Section A-Research paper

STUDY ON CARDIAC MANIFESTATIONS IN CKD PATIENTS IN A TEACHING HOSPITAL

[1]Dr. B. Vinayak Inkalagi , [2]Dr B. Priyanka katti,

[1]Assistant Professor: Department of General Medicine , Al Ameen medical college, Bijapur, Karnataka 586108

[2]Assistant Professor, Department of Obstetrics and Gynaecology, Belgaum Institute of Medical Sciences, Sadashiv Nagar, Belagavi, Karnataka 590019

***Corresponding author**
Dr. B. Vinayak Inkalagi,
Assistant Professor,
Department of General Medicine ,
Al Ameen medical college ,
Bijapur , Karnataka 590019

Received: 07-04-2023 Revised:13-04-2023 Accepted: 11-05-2023

ABSTRACT

Introduction: Chronic kidney disease (CKD) carries a significant association with cardiac diseases, which suggests a minor reduction in the glomerular filtration rate (GFR) can act as an independent risk factor for causing cardiovascular abnormalities . The combination of risk factors accelerates the progression of arterial disease and is associated with a greater prevalence of ventricular hypertrophy, myocardial fibrosis, valvopathy, arrhythmia, ischemia and sudden death. Early detection of cardiovascular abnormalities in CKD helps in reducing morbidity and mortality and improving the quality of life.

Aim: To study cardiac manifestations in CKD

Materials and methods : The study was conducted in patients with chronic kidney disease admitted in the department of General Medicine , Al Ameen medical college ,Bijapur ,Karnataka on 140 CKD cases.

Result: In our study Left ventricular hypertrophy noted in 31.4% (44/140) cases , LAD in 13.5% (19/140), Conduction disturbances 18.1 %(20/140) , Ischemia in 15.7%(22/140) , Arrhythmias in 2.1 %(3/140) , P -mitrale in 2.8% (4/140) and normal in 21.4% (30/140)

Conclusion: Echocardiography is non-invasive, safe, easily performed and accurate in assessment of cardiac function in chronic kidney disease. Echocardiography is more sensitive in diagnosing left ventricular hypertrophy . Cardiovascular diseases are the leading cause of morbidity and mortality among CKD patients.

Key words : Chronic kidney disease, Echocardiography, left ventricular hypertrophy**.**

INTRODUCTION

Chronic Kidney Disease (CKD) is a global problem equally affecting the people of developed countries as well as developing countries. Cardiovascular disease is by far the leading cause of morbidity and mortality in CKD patients, accounting for almost 40% of hospitalizations1 and almost 50% of deaths [1,2] .

Established 'traditional' atherosclerotic risk factors, such as diabetes, hypertension, dyslipidemia, and older age, have been found to be independent predictors of CVD in CKD. In addition, hemodynamic and metabolic factors such as volume overload, anemia, calcium and phosphorus imbalance, chronic infl ammation, and a hypercoagulable milieu are unique features of renal insuffi ciency that may contribute to the risk and pathogenesis of CVD[3]
Chronic kidney disease (CKD) is defined as a systemic pathology that affects approximately 10% of the population; however, data showed differences in the prevalence of CKD between countries [4]
The prevalence of CKD has increased markedly over the past decades due to aging of the population worldwide and increase in incidence of diabetes mellitus, which has become the primary cause of CKD. Nowadays, CKD is considered a public health problem that causes high rates of mortality in the population due to the association with cardiovascular diseases (CVDs)[5] **.**Thus, CVDs are prevalent in patients with CKD, and subsequent CKD is a significant risk factor for CVDs. Furthermore, patients with CKD are at increased risk for cardiovascular events or death than for progression to end-stage renal disease (ESRD) [6] Multiple studies support the notion that patients with renal disease suffer accelerated aging, which precipitates the appearance of pathologies, including CVDs, usually associated with advanced age [7]

The definition and classification of CKD have evolved over time, but current international guidelines define CKD as decreased kidney function shown by GFR of less than 60 mL/min per 1·73m2 , or markers of kidney damage, or both, of at least 3 months duration, regardless of underlying cause. Early detection of cardiovascular abnormalities in CKD helps in reducing morbidity and mortality and improving the quality of life.[8] Our aim is to study cardiac manifestations in CKD

MATERIALS AND METHODS

The study was conducted in patients with chronic kidney disease admitted in department of General Medicine , ,Al Ameen medical college ,Bijapur ,Karnataka

inclusion criteria

1) patients who were known chronic kidney disease patients.
2) Patients who were symptomatic for 3 months or more.
3) Patients with serum creatinine more than 3 mg% and creatinine clearance < 30 ml/min
4) Patients with bilateral contracted kidneys on abdominal ultra sonogram with poor corticomedullary differentiation and type 2 or type 3 parenchymal changes. Patients with Autosomal Dominant Polycystic Kidney Disease and Obstructive Nephropathy were also included in the study though they did not have contracted kidney due to the underlying disorder.

Exclusion criteria:

1) Patients who were known valvular heart disease, coronary heart disease, diabetes mellitus,
2) Patients who were known hypertensive for years before the onset of chronic kidney disease.
3) Patients who underwent dialysis after admission.
4) Patients above 50 years of age.
5) Patients who were alcoholics.

