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Original Research Article

Association of Electrocardiographic Changes and its Role in Predicting Outcome in CKD Patients on Maintenance Hemodialysis

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Conflict of interest: Nil

Abstract:

Background: Chronic kidney disease is associated with markedly increased risk for cardiovascular accidents and mortality. Cardiovascular disease is the most common cause of death in CKD. Cardiovascular mortality is very high in chronic and end-stage kidney disease (ESKD). However, risk stratification data is lacking to certain extent. The echocardiogram has been a useful instrument with remarkable accuracy in assessing ventricular mass and volume, systolic function measurement, hypertrophy detection, and determination of its geometric pattern (concentric or eccentric). So, the present study focuses on impact of routine electrocardiography for predicting prognosis in patientsof CKD on maintenance haemodialysis and need for early intervention in best patient interest.

Aims and Objectives: To study ECG changes in patients with CKD on maintenance haemodialysis.

To classify ECG changes for predicting outcome in patients of CKD in Maintenance hemodialysis.

Methodology

Study type/design: Prospective observational clinical study.

Study setting: The study was done in department of medicine in a tertiary care centre. In this study ECG changes diagnosed to have chronic kidney disease was studied.

Patient evaluation was done on day of admission, during each dialysis and at time of discharge. Informed consent was taken from every patient.

Result and Discussion: This study suggests a significant association was seen between the CKD stage and the presence of ECG changes.

- The heart rate was almost normal in all the CKD patients in 24 months of ECG monitoring.
- 57.85% of cases had a P-wave of more than 0.25 mV initially the number of percentage p-

wave after 24 months was reduced to 35.53%.
- QRS complex of more than 100 ms was in 35.05 % of patients at initial monitoring.
- There was a fluctuation in the changes in the T- wave in 24 months of monitoring.
- 19.83 % of patients had QTc interval between 401- 450 ms initially.
- ST segment was elevated in 14.87 % of cases initially and after 24 months the numberof patients with elevated ST segment was 1.65%.
- 28.09 % reported LVH at an initial screening at the end of 24 months the number of patients with LVH was 21.48%.

Conclusion: Electrocardiography is a non-invasive tool that can be used to identify cardiovascular disease early in the course of CKD. ECG abnormality observed in CKD patients was left ventricular hypertrophy followed by ST depression. The ECG changes observed after the 3 month of intervals for 24 months in the CKD patient with maintenance on hemodialysis showedvaried changes at each interval. The present study observed a high prevalence of ECG abnormalities in CKD patients. In viewof the above findings, the present study recommends periodic electrocardiographic examination for diagnosis and early treatment of cardiac abnormalities in patients with CKD at regular intervals to prevent complications in the longer run. It is crucial to periodically checkon CKD patients to evaluate any changes to their ECG. The probability of abnormal ECG readings increases as the CKD stage progresses, especially in the later stages.

Introduction

Chronic kidney disease is associated with markedly increased risk for cardiovascular accidents and mortality. Cardiovascular disease is the most common cause of death in CKD. [1] If kidney does not function normally for more than three months or long, it is identified by structural or functional disorders of the kidney, that reduces in glomerular filtration rate less than 60 mL/min/1.73 m. [2] It presents as either clinical abnormalities or indicators of kidney injury, such as changes in the blood or urine's composition or abnormalities in imaging studies.[3]

Nearly every system in the body is impacted by CKD, which leads to a number of structural and functional problems. Cardiovascular events are the main contributors to morbidity and mortality among the many causes. Dialysis patients have a death rate from cardiovascular disease that is 15–30 times greater.[3] Cardiovascular mortality is very high in chronic and end- stage kidney disease (ESKD). However, risk stratification data is lacking to certain extent. Sudden cardiac deaths are among the most common cardiovascular causes of death in these populations. As aresult, many studies have assessed the prognostic potential of various electrocardiographic parameters in the renal population. Recent data from studies of implantable loop recordings in haemodialysis patients from five different countries have shed light on a pre-eminent bradyarrhythmia risk of mortality.

According to statistics from 2017, chronic kidney disease was the 12th leading cause of mortality worldwide. According to a Lancet[4] article, the number of individuals needing dialysis increased by nearly 40% in 2020. 1.23 million deaths from CKD were thought to have occurred. Majorities of which were brought on by cardiovascular diseases (CVD) brought on by a reduction in renal function.

Standard electrocardiogram is inexpensive, non-invasive and easily accessible tool.

Hence, risk prediction models using this simple investigation tool could easily be translated into clinical practice. We believe that electrocardiographic assessment is currently under-valued in renal populations perhaps. For this review, we identified studies from the preceding 10 years that assessed the use of conventional and novel electrocardiographic biomarkers as risk predictors in chronic and ESKD.[5] Chronic kidney disease (CKD) is associated with increased risk of cardiovascular disease. Electrocardiographic (ECG) abnormalities are common in CKD patients. However, there is variation in literature regarding frequency of ECG abnormalities in CKD patients and limited information in local population.[6]

Prolonged QT interval and greater QT depression have been reported among uncontrolled case series of long-term haemodialysis patients. ECG abnormalities may be particularly strong predictors of CV events among people with CKD, as a result of their considerable baseline CV risk. Associations of resting ECG markers with clinical CV events could promote the 12 lead ECG as a useful clinical tool for CV risk stratification in security setting.[7]

