morbidity and mortality rate and will also improve the quality of life of CRF patients.²¹

In our study also participants with dyslipidaemia were more in CKD stage 3 & 4. There is high level of triglyceride and LDL level with low HDL level in CKD stage-3 & 4. Both ventricular and supraventricular arrhythmia are very common in ESRD patients receiving haemodialysis therapy. CAD, hypertension, and QTc dispersion appeared as independent factors predictive of CVA development. Duration of dialysis therapy is an independent factor affecting development of supraventricular arrhythmia. The increased rate of CVA may be responsible for the high sudden mortality and death rate seen in ESRD patients receiving haemodialysis.²² The prevalence of dyslipidaemia in non-diabetic CKD is high enough to pose a health problem in the society and this problem of dyslipidaemia increases with the severity of CKD. A high degree of abnormality is found in triglycerides in the form of hypertriglyceridemia in nondiabetic CKD patients. Haemodialysis could be a potential risk factor for development of dyslipidaemia in non-diabetic CKD as the prevalence is high in this group of patients compared to conservative management group.

CONCLUSIONS

Cardiovascular Disease (CVD) is emerging as the most common cause of death in patients with End Stage Renal Disease (ESRD). Left Ventricular Hypertrophy (LVH) is an independent predictor of mortality in chronic kidney disease patients. Hypertension is highly prevalent in CKD patients. Left ventricular hypertrophy is the commonest abnormality observed in CKD both on ECG and Echocardiography. Anaemia is anticipated as renal function declines, and can develop at any stage of CKD. Both ventricular and supraventricular arrhythmia are very common in ESRD patients receiving haemodialysis therapy. CAD, hypertension, and QTc dispersion appeared as independent factors predictive of CVA development. These observations are comparable with the data of various national and international studies. Hence, cardiac disorders are highly prevalent in patients with progressive CKD. All CKD patients

must be evaluated for cardiac co-morbidities, since it might help to establish adequate treatment that may potentially improve patient's prognosis. In my study, maximum participants were male, 78% participants were hypertensive and almost 30% were having left ventricular hypertrophy. Most of the participants were in the age group of 60-70 years and in the CKD stage 3 & 4. This study has some limitations. The sample size was less. Absence of a control group limits a definite assessment of the role of CKD in the pathogenesis of cardiac disorders. The study had a cross-sectional design, so no causal relationships with clinical outcomes could be established. Studies with larger sample size with a longer duration will be required to assess the outcome. The other comorbidities in CKD should have been taken for study considering the individual as a whole.

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