In all patients, a detailed history was taken, with special interest to the duration of symptoms was noted. Cardiovascular symptoms, like dyspnoea, chest pain, pedal edema, pallor were noted. Blood pressure was measured thrice and the average was taken. Cardiovascular examination was done. Complete hemogram, blood urea, serum creatinine, serum electrolytes, serum calcium, phosphorus and uric acid, serum lipid profile were measured. Patients were also subjected to abdominal ultra sonogram and chest X-ray. Creatinine clearance had been calculated in all patients using the CockCroft-Gault equation:

Estimated Creatinine = $\underline{(\ 140 - \text{age}\ ) \times \text{body weight (kg)}}$ clearance(ml/min)

72 x serum creatinine (mg / dl)

This equation is for men. It is multiplied by 0.85 for women. Presence of cardiomegaly, pulmonary interstitial edema, pleural effusion were looked for in chest X-ray posteroanterior view. Evidence of left ventricular hypertrophy, low voltage complexes, ischemic changes were looked for in electrocardiogram.

Finally Echocardiography was done. The following parameters were looked for:

Chamber size: In the 2D and M-mode echocardiography the measurements of the interventricular septum, left ventricular posterior wall thickness, left ventricular internal diameter was made in both systole and diastole. Patients with interventricular septal thickness and left ventricular posterior wall thickness in diastole more than 1.1 cm represents concentric left ventricular hypertrophy. It is difficult to differentiate physiologic hypertrophy and pathologic hypertrophy.

To avoid this, Relative wall thickness was calculated in all patients using the following equation:

Relative wall thickness = IVS(D) X LVPW(D) LVID(D)

Relative wall thickness > 0.45 cannot occur in physiologic hypertrophy and it signifies pathologic hypertrophy.

In the parasternal long axis view, left ventricular internal diameter in diastole more than 5.6 cm represents dilated left ventricle.

Left atrial antero posterior diameter more than 3.8 cm represents dilated left atrium.

2) Systolic function: The systolic function is assessed mainly by M-mode measurements. Ejection fraction and fractional shortening are the two parameters used.

The Ejection fraction is defined as the ratio of stroke volume to end-diastolic volume.

Ejection fraction = Enddiastolic volume - Endsystolic volume x 100 End diastolic volume Normal values of Ejection fraction are 55 to 75 45. Grading of systolic dysfunction:

i) Mild 45 to 55 %.

ii) Moderate 35 to 45 %.

iii) Severe less than 35%. Fractional shortening is calculated by the following equation: Fractional shortening = LVID(D) - LVID(S) X 100 LVID(D)

3) Diastolic function: Diastolic function is assessed by Pulsed wave Doppler using the E/A measurements. E (m/s) indicate mitral flow which causes ventricular filling following opening of the mitral valve. A (m/s) indicates ventricular filling due to atrial systole. E/A is normally more than 1.

Less than 1 indicates diastolic dysfunction. Diastolic dysfunction can be graded as follows:

Grade 1 = impaired relaxation

Grade 2 = pseudo normalised pattern

Grade 3 = reversible restrictive pattern

Grade 4 = irreversible restrictive pattern

4) Left ventricular wall motion abnormalities: Left ventricular performance is assessed by many ways. Left ventricular wall is divided into a number of segments. Determining the motion of each segment provides the wall motion score.

5) Pericardial effusion: The Pericardial effusion is quantified by the amount of echo-free space surrounding the heart.

The Pericardial effusion can be graded as Minimal pericardial effusion: Posterior atrioventricular groove shows echo free space, this is seen in systolic phase only. It represents normal pericardial fluid.

Mild pericardial effusion: Echo free space < 1 cm.

Moderate pericardial effusion: Echo free space 1 – 2 cm.

Large Pericardial effusion: Echo free space > 2 cm

. 6) Valvular abnormalities : The valves were looked for stenotic lesions, regurgitant lesions, calcifications or vegetations

Statistical analysis

Data collected was analyzed by using tests like Chisquare, Anova and represented in the form of frequency tables, Bar diagrams and Pie charts.

RESULTS

In the present study age distribution varies from 20 years to more than 80 years and majority noted among 41 – 60 years and 61-80 years. Mean ± SD is 59.83 ± 11.19 years .
In our study males (71.4%)were predominant when compared to females (28.5%) .Male : Female ratio 2.5:1.
In our study SBP 140 -159 mm hg note din 68.5% (96/140) and >160 mm hg noted in 31.4% (44/140)cases . In our study DBP 80-89 mm hg noted in 50.7% (71/140) and 90-99 mm hg noted in 42.1% (59/140)cases and >100 mm hg in 7.1 % (10/140) cases.
In the present study 21.4% (30/140) more than 5 years ,1- 5 years noted among 64.2% (90/100) cases , only 14.2 % (20/100) were having 6 months duration
Easy fatiguability was present in 92.8% cases (130/140) Pedal edema and dyspnoea were the other common symptoms present constituting 37.15 (52/140) and 27.1 (38/140), 7.1 % (10/140)had chest pain and 14.2 % cases had palpitations and vomitings (20/140) each .

In our study Left ventricular hypertrophy noted in 31.4% (44/140) cases , LAD in 13.5% (19/140), Conduction disturbances 18.1 %(20/140) , Ischemia in 15.7%(22/140) , Arrhythmias in 2.1 %(3/140) , P -mitrale in 2.8% (4/140) and normal in 21.4% (30/140) c
In 2D echo findings EF < 35 % seen in 78.9% (110/140) cases, and >35 % seen in 21.4% (30/140), Left ventricular hypertrophy 55.7% (78/140) Pericardial effusion in 7.1% (10/140), Diastolic dysfunction 40%(56/140), Systolic dysfunction 18.5%(26/140), Dilated LV 7.1%(10/140), Dilated LA 14.2 % (20/140).