Chronic kidney disease (CKD) patients have a markedly higher risk of overall and cardiovascular (CV) mortality than the general population.[8] Data from ADHERE database shows that as renal function worsens, prognosis deteriorates as well. The mortality rate for all patients in ADHERE was >4.0% whereas patients with severe renal dysfunction (serum creatinine >3.0 mg/dl) not yet receiving dialysis had an in-hospital mortality rate of 9.4%.[9]

Patients with chronic kidney disease (CKD) are susceptible to the occurrence of ventricular arrhythmias. The leading cause of death in dialysis patients is cardiac arrhythmias. The pathophysiology of arrhythmias in this population is complex and seems to be related to structural cardiac abnormalities caused by CKD, associated with several triggers, such as water and electrolyte disorders, hormonal conditions, arrhythmogenic drugs, and the dialysis procedure itself.[10] Because myocyte depolarization and repolarization depends on intra and extra cellular shifts in ion gradients, abnormal serum electrolytes can have profound effects oncardiac conduction and the electrocardiogram.[11,12]

The echocardiogram has been a useful instrument with remarkable accuracy in assessing ventricular mass and volume, systolic function measurement, hypertrophy detection, and determination of its geometric pattern (concentric or eccentric).

So, the present study focuses on impact of routine electrocardiography for predicting prognosis in patients of CKD on maintenance haemodialysis and need for early intervention in best patient interest.

Aims and Objectives:

1. To study ECG changes in patients with CKD on maintenance haemodialysis.
2. To classify ECG changes for predicting outcome in patients of CKD in Maintenance hemodialysis.

Methodology

Study type/design: Prospective observational clinical study.

Study setting: The study was done in department of medicine in tertiary care centre.This is a prospective observational clinical study.

Inclusion Criteria: Both sexes and all age groups.

Exclusion Criteria: Patients who refused to give consent.

In this study ECG changes diagnosed to have chronic kidney disease was studied.

Patient evaluation was done on day of admission, during each dialysis and at time of discharge.
Informed consent was taken from every patient.

➢ ECG

ECG was taken in all cases after admission. Routine conventional limb leads, chest leads and long strips were recorded. Continuous cardiac monitoring was done in some needful patients. ECG was done to determine.

1. Heart rate
2. Rhythm
3. Atrial rate ventricular rate
4. PR interval
5. QRS interval
6. QTC
7. ST changes
8. T wave
9. Axis- P, QRS, T wave
10. U wave
11. Any other miscellaneous observation
12. avr abnormality

This all test are done in our study to understand the routine electrocardiography for predictingoutcome in patients of CKD on maintenance haemodialysis.

Statistical Analysis: All the data was collected in the excel spread sheet and the quantitative data was represented as their mean ± SD. Categorical and nominal data was expressed in percentage. The t-test was used for analyzing quantitative data, or else non-parametric data was analyzed by Mann Whitney test and categorical data was analyzed by using chi-square test. The significance threshold of p-value was set at < 0.005. All the analysis was carried in SPPS version 25.

Result: ECG Changes

The ECG changes were observed for 24 months in the CKD patients. In the study 5 patients failed to come for follow up after 12 months and 1 patient died due to severe complication in 15 months and 2 patients died in a span of 18 month.
Effective Sample size 121 patients.

Table 1: Changes in heart rate in CKD patients in 24 months

Heart Rate perminutes	F (N) at initialstage	F(N) after3 month	F(N) after6 month	F(N) after9 month	F(N) after12 month	F(N) after15 month	F(N) after18 month	F(N) after21 month	F(N) after24 month
Less the 60 per Minute	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Between 60 – 99 PerMinute	121 (100%)	117 (96.69%)	115 (95.04%)	115 (95.04%)	108 (89.25%)	107 (88.42%)	105 (86.77%)	104 (85.95)	102 (84.29%)
More than 100	0 (100%)	4 (3.30 %)	6 (4.95%)	6 (4.95%)	8 (6.61%)	8 (6.61%)	8 (6.61%)	9 (7.43%)	11 (9.09%)
Total	**121**	**121**	**121**	**121**	**116**	**115**	**113**	**113**	**113**

F=Frequency

Table 1 represents the ECG changes in heart rate in 24 months. It is observed that there was a slow improvement in heart rate in some of the patients in 24 months.

Table 2: Changes in P-wave in CKD patients in 24 months

P - wave (mV)	F (N) at initialstage	F (N) after 3m	F (N) after 6month	F (N) after 9 month	F (N) after 12 month	F (N) after 15 month	F (N) after18 month	F (N) after21 month	F (N) after 24 month
Less than or equal to 0.25	51 (42.12%)	55 (45.45%)	55 (45.45%)	60 (49.58%)	62 (51.23%)	64 (52.89%)	65 (53.71%)	67 (55.37%)	70 (57.85%)
More than 0.25	70 (57.85%)	66 (54.54%)	66 (54.54%)	61 (50.41%)	54 (44.62%)	51 (42.14%)	48 (39.66%)	46 (38.01%)	43(35.53 %)
Total	121	121	121	121	116	115	113	113	113

F= Frequency

Table 2 represents the p-wave changes in CKD patients in 24 months. It is observed that there are some p-wave changes in CKD patients in 24 months. Initially 42.12 % patients had normal p-wave value and at the end of 24 months the numbers of patients were increased to 57.85%.