In the present study Stage II CKD were seen in 11% cases; Stage III CKD constituted 49.2%, 21.4% cases in stage IV CKD ,and 14.2% cases were in stage V CKD.

The most common cause of chronic kidney disease in the study was chronic glomerulonephritis and it constituted 83.5%(117/140) .IGA nephropathy 12.1%(17/140%) obstructive nephropathy 2.8%(4/140) and ADPKD 1.4%(2/140).

Table 1 : Correlation of CKD diagnosis with LVH findings

CKD diagnosis	LVH		
	No. of cases		P value
	Present	Absent	
CGN	62	55	0.4402 ns
IGA NEPHROPATHY	11	6	
OBSTRUCTIVE NEPHROPATHY	4	0	
ADPKD	1	1	
Total	78	62	

Fischer's exact test, *,p<0.05= significant, ns= not significant

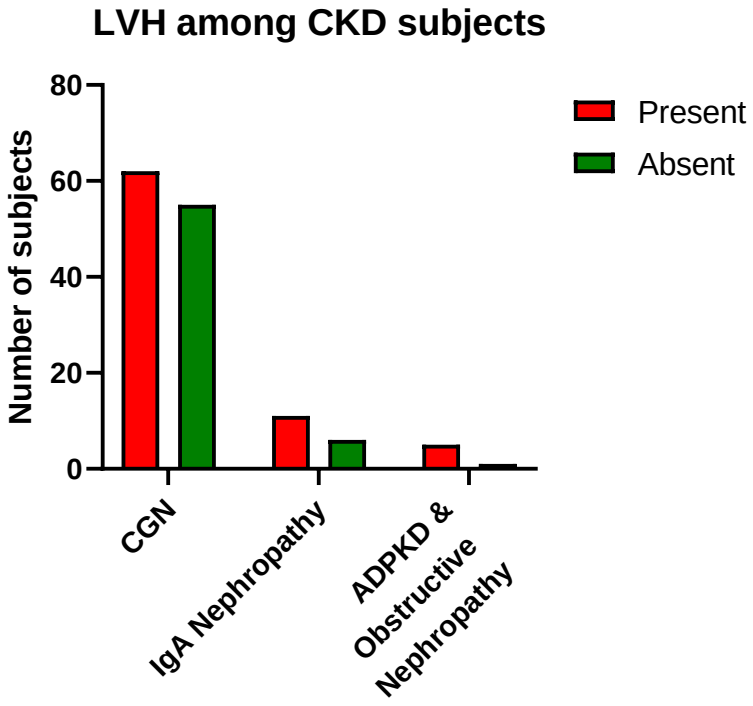


Table 2: Correlation of CKD diagnosis with ISCHEMIA findings

CLINICAL DIAGNOSIS	ISCHEMIA		P value
	No. of cases		
	Present	Absent	
CGN	62	55	>0.9999 ns
IGA NEPHROPATHY	11	6	
OBSTRUCTIVE NEPHROPATHY	4	0	
ADPKD	1	1	
Total	78	62	

Fischer's exact test, *,p<0.05= significant, ns= not significant

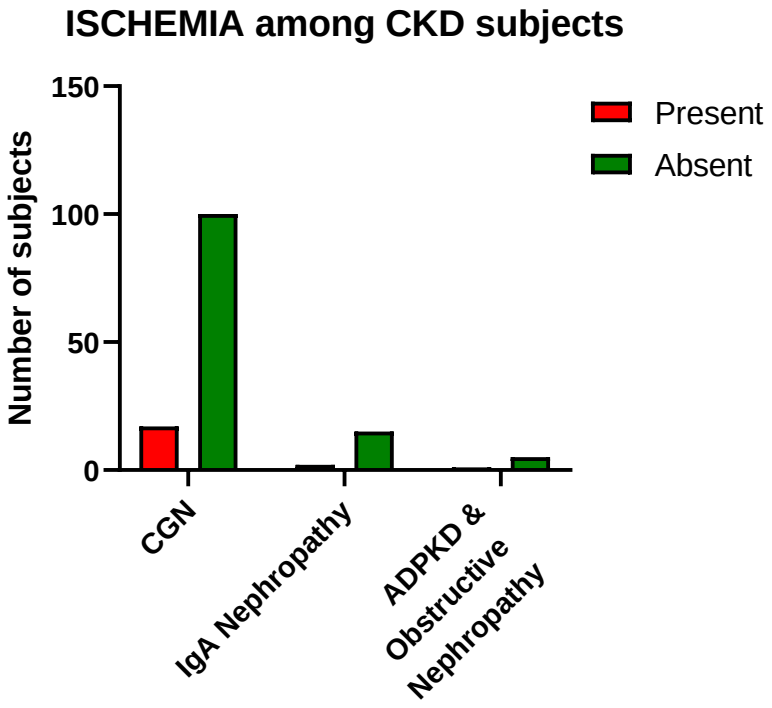


Table 3: Correlation of CKD diagnosis with Pericardial Effusion findings

CKD diagnosis	Pericardial Effusion		P value
	No. of cases		
	Present	Absent	
CGN	4	113	0.0093**
IGA NEPHROPATHY	4	13	
OBSTRUCTIVE NEPHROPATHY	2	2	
ADPKD	1	1	
Total	11	129	

Fischer's exact test, *,p<0.05= significant, ns= not significant

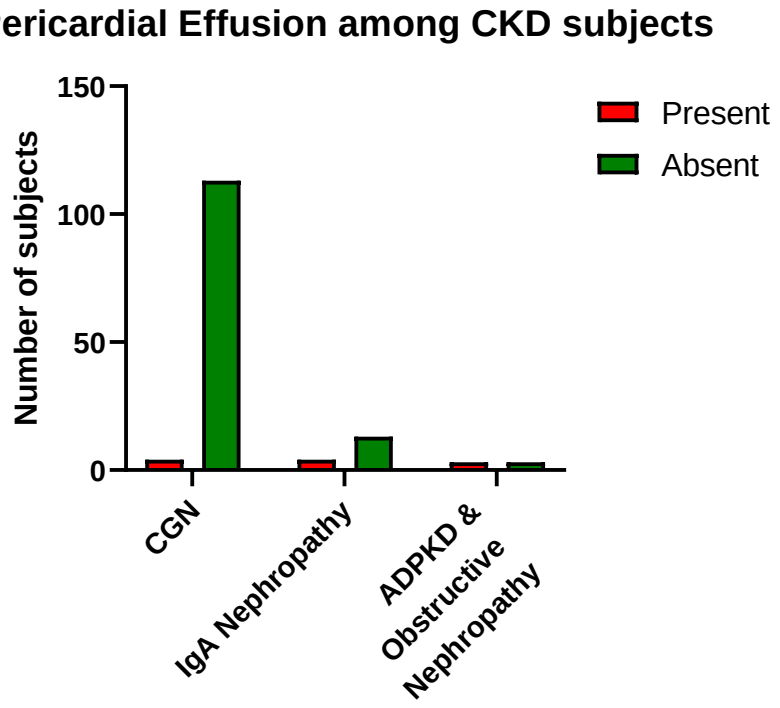


Table 4: Correlation of CKD diagnosis with Pericardial Effusion findings

CKD diagnosis	Diastolic Dysfunction		P value
	No. of cases		
	Present	Absent	
CGN	61	56	0.2236 ns
IGA NEPHROPATHY	13	4	
OBSTRUCTIVE NEPHROPATHY	4	0	
ADPKD	1	1	
Total	79	61	

Fischer's exact test, *,$p<0.05$= significant, ns= not significant

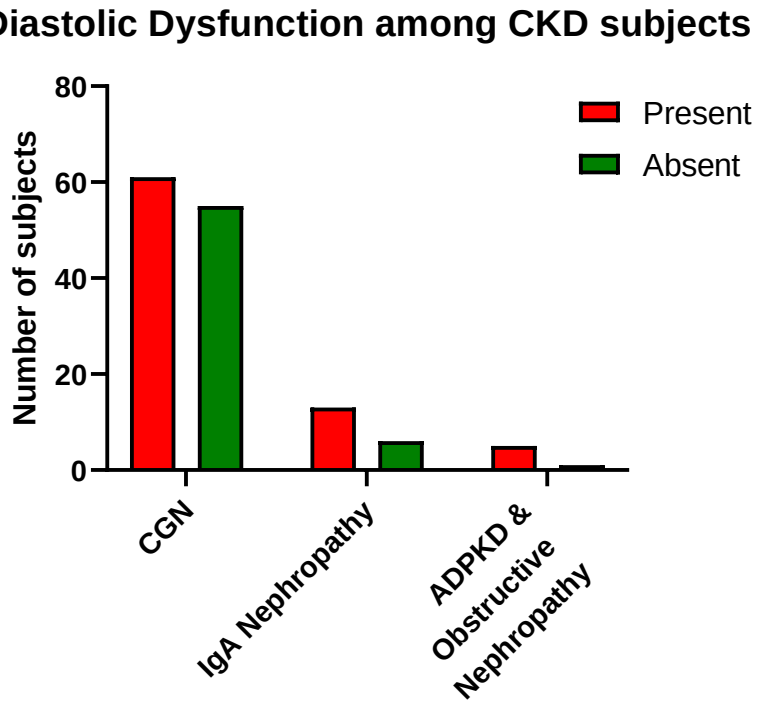


Table 5: Correlation of CKD diagnosis with Systolic Dysfunction findings

CKD diagnosis	Systolic Dysfunction		P value
	No. of cases		
	Present	Absent	
CGN	10	107	0.2236 ns
IGA NEPHROPATHY	7	10	
OBSTRUCTIVE NEPHROPATHY	3	1	
ADPKD	1	1	
Total	21	119	