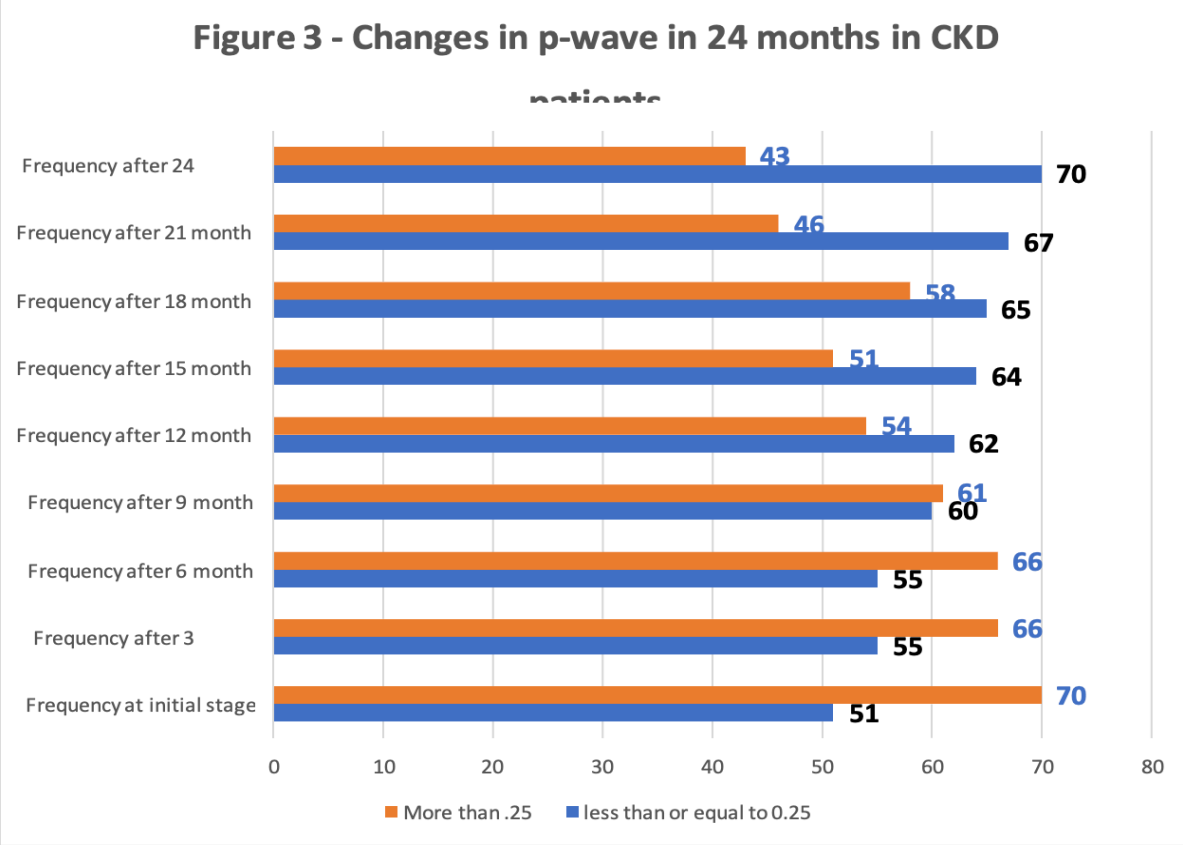


Table 3: Changes in QRS complex in CKD patients in 24 month

QRS complex (ms)	F (N) at initial stage	F(N) after3 month	(N) after6 month	F (N) after9 month	F (N) after12 month	F (N) after15 month	F (N) after18 month	F(N) after21 month	F (N) after24 month
Less than 80 ms	6 (4.95%)	5 (4.13 %)	5 (4.13%)	5 (4.13%)	5 (4.13%)	5 (4.13%)	4 (3.30%)	4 (3.30%)	4 (3.30%)
Between 80 - 100 ms	75 (61.98 %)	77 (62.62%)	79 (65.28%)	79 (65.28%)	81 (66.94%)	81 (66.94%)	84 (69.24%)	86 (71.07%)	90 (74.38%)
More than 100 ms	40 (33.05%)	39 (32.23%)	37 (30.57%)	37 (30.57%)	30 (24.79%)	29 (23.96%)	25 (20.66%)	23 (19.00%)	19 (15.70%)
Total	**121**	**121**	**121**	**121**	**116**	**115**	**113**	**113**	**113**

F=Frequency

Table 4 represents QRS complex changes in CKD patients in 24 month. In 24 month It is observedthat in there is improvement in QRS complex. Initially there were 61.98% of patients having normalQRS complex and at the end of 24 months the number of patients with normal QRS complex valvewas increased to 74.38%.