Fischer's exact test, *,p<0.05= significant, ns= not significant

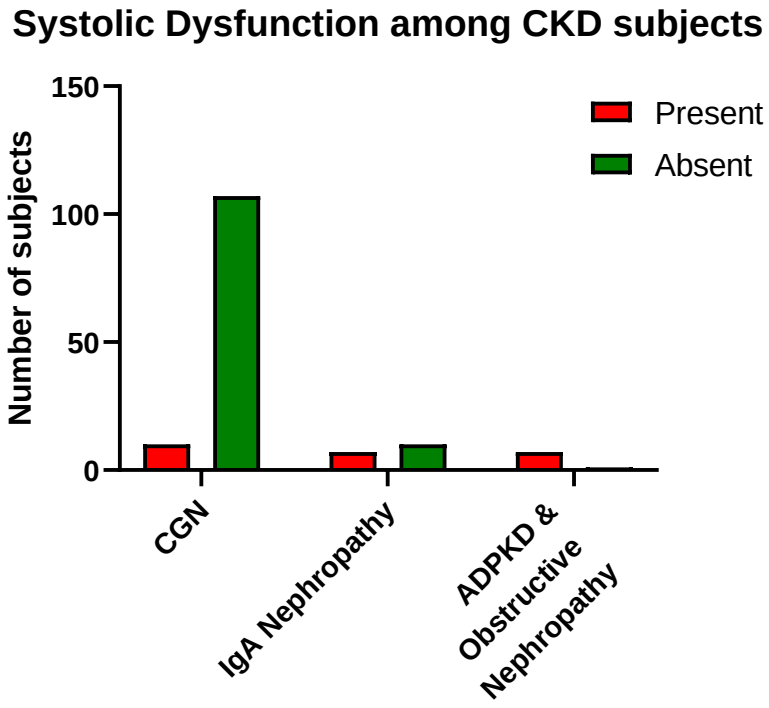


Table 6: Correlation of CKD diagnosis with Dilated LV findings

CKD diagnosis	Dilated LV		P value
	No. of cases		
	Present	Absent	
CGN	4	113	0.0093**
IGA NEPHROPATHY	4	13	
OBSTRUCTIVE NEPHROPATHY	2	2	
ADPKD	1	1	
Total	11	129	

Fischer's exact test, *,p<0.05= significant, ns= not significant

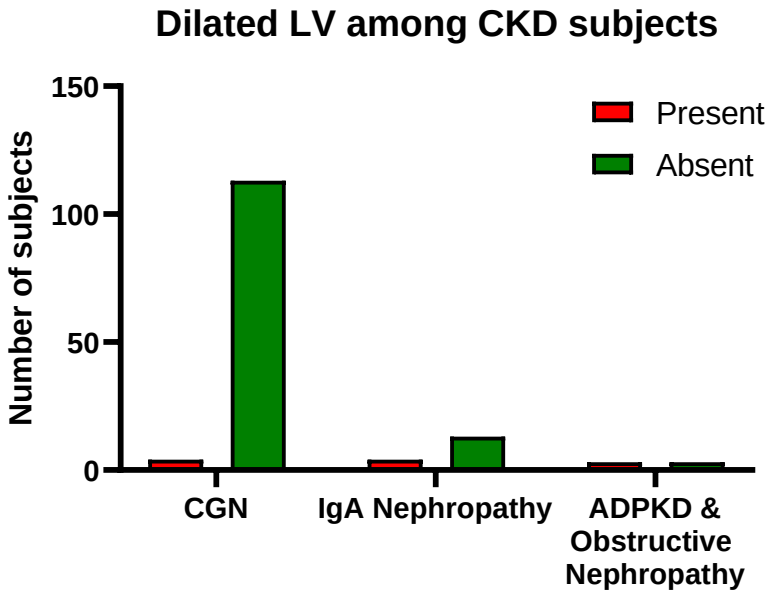


Table 7: Correlation of CKD diagnosis with Dilated LA findings

CKD diagnosis	Dilated LA		P value
	No. of cases		
	Present	Absent	
CGN	4	113	0.0093**
IGA NEPHROPATHY	4	13	
OBSTRUCTIVE NEPHROPATHY	2	2	
ADPKD	1	1	
Total	11	129	

Fischer's exact test, *,p<0.05= significant, ns= not significant

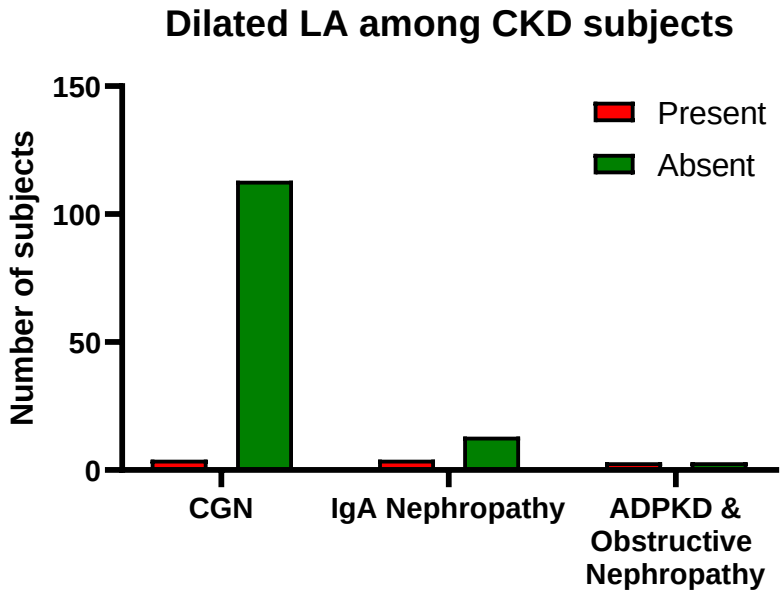


Table 8: Correlation of CKD diagnosis with Ejection Fraction % findings

CKD diagnosis	One way ANOVA		P value
	Ejection Fraction %		
	Mean ± SD	SEM	
CGN	36.94 ± 7.583	0.7071	0.9698 ns
IGA NEPHROPATHY	36.47 ± 8.690	2.108	
OBSTRUCTIVE NEPHROPATHY and ADPKD	37.17 ± 9.261	3.781	