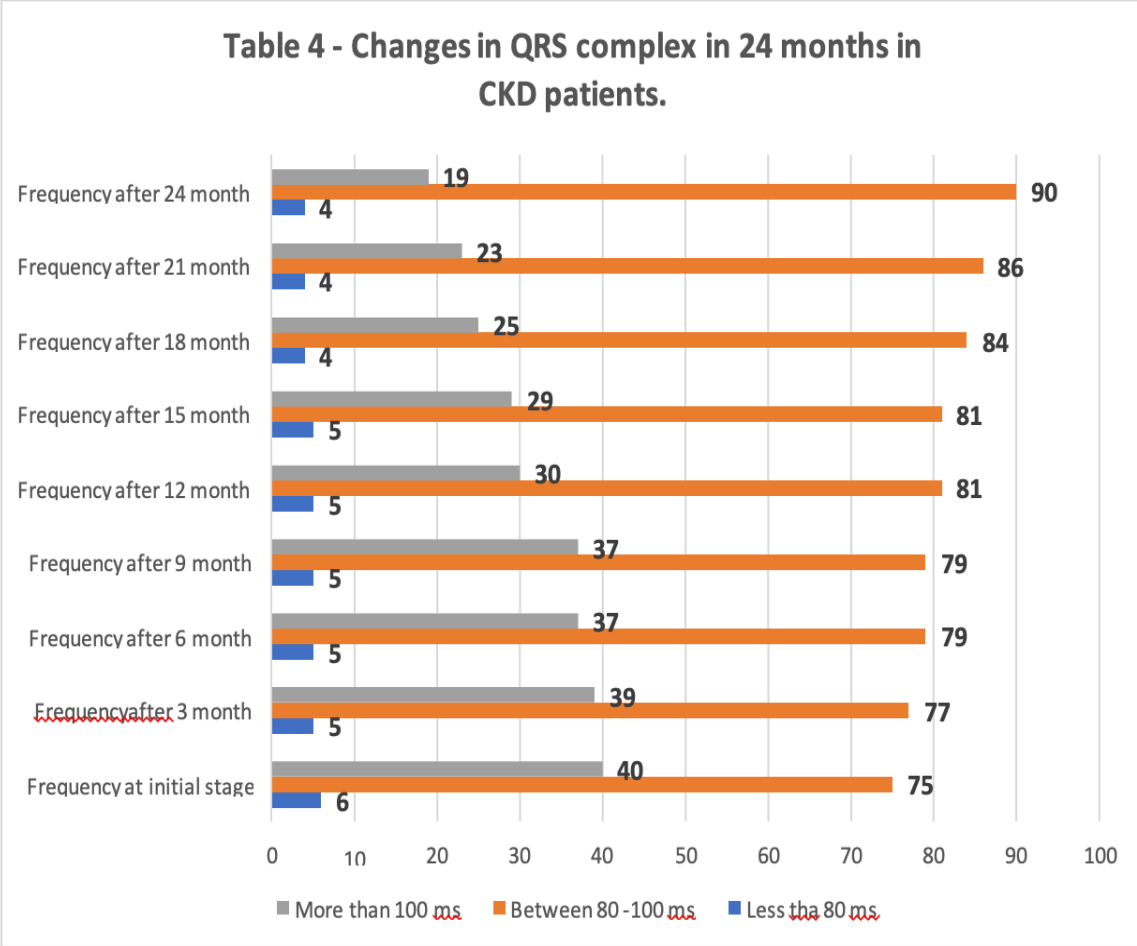


Table 5: Changes in T-wave in CKD patients in 24 month

T wave (mm)	F (N) at initial stage	F (N) After 3 month	F (N) after 6 month	F (N) after 9 month	F (N) After 12 month	F (N) After 15 month	F (N) after 18 month	F (N) After 21 month	F (N) after 24 month
5 - 6	75 (61.98%)	76 (62.80%)	78 (64.46%)	78 (64.46%)	79 (65.28%)	79 (65.28%)	77 (63.63%)	80 (66.11%)	81 (66.94%)
7 -8	16 (13.22%)	15 (12.39%)	13 (10.74%)	13 (10.74%)	14 (11.57%)	15 (12.39%)	13 (10.74%)	15 (12.39%)	14 (11.57%)
9 - 10	24 (19.83%)	25 (20.66%)	27 (22.39%)	29 (23.96%)	21 (17.35%)	19 (15.70%)	18 (14.87%)	14 (11.57%)	15 (12.39%)
11 -12	6 (4.95%)	5 (4.13%)	3 (2.47%)	1 (0.82%)	2 (1.65%)	2 (1.65%)	5 (4.13%)	4 (3.30%)	3 (2.47%)
Total	121	121	121	121	116	115	113	113	113

Table 5 represents T wave changes in 24 months in CKD patients. Within 24 months there were some T-wave changes in ECG findings. At initial stage 61.98% patients had T-wave in range between 5mm -6mm and end of 24 months the number of patients in that ranged had increased to 66.94%.

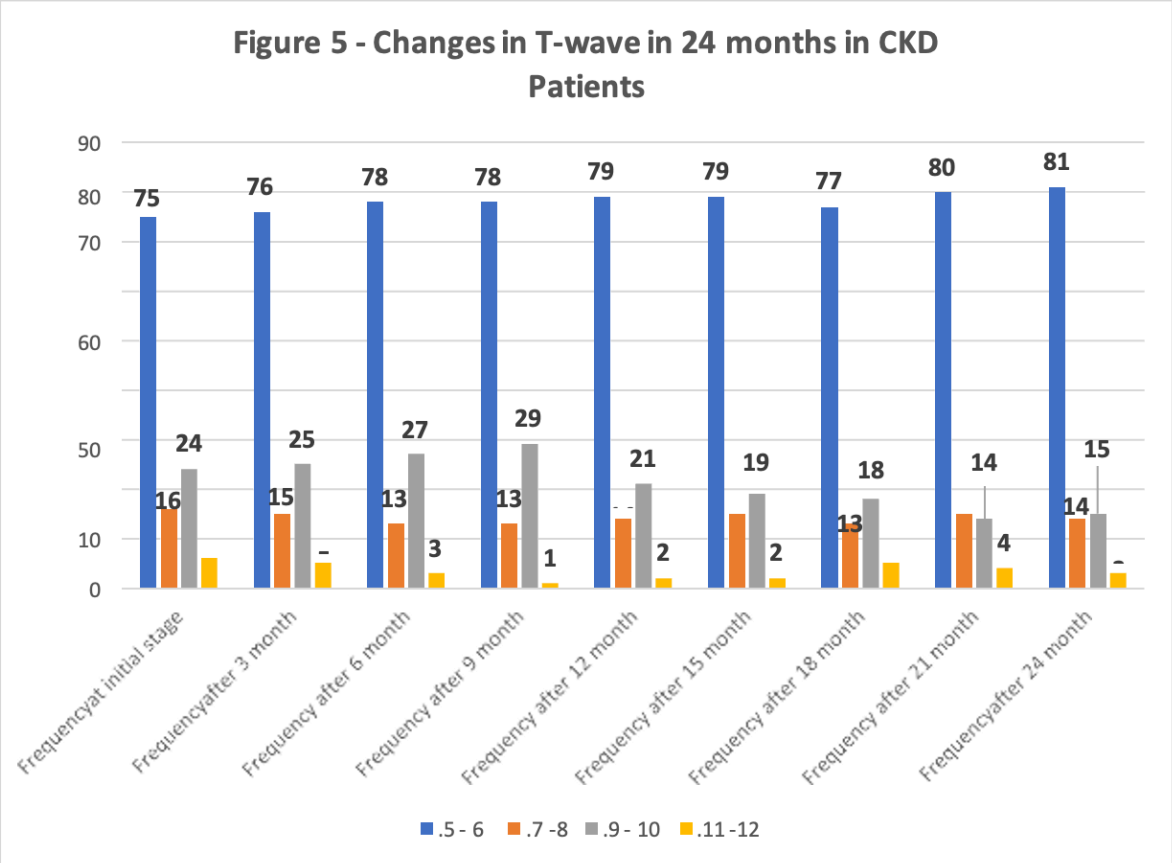


Table 6: QTc changes in 24 months in CKD patients

QTc Interval (ms)	F (N) At Initial stage	F (N) after 3 month	F (N) After 6 month	F (N) after9 month	F (N) after12 month	F (N) after 15 month	F (N) after 18 month	F (N) After 21 month	F(N) after 24 month
350 - 400 ms	97 (80.16%)	96 (79.33%)	96 (79.33%)	94 (77.68%)	93 (76.85%)	96 (79.33%)	97 (80.16%)	98 (80.99%)	99 (81.81%)
401 - 450 ms	24 (19.83%)	25 (20.66%)	25 (20.66%)	27 (22.31%)	23 (19.0%)	19 (15.70%)	16 (13.22%)	15 (12.39%)	14 (11.57%)
Total	**121**	**121**	**121**	**121**	**116**	**115**	**113**	**113**	**113**

Table 6 represents the QTc interval changes in CKD patients. In 24 months it was observed that at initial stage there were 80.16% patients in range of 350-400ms and at the end of 24 months the number of patients in this range was increased to 81.18%.

Table 7: Change in ST segment in 24 months in CKD patients

ST Segment	F (N) at initial stage	F (N) After 3 month	F (N) after 6 month	F (N) after 9 month	F (N) after 12 month	(N) after15 month	F (N) after 18 month	F (N) after 21 month	F (N) after 24 month
Decrease	12 (9.91%)	11 (9.09%)	11 (9.09%)	10 (8.26%)	9 (7.43%)	9 (7.43%)	7 (5.78%)	6 (4.95%)	7 (5.78%)
Normal	91 (75.20%)	93 (76.85%)	95 (78.51%)	96 (79.33%)	98 (80.99%)	99 (81.81%)	98 (80.99%)	98 (80.99%)	104 (85.95%)
Elevated	18 (14.87%)	17 (14.04%)	15 (12.39%)	15 (12.39%)	9 (7.43%)	7 (5.78%)	6 (4.95%)	7 (5.78%)	2 (1.65%)
Total	**121**	**121**	**121**	**121**	**116**	**115**	**113**	**113**	**113**

F=Frequency

Table 7 represents the ST segment changes within 24 months in CKD patients. It was observed

that at initial stage 75.20% were in normal range and at the end of 24 months the number of patientsin normal range was increased to 85.95%.