One way ANOVA*,$p<0.05$= significant, ns= not significant

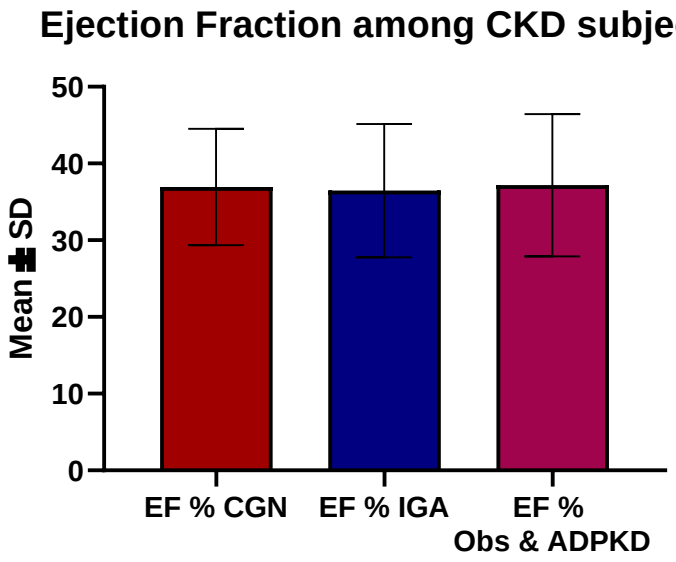


Table 9: Correlation of CKD diagnosis with SBP findings

CKD diagnosis	One way ANOVA		P value
	SBP		
	Mean ± SD	**SEM**	
CGN	150.4 ± 27.12	2.507	0.3681 ns
IGA NEPHROPATHY	141.0 ± 19.17	4.649	
OBSTRUCTIVE NEPHROPATHY and ADPKD	152.5 ± 22.22	9.073	

One way ANOVA*,p<0.05= significant, ns= not significant

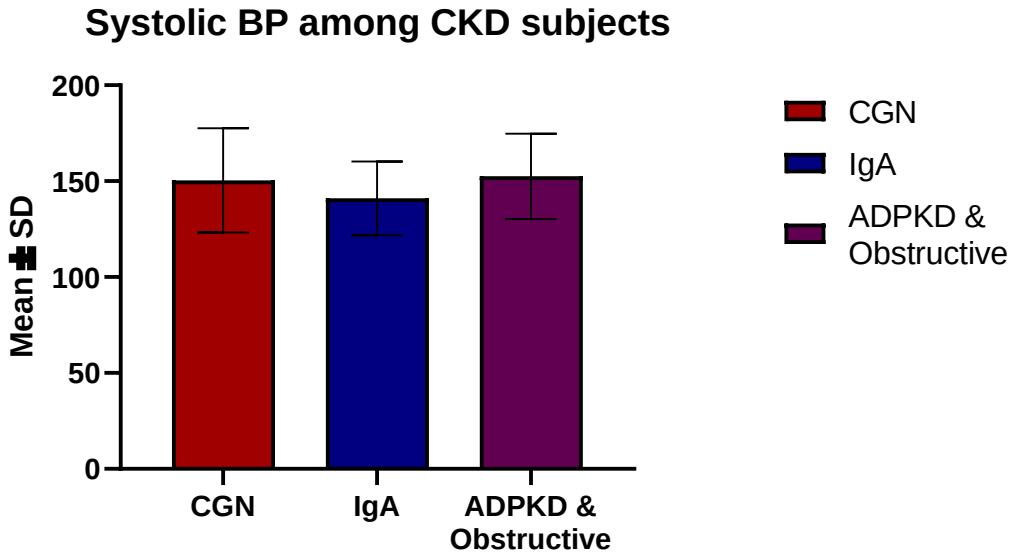
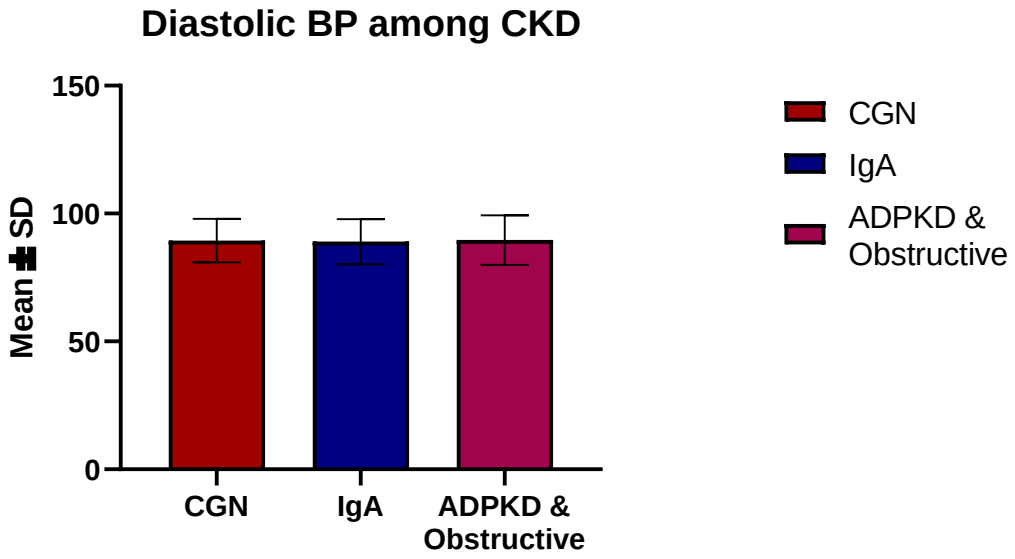


Table 10: Correlation of CKD diagnosis with DBP findings

CKD diagnosis	One way ANOVA	P value
	DBP	

	Mean ± SD	**SEM**	
CGN	89.45 ± 8.470	0.7830	0.9766 ns
IGA NEPHROPATHY	89.00 ± 8.846	2.145	
OBSTRUCTIVE NEPHROPATHY and ADPKD	89.67 ± 9.688	3.955	

One way ANOVA*,p<0.05= significant, ns= not significant



DISCUSSION

In the present study age distribution varies from 20 years to more than 80 years and majority noted among 41 – 60 years and 61-80 years. Mean ± SD is 59.83 ± 11.19 years.In Saha et al [9]study 22.7% was below 30 years of age, 19.3% between 30-40 years, 17% between 40- 50 years, 19.3% between 50-60 years and 21.7% 60 years or above. The mean age of the patients was 43.5±15.3 years; the lowest and highest ages were 14 and 80 years respectively.In Girish et al[10] study age distribution range from 18 years to 70 years .Majority of the cases were among 41-50 years i.e, 50%(50/100),followed by 51-60 years age group i.e 25%(25/100),18% (18/100) among 61-70 years ,least were among 18-30 years i.e, 2%(02/100). In the present.In Adarsh et al [11] study the mean age of the patients was 59 varied from 47 to 73 years.Sanath kumar [12] noted cardiovascular manifestations are mostly prevalent among 41 – 50 years of age with the frequency of 40% (36 cases) followed by 51-60 yr, 61-70 yr, 31-40 yr and 21- 30 yr with the incidence of 24.44% (22 cases), 18.88%(17 cases), 13.33%(12 cases) and 3.33% (3 cases).

In our study males (71.4%)were predominant when compared to females (28.5%) .Male : Female ratio 2.5:1.In Saha[9] study 58% were male and the rest (42%) were female, giving a male to female ratio of roughly 3:2 respectively.In Girish et al [10]study males were predominant with 62% (62/100) as compared to females with 38% (38/100), with Male to Female ratio1.6:1.In Sanath kumar study [12]male patients 64.44% (58 cases) followed by females with the prevalence of 35.55% (32 cases) In Adarsh et al [11] study 168(67.2%) males and 82(32.8%) females.

In the present study 21.4% had more than 5 years ,1- 5 years noted among 64.2% cases , only 14.2 % were having 6 months duration . In Girish et al [10]study 53% of cases had history of symtoms more than 5 years ,1- 5 years among 40% cases , only 7 % were having 6 months duration .

In our study Easy fatiguability was present in 92.8% cases (130/140) Pedal edema and dyspnoea were the other common symptoms present constituting 37.15 (52/140) and 27.1 (38/140), 7.1 % (10/140)had chest pain and 14.2 % cases had palpitations and vomitings (20/140) each . Girish et al [10]noted Dyspnoea (75%) in majority cases , followed by chest pain in 65% cases, pedal edema was seen in 40% cases and palpitation in 35% cases

In the present study 70% had Hypertension and 20% had Diabetes mellitus.10%had raised LDL cholesterol. .In Saha et al study [9]among traditional risk factors, 83.3% had Hypertension and 23% had Diabetes mellitus. Regarding Dyslipidaemia, 46.6% had raised LDL cholesterol and 57.3% had raised Triglyceride level. Of them, 27% had habit of smoking where as 20% was suffering from overweight and obesity.In Girish et al [10]study 43% (43/100) had history of DM ,32%(32/100) had history of HTN ,18% (18/100) of the cases had past history of both DM + HTN, 7% (07/100) had no past history.in Sanath kumar [12]et al study 45.55% (41) cases DM + HTN is the most common etiology in CKD succeeded by DM alone in 26.66% cases, HTN was the only etiology in 13.33% cases and chronic glomerulonephritis and otherswere in only 10% and 4.44% cases respectively.

In the present study Stage II CKD were seen in 11% cases; Stage III CKD constituted 49.2% , 21.4% cases in stage IV CKD ,and 14.2% cases were in stage V CKD. In Girish et al study [10]stage II CKD were seen in 6% cases; Stage III CKD constituted 54% , 30% cases in stage IV CKD ,and 10% cases were in stage V CKD.

In our study Left ventricular hypertrophy noted in 31.4% (44/140) cases , LAD in 13.5% (19/140), Conduction disturbances 18.1 %(20/140) , Ischemia in 15.7%(22/140) , Arrhythmias in 2.1 %(3/140) , P -mitrale in 2.8% (4/140) and normal in 21.4% (30/140) .In 2D echo findings EF < 35 % seen in 78.9% (110/140) cases, and >35 % seen in 21.4% (30/140), Left ventricular hypertrophy 55.7% (78/140) Pericardial effusion in 7.1% (10/140), Diastolic dysfunction 40%(56/140), Systolic dysfunction 18.5%(26/140), Dilated LV 7.1%(10/140), Dilated LA 14.2 % (20/140). In Saha et al study[9] 18.3% had ischemic heart disease, 38% heart failure, 4.7% arrhythmia and 9% left ventricular hypertrophy. Half of the patients did not have any cardiovascular events, about one-third (32.3%) had single event, 15% two events and 2.7% had three events. Girish et al [10]study 59% cases showed LVH on ECG. Ischemia in 24 % cases, Conduction disturbances in 16% cases. Arrhythmias in 10% cases, P- mitrale in 05 cases and 6% cases were showing normal study. 2D ECHO findings showed LVH as most common abnormality in 59% of cases. Next common abnormality noted was Systolic dysfunction in 36% cases. Valvular calcifications were seen in 20% cases. Diastolic dysfunction and Dilated LV in 9% cases each. Pericardial effusion and RWMA in 6% cases each. Dilated LA in 3% cases. In the present study, 36 cases presented with systolic dysfunction. Among them 6% cases had mild systolic dysfunction, 18% had moderate systolic dysfunction and 12% had severe systolic dysfunction. In the present study, 09 cases presented with diastolic dysfunction and 05 cases constituted grade 1 diastolic dysfunction, 04 cases constituted grade II diastolic dysfunction. Adarsh et al study [11]LVH with pressure overload pattern – 90(36%) cases. Low voltage QRS complexes – 43(17.2%) cases. Sinus tachycardia- 135(54%).The mean ejection fraction as found to be 55.21 with standard deviation of 6.13 LVH (left ventricular hypertrophy) 106(42.4%) patients had LVH in echocardiography and ECG. Table 4 represents the stages of LVH in CKD. LVDD (left ventricular diastolic dysfunction) 130 (52%) patients had left ventricular diastolic dysfunction out of which 80(32%) had grade 1,40(16%) had grade 2 and