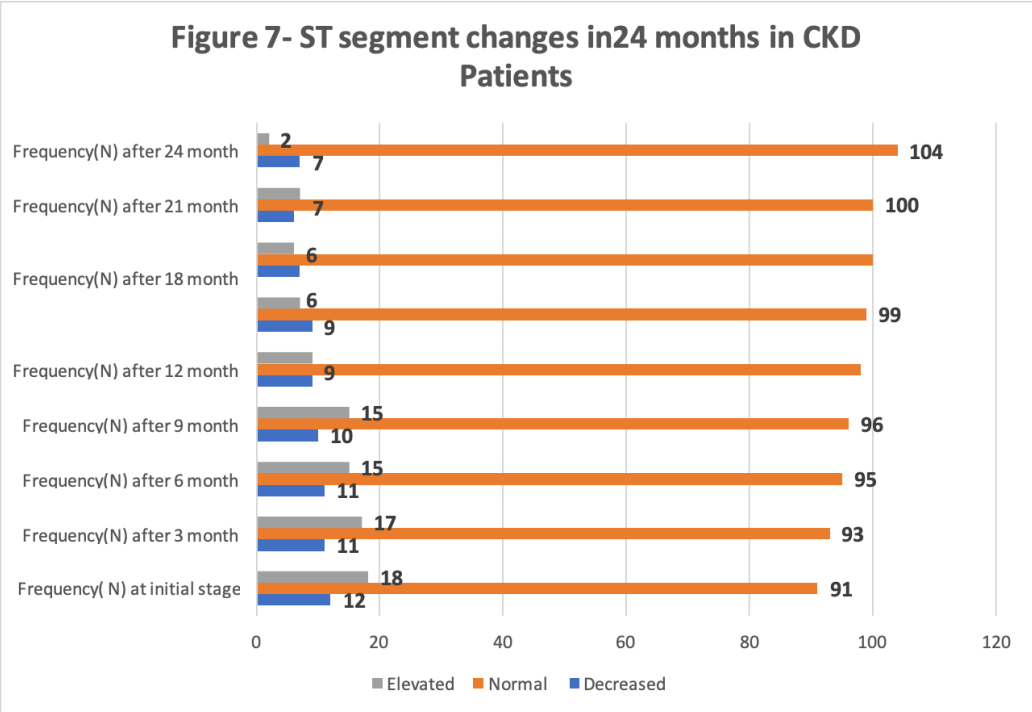
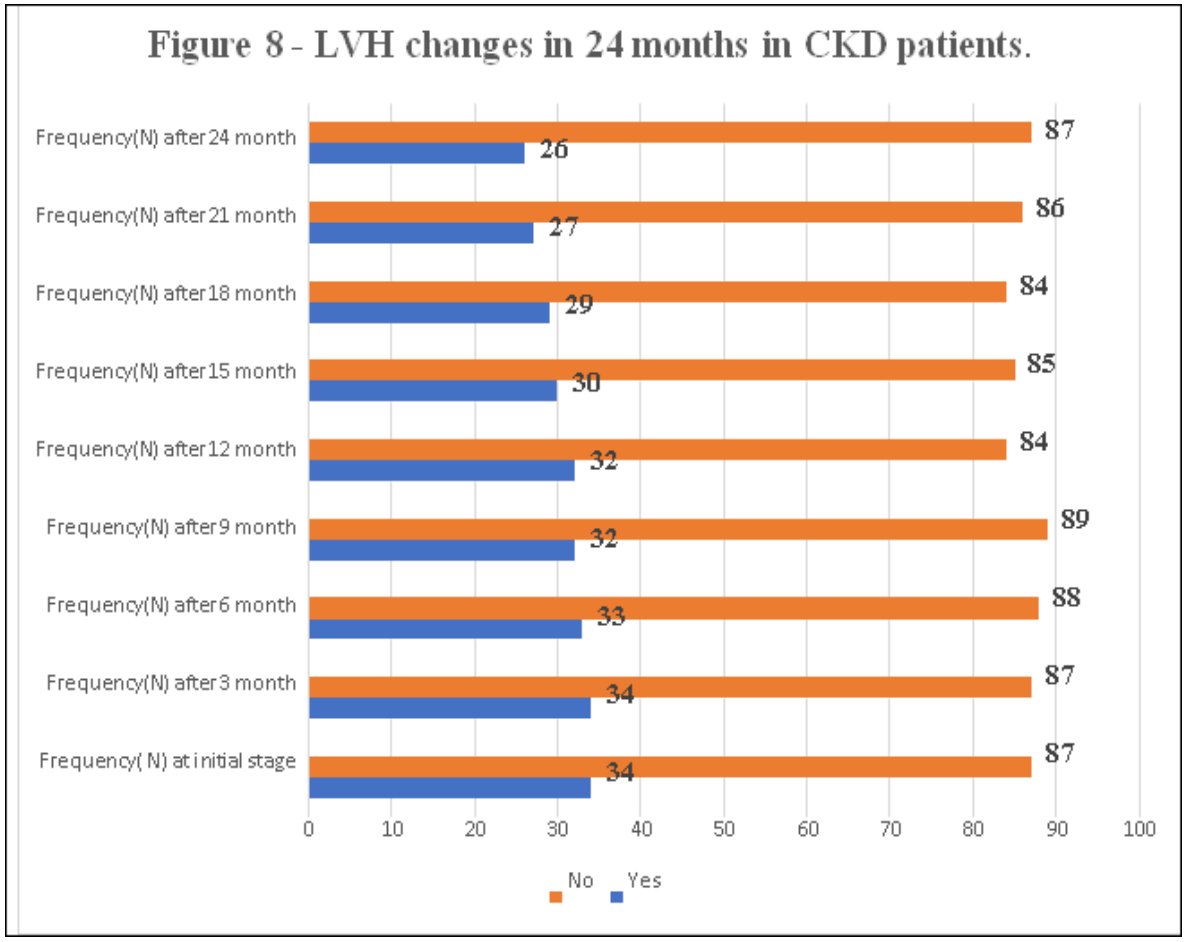


Table 8: Left ventricular hypertrophy changes in 24 months in CKD patients.