10(4%) had grade 3 LVDD. In Sanath kumar[12] study out of 90 subjects mostly 32.22% cases shown ischemic changes succeeded by 22.22% with ST-T changes20% with LVH changes and 10%, 8.88%, 6.66% cases shown ECG changes of LVC, LBBB, VPC respectively. Out of 90 cases 28.88% cases shown LVH ECHO changes followed by 22.22%, 20%, 15.55%, 13.33% cases with calcified valves, diastolic dysfunction, regurgitation and pericardial effusion type of ECO changes respectively. Out of included individuals mostly 43.33% cases were with mild systolic dysfunction with 45-55 EF% succeeded by moderate systolic dysfunction 23.33% and severe systolic dysfunction 13.33% cases with EF% of 35-45%

In our study the most common cause of chronic kidney disease in the study was chronic glomerulonephritis and it constituted 83.5%(117/140) .IGA nephropathy 12.1%(17/140%) obstructive nephropathy 2.8%(4/140) and ADPKD 1.4%(2/140).In Girish et al study[10] the most common cause of chronic kidney disease was Diabetic nephropathy ie, 45% next common cause was HTN associated CKD ie, 31%,Chronic glomerulonephritis consituted15% Adult polycystic kidney disease occupied 5% (05/100), about 2% (02/100) each constituted IgA nephropathy and Adult polycystic kidney disease.

CONCLUSION

In our study Left ventricular hypertrophy noted in 31.4% cases , LAD in 13.5%, Conduction disturbances 18.1 % , Ischemia in 15.7% , Arrhythmias in 2.1 % , P -mitrale in 2.8% and normal in 21.4% .In 2D echo findings EF < 35 % seen in 78.9% cases, and >35 % seen in 21.4% , Left ventricular hypertrophy 55.7% . Pericardial effusion in 7.1% , Diastolic dysfunction 40%, Systolic dysfunction 18.5%, Dilated LV 7.1%, Dilated LA 14.2 % . Echocardiography is non-invasive, safe, easily performed and accurate in assessment of cardiac function in chronic kidney disease. Echocardiography is more sensitive in diagnosing left ventricular hypertrophy . Cardiovascular diseases are the leading cause of morbidity and mortality among CKD patients.

References

1. US Renal Data System. 2002 Annual Data Report, The National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD; 2002
2. Locatelli F, Marcelli D, Conte F et al. Cardiovascular disease in chronic renal failure: the challenge continues. Nephrol Dial Transplant 2000; 15 [Suppl 5]: 69–80.
3. K. Kundhal C.E. Lok Clinical Epidemiology of Cardiovascular Disease in Chronic Kidney Disease Nephron Clin Pract 2005;101:c47–c52.
4. Hill NR, Fatoba ST, Oke JL, Hirst JA, O'Callaghan CA, Lasserson DS, Hobbs FD. Global Prevalence of Chronic Kidney Disease - A Systematic Review and Meta-Analysis. PLoS One. 2016 Jul 6;11(7):e0158765.
5. Go, A. S., Chertow, G. M., Fan, D., McCulloch, C. E., and Hsu, C. Y. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N. Engl. J. Med. 2014:351, 1296–1305.
6. Keith, D. S., Nichols, G. A., Gullion, C. M., Brown, J. B., and Smith, D. H. Longitudinal follow-up and outcomes among a population with chronic kidney disease in a large managed care organization. Arch. Intern. Med. 2014:164, 659–663.
7. Stenvinkel, P., and Larsson, T. E. (2013). Chronic kidney disease: a clinical model of premature aging. Am. J. Kidney Dis.2013: 62, 339–351.
8. Sulemane S, Panoulas VF, Nihoyannopoulos P. Echocardiographic assessment in patients with chronic kidney disease: Current update. Echocardiography. 2017 Apr;34(4):594-602.
9. Saha M, Faroque MO, Alam KS, Alam MM, Ahmed S. Chronic kidney disease specific cardiovascular risk factors among non dialytic patients with chronic kidney disease stage-V--an experience of a specialized hospital. Bangladesh Med Res Counc Bull. 2012 Apr;38(1):18-22.

10. Girish Ronad, Anand Shankar, Ravi Kumar. A clinical study of cardiac manifestations in chronic kidney disease. MedPulse International Journal of Medicine. August 2021; 19(2): 35-41.
11. Adarsh L. S., Sravanthi Reddy, Manjunath S. Shetty: Asymptomatic cardiac manifestations in CKD: Int J Res Med Sci. 2018 Mar;6(3):822-827.
12. Dr. Sanath Kumar, Dr. Bandi Suman, Dr. Chiluka Kiran: A study on diagnostic evaluation of ecg and echo results in ckd patients :Journal of Cardiovascular Disease 2022: vol13, issue 05, 2039-2051.