Left ventricular hypertrophy	Frequency (N) At initial stage	Frequency (N) At after 3 months	Frequency (N) At after 6 months	Frequency (N) At after 9 months	Frequency (N) At after 12 months	Frequency (N) At after 15 months	Frequency (N) At after 18 months	Frequency (N) At after 21 months	Frequency (N) At after 24 months
Yes	34 (28.09%)	34 (28.09%)	33 (27.27%)	32 (26.44%)	32 (26.44%)	30 (24.79%)	29 (23.96%)	27 (22.31%)	26 (21.48%)
No	87 (71.90%)	87 (71.90%)	88 (72.72%	89 (73.55%)	84 (69.42%)	85 (70.24%)	84 (69.42%)	86 (71.07%)	87 (71.90%)
Total	121	121	121	121	116	115	113	113	113

Table 8 represents the Left ventricular hypertrophy (LVH) changes in patients within 24 months.It was observed at initial stage 28.09 % patients had LVH in the ECG scanning and at the end of 24months the number of patients with LVH was decreased to 21.48%.



Result and Discussion

The current prospective observational clinical study of 121 cases on routine electrocardiography in predicting outcomes in patients of CKD on maintenance hemodialysis was conducted. All the cases satisfying the inclusion criteria were selected for the study. ECG changes and outcomes of patients diagnosed to study chronic kidney disease. The patient evaluation was done on the day of admission, during each dialysis, and at the timeof discharge. In terms of hemodynamic and regulatory functions, the kidney and heart are closely related. Their association is currently on various levels.

Recent studies have shown that CKD is linked to high rates of cardiovascular mortality and morbidity. Because CKD's harmful consequences start to manifest in its early stages, preventive measures must be taken as soon as possible. However, renal failure's asymptomaticcharacter and early, unsuccessful detection costs patients important time, and proper consultation is hindered.[13] This study analysed patients at the initial stage and the ECG changes in 9 intervals that are at 0, 3, 6, 9, 12, 15, 18, 21, 24 months are recorded in the excel spreadsheet. The data were analysed by SPSS – 25 software and the results obtained are discussed as under. ECG changes.

In the current study, the ECG changes were observed for 24 months in CKD patients. In the study, 5 patients failed routine follow-ups after 12 months and 1 patient died due to severe complications in 15 months and 2 patients died in 18 months.

Changes in heart rate in CKD patients in 24 monthsIn the current study, the changes in heart rate were observed in 9 intervals that is after 3, 6, 9, 12, 15, 18, 21, and 24 months. It was observed that no patient had a heart rate of less than 60in per minute. Maximum patients had heart rate between 60 -90 per minute. Few patients were observed with a heart rate of more than 100 per minute. It is observed that there was a

slow improvement in heart rate in some of the patients in 24 months.

Changes in P-wave in CKD patients in 24 months.

In the current study of the p-wave changes in CKD patients in 24 months. It is observed that there are some p-wave changes in CKD patients in 24 months. Initially, 42.12 % of patients had normal p-wave values and at the end of 24 months, the number of patients increased to 57.85%.

Changes in QRS complex in CKD patients in 24 month

In the current study of QRS complex changes in CKD patients in 24 months. In 24 months it is observed that there is improvement in the QRS complex. Initially, there were 61.98% of patients had normal QRS complex and at the end of 24 months the number of patients with normal QRS complex valve increased to 74.38%.

Changes in T-wave in CKD patients in 24 month

In the current study of T wave changes in 24 months in CKD patients. Within 24 months there weresome T-wave changes in ECG findings. At the initial stage, 61.98% of patients had T-wave in the range between 5mm -6mm, and end of 24 months the number of patients in that range had increasedto 66.94%.

QTc changes in 24 months in CKD patients

In the current study of QTc interval changes in CKD patients. In 24 months it was observed that atthe initial stage, there were 80.16% of patients in a range of 350-400ms and at the end of 24 months the number of patients in this range increased to 81.18%.

Change in ST segment in 24 months in CKD patients in the current study of ST segment changes within 24 months in CKD patients. It was observed thatat the initial stage, 75.20% were in the normal range and at the end of 24 months the number of patients in the normal range increased to 85.95%.

CKD patients experience frequent cardiac abnormalities such as systolic dysfunction, left ventricular dilatation (LVD), or left ventricular hypertrophy. This condition is known as Uremic cardiomyopathy. The incidence of Left Ventricular Hypertrophy rises along with a steady deterioration in renal function. Left Ventricular Hypertrophy is extremely common in chronic kidney disease and is linked to a very unfavorable prognosis.[14]

Patients with chronic kidney disease (CKD) with stable ischemic heart disease are at much higher risk for cardiovascular events. Clinical results for these individuals are improved by the initial invasive management method.

Sachdeva S et al.[15] in their study of ECG changes in CKD patients reported in his study that there were cardiovascular abnormalities in 60 patients with CKD, using electrocardiography. ECG was abnormal in 45 out of 60 cases of CKD (75%). Common ECG changes seen were: LVH present in20 out of 60 (33.33%), Left axis deviation in 9 out of 60 (15%), Conduction disturbances in 10 out of 60 (16.67%), Ischemia in 12 out of 60 (20%), Arrhythmias in 2 out of 60 (3.33%) and P-mitral was found in 4 out of 60 cases (6.67%). ECG changes were observed more in cases on hemodialysis as compared to those not on hemodialysis.[15]

Many studies have reported echocardiographic changes in CKD patients but the comparison study with the current study showing the ECG changes in CKD for 24 months is not found. This study suggests a significant association was seen between the CKD stage and the presence of ECG changes.

- The heart rate was almost normal in all the CKD patients in 24 months of ECGmonitoring.
- 57.85% of cases had a P-wave of more than 0.25 mV initially the number of percentage p-wave after 24 months was

reduced to 35.53%.

- QRS complex of more than 100 ms was in 35.05 % of patients at initial monitoring.
- There was a fluctuation in the changes in the T- wave in 24 months of monitoring.
- 19.83 % of patients had QTc interval between 401- 450 ms initially.
- ST segment was elevated in 14.87 % of cases initially and after 24 months the number of patients with elevated ST segment was 1.65 %.
- 28.09 % reported LVH at an initial screening at the end of 24 months the number of patients with LVH was 21.48%.

Thus from the current study, we summarize that a higher amount of ECG abnormalities are observed in CKD patients on hemodialysis. The changes are observed in the current study with continuous follow-up every 3 months for 24 months. . The study suggests that routine ECG monitoring in CKD patients helps in early identification and treatment to avoid long-term consequences.

Conclusion

lectrocardiography is a non-invasive tool that can be used to identify cardiovascular disease early in the course of CKD. ECG abnormality observed in CKD patients was left ventricular hypertrophy followed by ST depression. The ECG changes observed after the 3 month of intervals for 24 months in the CKD patient with maintenance on hemodialysis showed varied changes at each interval.

The present study observed a high prevalence of ECG abnormalities in CKD patients. In viewof the above findings, the present study recommends periodic electrocardiographic examination for diagnosis and early treatment of cardiac abnormalities in patients with CKD at regular intervals to prevent complications in the longer run. It is crucial to periodically check on CKD patients to evaluate any changes to their ECG. The probability of abnormal ECG readings increases as the CKD stage progresses, especially in the later stages.

Bibliography

1. Clinical journal of the American Society of Nephrology. 2012; 7(6): 949-956.
2. Di Lullo L., et al., chronic kidney disease and cardiovascular complications. Heart Fail Rev, 2015; 20(3): 259-72.
3. Levey, A.S., et al., Definition and classification of chronic kidney disease: a position statement from kidney disease: Improving Global Outcomes (KDIGO). Kidney Int, 2005; 67(6): 2089-100.
4. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017, The lancet. 2020; 395(10225): P709-733.
5. Sofia Skampardoni, Dimitrios Poulikakos, Marek Malik, Darren Green, Philip A Kalra. Nephrology Dialysis Transplantation. 2019; 34(7): 1089-1098.
6. Salman Shafi et al. J Ayub Med Coll Abbottabad. Jan-Mar 2017.
7. Mirela Dobre, Andrei Brateanu, Arash Rashidi and Mahboob Rahman CJASN. June 2012;7(6):949-956.
8. Bryan Kestenbaum, Kyle D. Rudser, Michael G. Shlipak, Linda F. Fried, Anne B. Newman, Ronit Katz, Mark J. Sarnak, Stephen Seliger, Catherine Stehman-Breen, Ronald Prineas and David S. Siscovick CJASN. May 2007.
9. Levin A, Foley RN. Cardiovascular disease in chronic renal insufficiency, Am J Kidney Dis, 2000; 36: S24-S30.
10. Dries DL, Exner DV, Domanski MJ, Greenberg B, Stevenson LW. The prognostic implications of renal insufficiency in asymptomatic and symptomatic patients with left ventricular systolic dysfunction. Journal of the American College of Cardiology.

2000 Mar1;35(3):681-9.
11. Brazilian Journal of Nephrology. 2017; 39(2): 186-195.
12. The Journal of emergency medicine 2004; 27(2): 153-160.
13. Lote CJ. Principles of Renal Physiology, 5th edition. Springer. 2012;21.
14. Parfrey P., et al., Outcome and risk factors for left ventricular disorders in chronic uraemia. Nephrology Dialysis Transplantation, 1996. 11(7):1277-1285.
15. Satish Sachdeva, Tarvinderjit Khurana, Satinderpal Kaur, Kamalpreet Rajiv Aggarwal et al ECG and ECHO Changes in CKD Annals of International Medical and Dental Research, 2017;3(5): 160-169.